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Semi-quantitative assessment of right ventricular function in comparison to a 3D volumetric approach: A cardiovascular magnetic resonance study

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Abstract Right ventricular (RV) volume measurements with cardiovascular magnetic resonance (CMR) is considered the gold standard, but acquisition and analysis remain time-consuming. The aim of our study was therefore to investigate the accuracy and performance of a semi-quantitative assessment of RV function in CMR, compared to the standard quantitative approach. Seventy-five subjects with pulmonary hypertension (15), anterior myocardial infarction (15), inferior myocardial infarction (15), Brugada syndrome (15) and normal subjects (15) underwent cine CMR. RV end-systolic and end-diastolic volumes were determined to calculate RV ejection fraction (EF). Four-chamber cine images were used to measure tricuspid annular plane systolic excursion (TAPSE). RV fractional shortening (RVFS) was calculated by dividing TAPSE by the RV end-diastolic length. RV EF correlated significantly with TAPSE ($r = 0.62$, $p < 0.01$) and RVFS ($r = 0.67$, $p < 0.01$). Sensitivity to predict RV dysfunction was comparable between TAPSE and RVFS, with higher specificity for RVFS, but comparable areas under the ROC curve. Intra- and inter-observer variability of RV EF was better than TAPSE (3%/4% versus 7%/15%, respectively). For routine screening in clinical practice, TAPSE and RVFS seem reliable and easy methods to identify patients with RV dysfunction. The 3D volumetric approach is preferred to assess RV function for research purposes or to evaluate treatment response.

Keywords Cardiovascular magnetic resonance · Right ventricular function · TAPSE

Introduction

Right ventricular (RV) function has proven to be of significant importance in a wide range of cardiac disease. It is a major determinant of clinical outcome in chronic heart failure, a prognostic marker for adverse outcome after acute myocardial infarction and an important measure in the evaluation and follow-up of patients with pulmonary arterial hypertension [1–4]. Thus, the need for diagnosis of RV dysfunction is evident. Various (non)invasive imaging modalities are available for the evaluation of RV function [5–10], of which cardiovascular magnetic resonance (CMR) is considered the gold standard for quantitative assessment [11, 12]. Although assessment of RV volumes and function using CMR is highly accurate and reproducible [13, 14], both acquisition and analysis are still time-consuming and require dedicated post-processing software. In clinical practice, 2D echocardiography is generally used to acquire functional information of the RV. A quick semi-quantitative approach to assess RV function in 2D echocardiography is to measure the tricuspid annular plane systolic excursion (TAPSE), which can easily be obtained, and correlates well with RV function on radionuclide angiography [15–17].

The increasing interest and availability of clinical CMR generates the need for fast and accurate methods to obtain information on RV function and dimensions. For left ventricular analysis, geometrical models have been developed to accurately determine left ventricular function and

dimensions and to substantially reduce acquisition and analysis duration [18]. However, this approach often fails in RV analysis, while its geometrical complexity impedes the accuracy of such models to determine function and volumes. Some clinicians therefore measure a modified TAPSE, adapted from echocardiography. However, it is unknown whether this semi-quantitative approach can be legitimately used in CMR and how it relates to the quantitative assessment of RV function. Furthermore, it is disputable whether an absolute TAPSE value accurately represents RV function in all patients, while this measure disregards the dimensions of the RV. Therefore, it may be more accurate to use a semi-quantitative measure that involves RV dimensions to determine RV function.

The present study was designed to determine the accuracy of a semi-quantitative assessment of RV function in CMR and to evaluate its diagnostic performance for identifying different degrees of RV dysfunction. Furthermore, we sought to investigate the intra-observer and inter-observer reproducibility of this method, compared to the standard quantitative approach.

