

Assessment of left ventricular systolic function by deformation imaging derived from speckle tracking: a comparison between 2D and 3D echo modalities

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Aims

Deformation imaging is undergoing continuous development with the emergence of new technologies allowing the evaluation of the different components of strain simultaneously in three dimensions. Assessment of all global strain parameters in 2D and 3D modes and comparison with LVEF have been the focus of our study.

Methods and results

Out of 166 patients, 147 were evaluated with the use of both 2D and 3D speckle-tracking echocardiography (STE). Global strain parameters including longitudinal (GLS), circumferential (GCS), radial (GRS) and area strain (AS), as well as left ventricular volumes and ejection fraction were examined. Analysis of strain with 3D STE was faster than with 2D STE (7 ± 2 vs. 24 ± 4 min, $P < 0.05$). GLS values were similar between 2D and 3D modes (-14 ± 4 vs. -13 ± 3 , NS), while slight differences were observed for GCS (-24 ± 7 vs. -27 ± 7 , $P < 0.05$) and GRS (27 ± 9 vs. 24 ± 9 , $P < 0.05$). All 2D and 3D strain parameters showed good accuracy in the identification of 2D-LVEF $< 55\%$ with AS demonstrating superiority over GCS and GRS but not GLS.

Conclusion

Three-dimensional STE allows accurate and faster analysis of deformation when compared with 2D STE and might represent a viable alternative in the evaluation of global LV function.

Keywords

Deformation imaging • Three-dimensional echocardiography • Speckle-tracking echocardiography • Global strain • Area strain

Introduction

Recently, published EAE/ASE guidelines recommend the use of 3D echocardiography in assessing LV volumes and ejection fraction as a more accurate and reliable modality.¹ Latest advances in speckle-tracking echocardiography (STE) also allow us to track speckles in all three dimensions simultaneously in a full-volume data set. Whether 3D strain assessment is superior to 2D is not yet clear as evident from the conflicting reports about the level of correlation between 2D and 3D STE.^{2–4}

Moreover, 3D strain offers unique opportunity to quantify the endocardial area change ratio by area strain (AS), which combines the analysis of both longitudinal and circumferential deformations of the left ventricle.⁵ AS has been shown to accurately assess LVEF in patients with and without heart failure but its accuracy has not been compared with all other strain parameters obtained by 2D and 3D STE.⁶

We aimed (i) to evaluate and compare global longitudinal, circumferential, and radial strains between 2D and 3D modes in a large series of patients, (ii) to compare the correlations of these deformation parameters with 2D and 3D-LVEF, (iii) to specifically assess potential

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superiority of AS over longitudinal, circumferential, and radial strain components.

Methods

Study population and protocol

This study prospectively recruited 166 consecutive patients with adequate 2D acoustic window who were scheduled for routine evaluation in our echocardiography department. All the patients were evaluated with the use of 2D and 3D modes by a single operator (M.A.) with all the analysis being performed offline.

Data acquisition

Echocardiography was performed with the use of Artida 4D (Toshiba Medical Systems). All the patients were scanned in the left lateral decubitus position with the use of both standard 2D transducer (PST-30SBT) and 2.5 MHz fully sampled 3D matrix array transducer (PST-25SX). An average frame rate for 2D acquisition was 58 ± 4 fps, whereas an average volume rate for the 3D mode was 24 ± 3 vps. In the 2D mode, standard three parasternal short-axis views (basal, mid, and apical levels) were obtained for the assessment of global radial (GRS) and global circumferential (GCS) strains and three apical views for the assessment of global longitudinal strain (GLS). Standard techniques were used to obtain M-mode, 2D, and Doppler measurements in accordance with the American Society of Echocardiography guidelines.⁷ End-diastolic (EDV) and end-systolic (ESV) volumes and LV ejection fraction (LVEF) were measured manually using the biplane Simpson's method in the 2D mode and were automatically calculated by the wall motion tracking (WMT) software in the 3D mode (Toshiba Medical Systems).

