Two- and Three-dimensional Speckle-tracking Global Longitudinal Strain Are Strongly Correlated, in General but Not Per Segment, According to the 17-segment American Heart Association Model

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Research Article

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Abstract

Purpose

Two-dimensional (2D) and three-dimensional (3D) speckle-tracking echocardiography (STE) enable objective assessment of myocardial function. Here we examined the agreement between 2D and 3D STE measurement of global longitudinal strain (GLS) in patients with normal left ventricle, reduced ejection fraction, and cardiac pacing.

Methods

Our analysis included 90 consecutive patients (59% males; average age: 73.2 ± 11.2 years) examined between May 2019–December 2020, with valid 2D and 3D loops for further speckle-tracking strain analysis. Linear regression and Pearson correlation were used to quantify the association between 2D and 3D GLS, and related segments using the 17-segment American Heart Association (AHA) model. Analyses were performed in the entire study group and subgroups.

Results

We observed a strong correlation between 2D and 3D GLS measurements (R = 0.76, $P < 0.001$), which was higher in males (R = 0.78, $P < 0.001$) than females (R = 0.69, $P < 0.001$). Associated segment correlation was poor (R = 0.2–0.5, $P < 0.01$). The correlation between 2D and 3D GLS was weaker in individuals with ventricular pacing of >50% (R = 0.62, $P < 0.001$) than <50% (R = 0.8, $P < 0.001$), and in patients with LVEF of <35% (R = 0.69, $P = 0.002$) than >35% (R = 0.72, $P < 0.001$).

Conclusion

verall 2D and 3D GLS were closely associated, but not when analyzed per segment. Right ventricular pacing and reduced left ventricular ejection fraction were associated with reduced correlation between 2D and 3D GLS.

Introduction

Speckle-tracking echocardiography (STE) is a promising method for non-invasive myocardial deformation analysis [1]. Compared to magnetic resonance imaging (MRI), two-dimensional (2D) STE enables angle-independent and reliable measurement of left ventricular dimensions and strains [1]. Despite years of research showing advantages over conventional parameters, 2D STE is not commonly used in clinical practice. Reasons include that the analysis is time-consuming, the lack of standardization, inter-vendor differences, and the need for manual adjustments to the cardiac regions of interest [2-4]. Moreover, different modalities—such as 2D STE, three-dimensional (3D) STE, and cardiac (MRI)—are available to acquire myocardial strain measurements, raising questions regarding the agreement between methods[4,5].

Two-dimensional STE has been validated against MRI tagging, as a gold standard of deformation analysis[1,5]. However, based on the expert consensus statement, there is no true gold standard technique for non-invasive quantification of left ventricular (LV) mechanics[6]. MRI tagged myocardial strain showed an excellent correlation to 2D STE[1], similar to the agreement previously described between tissue Doppler imaging (TDI)-based strain and MRI-tagging [7].

Two-dimensional STE enables feasible objective assessment of global and regional myocardial function[4]. The model is reconstructed and segmented from three 2D planes, in contrast to 3D volumetric speckle-tracking analysis. Three-dimensional STE is an emerging ultrasonographic modality that may provide us with more physiological, and probably faster, analysis of myocardial deformation. The results of 3D STE should be cautiously evaluated. Compared to 2D STE, 3D STE involves a considerably lower average frame rate and a higher level of automatization of the analysis. Therefore, there remains a need to examine the agreement between 2D and 3D STE.

Global longitudinal strain (GLS) predominantly reflects the contractile function of the subendocardium and subepicardium of the left ventricular wall due to myofiber orientation [8]. Notably, the subendocardium is more susceptible to both ischemia/stunning and mechanical overload related to either valvular disease or aging [8-10]. Therefore, GLS is likely to decrease in early stages of various cardiac diseases [8]. GLS is by far the most frequently used, reliable, and reproducible parameter, even when compared to left ventricular ejection fraction (LVEF) [11].

Based on its reliability, sensitivity, and reproducibility, GLS was the main parameter investigated in our present study. We aimed to analyze the level of agreement between GLS measured by 2D vs. 3D STE, gender differences in 2D vs. 3D GLS analysis, and factors influencing the level of agreement between 2D vs. 3D GLS.

Methods

Patients

For this study, we retrospectively enrolled echocardiographic examinations from 120 consecutive patients. The analysis included only cases with adequate image quality and complete loops for 2D and 3D STE (N = 90). There were no significant differences in baseline clinical parameters between included and excluded patients (not tabulated). We included a mixed sample of patients with various cardiovascular diseases to assess the correlation between 2D and 3D STE across a heterogenous patient population. This study was approved by the institutional review board, and conducted in accordance with the Helsinki declaration. The need for informed consent was waived for this study.

Echocardiography

Two-dimensional grayscale echocardiography was performed using a Vivid E95 scanner (GE Vingmed Ultrasound, Horten, Norway). The frame rate was >50/s for 2D STE, and >25/s for 3D STE. Images were analyzed using EchoPAC version 203 revision 73 (GE Vingmed Ultrasound, Horten, Norway). The endocardial border was traced at end-systole, and the thickness of the region of interest (ROI) was adjusted to include most of the myocardium, while avoiding stationary speckles near the pericardium.

For 2D STE, we used automatic function imaging (AFI) of the EchoPAC (*Fig. 1*). The AFI feature involves the manual placement of markers on each side of the mitral annulus and left ventricular (LV) apex in three standard apical views. Next, the program automatically tracks the endocardial border and calculates the myocardial (ROI). When necessary, manual adjustments were made to the ROI and/or the endocardial/epicardial borders, which are important for the strain analysis (*Fig. 1, Fig. 2*).