Materials and methods

Subject selection

Patients for the study were recruited from the clinic at the cardiology department of the VU University Medical Center, Amsterdam, the Netherlands. We prospectively investigated 60 patients (39 men; mean age, 50±13 years), consecutively enrolled per each patient group. The study population consisted of 15 patients with pulmonary arterial hypertension, 15 patients with anterior acute myocardial infarction (AMI), 15 patients with inferior AMI and 15 patients with Brugada syndrome. Pulmonary arterial hypertension (11 idiopathic, 4 systemic sclerosis) was confirmed by cardiac catheterization (mean pulmonary artery pressure, 54 ± 16 mmHg). Patients with AMI were scanned 5 ± 2 days after primary percutaneous coronary intervention with stenting and were treated with aspirin, heparin, abciximab, clopidogrel, statins, beta-blockade and ACE-inhibitors. The Brugada syndrome was confirmed by typical ECG-pattern and a positive ajmaline test [19]. We also included 15 healthy controls without cardiac history or risk factors in the study (5 men; mean age, 41 ± 12 years). Exclusion criteria comprised contraindications for CMR (e.g., claustrophobia, pacemakers, very irregular heart rhythm and intracerebral aneurysm clips). The study was approved by the local ethics committee, and all patients gave written informed consent.

CMR study protocol

CMR examination was performed on a 1.5-T clinical MR system (Magnetom Sonata, Siemens, Erlangen, Germany) using a four-element phased-array cardiac receiver coil. ECG-gated cine imaging was performed using a balanced steady-state free precession pulse sequence, during repeated breath-holds of approximately 10 s. Long axis slices were acquired in the three standard views (four-, three- and two-chamber view), as well as a stack of short axis slices with a typical slice thickness of 5 mm and a gap of 5 mm between the slices, fully covering both ventricles from base to apex. MR parameters were as follows: temporal resolution between 35 to 50 ms, typical voxel size 1.5× 1.8 ×5.0 mm^3, excitation angle 60°, receiver bandwidth 930 Hz/pixel, TR/TE 3.2/1.6 ms, matrix 256×156.

Data analysis and definitions

CMR data for the assessment of RV volumes were analyzed on a personal computer using dedicated software (Mass, Medis, Leiden, the Netherlands). On all short axis cine slices, the endocardial borders of the RV were outlined manually on end-diastolic (first cine phase of the R-wave triggered acquisition) and end-systolic (image phase with smallest cavity area) images, excluding trabeculae and papillary muscles. RV end-diastolic volumes (EDV, ml) and RV end-systolic volumes (ESV, ml) were calculated by summation of discs, from which RV ejection fraction (EF, %) could be derived. TAPSE measurements were calculated on a separate workstation (Centricity Radiology v6.1, GE Medical Systems, Zeist, the Netherlands). On the four-chamber view, the distance between the cutting edge of the tricuspid annulus with the RV free wall and the RV apex was measured in end-diastole (end-diastolic length, EDL, mm) and end-systole (ESL, mm) (Fig. 1). TAPSE was defined as the difference between RV EDL and ESL. An additional relative measure was obtained, which corrects TAPSE for the length of the RV. This right ventricular fractional shortening (RVFS) was calculated as follows:

$$RVFS(\%) = \frac{(EDL - ESL)}{EDL} * 100$$

To test intra-observer and inter-observer variability of RV EF and TAPSE measurements, analyses were repeated by the same investigator, and a second investigator respectively on the same images in 25 subjects, from 5 consecutive subjects in each group (RN, TG). Analysis of the scans was performed in random order, with the investigators blinded to medical history of the subject and previous results.

Statistical analysis

Continuous variables with normal distribution are expressed as mean ± SD. Analysis of variances (ANOVA) was used to compare differences between patient groups, and