Strain analysis

Both 2D and 3D echocardiographic images were analysed using the WMT software. The best cardiac cycle was selected based on optimal endocardial definition and quality of ECG tracing with all the measurements performed by single operator. Endocardial border was manually traced at the end of diastole with papillary muscles included in LV cavity. The WMT software automatically tracked the endocardial and epicardial borders frame by frame throughout the whole cardiac cycle with minimal adjustments made to the endocardial contours when necessary to optimize the boundary position and tracking. Tracking quality was assessed by visual assessment of the adequacy between endocardial border and its delineation by the software. Anyone with more than three inadequately tracked segments was excluded from the study.

In the 2D mode, GLS values were calculated as an average of strain values obtained from the three apical views, whereas GCS and GRS values were calculated as an average of strain values obtained from the basal, mid, and apical parasternal short-axis views. In the 3D mode, GLS, GCS, and GRS as well as AS were measured automatically by the software from the single full-volume acquisition. To ensure comparable results between 2D and 3D modes, strain values were recorded at the time of the aortic valve closure, which was manually entered.

Statistical analysis

Statistical analysis was performed using SPSS for Windows version 15.0 (SPSS, Inc., Chicago, IL, USA) and R version 2.15.2 (2012, the R Foundation for Statistical Computing). Continuous and normally distributed variables were expressed as mean \pm standard deviation, and variables

deviating from normality were expressed as median (inter-quartile range). Categorical variables were expressed as percentage. Correlations were tested between 2D and 3D strains, and the Bland–Altman method was used to assess the agreements between different indices.⁸ Linear regressions were performed between (i) each component of 2D strain and 2D LVEF; (ii) each component of 3D strain including AS with both 2D LVEF and 3D LVEF. Receiver-operating characteristic (ROC) curves were constructed for each component of 2D and 3D strains for the proper identification of 2D LVEF and 3D LVEF $<55\%$. Area under the curve (95% CI), sensitivity, specificity, and optimal cut-off value were given for each ROC curve. Formal paired comparisons of ROC curves for the prediction of 2D or 3D LVEF $<55\%$ were performed using the DeLong method.⁹ Different logistic regression models were applied to test any difference between (i) each component of 2D strain, (ii) each component of 3D strain, (iii) 2D and 3D longitudinal, (iv) 2D and 3D circumferential, (v) 2D and 3D radial strains. Finally, AS was added to the model (2). Differences were considered to be statistically significant when $P < 0.05$.

Reproducibility analysis

Intra- and inter-observer variability of both LVEF and strain measurements was evaluated in 10 randomly selected patients. To test intra-observer variability, the same primary operator analysed selected data sets twice at least 2 weeks apart. Operator was blinded to the result of the previous measurements during second evaluation. To test inter-observer variability, a second experienced observer was given data sets with no access to information regarding all prior measurements. Intra- and inter-observer variability was calculated as an absolute difference between two measurements over the mean of those measurements and presented as the mean percentage error.

Results

Out of 166 patients prospectively enrolled in this study, 19 were excluded due to inadequate myocardial tracking ($n = 13$ both in 2D and 3D modes; $n = 3$ only in the 3D mode) or rhythm disturbances ($n = 3$).

Among the remaining 147 examined subjects (mean age: 54 ± 15 years, 76% males), 70 patients were included with a diagnosis of ischaemic cardiomyopathy, 23 with heart failure and preserved ejection fraction, 11 with hypertrophic cardiomyopathy, 3 with Fabry disease, 34 with hypertensive heart disease, and 6 healthy volunteers with no previous cardiac history. Such mix of pathologies provided a wide spectrum of LVEF (ranging between 21 and 72%).

The mean 2D-LVEF was slightly but significantly higher than the mean 3D-LVEF (58 ± 9 vs. $57 \pm 9\%$, $P < 0.05$). The correlation of LVEF values obtained by two modes was good ($r = 0.9$, $P < 0.05$). The mean EDV was higher in 2D than in the 3D mode (91 ± 27 vs. 85 ± 23 mL $P < 0.05$), whereas ESV was similar in both modes (38 ± 17 vs. 37 ± 16 mL, $P = 0.07$).