For 3D STE analysis, we used the automatic left ventricular quantification function (AutoLVQ) of EchoPAC. Topographic markers were placed in the middle of the mitral valve and the LV apex. The endocardial border was automatically delineated, and manual adjustments were made when necessary. For both 2D and 3D STE, end-diastole and end-systole were determined by automatic identification of the aortic valve opening and closure, and manual adjustments were made when necessary (*Fig. 3*). All the 2D and 3D global longitudinal strain values were calculated using the software, and presented as a 17-segment bull's eye model.

Statistics

Continuous variables were expressed as mean ± standard deviation, and compared by t-test or Mann-Whitney U test, as appropriate. Categorical variables were expressed as percentages, and compared by the chi-square test, Fisher's exact test, or logistic regression, as appropriate. We investigated the association of 2D GLS with 3D GLS using linear regression analysis and Pearson's correlation. A two-tailed α value of <0.05 was considered statistically significant—except for the test of equality of covariance matrices, for which $P < 0.005$ was considered significant. The majority of analyses were performed on the entire group of patients, some analyses were performed separately for males and females. All analyses were performed using IBM SPSS for MAC version 23 (IBM, New York, USA) and MS Excel (Redmond, Washington, USA) for MAC version 16.5.

Results

Our analysis included a total of 90 patients. *Table 1* shows the baseline clinical characteristics, including gender differences. Except for LVEF and heart failure, there were no meaningful differences between males and females. We observed an overall strong positive correlation between 2D GLS and 3D GLS (R = 0.76, $P < 0.001$) (*Fig. 4*). Separate analyses revealed that this correlation coefficient was greater in males (R = 0.78, $P < 0.001$) and lesser in females (R = 0.69, $P < 0.001$). Bland-Altman analysis demonstrated a small bias (0.1%) and relatively narrow limits of agreement (SD: 2.9%) between 2D and 3D GLS (*Fig. 5*).

Analysis of every 2D vs. 3D segment of the 17-segment AHA model revealed a poor associated segment correlation, with R values ranging from 0.2 to 0.5 ($P < 0.01$) (*Table 2*). Not all of the segments even reached the level of significance. The anteroseptal segments seem to produce higher correlation between 2D and 3D GLS irrespective whether they were apical, middle or basal (*Table 2*). The correlation between 2D and 3D GLS was weaker among individuals with >50% ventricular pacing (R = 0.62, $P < 0.001$) than in individuals with <50% ventricular pacing or no pacing (R = 0.8, $P < 0.001$) (*Fig. 6, Table 3*). Moreover, the correlation coefficient between 2D vs. 3D GLS was lower with LVEF < 35% (R = 0.69, $P = 0.002$) than LVEF > 35% (R = 0.72, $P < 0.001$) (*Fig. 7*, *Table 3*).

Discussion

The main findings of our retrospective analysis can be summarized as follows: 1) we found high agreement between two-dimensional and three-dimensional global longitudinal strain, 2) the degree of agreement differed between genders, and 3) cardiac pacing and reduced LVEF were associated with a lower numerical correlation between two-dimensional and three-dimensional global longitudinal strain.

Previous studies

Two-dimensional speckle-tracking echocardiography has been proven to be efficient and reliable for the quantification of regional and global LV myocardial motion in different clinical scenarios, yet it has some limitations[1-5,8,11]. Three-dimensional speckle-tracking echocardiography has attracted interest because it may overcome the "out of plane" movement limitation of 2D STE. However, the greater complexity of 3D STE acquisition and image analysis make it vulnerable to low image quality, tracking artifacts, and low frame rate interactions. Although it has been shown that 3D STE performance is not compromised by frame rates as low as 18–25 frame/s [12].

Many recent comparative studies have examined 2D STE, 3D STE, and MRI tagging or feature tracking, showing varying results. Altman et al. conducted a trial comparing different 2D STE and 3D STE measures, and found that GLS was similar between 2D and 3D modes (−14 ± 4 vs. −13 ± 3, non-significant) [13]. Another trial evaluated the agreement between 3D and 2D speckle-tracking GLS, and found a Pearson correlation of 0.95 [14]. On the other hand, a comparison of 2D vs. 3D GLS detected a correlation coefficient of only 0.4 in healthy volunteers, compared to 0.9 in patients with mitral stenosis [5]. Another study reported a good correlation between GLS determined by cardiac magnetic resonance feature tracking (CMRFT) compared to 2DST (r = 0.83) and 3DSTE (r = 0.87) [15]. In one investigation, GLS values were consistently lower in the 3D mode compared to the 2D mode, and the sensitivity for predicting coronary artery disease was 80% for 2D GLS compared to 93% for 3D GLS [16]. Notably, 3D strain data were acquired faster than 2D data (2.2 ± 1 vs. 3 ± 1, respectively) [16]. The varying levels of agreement between 2D and 3D strain data may be explained by the different vendors, intra- and interobserver variability, differences in patient comorbidities and gender, cine loops image quality, and the magnitude of manual adjustments.