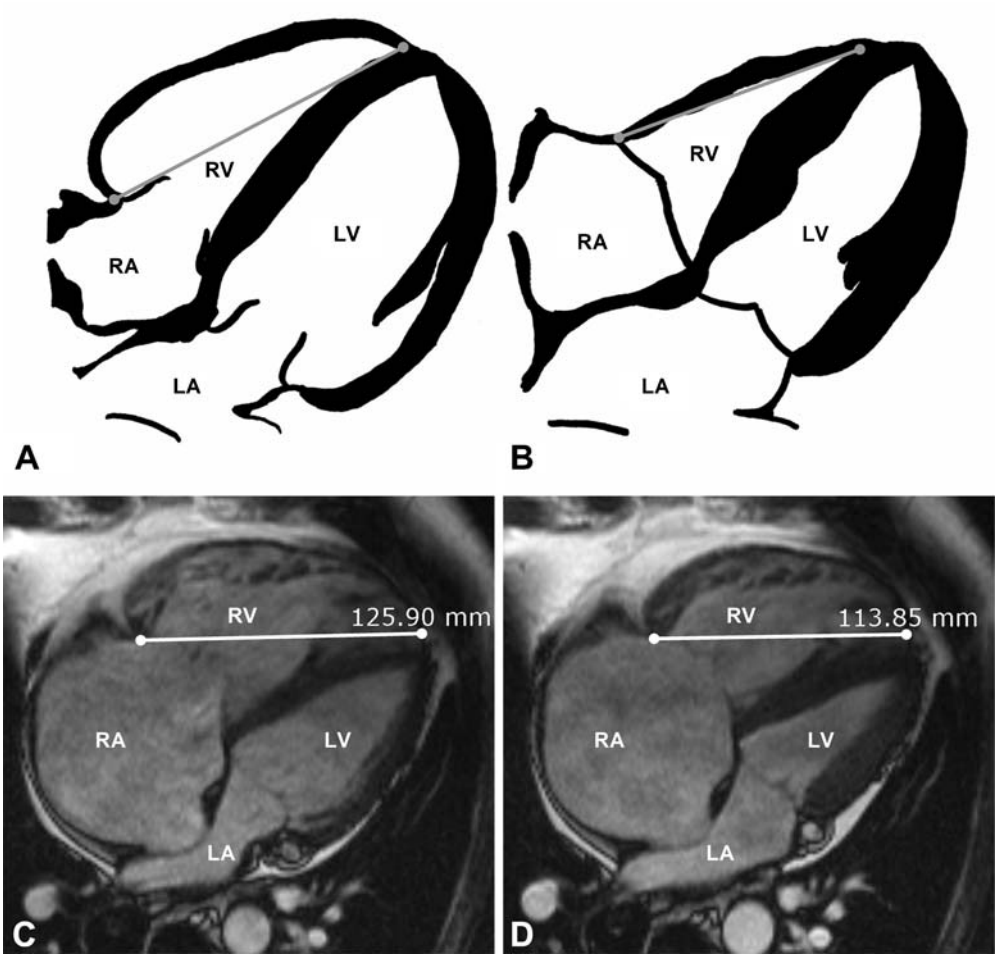

Fig. 1 Schematic figure of TAPSE measurement using a four-chamber cine image in end-diastole (**A**) and end-systole (**B**). TAPSE is calculated by subtracting the right ventricular end-systolic length (grey line in panel B) from the end-diastolic length (gray line in panel A). Clinical example of a four-chamber cine image in end-diastole (**C**) and end-systole (**D**) in a patient with pulmonary hypertension. The TAPSE measures 125.90−113.85=12.05 mm, and the RVFS is $\frac{(125.90-113.85)}{125.90} * 100 = 9.57\%$. RA: right atrium, RV: right ventricle, LA: left atrium, LV: left ventricle

Tukey's post-hoc test was used for pair-wise comparison of means. Pearson's correlation coefficients (r) were calculated for the relation between RV EF, TAPSE and RVFS. Correlation coefficients were compared using a Fisher's Z transformation. The TAPSE and RVFS value with the highest sensitivity and specificity for predicting RV dysfunction were calculated for RV EF <35%, <40% and <45%, using receiver-operating characteristic (ROC) analysis. Comparison between ROC curves following the method described by Hanley and McNeil [20] was performed using Analyse-it Clinical Laboratory 1.73 (Analyse-It Software, Ltd.).

Intra-observer and inter-observer variability of RV EF and TAPSE measurements was assessed as previously described by Bland and Altman [21], and the coefficients of variability (SD of the differences of two measurements divided by their mean) were calculated. A one-sample *t* test against zero was performed to test for statistical significance of the observed differences in intra-observer and inter-observer variability.