Average acquisition and analysis time was significantly shorter for 3D STE (7 ± 2 min) than 2D STE (24 ± 4 min), which included GLS, GCS, and GRS analysis in six standard views ($P < 0.05$).

Comparison between 2D and 3D global strain values and their correlations

Table 1 presents the comparison between 2D and 3D strain values. Although GLS values were similar between 3D STE and 2D STE

Table 1 Global strain values obtained by 2D and 3D speckle-tracking echocardiography

Deformation index	2D STE	3D STE
Global longitudinal strain %	-14 ± 4	-13 ± 3
Global circumferential strain %	-24 ± 7	-27 ± 7*
Global radial strain %	27 ± 9	24 ± 9*
Area strain %		-39 ± 8

*P < 0.05, 3D STE vs. 2D STE.

(-13 ± 3 vs. -14 ± 4%; P = NS), GCS values were slightly higher in 3D STE than in 2D STE and GRS values were lower in 3D STE than in 2D STE. All strain parameters significantly correlated between 2D and 3D modes (Figure 1).

Intra- and inter-observer variability is presented in Table 2. Although variability for GLS and GCS were comparable using 2D and 3D STE, GRS variability was consistently improved by 3D STE when compared with 2D STE, approaching similar reproducibility as GLS and GCS. AS had the lowest intra-observer variability (7.3%) and similar inter-observer variability as all other 3D STE strain parameters (10.2%).

