

Importance of Nonlongitudinal Motion Components in Right Ventricular Function: Three-Dimensional Echocardiographic Study in Healthy Volunteers



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Background: Global right ventricular (RV) function is determined by the interplay of different motion components related to the myofiber architecture, and the relative importance of these components is still not thoroughly characterized. The aims of this study were to quantify the relative contributions of longitudinal, radial, and anteroposterior motion components to global RV function and to examine their determining factors in a large cohort of healthy volunteers using three-dimensional echocardiography.

Methods: Three hundred healthy adults with a balanced age range and an equal sex distribution were investigated at two centers. A three-dimensional mesh model of the right ventricle was generated, and its motion was decomposed along the three anatomically relevant axes. Multiplicative relative contributions were measured by dividing the ejection fraction (EF) values generated by shortening in the longitudinal, radial, and anteroposterior directions by global RV EF (longitudinal EF index [LEFi], radial EF index [REFi], and anteroposterior EF index, respectively). The circumferential contribution was defined as shortening in the radial and anteroposterior directions, omitting only longitudinal shortening.

Results: Circumferential EF index was markedly higher compared with LEFi ($79 \pm 7\%$ vs $47 \pm 9\%$, $P < .001$). LEFi ($47 \pm 9\%$) and anteroposterior EF index ($49 \pm 7\%$) were found to be similar in the pooled population, whereas REFi ($44 \pm 10\%$) was lower ($P < .001$). In younger individuals (20–39 years of age), the relative contribution of longitudinal shortening was significantly higher compared with the radial component; however, in the older age groups, LEFi and REFi were comparable. Age, body surface area, heart rate, and RV end-diastolic volume were independent predictors of LEFi and REFi, but all with opposite effects on the two motion directions.

Conclusions: In contrast to the traditional viewpoint, the contributions of the radial and anteroposterior motion directions may be of comparable significance with that of longitudinal shortening in determining global RV function. Standard parameters referring only to longitudinal shortening of the right ventricle may be inadequate to characterize RV function thoroughly. (J Am Soc Echocardiogr 2020;33:995–1005.)

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Abbreviations

2D = Two-dimensional
3D = Three-dimensional
AEFI = Anteroposterior ejection fraction index
BSA = Body surface area
EF = Ejection fraction
FAC = Fractional area change
GAS = Global area strain
GCS = Global circumferential strain
GLS = Global longitudinal strain
HR = Heart rate
LEFI = Longitudinal EF index
LV = Left ventricular
LVEF = Left ventricular ejection fraction
PASP = Peak pulmonary artery systolic pressure
REFI = Radial EF index
RV = Right ventricular
RVEDVi = Right ventricular end-diastolic volume index
RVEF = Right ventricular ejection fraction
TAPSE = Tricuspid annular plane systolic excursion

Right ventricular (RV) morphology and function have a strong prognostic role in several cardiovascular diseases, such as myocardial infarction, heart failure, pulmonary arterial hypertension, and congenital heart diseases.¹⁻⁵ Because of the complex anatomy and functional characteristics of the right ventricle, two-dimensional (2D) echocardiography has limited value in the assessment of the chamber. Three-dimensional (3D) echocardiography-based techniques overcome these challenges by providing precise quantification of RV volumes and ejection fraction (EF) with high reproducibility and good agreement with cardiac magnetic resonance imaging as a reference.⁶ However, global RV function is determined by the interplay of different motion components related to the myofiber architecture, and the relative importance of these components is still not thoroughly characterized.

Evidence suggests that RV global longitudinal strain (GLS) may be a more sensitive diagnostic and prognostic parameter compared with traditional RV functional parameters.² Nevertheless, it refers only to a single aspect of the more com-

plex RV contraction. Other components of RV mechanics, such as the inward movement of the RV free wall ("bellows effect" [radial motion]) and the traction of the RV free wall insertion points into the ventricular septum (as viewed from the short-axis [anteroposterior motion]), may also have considerable impact on RV ejection. Still, shortening along the nonlongitudinal (radial and anteroposterior) directions is often neglected in routine clinical practice; moreover, even the native contributions of these motion components of global RV function remain to be quantified.⁷⁻⁹

Accordingly, our aim was to quantify the relative contributions of the longitudinal, radial, and anteroposterior motion components of global RV function and to examine their determining factors in a large cohort of healthy volunteers from two centers using 3D echocardiography. We hypothesized that shortening along the radial and anteroposterior directions is of comparable significance with longitudinal contraction.

METHODS

Healthy volunteers of a wide age range were included from two centers (Semmelweis University, Budapest, Hungary, and the University of Occupational and Environmental Health, School of

Medicine, Kitakyushu, Japan). Subjects were recruited from a community screening program, medical students, hospital employees, their relatives, and patients referred for cardiologic examination without known or subsequently established cardiovascular disease. The study protocol was approved by both centers' institutional ethical review boards (Semmelweis University: 169/2018; University of Occupational and Environmental Health: UOEHC18-015), and all participants gave written informed consent to participate in the study. To adequately assess the effects of ethnicity, age, and sex, both participating centers aimed to enroll ≥ 150 patients with an equal sex distribution across predefined age groups (30 men and 30 women per group). A total of 486 subjects (Hungary, $n = 223$; Japan, $n = 263$) were screened to achieve the desired sample size. Thirty-three patients were excluded because of the presence of exclusion criteria, and 3D RV analysis was not feasible in 15% of the subjects ($n = 68$). The final study population, with balanced age, sex, and ethnic distributions, was selected from this pool ($n = 385$). A routine physical examination, including anthropometric measurements, was performed in each subject, followed by blood pressure measurement and 12-lead electrocardiography. Body surface area (BSA) was calculated using the Mosteller formula.¹⁰ Inclusion criteria were age > 20 years; no history and/or symptoms of any cardiovascular or pulmonary disease; and absence of cardiovascular risk factors such as arterial hypertension, diabetes, smoking, and dyslipidemia. Exclusion criteria were body mass index ≥ 30 kg/m², any abnormality on electrocardiography, moderate or severe valvular heart disease or wall motion abnormality and/or left ventricular (LV) EF $< 50\%$ found during echocardiography, poor echocardiographic windows, and factors that might affect cardiac morphology and function, such as pregnancy and regular high-intensity sport activity (> 3 h/wk).