Current study

To our knowledge, no prior studies have compared 2D and 3D GLS between particular segments of the 17-segment AHA model. Surprisingly, although we found a high overall agreement between 2D and 3D GLS, the numerical correlation per segment was quite low. This is probably due to the different manners of acquisition and segmentation processes. In the 3D mode, the calculation originates from the volumetric matrix. On the contrary, in the 2D mode, an extrapolation is created from three 2D apical planes. Moreover, we may speculate that the strain segment annotation differs between 2D and 3D mode, which could explain why there was a generally strong correlation between the two modes overall, but not per segment. On the other hand, there is some pattern to the level of correlation related to broader areas of the myocardium. Particularly anterior and anteroseptal areas demonstrated higher 2D vs. 3D GLS correlation than the rest of the heart. We may only speculate, that better visualization of anterior and septal areas, which are usually in direct beam of the ultrasound transducer, may lead to more reliable speckle tracking acquisition. On the lateral, posterior and inferior myocardial wall the tracked border may more easily depart from the visible boundary [17].

In our study, we also found that a low LVEF of <35% and significant amount (>50%) of right ventricular pacing were associated with a decreased correlation between 2D and 3D GLS. Both factors have the same denominator of asynchronous and/or impaired ventricular contraction. It has been also shown that the left ventricle geometry may act as a confounder. A significant reduction of GLS could be compensated by a small increase in global circumferential strain, wall thickness, and/or reduced LV diameter [18].

Implications

Our observations may have implications for clinical practice. Compared to 2D STE, 3D STE is a promising and less time-consuming method. Global longitudinal strain is a reliable and reproducible measure of myocardial deformation, even when assessed using different modes of acquisition (2D vs. 3D). In patients with reduced left ventricular ejection fraction and a significant amount of right ventricular pacing, strain data must be evaluated cautiously.

Limitations

The study has several limitations. First, it was a retrospective study, and many aspects of the acquisition were not prespecified. Therefore, a substantial number of patients had to be excluded from the study due to inadequate image quality, which may have produced a selection bias. Moreover, the agreement between 2D and 3D strain was determined purely based on echocardiographic methods, without comparison to the "golden standard" of MRI tagging or feature tracking. Notably, although there is no real golden standard for myocardial deformation, MRI is historically considered the most accurate and reliable method.

Conclusion

We found that 2D and 3D GLS measurements exhibited a close association overall, but not when analyzed per segment according to the 17-segment AHA model. Moreover, high levels of right ventricular pacing and reduced left ventricular ejection fraction were associated with a numerically lower correlation between 2D and 3D GLS.

Declarations

Statements and Declarations:

The authors have no financial or non-financial conflict of interest related to this article.

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Tables

Table 1. Baseline characteristics of the study population

	Total population	Males	Females	P value
	N = 90	N = 53	N = 37	
Age (years)	73.2 ± 11.2	70.5±12.3	76.7 ± 8.3	0.681
Males (%)	59	-	-	
Body weight (kg)	85.1 ± 18.4	91.4 ± 16.5	77 ± 17.7	0.882
Body height (cm)	169.1 ± 9.9	175.5 ± 6.4	160.7 ± 7	0.068
Body mass index (kg/m^2)	29.6 ± 5.4	29.5 ± 4.6	29.8 ± 6.4	0.92
LV EF	48±12.7	45±12.9	51±11.8	0.039
Coronary artery disease (%)	46.5	49	43.2	0.269
Hyperlipoproteinaemia (%)	52.6	55.1	48.6	0.726
Myocardial infarction (%)	27.9	32.7	21.6	0.744
Peripheral arterial disease (%)	4.7	8.2	2.7	0.660
Hypertension (%)	79.1	73	86.5	0.371
Heart failure (%)	8.1	18.0	10.8	0.021
Diabetes mellitus (%)	25.6	24.5	27	0.732
Previous stroke/TIA (%)	9.3	10.2	8.1	0.585
COPD (%)	8.1	8.2	8.1	0.314
DCM	8.1	10.2	5.4	0.27
HCM	1.2	2	0	N/A
CABG (%)	16.3	24.5	5.4	0.027

Indices are shown as mean ± standard deviation or proportion in percentages and compared for male and females.; CABG, Coronary artery by-pass graft;COPD, Chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; LV, left ventricle; TIA, transient ischemic attack;

Table 2. Comparison of 2D vs. 3D global longitudinal strain, analyzed on entire group and separately by gender