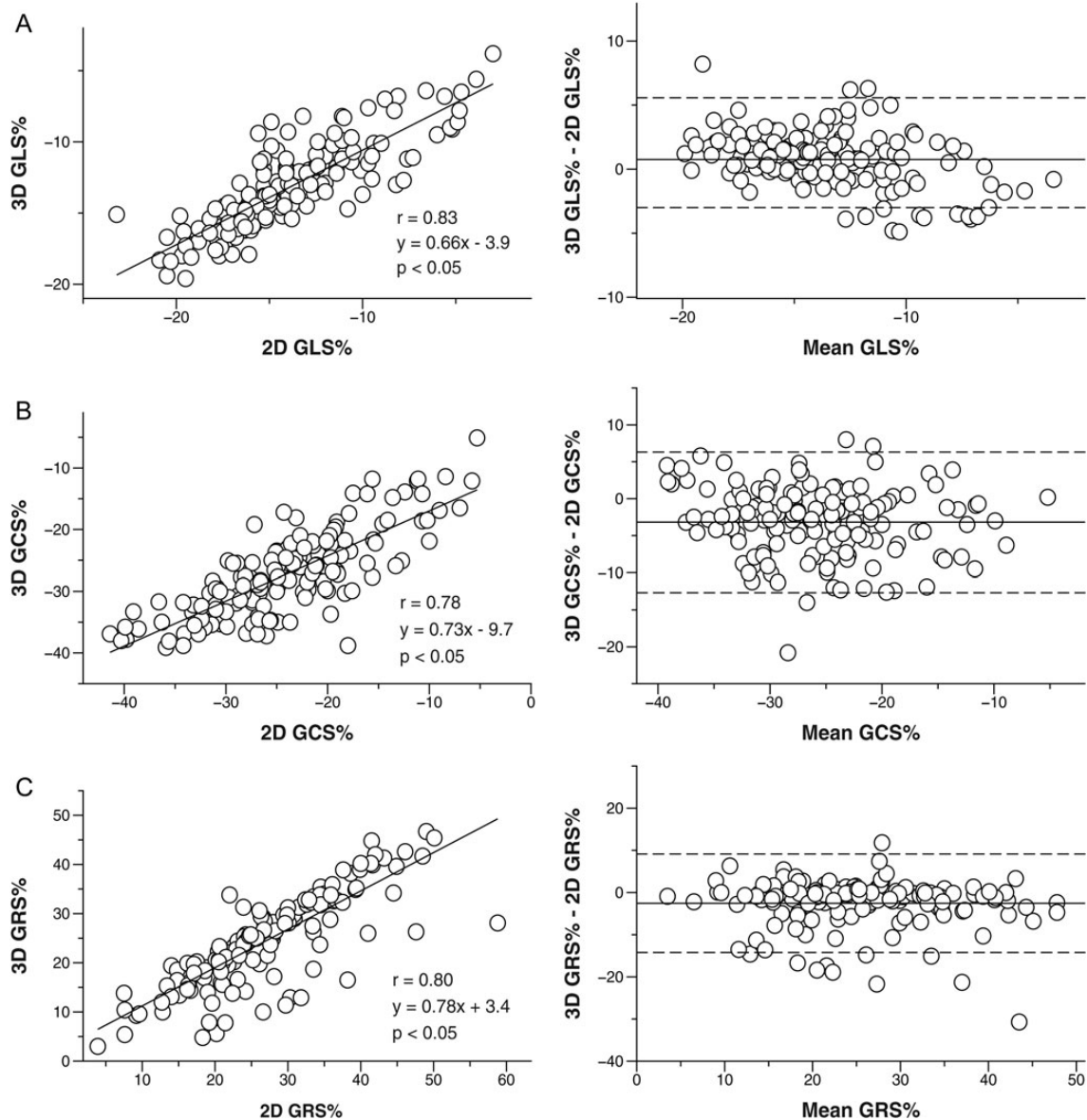


Figure 1 Linear regression and Bland–Altman analyses for global strain parameters between 2D and 3D modes. (A) global longitudinal strain, (B) global circumferential strain and panel (C) global radial strain.

Table 2 Intra- and inter-observer variability of 2D and 3D LVEF and strain parameters

Parameter	Intra-observer variability		Inter-observer variability	
	2D mode (%)	3D mode (%)	2D mode (%)	3D mode (%)
Left ventricular ejection fraction	5.7	2.1	10.6	7.3
Global longitudinal strain	8.7	11.0	11.9	10.9
Global circumferential strain	10.5	10.9	12.0	11.9
Global radial strain	14.9	11.2	21.2	13.2
Area strain	–	7.3	–	10.2

Correlation between LVEF and deformation indices in 2D and 3D modes

Figure 2 illustrates the correlations between LVEF and deformation indices in 2D and 3D modes.

In the 2D mode, all strain parameters significantly correlated with 2D-LVEF with GCS presenting a higher coefficient of the correlation value ($r = -0.72$, $P < 0.05$) than GLS ($r = -0.67$, $P < 0.05$) or GRS ($r = 0.55$, $P < 0.05$).

Similar findings were observed when 3D strain values were compared with 2D-LVEF [GCS ($r = -0.85$, $P < 0.05$); GLS ($r = -0.68$, $P < 0.05$); and GRS ($r = 0.57$, $P < 0.05$)] and with 3D-LVEF [GCS ($r = -0.89$, $P < 0.05$); GLS ($r = -0.69$, $P < 0.05$); and GRS ($r = 0.65$, $P < 0.05$)]. Among the different deformation parameters, 3D GCS showed a higher correlation with LVEF than 2D GCS. However, when compared with 2D GCS, 3D GCS did not improve the identification of patients with LVEF $< 55\%$ as demonstrated by similar AUC values by ROC curve analysis (Table 3).

Furthermore, AS, an exclusive 3D parameter, provided a higher value of coefficient of correlation with both 2D-LVEF ($r = -0.87$) and 3D-LVEF ($r = -0.91$), when compared with GLS, GCS, and GRS (Figure 3). ROC curve analysis demonstrated that for the identification of 2D-LVEF $< 55\%$ AS [AUC = 0.92 (0.87–0.97)] was superior to 3D GCS [AUC = 0.89 (0.83–0.95), $P < 0.008$] and 3D GRS [AUC = 0.83 (0.76–0.91), $P < 0.007$] but not 3D GLS [AUC = 0.85 (0.79–0.92), $P < 0.0187$].

To identify 3D-LVEF $< 55\%$, AS [AUC = 0.95 (0.92–0.98)] was superior to 3D GLS [AUC = 0.84 (0.78–0.90), $P < 0.0001$] and 3D GRS [AUC = 0.86 (0.80–0.93), $P < 0.007$], but not 3D GCS [AUC = 0.94 (0.90–0.97), $P < 0.06$] (Figure 4).