Two-Dimensional Echocardiography

Echocardiographic acquisitions were performed using Philips EPIQ 7 (equipped with an X5-1 transducer; Philips Medical Systems, Best, the Netherlands) and GE Vivid E95 (equipped with 4V-D or 4Vc-D transducers; GE Healthcare, Horten, Norway) ultrasound systems. A standard acquisition protocol consisting of loops from parasternal, apical, and subxiphoid views was used according to current guidelines.¹¹ RV basal diameter was measured as the maximal transverse dimension in the basal third of the RV inflow from the RV-focused apical four-chamber view in the end-diastolic frame. RV areas and fractional area change (FAC) were measured by manual tracing of the RV endocardial border in end-diastole and end-systole. M-mode-derived tricuspid annular plane systolic excursion (TAPSE) was calculated as the peak longitudinal excursion of the tricuspid annulus. Right atrial volume was estimated using the Simpson method. Systolic (s'), early (e'), and late diastolic (a') velocities at the tricuspid free wall annulus were measured using pulsed-wave Doppler tissue imaging. Peak pulmonary artery systolic pressure (PASP) was calculated from the tricuspid regurgitant jet signal velocity and right atrial pressure, which was estimated using inferior vena cava diameter and collapsibility. Reliable measurement of PASP was achievable in only 195 cases, but the distribution was consistent across age categories and sexes (P for trend = .85).

Three-Dimensional Echocardiography

Beyond the routine echocardiographic protocol, electrocardiographically gated full-volume 3D data sets reconstructed from four or six cardiac cycles optimized for the right or left ventricle were obtained for offline analysis. Image quality was verified at the bedside

HIGHLIGHTS

- Global RV function is determined by different motion components.
- Longitudinal, radial, and anteroposterior motion may be of comparable significance.
- Age and other anthropometric factors may correlate with RV deformation pattern.
- Elderly individuals show a distinct RV deformation pattern.

to avoid “stitching” and “dropout” artifacts of the 3D data. Further measurements were performed on a separate workstation using dedicated software (4D RV-Function 2 and 4D LV-Analysis 3; TomTec Imaging, Unterschleissheim, Germany). The algorithm detects the endocardial surface of the right and left ventricles, and following manual correction, it traces its motion throughout the cardiac cycle. We determined end-diastolic volume index, end-systolic volume index, and stroke volume index normalized to BSA, and to characterize global RV and LV functions, EFs were also assessed. We measured LV mass index normalized to BSA by tracing the end-diastolic epicardial contour. Moreover, LV GLS and global circumferential strain (GCS) and 2D RV free wall longitudinal strain were also calculated.

In-Depth Analysis of 3D RV Deformation

The 3D RV deformation analysis was previously described in detail.¹² All analyses were performed on a standard computer. First, a series of 3D meshes were exported from TomTec 4D RV-Function 2, taken at even time instants during the cardiac cycle. Then, using our software (ReVISION method; Argus Cognitive, Lebanon, New Hampshire), the work flow consists of the following steps: (1) standardization of the 3D mesh orientation, (2) movement decomposition, (3) calculation of strain values.

The input to our software (ReVISION method) is a series of 3D meshes exported from TomTec 4D RV-Function 2, taken at even time instants during the cardiac cycle (Supplemental Video 1 available at www.onlinejase.com). The first step of the analysis is the reorientation of the 3D RV mesh. To standardize the orientation of the models, we align them to a reference mesh using Procrustes superimposition (without scaling). Therefore, the Euclidean axes of the model correspond to the anatomically relevant axes (longitudinal, radial, and anteroposterior).

Second, the wall motions of the 3D RV model are decomposed in a vertex-based manner (e.g., for quantifying the magnitude of longitudinal motion, we took into account only the movement of the vertices along the vertical axis). This decomposition step transforms the original mesh series into several series of meshes, each corresponding to a decomposition type (i.e., which movement directions are enabled and which ones are not).

In the final step of the algorithm, we used the decomposed 3D models to calculate several measures characterizing the right ventricle. The volumes of the models accounting for only one motion direction were calculated at each time frame using the signed tetrahedron method.¹³ By the decomposition of the model's motion along the three anatomically relevant orthogonal axes, we can measure the volume change of the right ventricle attributable to the specific direction separately (Figure 1). Therefore, we were able to measure component

EF values indexed to global RVEF: the so-called longitudinal EF index (LEFi; Supplemental Video 2 available at www.onlinejase.com), radial EF index (REFi; Supplemental Videos 3 and 4 available at www.onlinejase.com), and anteroposterior EF index (AEFi; Supplemental Video 5 available at www.onlinejase.com). These measures quantify the relative contribution of the given direction to global RV performance (Figure 1). Note that the absolute volume change of the chamber is generated by the aggregated contribution of the three motion components. This composition is not additive, and consequently, the sum of the decomposed volume changes is not equal to the global volume change; in other words, the relative contribution of the motion components do not add up to 100%. This is attributable to the fact that the decomposition of RV motion is performed on the end-diastolic frame. By permitting the motion in only one axis, and omitting motion in the other axes of the right ventricle, the contribution of a given motion direction to global RV volume loss will be mathematically overestimated.

By blocking only the longitudinal motion of the RV model, we have also calculated circumferential EF indexed to global RVEF (Supplemental Video 6 available at www.onlinejase.com), which serves as a composite marker of the relative contribution of nonlongitudinal motion components.

To assess longitudinal and circumferential myocardial deformation, we computed 3D GLS and GCS as well. For GCS, we created 15 equidistant circumferential contours on the first mesh of each series and calculated their positions at later time instants. For GLS, 45 longitudes are generated by connecting the apex, the predefined vertices of the base, and vertices in equidistant latitude to the latter by fitting geodesic lines (the shortest path between two points on a curved surface). The pulmonary and tricuspid annular planes are excluded from this part of the analysis. Our software evaluates 3D RV GCS and GLS by averaging the length changes of each circumferential contour or longitude referenced to their end-diastolic length. Global area strain (GAS) is also calculated by the relative change of the endocardial surface between end-diastole and end-systole.

A beta version of the ReVISION method is freely available for research purposes at <http://www.revisionmethod.com>.

Statistical Analysis

Data are presented as mean $\pm$ SD. The normal distribution of our variables was confirmed using a Shapiro-Wilk test. Unpaired Student's *t* tests were used to compare groups, and Pearson tests were performed for correlation analysis. In the case of 3D RV parameters, two-way analysis of variance was used with two factors (age and sex), and their interactions were assessed to compare age groups. Repeated-measures analysis of variance was used to compare the relative contributions in the pooled population and across age categories as well. Multiple linear regression analysis was applied to find independent predictors that determine RV motion components. To avoid multicollinearity issues, tolerance was set at >0.5 . *P* values <0.05 were considered to indicate statistical significance. Intraobserver and intercenter variability was evaluated using the coefficient of determination and coefficient of variation (Supplemental Table 3).¹⁴ To assess the intraobserver variability of the most relevant RV parameters, the same operator repeated the 3D analysis in a randomly chosen subset of 20 patients, blinded to previous results. Intercenter reproducibility was determined by sending the same 20 data sets to the other center for analysis.