LINEAR REGRESSION + PEARSON‘S CORRELATION

	ALL					MALES					FEMALES			
	SLOPE±SEM	R	P	r	P	SLOPE±SEM	R	P	r	P	SLOPE±SEM	R	P	r
2D vs.3D GLS	0.768±0.273	0.76	<0.001	0.76	<0.001	0.818±0.353	0.78	<0.001	0.78	<0.001	0.687±0.395	0.69	<0.001	0.69
Seg.1	0.382±0.392	0.27	0.019	0.27	0.02	0.356±0.364	0.16	0.3	0.18	0.23	0.256±0.566	0.15	0.41	0.16
Seg.2	0.661±0.521	0.55	<0.001	0.55	<0.001	0.794±0.511	0.54	<0.001	0.54	<0.001	0.579±1.032	0.58	<0.001	0.58
Seg.3	0.198±0.594	0.18	0.123	0.20	0.09	0.287±0.738	0.3	0.05	0.32	0.04	0.086±0.910	0.07	0.715	0.08
Seg.4	0.464±0.605	0.35	0.002	0.35	0.002	0.458±0.818	0.35	0.023	0.35	0.02	0.440±0894	0.33	0.075	0.32
Seg.5	0.424±0.678	0.318	0.006	0.30	0.009	0.377±0.786	0.26	0.096	0.24	0.119	0.496±1.193	0.40	0.03	0.39
Seg.6	0.049±0.601	0.068	0.569	0.04	0.733	-0.008±0.652	0.05	0.750	0.01	0.970	0.064±1.110	0.06	0.745	0.06
Seg.7	0.502±0.428	0.44	<0.001	0.44	<0.001	0.427±0.604	0.42	0.006	0.42	0.004	0.612±0.570	0.432	0.019	0.43
Seg.8	0.448±0.482	0.47	<0.001	0.47	<0.001	0.588±0.539	0.53	<0.001	0.53	<0.001	0.331±0.884	0.42	0.024	0.41
Seg.9	0.500±0.466	0.41	<0.001	0.41	<0.001	0.566±0.592	0.49	0.001	0.49	0.001	0.400±0.756	0.32	0.086	0.31
Seg.10	0.321±0.522	0.27	0.02	0.27	0.02	0.595±0.649	0.53	<0.001	0.52	<0.001	-0.06±0.847	0.04	0.850	0.05
Seg.11	0.531±0.528	0.45	<0.001	0.45	<0.001	0.632±0.632	0.51	<0.001	0.50	<0.001	0.385±0.912	0.36	0.05	0.37
Seg.12	0.496±0.515	0.45	<0.001	0.45	<0.001	0.602±0.592	0.54	<0.001	0.54	<0.001	0.395±0.925	0.36	0.05	0.37
Seg.13	0.291±0.648	0.48	<0.001	0.48	<0.001	0.375±0.754	0.51	<0.001	0.51	<0.001	0.165±1.154	0.38	0.05	0.37
Seg.14	0.458±0.657	0.52	<0.001	0.52	<0.001	0.565±0.754	0.56	<0.001	0.57	<0.001	0.386±1.173	0.49	0.007	0.49
Seg.15	0.228±0.614	0.32	0.007	0.26	0.03	0.284±0.755	0.42	0.006	0.31	0.05	0.166±1.011	0.23	0.220	0.2
Seg.16	0.143±0.559	0.19	0.103	0.18	0.129	0.330±0.752	0.45	0.003	0.42	0.006	-0.155±0.764	0.17	0.359	0.17
Seg.17	0.269±0.495	0.3	0.01	0.29	0.01	0.42±0.662	0.47	0.002	0.44	0.003	0.03±0.712	0.04	0.830	0.03

Indices are shown as mean ± standard error of the mean (SEM);2D, Two-dimensional;3D, Three-dimesnional;GLS, Global longitudinal strain; values of Pearson’s correlation coefficient (r) and linear regression coefficient (R) coincide while the data are in the same units, thus “naturally” normalized

Table 3. 2D and 3D global longitudinal strain, subgroup analysis

	N	R	P value
LV EF <35%	17	0.699	0.002
LV EF > 35%	73	0.727	<0.001
VP > 50%	41	0.62	<0.001
VP < 50%	49	0.8	<0.001

EF, Ejection fraction;LV, Left ventricle;VP, Ventricular pacing, R- Pearson’s correlation coefficient