Discussion

Our study has specifically focused on (i) the comparison of 2D and 3D speckle tracking in assessing longitudinal, circumferential, and radial strains, (ii) the validation of the reproducibility and feasibility of 3D strain parameters including AS across a wide range of LVEF, and (iii) the potential superiority of AS over other strain components.

Our main results are: (i) GLS values were similar in 2D and 3D modes, while slight but significant differences were observed for GCS and GRS; (ii) none of the 3D strain indices (GLS, GCS, and GRS) was proved to be superior to the corresponding 2D strain indices in assessing LVEF; (iii) AS was accurate but not superior to GLS in identifying 2D-LVEF $< 55\%$.

Our study has confirmed the feasibility of 3D STE in the evaluation of global systolic function. While AS, a new parameter combining longitudinal and circumferential deformations appears to be of potential interest in our series it did not demonstrate clear advantage over 3D GLS in identification of decreased 2D LVEF.

There are ongoing arguments for the use of 3D deformation imaging and its ability to overcome well-known limitations of 2D STE. Indeed, the 3D mode avoids foreshortening of apical views, consumes less time in acquisition and analysis, and is able to track motion of speckles in all three dimensions and therefore helps to eradicate the problem of out-of-plane motion inherently present in 2D modality.² However, this advantage comes at a cost of lower volume rate, which might alter the correlations with measurements obtained by 2D STE.¹⁰

Since, we did not firmly establish the superiority of 3D STE over 2D STE for the evaluation of all three components of LV deformation (GLS, GCS, and GRS) we therefore agree that strain values are not interchangeable between 2D and 3D modes due to the differences in acquisition rates,¹⁰ problems of adequate tracking of the apical segments and out-of-plane motion inherent to 2D acquisition.¹¹ While we observed similarity between 2D and 3D GLS values which in part might be due to the fact that with this vendor's algorithm both are measured predominantly in the endocardium, our results did not support previous observations demonstrating that 3D STE underestimated longitudinal strain when compared with 2D STE.^{3,4,12} In addition, the feasibility of 3D STE when compared with 2D STE may be an issue.¹⁰ Importantly, our data cannot be extended to other echo machines because of the high variability that exists between ultrasound systems.^{12–14} Indeed, Badano *et al.* have recently pointed out poor intervendor reproducibility by comparing the Artida™ (Toshiba) with the Vivid 9 system (GE Vingmed Ultrasound AS).¹³

In our study, we also paid attention to measure strain values in both modes at the same time (i.e. aortic valve closure), which was manually entered. The importance to standardize the timing of the measurements is crucial, since 3D strain values are usually measured at the time of the minimal systolic volume, which is automatically determined by the software and is often observed just before the mitral valve opening. As a consequence of such standardization, we did not observe any significant difference in longitudinal strain values between 2D and 3D modes, but we reported slightly higher values of circumferential strain and lower radial strain values using 3D STE. In addition, 3D STE improved the intra- and inter-observer reproducibility for GRS when compared with 2D STE. These results are not concordant with previous studies pointing out lower reproducibility of 3D radial strain values.^{15,16}

Furthermore, we evaluated the interest of 3D STE in assessing AS, a new deformation parameter exploring the variation in the endocardial surface area during the cardiac cycle by combining the data from longitudinal and circumferential components. Accuracy of the AS in identifying abnormal regional myocardial function has been previously tested against sonomicrometry during acute experimental