All statistical tests were two-sided with a significance level of $p < 0.05$. SPSS 12.0.1 for Windows (SPSS Inc.) was used for all analyses, except for the comparison between ROC curves.

Results

RV volumes, EF, lengths, TAPSE and RVFS are listed in Table 1 according to patient groups. Healthy volunteers and patients with Brugada syndrome were significantly younger than patients with anterior/inferior AMI ($p < 0.05$). Patients with anterior AMI had larger infarcts than patients with inferior AMI (21 ± 12 versus 13 ± 9 percent of

Table 1 Subject characteristics and CMR measurements of the right ventricle per patient group and as a whole

	Controls (n=15)	PHT (n=15)	Anterior AMI (n=15)	Inferior AMI (n=15)	Brugada (n=15)	Total (n=75)
Age (years)	41 ± 12	47 ± 13	56 ± 10	55 ± 10	42 ± 12	48 ± 13
Peak CK (U/l)	–	–	3,755 ± 1,856	2,736 ± 1,939	–	–
Infarct size (% LV)	–	–	22 ± 12	13 ± 9	–	–
EDV (ml)	192 ± 37	248 ± 93	158 ± 34	175 ± 57	188 ± 47	192 ± 64
EDVi (ml/m^2)	103 ± 15	130 ± 38	80 ± 14	87 ± 27	101 ± 17	100 ± 29
ESV (ml)	96 ± 20	188 ± 97	79 ± 24	89 ± 31	97 ± 28	110 ± 62
ESV i (ml/m^2)	52 ± 10	98 ± 44	40 ± 10	44 ± 15	52 ± 12	57 ± 30
SV (ml)	96 ± 21	61 ± 30	79 ± 19	86 ± 30	92 ± 24	83 ± 27
SV i (ml/m^2)	51 ± 8	32 ± 15	40 ± 10	42 ± 14	49 ± 10	43 ± 13
EF (%)	50 ± 5	27 ± 14	51 ± 8	49 ± 8	49 ± 7	45 ± 13
EDL (mm)	91 ± 8	103 ± 12	93 ± 10	98 ± 13	95 ± 9	96 ± 11
ESL (mm)	69 ± 7	89 ± 13	76 ± 12	78 ± 11	72 ± 9	77 ± 12
TAPSE (mm)	23 ± 3	15 ± 6	18 ± 5	20 ± 4	23 ± 4	20 ± 5
RVFS (%)	25 ± 3	14 ± 7	19 ± 6	21 ± 3	24 ± 4	21 ± 6

PHT: pulmonary arterial hypertension, AMI: acute myocardial infarction, CK: creatine kinase, LV: left ventricle, EDV: end-diastolic volume, ESV: end-systolic volume, SV: stroke volume, -i: indexed for body surface area, EF: ejection fraction, EDL: end-diastolic length, ESL: end-systolic length, TAPSE: tricuspid annular plane systolic excursion, RVFS: right ventricular fractional shortening
Values are expressed as mean ± SD

the left ventricle, $p < 0.05$). RV EDVi (indexed for body surface area) and RV ESVi were higher and RV EF was lower in patients with pulmonary arterial hypertension compared to patients with anterior/inferior AMI and Brugada syndrome ($p < 0.05$). RV ESVi, RV EDL and RV ESL were significantly higher and RV EF, TAPSE and RVFS lower in patients with pulmonary hypertension than in healthy volunteers ($p < 0.05$). There were no differences in RV indices between patients with anterior or inferior AMI (p = ns).