Figures

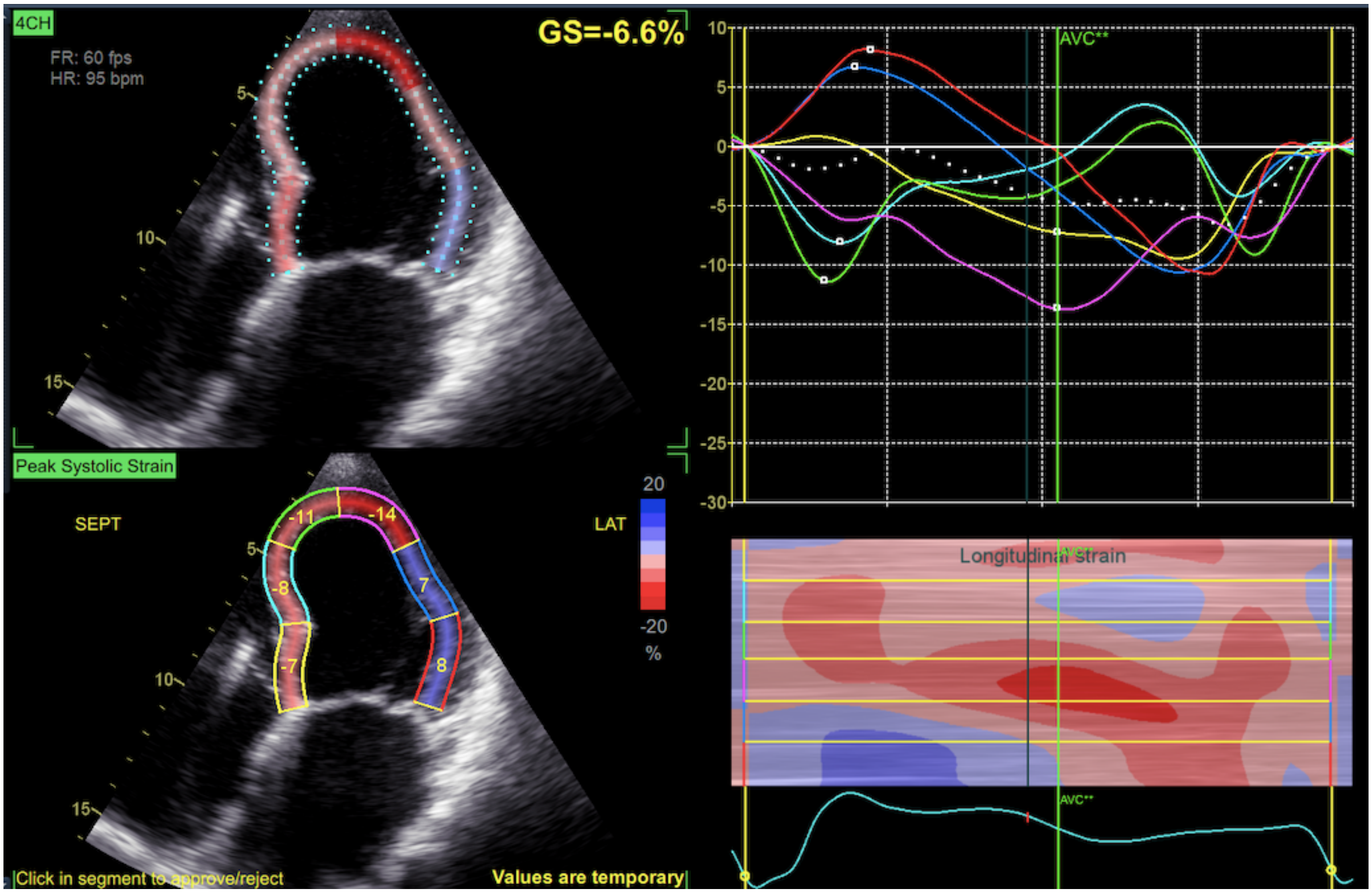

Figure 1

Four-chamber view of automatic function imaging (AFI). Peak systolic strain is visualized in the left lower part, global strain in the left upper part. The corresponding waveforms in the right upper and lower parts visualize the surface extrapolated color mapped strain.

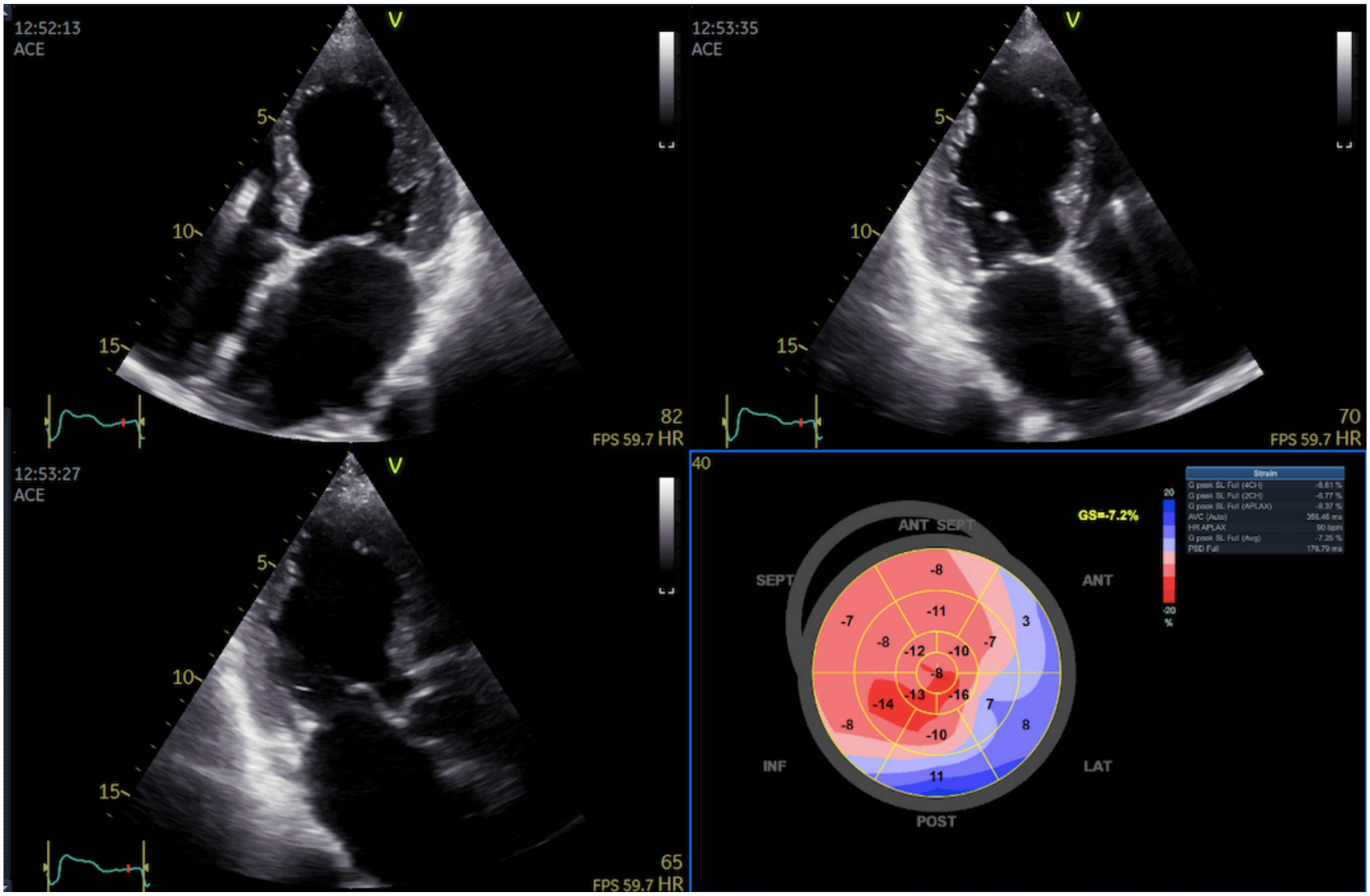

Figure 2

All three respective planes (left upper part, left lower part, and right upper part) giving rise to the automatic function imaging (AFI) bullseye reconstruction of 2D global longitudinal strain (right lower part).