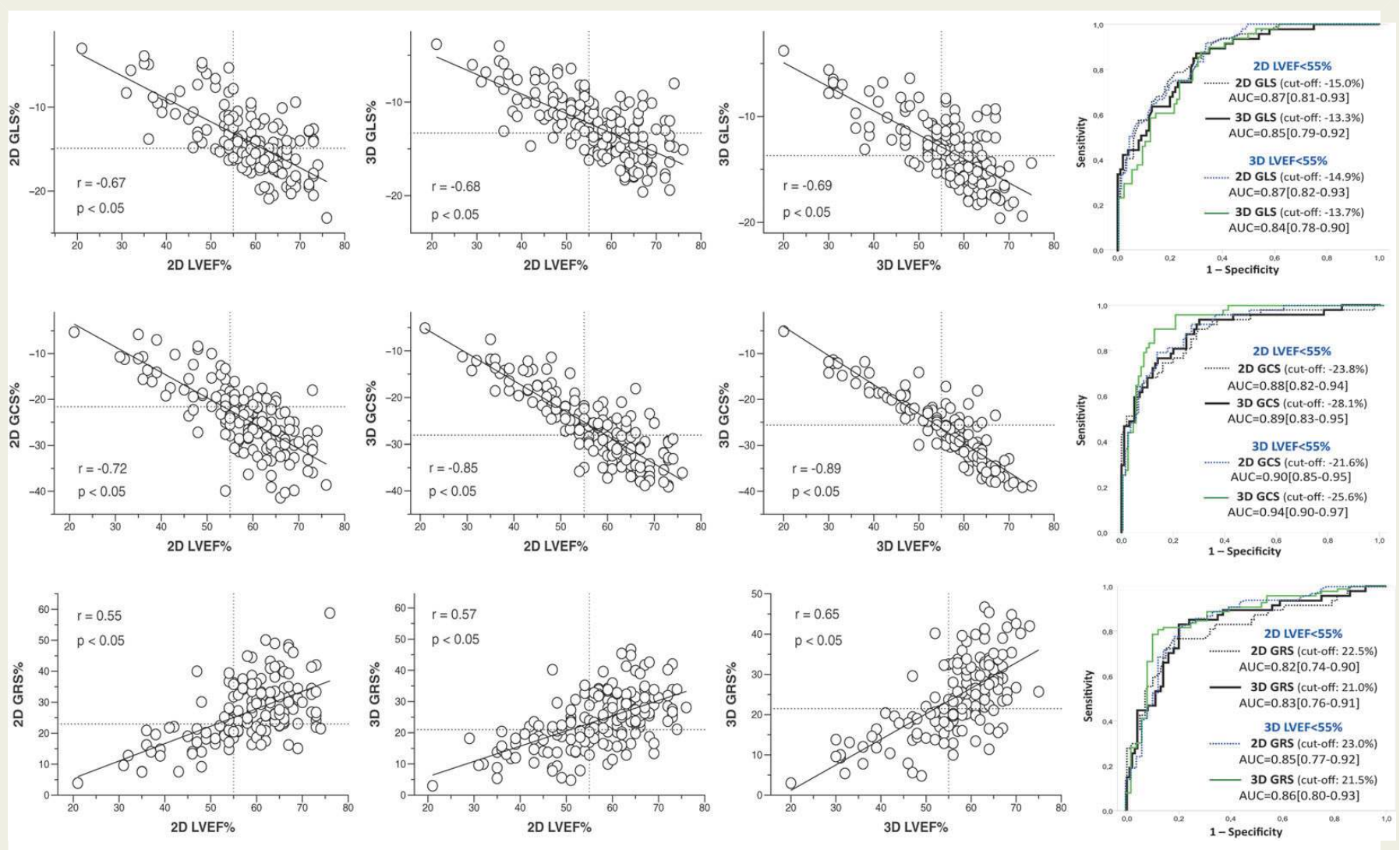


Figure 2 Linear regression analysis between global strain parameters and LVEF in 2D and 3D modes. Receiver-operating characteristic curves for global strain parameters in 2D and 3D modes. Upper panel: global longitudinal strain. Mid panel: global circumferential strain. Lower panel: global radial strain.

ischaemia studies⁵ and magnetic resonance imaging in patients with coronary heart disease.¹⁷ Recent report provided a normal value of global AS of $-38.9 \pm 5.9\%$ in a series of 60 healthy subjects that were close to our cut-off value of -36.7% to identify abnormal LVEF.¹⁸ Owing to its high reliability and reproducibility AS could be used to monitor changes in LV function in patients with chronic

heart failure and myocardial disease following therapeutic interventions including cardiac resynchronization therapy.¹⁹ Despite the fact that we agree with two previous studies establishing AS as a promising tool in characterization of LV systolic function, our data did not firmly established this parameter as a superior index when compared with GLS.^{6,15} Of note, these two studies established superiority of AS when compared with all other components of deformation on the sole interpretation of correlation coefficients between LVEF and deformation indices but not on the ROC curve analysis.^{6,15} In our study, we have deliberately constructed ROC curves in order to test the accuracy of each of the 2D and 3D deformation indices in the evaluation of LVEF. We can therefore conclude that AS was superior to GCS and GRS but not GLS in identification of 2D-LVEF < 55%.