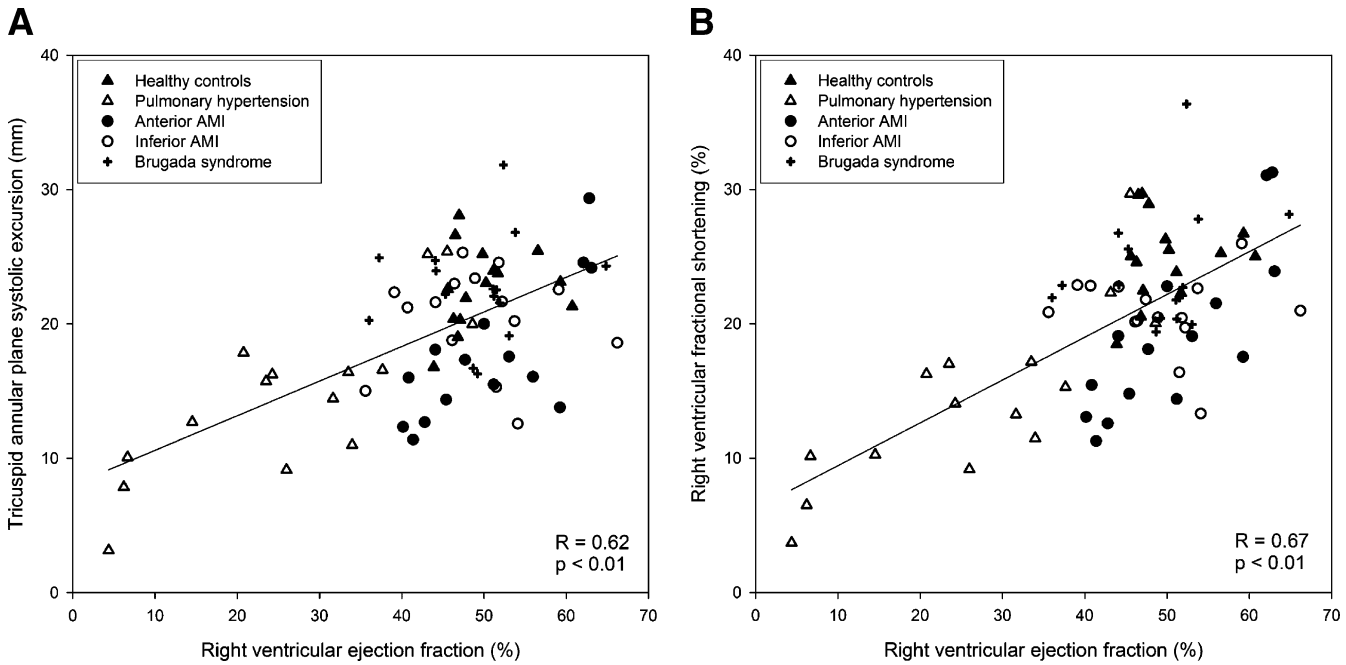

Fig. 2 Linear regression (solid line) of tricuspid annular plane systolic excursion (**A**) and right ventricular fractional shortening (**B**) by right ventricular ejection fraction. Symbols represent groups according to legend

Table 2 The TAPSE and RVFS cut-off values with the highest sensitivity and specificity for predicting RV EF <35%, <40% and <45%

RV EF	TAPSE			RVFS		
	Cut-off value	Sensitivity	Specificity	Cut-off value	Sensitivity	Specificity
<35%	18	100	73	17	100	86
<40%	17	75	81	17	75	86
<45%	18	70	79	19	67	85

The RV EF as estimated by CMR showed significant correlation to TAPSE (r=0.62, p<0.01, Fig. 2A). The relationship between RV EF and RVFS was also statistically significant (r=0.67, p<0.01, Fig. 2B). There were no significant differences between both correlation coefficients (Z_{obs}=0.52). The TAPSE and RVFS cut-off values with the highest sensitivity and specificity for predicting RV EF <35%, <40% and 45% are listed in Table 2. Figure 3 displays the ROC curves of TAPSE and RVFS to indicate RV EF <35%. Specificity of RVFS was higher than TAPSE to detect RV dysfunction; however, comparison between the areas under the ROC curves of TAPSE and RVFS revealed no statistical differences.

Figure 4 represents the Bland-Altman analyses of intra-observer and inter-observer variabilities of RV EF and TAPSE measurements. Intra-observer and inter-observer variability of RV EF calculations was low (3% and 4%, respectively). Although the intra-observer and inter-observer variability of TAPSE measurements were substantially higher (7% and 15%, respectively), the differences in intra- and inter-observer variabilities of both RV EF (p=0.74 and p=0.40, respectively) and TAPSE (p=0.40 and p=0.56, respectively) were not statistically significant.