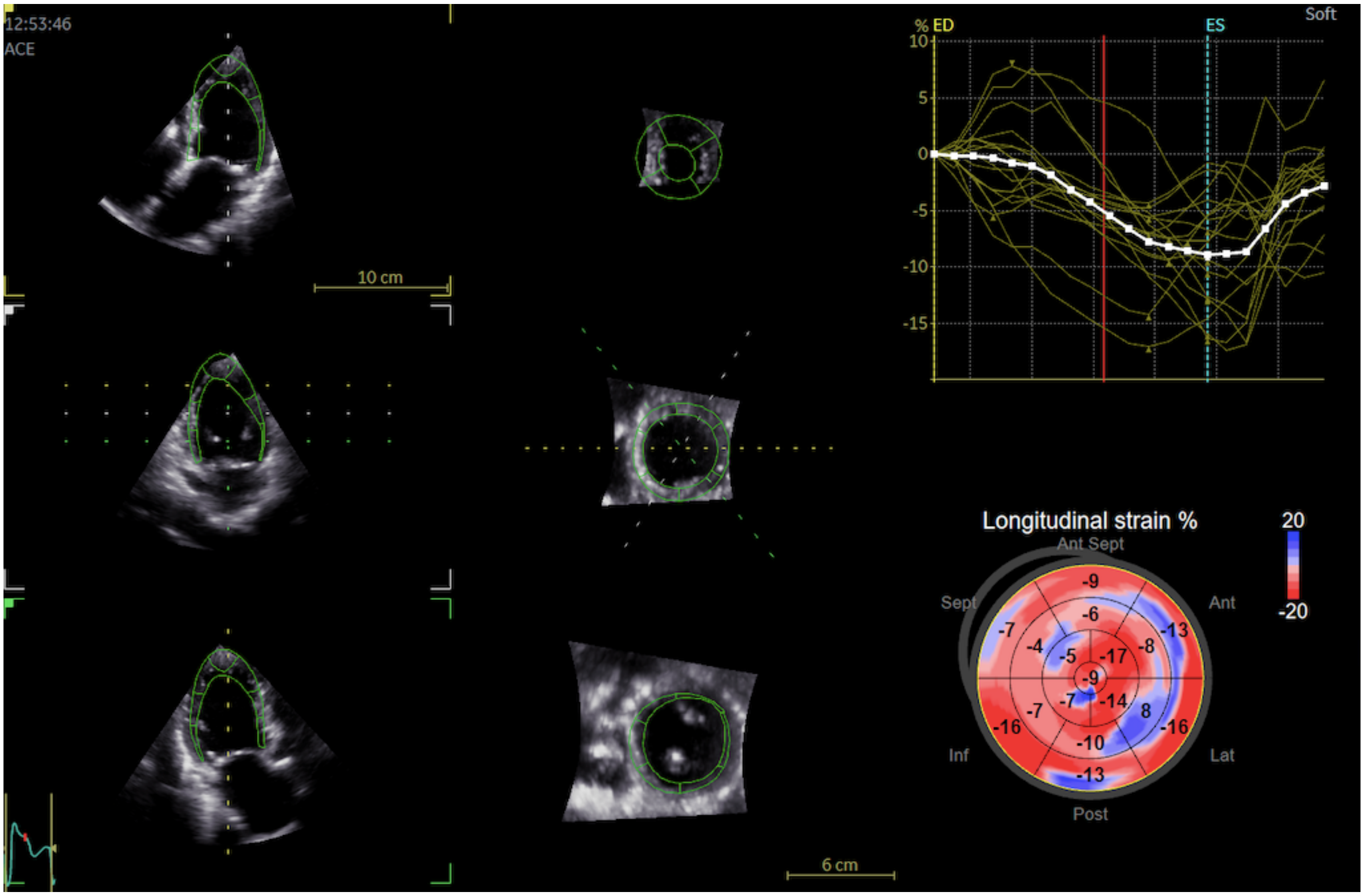

Figure 3

Automatic left ventricular quantification (AutoLVQ) plane after segmentation process with bullseye reconstruction of 3D global longitudinal strain.