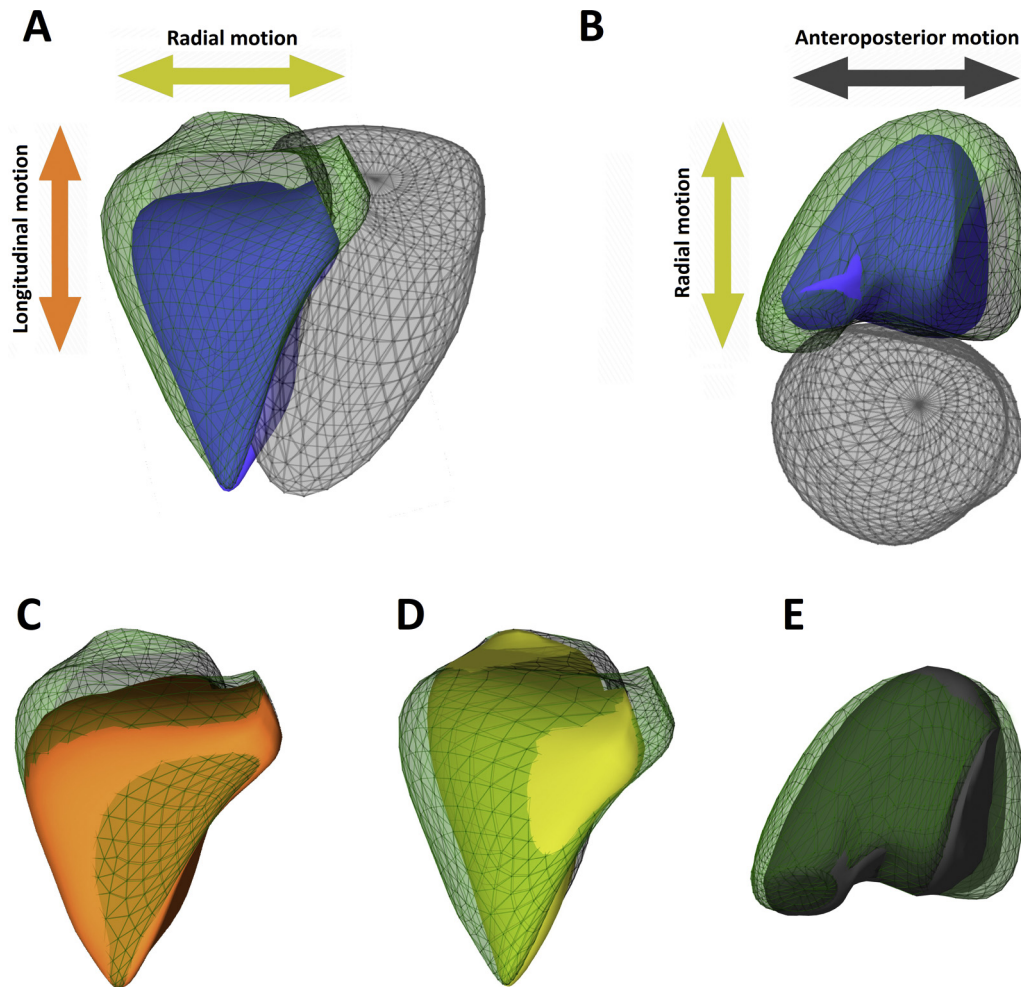


Figure 1 The three different motion components of the right ventricle. The motion of the right ventricle can be appreciated in anterior (A) and superior (B) aspects (green mesh, RV end-diastolic volume; blue surface, end-systolic volume of global function). The 3D model of the left ventricle (gray mesh) is also visualized. By decomposition of RV motion along the three anatomically relevant axes, theoretical RV end-systolic meshes can be generated in which RV motion is “locked” in two directions and enabled along only one axis. Therefore, the volume decrease attributable only to the longitudinal (C, orange surface), radial (D, yellow surface), and anteroposterior (E, black surface) shortening can be separately quantified, and the relative contribution of these components can be calculated.

RESULTS

Basic demographic and morphometric data of the entire study population and the two sexes are summarized in Table 1. The mean age of the enrolled patients was 45 ± 15 years. Men were characterized by significantly higher morphometric parameters, higher systolic and diastolic blood pressure, and lower heart rate (HR; Table 1).

Conventional echocardiographic measures of RV and 3D LV parameters are shown in Table 2. Male sex was associated with higher RV basal diameter, RV areas, right atrial volume index, and LV volumes and LV mass index. RV FAC and RV free wall longitudinal strain were higher in women, but TAPSE did not differ between sexes. Doppler tissue imaging–derived tricuspid annular velocities and PASP were comparable between men and women (Table 2).

Three-dimensional RV volumes and contraction pattern of the study population and for each sex and age category are summarized in Table 3. Men had significantly higher RV end-diastolic volume index (RVEDVi) and RV end-systolic volume index, while RVEF, RV GLS, RV GCS, and RV GAS were significantly higher in women.

Values of LEFi, REFi, and AEFi showed that there were no sex differences in the relative contributions of the longitudinal, radial, and anteroposterior motion components. RV volumetric indices, RVEF, RV GLS, RV GAS, and circumferential EF index significantly differed across age categories. No significant interaction between age and gender was found regarding 3D RV parameters.

The contribution of nonlongitudinal motion components measured by circumferential EF index was markedly higher in the pooled population and in every age category compared with longitudinal shortening ($P < .001$ for all). Circumferential shortening was further decomposed to radial and anteroposterior shortening. Comparison of the relative contributions of the longitudinal, radial, and anteroposterior motion directions in the age categories and the entire study population is illustrated in Figure 2 and Supplemental Table 1. Anteroposterior ($49.1 \pm 6.8\%$) and longitudinal shortening ($46.6 \pm 8.7\%$) were found to be the most prominent motion components of the right ventricle in the pooled population, while radial shortening ($43.5 \pm 10.3\%$) was of inferior significance. When analyzing the age categories separately, the relative contribution of longitudinal

Table 1 Clinical and demographic characteristics of the study group

	All (N = 300)	Female (n = 150)	Male (n = 150)	P
Age, y	44.8 ± 15.6	44.9 ± 15.6	44.7 ± 15.6	.87
Height, cm	167.2 ± 10.1	160.6 ± 7.6	173.9 ± 7.6	<.001
Weight, kg	66.7 ± 14.6	59.1 ± 12.1	74.3 ± 12.8	<.001
BMI, kg/m ²	23.7 ± 3.9	22.8 ± 4.0	24.5 ± 3.6	<.001
BSA, m ²	1.75 ± 0.23	1.62 ± 0.19	1.89 ± 0.19	<.001
SBP, mm Hg	131.6 ± 15.4	128.3 ± 15.4	135.2 ± 14.8	<.001
DBP, mm Hg	76.7 ± 11.2	75.3 ± 12.0	78.2 ± 10.1	<.05
HR, beats/min	68.8 ± 13.5	70.4 ± 14.5	67.0 ± 12.1	<.05

BMI, Body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Data are expressed as mean ± SD.

shortening was significantly higher compared with the radial component in younger age categories (20–29 and 30–39 years). In the older groups, however, LEFi and REFi were comparable. Anteroposterior shortening had a higher contribution compared with longitudinal shortening in the 30 to 39 and 50 to 59 age groups, while it had a higher contribution compared with radial shortening in every age category except 50 to 59 years (Supplemental Table 1, Figure 2).