Discussion

In the present study, we evaluated the accuracy and performance of a semi-quantitative assessment of RV function in CMR, and the intra-observer and inter-observer reproducibility of this method, compared to the standard quantitative approach. Our data demonstrate that TAPSE in CMR correlates well with 3D volumetric assessment of RV function. Intra-observer reproducibility was better than the inter-observer reproducibility of TAPSE, but inferior to the 3D volumetric approach, which had comparable intra- and inter-observer variability. Right ventricular fractional shortening, which corrects for RV length, showed also significant correlation with quantitative analysis.

Previous reports have demonstrated a relationship between echocardiographic TAPSE and quantitative assessment of RV function, using different modalities [22–24]. In the present study, TAPSE acquired on CMR images showed comparable normal ranges with previous studies in echocardiography [25, 26], thus the described method for CMR seems valid. The reason for a higher level of correlation between TAPSE and RV EF in the present study may be a larger study population with a wider range of RV parameters than previously investigated. In addition, in CMR it is possible to correct TAPSE for RV length, which may offer a reliable semi-quantitative measure in small hearts as well. RVFS tended to correlate better with RV function than TAPSE and indicated impaired RV function with comparable sensitivity but higher specificity than TAPSE. Future research is needed to evaluate its possible statistical superiority and clinical applicability.

In this study we used short axis orientation for volumetric assessment of RV volumes [27–30]. Alfakih and colleagues demonstrated that axial orientation results in better observer variabilities than the short axis orientation [31]. They suggest that the better identification of the pulmonary and tricuspid valves, and the basal slice in the axial orientation are mostly responsible for the differences. In our study, we used the four-chamber view to verify whether the basal short axis slice was part of the RV and should be included in analysis, which resulted in good reproducibility as well. Furthermore, in clinical practice, short axis orientation allows both analysis of left and right ventricular volumes and is therefore most often used.

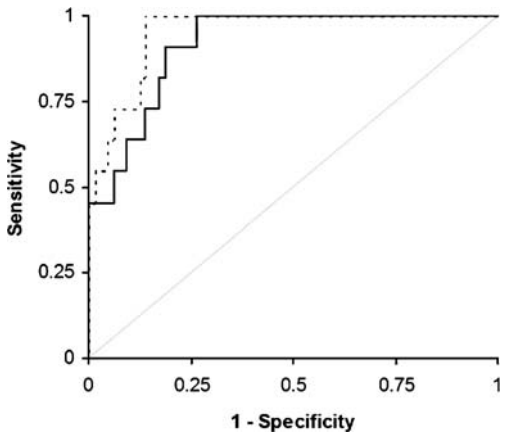

Fig. 3 Receiver-operating characteristic curves of the TAPSE (solid line) and RVFS (dashed line) to indicate right ventricular ejection fraction of less than 35%. Area under the curves was 0.92 (0.85–0.99) for TAPSE, versus 0.95 (0.90–1.00) for RVFS. There was no statistical difference between both areas under the curve