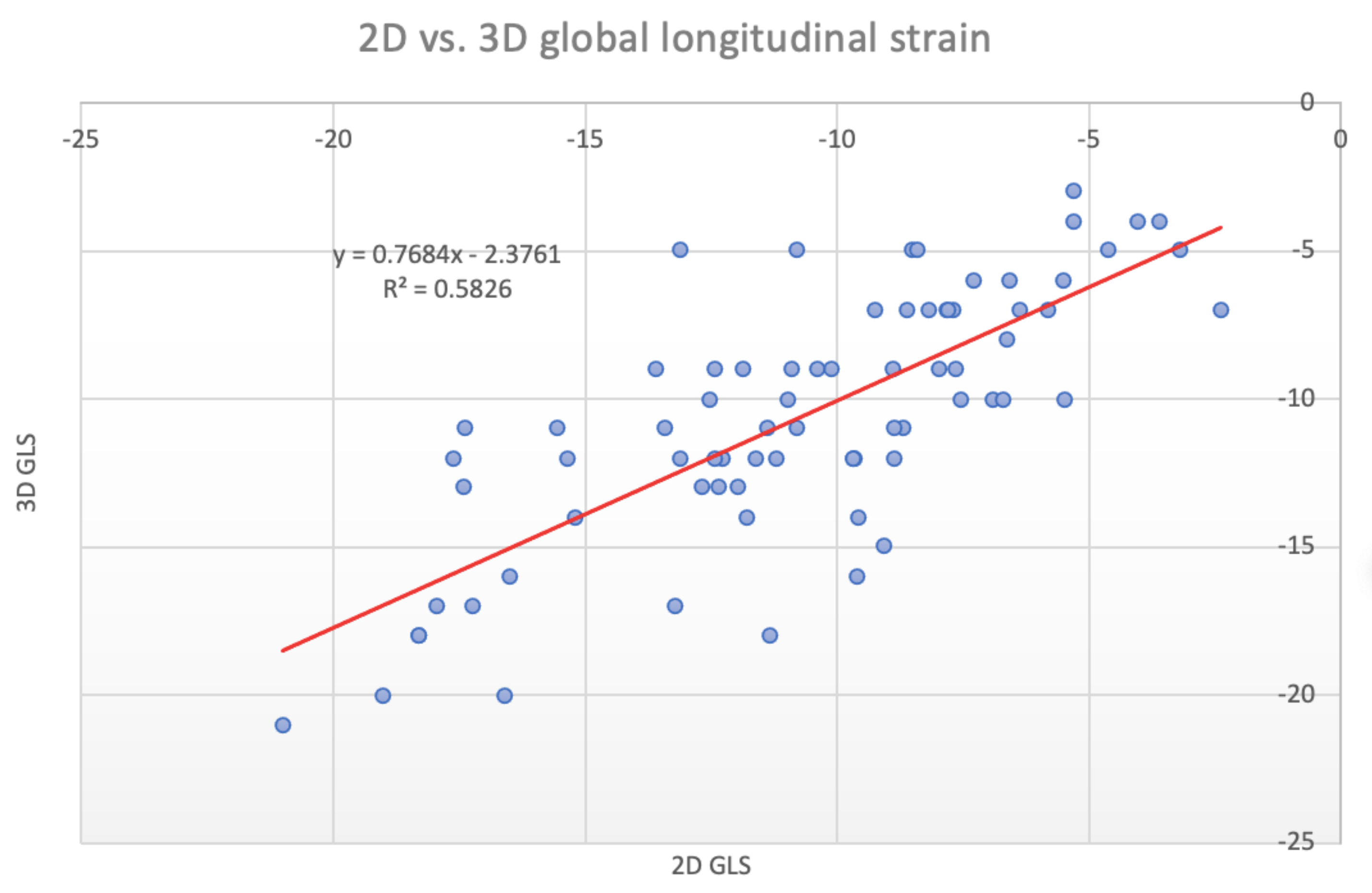

Figure 4

Scatter plot of 2D vs. 3D global longitudinal strain (GLS). Linear regression equation is displayed in the left upper section.