We compared subjects in the lowest quartile of LEFi with the rest of the study group ($37.7 \pm 4.0\%$ vs $48.9 \pm 5.2\%$, $P < .001$). A lower contribution of longitudinal shortening was not associated with lower RVEF ($59.5 \pm 6.3\%$ vs $59.0 \pm 5.4\%$, $P = .67$), and AEFi was also comparable between the two groups ($50.4 \pm 6.7\%$ vs $48.7 \pm 6.8\%$, $P = .12$); however, the contribution of radial shortening was significantly higher (REFi $50.5 \pm 7.2\%$ vs $41.0 \pm 10.0\%$, $P < .001$).

We also compared subjects in the lowest quartile of REFi with the rest of the population ($29.7 \pm 7.4\%$ vs $48.0 \pm 6.3\%$, $P < .001$). Although patients with the lowest REFi had significantly lower RVEFs ($55.4 \pm 6.2\%$ vs $60.4 \pm 4.9\%$, $P < .001$), LEFi ($52.1 \pm 6.1\%$ vs $43.8 \pm 6.2\%$, $P < .001$) and AEFi ($51.6 \pm 6.1\%$ vs $48.3 \pm 6.8\%$, $P < .001$) were significantly higher, suggesting that the other two motion directions may effectively compensate lower radial shortening.

We compared RV morphology and function between the two centers to examine racial differences in our cohort (Supplemental Table 2). RV volumes and RVEF were significantly lower in Japanese subjects compared with the Hungarian population. RV deformation also differed between the two groups: Japanese subjects were characterized by higher AEFi and LEFi, while REFi and RV GCS were significantly lower.

Several RV parameters showed weak but statistically significant correlations with age, BSA, and hemodynamic parameters (Table 4). Age correlated negatively with RVEDVi, RVEF, RV GLS, LEFi, and RV GAS. BSA showed negative relationships with RVEF, RV GLS, LEFi, and AEFi but correlated positively with RVEDVi and REFi. Regarding systolic and diastolic blood pressure, negative correlations were found with RV GLS and AEFi, while RVEDVi and REFi had positive correlations with blood pressure. Systolic blood pressure also correlated negatively with RVEF. HR showed positive relationships with RVEF, RV GCS, RV GAS, and REFi but correlated negatively with AEFi. PASP did not show any correlation with RV parameters in the pooled study group (Table 4). In subjects

Table 2 Basic echocardiographic characteristics of the study group

	All (N = 300)	Female (n = 150)	Male (n = 150)	P
RV basal diameter, mm	32.3 ± 5.9	30.2 ± 5.5	34.3 ± 5.0	<.001
RVEDA, cm ²	24.6 ± 5.8	21.6 ± 4.6	27.7 ± 5.2	<.001
RVESA, cm ²	15.0 ± 3.6	12.9 ± 2.7	17.2 ± 3.1	<.001
RV FAC, %	50.2 ± 7.5	51.9 ± 7.6	48.5 ± 7.0	<.001
TAPSE, mm	22.2 ± 4.8	21.9 ± 4.6	22.5 ± 5.0	.31
Tricuspid annular s', cm/sec	13.8 ± 2.5	13.7 ± 2.5	13.9 ± 2.4	.50
Tricuspid annular e', cm/sec	15.5 ± 4.2	15.7 ± 4.4	15.2 ± 4.0	.46
Tricuspid annular a', cm/sec	15.2 ± 6.7	14.6 ± 4.6	15.8 ± 8.2	.32
RV 2D FWLS, %	29.9 ± 5.4	30.8 ± 5.6	29.1 ± 5.0	<.01
PASP, mm Hg	25.3 ± 5.7	25.8 ± 5.3	24.8 ± 6.1	.20
RAVi, mL/m ²	20.8 ± 9.8	19.2 ± 8.8	22.3 ± 10.5	<.01
3D LVEDVi, mL/m ²	63.6 ± 12.8	60.0 ± 10.6	67.2 ± 13.7	<.001
3D LVESVi, mL/m ²	27.0 ± 7.5	24.5 ± 5.9	29.6 ± 8.0	<.001
3D LVEF, %	57.8 ± 6.1	59.1 ± 6.3	56.4 ± 5.6	<.001
3D LV GLS, %	20.0 ± 2.9	21.2 ± 2.6	18.9 ± 2.6	<.001
3D LV GCS, %	27.8 ± 4.4	28.4 ± 4.4	27.2 ± 4.2	<.05
3D LVMI, g/m ²	62.0 ± 11.0	59.4 ± 10.3	64.6 ± 11.0	<.001

FWLS, Free wall longitudinal strain; LVEDVi, LV end-diastolic volume index; LVESVi, LV end-systolic volume index; LVMI, LV mass index; RAVi, right atrial end-systolic volume index; RVEDA, RV end-diastolic area; RVESA, RV end-systolic area.

Data are expressed as mean ± SD.

≥60 years of age, however, RVEF ($r = -0.45$, $P < .05$) and REFi ($r = -0.49$, $P < .01$) showed weak negative correlations with PASP.

Multivariate models were built with relevant hemodynamic and echocardiographic variables to find independent predictors of LEFi, REFi, and AEFi (Tables 5, 6, and 7). Age, BSA, HR, and RVEDVi were independent predictors of LEFi and REFi as well, but all with the opposite effect on the two motion directions. Beyond these variables, LV mass index, LV GLS, and PASP were associated with LEFi in the multivariate analysis. Concerning REFi, RVEF and LVEF were found to be independent predictors. Race, LVEF, and RVEF were independent predictors of AEFi (Table 7).

We have included three representative cases, all with maintained RVEFs, to highlight the importance of a detailed analysis of RV deformation pattern (Figure 3).

The intraobserver variability of the key 3D RV mechanical parameters was comparable with previous data, with coefficients of variation <5% for all parameters (Supplemental Table 3).^{8,15} Intercenter reproducibility showed acceptable agreement between the repeated measurements (Supplemental Table 3).