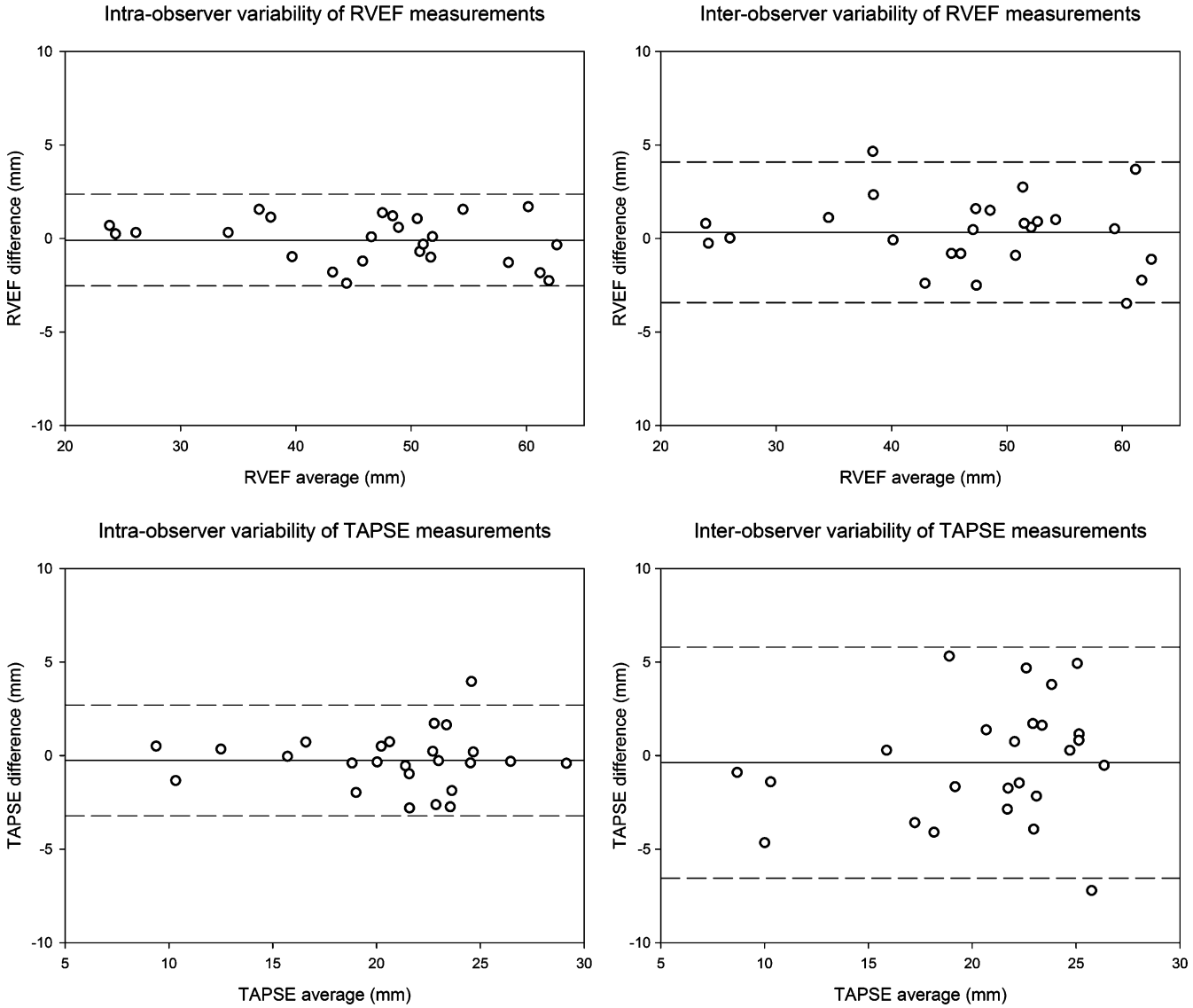

Fig. 4 Bland-Altman plot illustrating the intra- and inter-observer variability of RV EF and TAPSE measurements. Mean difference (solid line) and 95% limits of agreement (dashed lines) are shown

The status of CMR as a highly reproducible reference standard for the assessment of cardiac function is based on its flexible multi-plane capabilities. The present study offers directions to perform semi-quantitative measurements for right ventricular function using CMR. Since RV function provides important prognostic information, it is desirable to have a screening tool to identify patients with RV dysfunction. Both TAPSE and RVFS were validated for this purpose and showed good performance, but also had important limitations. For routine screening of the RV in a standard clinical CMR examination, TAPSE and RVFS seem reliable and easy methods to identify patients with RV dysfunction. However neither TAPSE nor RVFS were able to distinguish moderate and mildly depressed RV function. For research purposes or when small changes in RV function may have important clinical consequences, e.g., for the evaluation of response to treatment, the more time-consuming 3D volumetric approach is preferred to assess RV function.

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