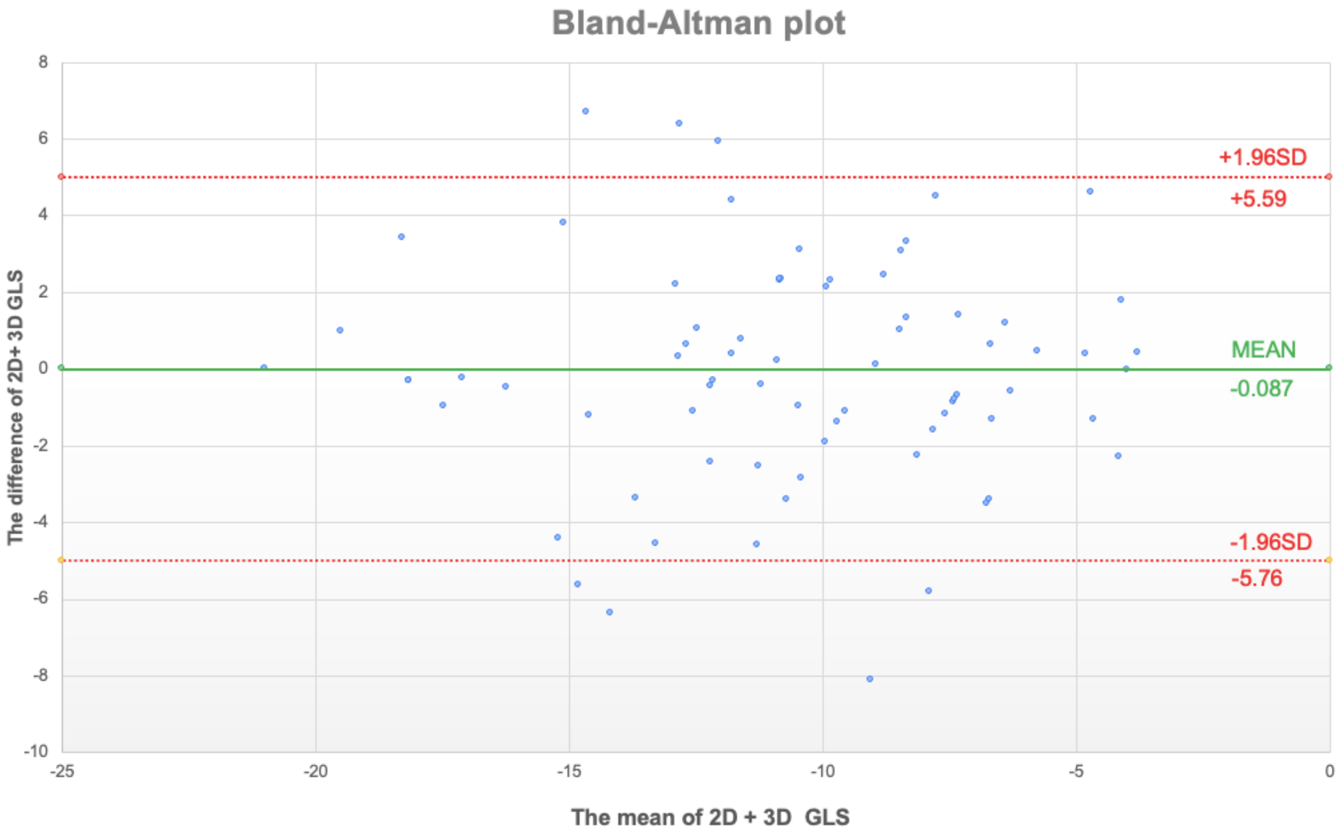

Figure 5

Bland-Altman plot of mean values of 2D and 3D global longitudinal strain (GLS; x axis) and the difference between 2D and 3D GLS. Upper and lower limit of agreement are displayed as red dotted lines with respective values.

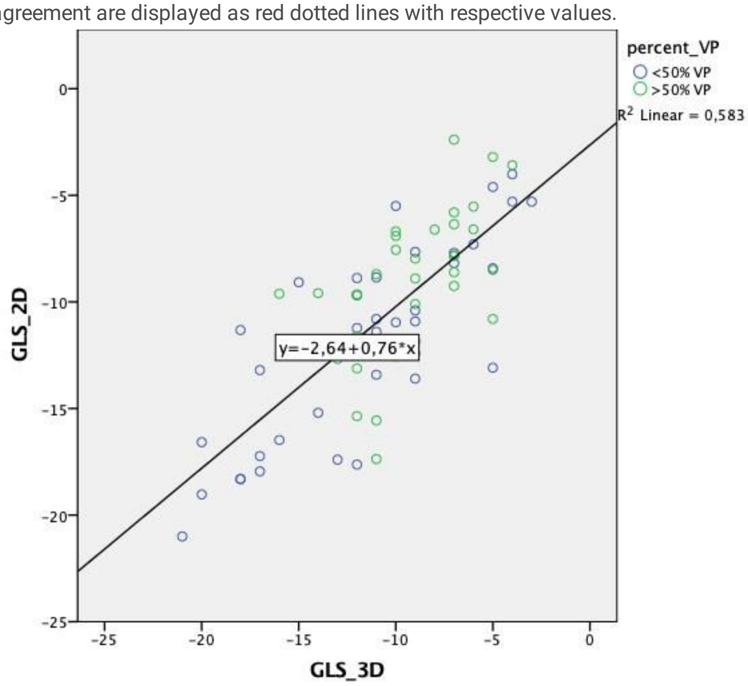

Figure 6

Scatter plot of 2D vs. 3D global longitudinal strain (GLS) sorted by the amount of right ventricular pacing (VP) with the regression equation displayed.

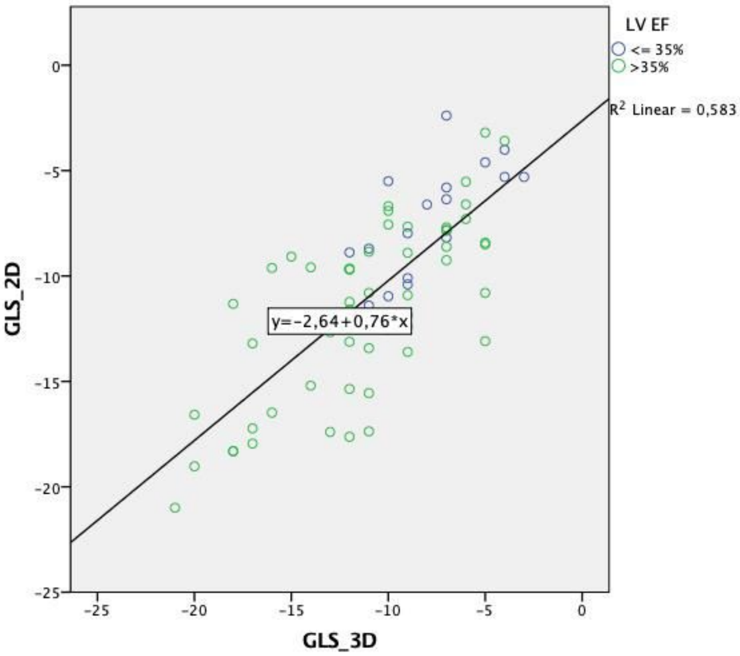

Figure 7

Scatter plot of 2D vs. 3D global longitudinal strain (GLS) sorted by left ventricular ejection fraction (LVEF) with the regression equation displayed.

Supplementary Files

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- centralillustrationIJCI.jpg