Table 3 Area under the curve and confidence interval values for 2D and 3D strain parameters in identification of 2D and 3D LVEF < 55%; P-values provided from the paired comparison of ROC curves by the DeLong method

LVEF	Strain index	AUC	95% CI	P-value
2D	2D GLS	0.87	0.81–0.93	0.46
	3D GLS	0.85	0.79–0.92	
	2D GCS	0.88	0.82–0.94	0.81
	3D GCS	0.89	0.83–0.95	
	2D GRS	0.82	0.74–0.90	0.59
	3D GRS	0.83	0.76–0.91	
3D	2D GLS	0.87	0.82–0.93	0.19
	3D GLS	0.84	0.78–0.90	
	2D GCS	0.90	0.85–0.95	0.25
	3D GCS	0.94	0.90–0.97	
	2D GRS	0.85	0.77–0.92	0.53
	3D GRS	0.86	0.80–0.93	

Study limitations

Despite the fact that we had a large cohort of patients in our study, the sample size could potentially benefit from a larger group of healthy volunteers. Also, the relationship between 3D strain parameters and LVEF might have been better assessed by adding a reference method for comparison. Indeed, we have compared 3D strain parameters to 2D LVEF since different algorithms are used to calculate the volumes and strain values. In addition a small subgroup of patients also underwent cardiac MRI for the assessment of LV function. Despite the small number of patients ($n = 9$), we found good correlation between 2D LVEF, 3D LVEF, and MRI LVEF ($r = 0.85$ and $r = 0.89$, $P < 0.05$, respectively) and between 3D strain parameters and MRI LVEF (AS: $r = -0.91$, $P < 0.05$) (data not shown).

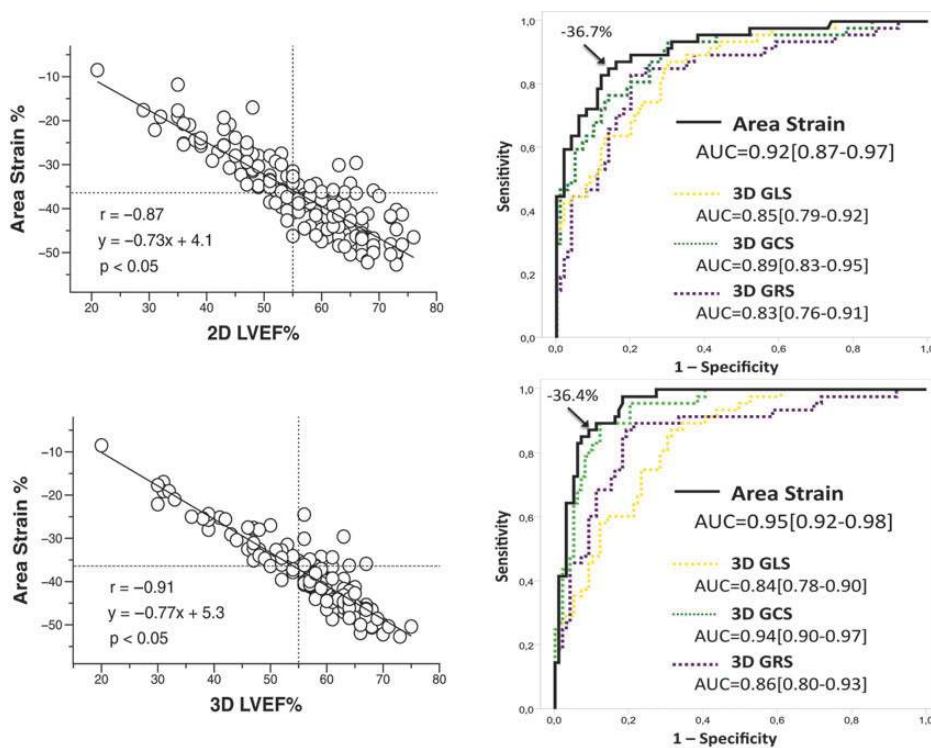


Figure 3 Linear regression analysis between area strain and 2D LVEF and 3D LVEF and receiver-operating characteristic curves.