DISCUSSION

The aim of our dual-center study was to determine the physiologic contributions of RV longitudinal, radial, and anteroposterior motion

Table 3 Three-dimensional RV mechanics of the study group by age categories and sex

	All	20–29 y	30–39 y	40–49 y	50–59 y	≥60 y	P value for age	P value for gender	Interaction P
RVEDVi, mL/m²									
Men	57.0 ± 12.3	62.7 ± 12.4	58.7 ± 14.0	53.1 ± 10.2	54.0 ± 10.2	56.3 ± 12.4			.72
Women	50.7 ± 11.6	54.6 ± 12.3	50.9 ± 10.6	46.2 ± 10.2	51.3 ± 13.4	50.5 ± 10.2			
All	53.8 ± 12.3	58.6 ± 12.9	54.8 ± 12.9	49.7 ± 10.7	52.7 ± 11.8	53.4 ± 11.7	<.01	<.001	
RVESVi, mL/m²									
Men	24.1 ± 6.2	26.6 ± 6.4	23.8 ± 6.5	22.1 ± 4.8	23.0 ± 6.5	25.2 ± 5.8			.91
Women	19.8 ± 5.3	21.4 ± 5.5	19.4 ± 4.6	18.1 ± 5.1	20.2 ± 6.4	20.2 ± 4.2			
All	22.0 ± 6.1	24.0 ± 6.4	21.6 ± 6.0	20.1 ± 5.3	21.6 ± 6.6	22.7 ± 5.6	<.01	<.001	
RVEF, %									
Men	57.3 ± 5.4	57.6 ± 4.8	59.5 ± 4.5	58.4 ± 5.1	56.0 ± 6.0	55.1 ± 5.8			.69
Women	61.1 ± 5.3	60.7 ± 4.6	61.9 ± 4.5	61.9 ± 4.2	60.9 ± 6.4	59.6 ± 6.4			
All	59.2 ± 5.7	59.1 ± 4.9	60.7 ± 4.6	60.1 ± 5.0	58.5 ± 6.6	57.3 ± 6.5	<.01	<.001	
RV GLS, %									
Men	29.2 ± 5.5	29.7 ± 5.1	31.9 ± 4.7	29.5 ± 5.2	27.3 ± 5.6	27.4 ± 5.8			.91
Women	33.1 ± 6.6	33.6 ± 4.6	35.6 ± 5.5	33.4 ± 5.7	33.3 ± 7.4	30.4 ± 8.3			
All	31.1 ± 6.4	31.7 ± 5.2	33.7 ± 5.4	31.5 ± 5.8	29.8 ± 7.0	28.9 ± 7.2	<.001	<.001	
RV GCS, %									
Men	27.2 ± 6.3	26.9 ± 6.5	28.9 ± 5.7	28.1 ± 7.1	26.3 ± 5.6	25.5 ± 6.2			.48
Women	29.9 ± 7.9	29.3 ± 6.6	29.9 ± 8.1	29.4 ± 7.1	31.5 ± 9.4	29.2 ± 8.2			
All	28.5 ± 7.2	28.1 ± 6.6	29.4 ± 7.0	28.8 ± 7.1	28.9 ± 8.1	27.4 ± 7.4	<.57	<.01	
RV GAS, %									
Men	38.2 ± 4.9	38.3 ± 4.2	39.6 ± 4.6	39.1 ± 4.7	37.4 ± 5.4	36.7 ± 5.1			.90
Women	41.8 ± 5.0	41.7 ± 3.8	43.1 ± 3.6	41.7 ± 4.1	41.6 ± 6.3	40.8 ± 6.5			
All	40.0 ± 5.2	40.0 ± 4.3	41.4 ± 4.5	40.4 ± 4.6	39.5 ± 6.2	38.7 ± 6.1	<.05	<.001	
LEFi, %									
Men	46.2 ± 8.8	46.8 ± 7.3	47.3 ± 10.0	46.9 ± 8.4	44.0 ± 10.8	45.8 ± 7.4			.92
Women	46.9 ± 8.6	47.0 ± 7.5	49.0 ± 9.5	48.7 ± 8.3	44.9 ± 7.5	45.1 ± 9.7			
All	46.6 ± 8.7	46.9 ± 7.3	48.2 ± 9.7	47.8 ± 8.3	44.5 ± 9.3	45.3 ± 8.5	.10	.43	
CEFi, %									
Men	79.0 ± 6.6	77.1 ± 6.3	80.3 ± 5.8	79.8 ± 6.1	80.4 ± 7.3	77.5 ± 7.4			.88
Women	78.8 ± 7.0	76.6 ± 7.7	78.9 ± 6.9	79.4 ± 5.2	80.9 ± 6.6	78.4 ± 8.0			
All	78.9 ± 6.8	76.8 ± 6.8	79.6 ± 6.3	79.6 ± 5.6	80.7 ± 6.9	77.9 ± 7.7	.02	.80	
REFi, %									
Men	43.6 ± 9.4	41.7 ± 8.9	42.5 ± 7.0	44.7 ± 10.1	46.4 ± 9.4	42.7 ± 11.0			.99
Women	43.2 ± 11.1	40.7 ± 9.9	42.9 ± 12.0	44.4 ± 9.3	46.0 ± 11.6	41.8 ± 12.4			
All	43.5 ± 10.3	41.2 ± 9.4	42.7 ± 9.7	44.5 ± 9.6	46.2 ± 10.5	41.8 ± 12.4	.07	.72	
AEFi, %									
Men	48.5 ± 6.4	47.6 ± 7.3	51.8 ± 6.9	48.7 ± 5.6	47.5 ± 5.3	47.0 ± 6.0			.50
Women	49.7 ± 7.1	49.2 ± 7.3	50.5 ± 5.7	49.5 ± 7.5	49.7 ± 7.4	49.8 ± 7.9			
All	49.1 ± 6.8	48.4 ± 7.3	51.2 ± 6.3	49.1 ± 6.6	48.6 ± 6.5	48.4 ± 7.1	.13	.12	

CEFi: circumferential ejection fraction index; RVEDVi, RV end-diastolic volume index; RVESVi, RV end-systolic volume index. Data are expressed as mean ± SD.

to global RV function and their relations to relevant morphometric and demographic parameters. According to our results, anteroposterior and longitudinal shortening are the most prominent motion directions of RV performance. However, there is an age-dependent

increase in the relative contribution of radial motion, with a concomitant decrease in the relative contribution of longitudinal shortening to global RV function. After 40 years of age, longitudinal and radial motion contribute equally to global RV function. Individuals

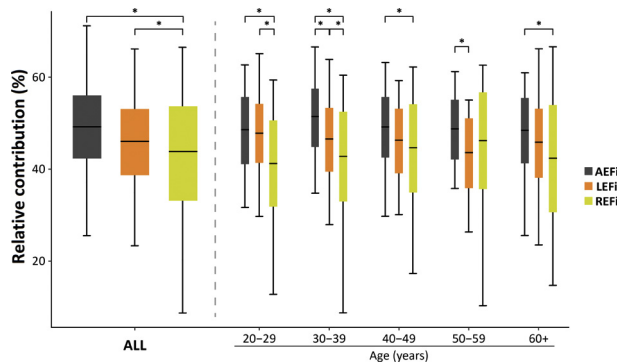


Figure 2 Comparison of the relative contributions of anteroposterior, longitudinal, and radial shortening to global RV function. Individual and mean values of AEFi, LEFi, and REFi are visualized in the pooled population ($n = 300$) and the different age categories, with statistical comparison among the three motion components. $*P < .05$.

>60 years of age represent a distinct group regarding RV contraction pattern, which may be attributable to the age-related increase in PASP.

Numerous studies have proved the independent prognostic value of RV morphology and function.¹⁻⁵ Despite these robust results, in everyday clinical practice, the assessment of RV geometry and function generally relies on simple linear measurements, with subsequent limitations. Conventional parameters of RV function, such as TAPSE and FAC, have demonstrated their correlation with RVEF and also their diagnostic and prognostic value in various cardiovascular conditions.¹⁶⁻¹⁸ On the other hand, TAPSE refers only to the longitudinal motion of the chamber, and several sources of measurement error must be taken into consideration. FAC also refers to the radial motion of the RV free wall; nevertheless,

similarly to TAPSE, it represents the function of the right ventricle in only a single 2D cut plane.¹² Three-dimensional echocardiography provides incremental data regarding RV morphology and function by precise measurements of volumes without geometric assumptions and, therefore, enables the establishment of reference values of RVEF.⁶ Notably, maintained RVEF does not preclude significant changes compared with the physiologic RV contraction pattern.¹⁶

Three main mechanisms generate RV ejection: shortening along the longitudinal axis with the traction of the tricuspid annulus toward the apex (longitudinal motion), inward movement of the RV free wall (radial motion), and traction of the RV free wall insertion points by the circumferential deformation of LV myocardium (anteroposterior motion).¹⁹ These motion components correspond to the myocardial architecture of the right ventricle. The RV myocardium consists of a complex 3D architecture of myofibers in which two main layers are present: a predominantly longitudinally aligned subendocardial layer and a dominantly circumferentially oriented subepicardial layer.^{20,21} By the shared interventricular septum and the fibers crossing the interventricular groove, LV contraction also has a significant impact on RV performance.^{22,23}

Previous data suggested that longitudinal shortening accounts for 80% of RV ejection, while the inward motion of the free wall plays only a minor role.²³ However, several studies have contradicted these observations, highlighting the potential importance of the “bellows” action (radial shortening) and anteroposterior shortening in healthy individuals and in patients with cardiovascular diseases as well.^{7,16,24,25} Although the longitudinal motion of the tricuspid annulus appears to be quite prominent, it is important to emphasize that because of its large surface, even subtle inward motion of the RV free wall can result in a considerable amount of volume change.²⁶ Nevertheless, current clinical practice lacks any RV functional parameter, which selectively represents the nonlongitudinal motions of the chamber. According to previous results, RV circumferential

Table 4 Univariate correlations between RV parameters and basic morphometric and demographic parameters

	Age	BSA	PASP	SBP	DBP	HR
RVEDVi	$r = -0.14$ $P = .02$	$r = 0.37$ $P < .001$	$r = 0.01$ $P = .90$	$r = 0.18$ $P < .01$	$r = 0.15$ $P = .02$	$r = -0.11$ $P = .07$
RVEF	$r = -0.18$ $P < .01$	$r = -0.18$ $P < .01$	$r = -0.09$ $P = .20$	$r = -0.14$ $P = .03$	$r = -0.05$ $P = .42$	$r = 0.17$ $P < .01$
RV GLS	$r = -0.23$ $P < .001$	$r = -0.26$ $P < .001$	$r = -0.08$ $P = .28$	$r = -0.17$ $P < .01$	$r = -0.13$ $P = .04$	$r = 0.001$ $P = .95$
RV GCS	$r = -0.07$ $P = .25$	$r = -0.05$ $P = .46$	$r = -0.02$ $P = .80$	$r = -0.09$ $P = .18$	$r = -0.03$ $P = .59$	$r = 0.14$ $P = .03$
RV GAS	$r = -0.16$ $P < .01$	$r = -0.13$ $P = .02$	$r = -0.08$ $P = .24$	$r = -0.10$ $P = .11$	$r = -0.04$ $P = .51$	$r = 0.19$ $P < .01$
LEFi	$r = -0.11$ $P = .048$	$r = -0.18$ $P < .01$	$r = -0.13$ $P = .07$	$r = -0.12$ $P = .06$	$r = -0.11$ $P = .09$	$r = -0.11$ $P = .08$
CEFi	$r = 0.04$ $P = .44$	$r = 0.09$ $P = .13$	$r = 0.05$ $P = .51$	$r = 0.02$ $P = .70$	$r = 0.09$ $P = .17$	$r = 0.11$ $P = .07$
REFi	$r = 0.06$ $P = .28$	$r = 0.20$ $P < .001$	$r = -0.02$ $P = .79$	$r = 0.15$ $P = .02$	$r = 0.24$ $P < .001$	$r = 0.23$ $P < .001$
AEFi	$r = -0.07$ $P = .24$	$r = -0.21$ $P < .001$	$r = 0.07$ $P = .33$	$r = -0.21$ $P < .01$	$r = -0.25$ $P < .001$	$r = -0.15$ $P = .02$

CEFi: circumferential ejection fraction index; DBP, Diastolic blood pressure; RVEDVi, RV end-diastolic volume index; SBP, systolic blood pressure. Values in boldface type are statistically significant ($P < .05$).

Table 5 Multivariate linear regression analysis: independent predictors of LEFi

Covariate	β	P
Age	-0.23	<.01
Sex	-0.13	.29
Race	-0.03	.29
BSA	-0.29	<.001
SBP	0.15	.07
DBP	0.05	.57
HR	-0.17	<.05
LVEDVi	-0.01	.88
LVEF	-0.17	.60
LVMi	0.21	<.05
LV GLS	0.16	<.05
LV GCS	0.23	.42
PASP	-0.15	<.05
RVEDVi	-0.20	<.05
RVEF	-0.15	.07
Adjusted R^2	0.15	
SE	6.41%	
Cumulative P value	<.0001	

DBP, Diastolic blood pressure; LVEDVi, LV end-diastolic volume index; LVMi, LV mass index; RVEDVi, RV end-diastolic volume index; SBP, systolic blood pressure.

Values in boldface type are statistically significant ($P < .05$).

Table 6 Multivariate linear regression analysis: independent predictors of REFi

Covariate	β	P
Age	0.24	<.001
Sex	0.05	.68
Race	0.009	.94
BSA	0.29	<.001
SBP	-0.13	.16
DBP	0.10	.23
HR	0.21	<.01
LVEDVi	-0.02	.86
LVEF	-0.22	<.01
LVMi	-0.10	.19
LV GLS	0.03	.83
LV GCS	-0.04	.86
PASP	0.001	.99
RVEDVi	0.22	<.01
RVEF	0.56	<.001
Adjusted R^2	0.32	
SE	8.39%	
Cumulative P value	<.0001	

DBP, Diastolic blood pressure; LVEDVi, LV end-diastolic volume index; LVMi, LV mass index; RVEDVi, RV end-diastolic volume index; SBP, systolic blood pressure.

Values in boldface type are statistically significant ($P < .05$).

Table 7 Multivariate linear regression analysis: independent predictors of AEFi

Covariate	β	P
Age	-0.005	.95
Sex	0.005	.96
Race	0.25	<.05
BSA	0.01	.92
SBP	-0.03	.79
DBP	-0.04	.66
HR	-0.06	.47
LVEDVi	0.15	.08
LVEF	0.44	<.05
LVMi	-0.08	.50
LV GLS	-0.09	.48
LV GCS	-0.25	.26
PASP	0.09	.25
RVEDVi	-0.17	.05
RVEF	0.26	<.01
Adjusted R^2	0.20	
SE	6.41%	
Cumulative P value	<.0001	

DBP, Diastolic blood pressure; LVEDVi, LV end-diastolic volume index; LVMi, LV mass index; RVEDVi, RV end-diastolic volume index; SBP, systolic blood pressure.

Values in boldface type are statistically significant ($P < .05$).

deformation (summation of radial and anteroposterior motions) appears to be higher than longitudinal deformation, which also supports our findings.^{9,27} These observations are similar to the LV deformation characteristics: although LV longitudinal shortening indeed has strong diagnostic and prognostic power, LV circumferential shortening contributes more to LVEF.²⁸

We found a functional shift with age (increasing radial and decreasing longitudinal contributions), which appears to be independent of the age-related changes in RV morphology. Previous studies using Doppler tissue imaging–derived velocities and speckle-tracking echocardiography found an age-dependent decrease in RV longitudinal contraction, which is concurrent with our data.^{29,30} Similarly to our results concerning LEFi, Muraru *et al.*²⁹ identified age, LV GLS, and PASP as independent predictors of RV longitudinal performance.

Compared with longitudinal function, the radial motion of the right ventricle has been scarcely investigated in clinical studies. In a pediatric study, a functional shift was observed from neonatal to early adulthood: the authors found radial predominance of RV systolic function at younger ages, with a shift to dominantly longitudinal shortening at older ages; however, they were using simple linear parameters to quantify these motion directions.³¹ Our results suggest that in adulthood, a less prominent but still considerable shift can be seen with decreasing longitudinal and increasing radial motion, which can be attributable to the age-related changes in RV myofiber architecture.³²

The anteroposterior shortening of the right ventricle is even more often neglected; therefore, clinical data are highly limited regarding this motion direction. We hypothesize that RV anteroposterior

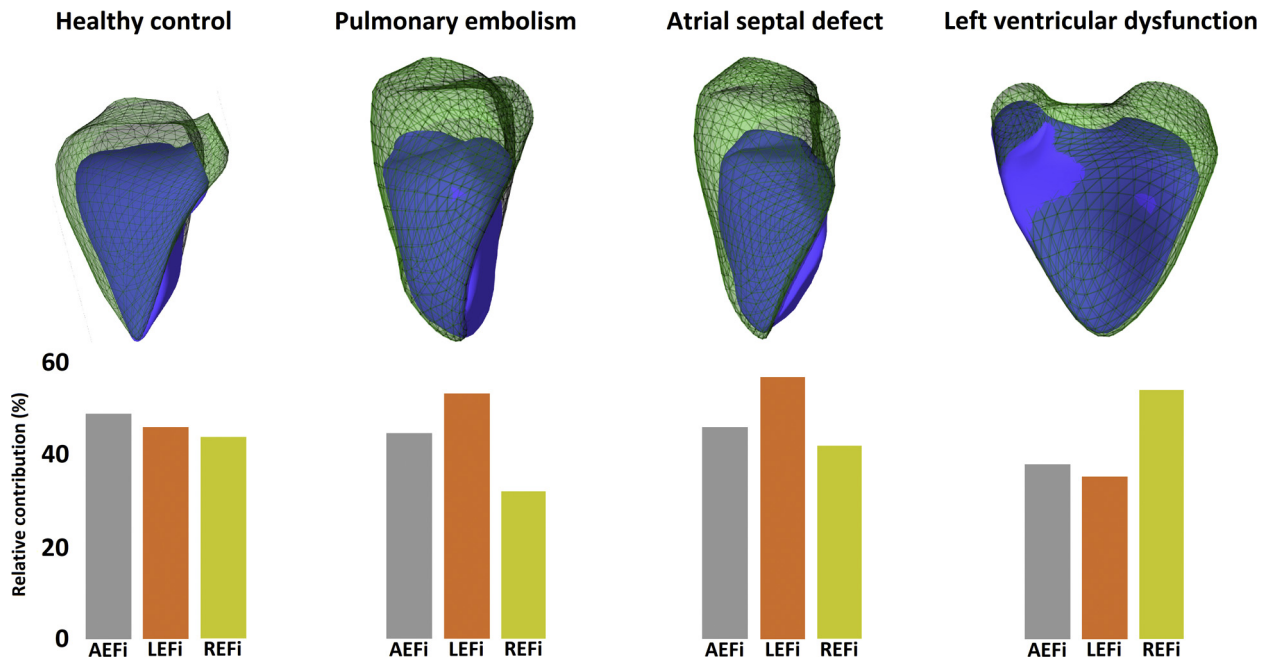


Figure 3 Significant changes in RV deformation pattern with maintained RVEF: representative cases. A healthy subject from our study group (RVEF 62%) demonstrates physiologic RV deformation with more or less equal contribution of the three motion directions. In a patient following massive pulmonary embolism (pressure overload; PASP 57 mm Hg) and maintained global RV function (RVEF 51%), radial motion (REFi) was significantly lower, while anteroposterior shortening (AEFi) remained unchanged, resulting in a higher contribution of longitudinal motion to global function (LEFi). A patient with a hemodynamically significant atrial septal defect (volume overload; Qp/Qs = 1.8) was characterized by hyperdynamic RV function (RVEF 66%). In this case, higher LEFi could be seen, with subsequently lower REFi and AEFi. In a patient with heart failure with nonischemic dilated cardiomyopathy, severely reduced LV function (LVEF 29%), and maintained RV systolic function (RVEF 48%), LEFi and AEFi were severely reduced, while REFi was relatively increased.

shortening may reflect the effect of LV contraction on RV function and, therefore, can refer to LV-RV interaction. Our research group found comparable AEFi values between heart transplant recipients and healthy control subjects and also between elite athletes and sedentary individuals.^{8,15} Nevertheless, further studies are needed to clarify the physiologic and pathophysiologic importance of RV anteroposterior shortening, especially in patients with reduced LVEFs.

Interestingly, the oldest age category (≥ 60 years) was characterized by a different RV deformation pattern. Moreover, in this group, REFi showed a negative correlation with RV afterload. Previous clinical and also experimental data suggest that decreased RV radial shortening may be an early marker of elevated PASP.^{7,33} Therefore, our finding may refer to early RV functional change in response to mildly elevated RV afterload in the elderly.³⁴ From a clinical viewpoint, however, it gains particular importance in the pathogenesis of heart failure with preserved EF, in which the significance of RV radial (transverse) function was emphasized in a recent position statement from the Heart Failure Association of the European Society of Cardiology.³⁵ In contrast to pressure overload, markedly increased contribution of radial motion can be observed in heart transplant recipients and after other forms of open heart surgery.⁸ Accordingly, several additional factors may determine RV radial function, such as loading conditions, pericardial constraint, and even autonomic innervation.^{33,36,37}

We observed no sex differences in the relative contribution of the three major components; however, RV GLS and RV GCS were higher in women, which could be associated with their lower RV volumes and higher RVEFs. By comparing the study cohorts of the two

enrolling centers, we have also evaluated racial differences. Japanese subjects were characterized by significantly lower RV volume indices and RVEFs, in accordance with preliminary data from the large-scale international World Alliance of Societies of Echocardiography study.³⁸ Interestingly, RV contraction pattern also differed, with significantly higher longitudinal and anteroposterior and significantly lower radial contributions to global function in the Japanese population. Final results from the World Alliance of Societies of Echocardiography study will more comprehensively address the racial differences in RV morphology and function.^{39,40}

When we compared patients in the lowest quartile concerning LEFi with the rest of the population, no difference in RVEF was found; however, REFi was markedly higher, further supporting that lower longitudinal function of the right ventricle may not be an unequivocal sign of dysfunction in every case.

Several demographic and hemodynamic parameters correlated with RV morphology and deformation pattern. Similar associations of RV EDVi and RVEF with age, BSA, HR, and systemic blood pressure were previously reported in the literature.^{6,41} The inverse relationships of REFi and LEFi with BSA suggest that body size also affects RV function, which may be attributable to the distinct hemodynamic load.^{42,43} We found a positive correlation of REFi and a negative correlation of AEFi with systemic blood pressure, which may also refer to the importance of ventricular interaction. Experimental data suggest that changes in LV systolic function in response to altered LV loading conditions result in opposite changes of radial and anteroposterior shortening, which is in line with our

results.⁴⁴ Moreover, in accordance with previous data, RV GLS and LEFi did not correlate with HR; whereas RV GCS and REFi had positive correlations and AEFi had a negative correlation with HR. According to these findings, the RV longitudinal and circumferential fibers may have a different inotropic response to the changes in HR (force-frequency relationship).⁴⁵

Limitations

Our study group consisted of a relatively large number of healthy subjects with a balanced sex and age distribution, also enabling us to compare European and Japanese subjects. Nevertheless, other racial differences could not be evaluated. Further multiethnic expansion of the population may strengthen our findings. Individuals >60 years of age formed one group, with a broader age distribution. Because there is no reference method for assessing RV longitudinal, radial, and anteroposterior motions, we cannot validate our results against a gold standard. Values of REFi had a higher SD compared with other motion components, which may relate to a higher variability of RV free wall inward motion. Examining RV deformation in the pediatric population, especially given its high relevance in congenital heart diseases, would also be of high interest. The value of RV motion decomposition remains to be tested in clinical practice, as data are scarce regarding the diagnostic and prognostic power of such measurements. Our method provides multiplicative rather than additive relative contributions of the different motion directions; therefore, the sum of the decomposed motion components exceeds 100%.

CONCLUSION

Despite the importance of altered RV deformation patterns in cardiovascular diseases, current clinical practice lacks methods of detailed RV functional assessment, particularly in the quantification of nonlongitudinal motions. We have demonstrated that the routinely neglected radial and anteroposterior motion directions of the right ventricle have comparable significance to longitudinal shortening in determining global RV function in healthy volunteers. These results emphasize the importance of 3D echocardiography in the assessment of RV function. Clinical data suggest that normal values of parameters that refer exclusively to RV longitudinal motion do not exclude RV dysfunction, while normal RV global function can be accompanied by abnormal longitudinal measures. Three-dimensional RVEF incorporates the contribution of all motion directions, which may be associated with additional diagnostic and prognostic power compared with conventional M-mode or 2D measurements. Even in the face of maintained global RV function, the relative contributions of the three major components may vary in different clinical scenarios (RV volume or pressure overload, cardiomyopathies, left-sided heart failure, etc.). Therefore, further studies are warranted to investigate whether the assessment of RV deformation pattern by quantifying longitudinal, radial, and anteroposterior wall motion components add to the established value of RVEF.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.echo.2020.04.002>.

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APPENDIX

Supplemental Table 1 Comparison of RV motion components by age groups

	LEFi	AEFi	REFi	LEFi vs AEFi	LEFi vs REFi	AEFi vs REFi
All (N = 300)	46.6 ± 8.7	49.1 ± 6.8	43.5 ± 10.3	<.001	<.001	<.001
20–29 y (n = 60)	46.9 ± 7.3	48.4 ± 7.3	41.2 ± 9.4	.12	<.001	<.001
30–39 y (n = 60)	48.2 ± 9.7	51.2 ± 6.3	42.7 ± 9.7	<.05	<.001	<.001
40–49 y (n = 60)	47.8 ± 8.3	49.1 ± 6.6	44.5 ± 9.6	.30	<.001	<.01
50–59 y (n = 60)	44.5 ± 9.3	48.6 ± 6.5	46.2 ± 10.5	.11	<.001	.13
≥60 y (n = 60)	45.3 ± 8.5	48.4 ± 7.1	41.8 ± 12.4	.06	<.05	<.001

Data are expressed as mean ± SD. Values in boldface type are statistically significant ($P < .05$).

Supplemental Table 2 Comparison of 3D RV parameters in the population of the two enrolling centers

	Japanese (n = 150)	Hungarian (n = 150)	P
RVEDVi, mL/m ²	50.1 ± 11.6	57.5 ± 11.9	<.001
RVESVi, mL/m ²	21.2 ± 6.2	22.9 ± 5.8	<.05
RVEF, %	57.9 ± 6.7	60.6 ± 4.1	<.001
RV GLS, %	30.9 ± 7.3	31.4 ± 5.3	.46
RV GCS, %	27.1 ± 7.3	29.9 ± 7.0	<.001
RV GAS, %	38.4 ± 5.9	41.6 ± 3.9	<.001
LEFi, %	46.9 ± 7.4	44.8 ± 6.8	<.05
REFi, %	40.0 ± 11.3	46.6 ± 7.9	<.001
AEFi, %	50.8 ± 6.6	47.4 ± 6.7	<.001

RVEDVi, RV end-diastolic volume index; RVESVi, RV end-systolic volume index.

Data are expressed as mean ± SD.

Supplemental Table 3 Intraobserver and intercenter variability of key 3D RV mechanical parameters

	Intraobserver variability		Intercenter variability	
	CV, %	R ²	CV, %	R ²
L_ESV	4.63	0.887	8.42	0.632
R_ESV	4.55	0.880	6.81	0.507
A_ESV	2.81	0.956	8.53	0.632

A_ESV, end-systolic volume after decomposition, anteroposterior motion only; CV, coefficient of variation; L_ESV, end-systolic volume after decomposition, longitudinal motion only; R_ESV, end-systolic volume after decomposition, radial motion only.