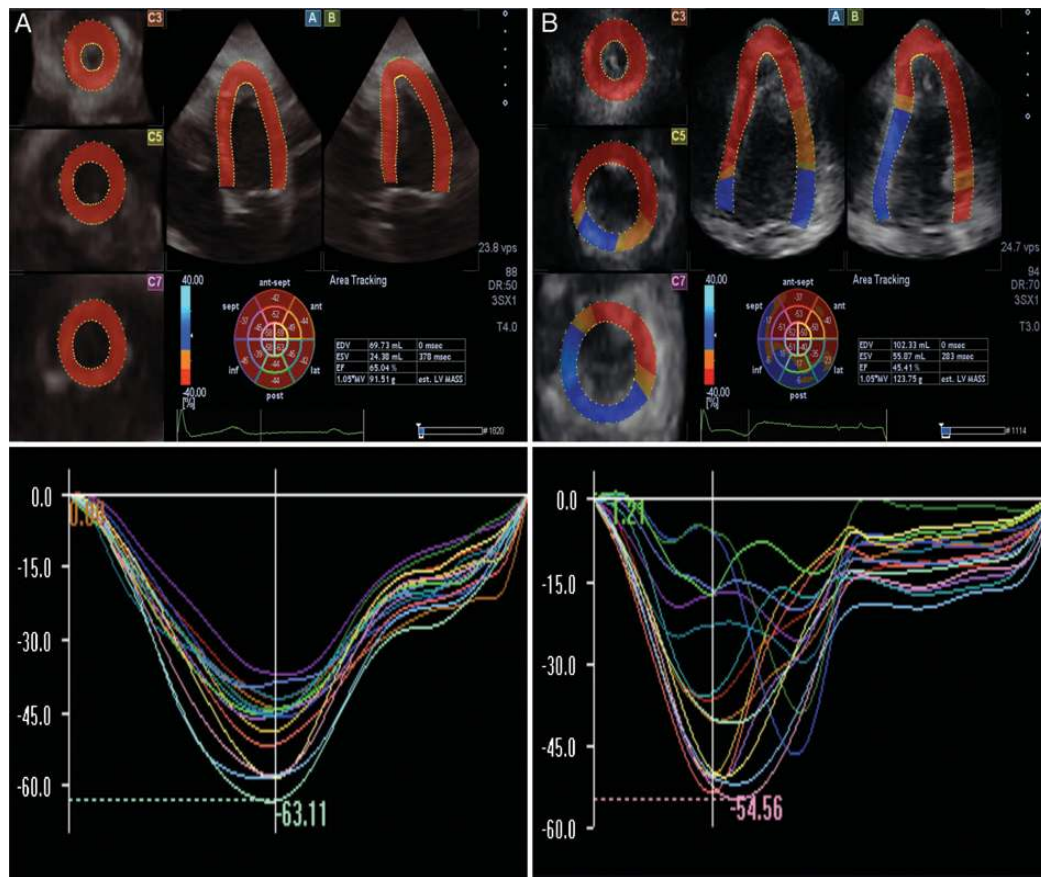


Figure 4 Measurements of the left ventricular volumes, ejection fraction and deformation parameter area strain, using three-dimensional speckle-tracking echocardiography. Visual information on area strain is shown in colour overlay superimposed on grey-scale image. (A) normal subject. (B) patient with ischaemic cardiomyopathy following inferior myocardial infarction.

The presence of a large proportion of patients with a documented history of ischaemic cardiomyopathy and patients with symptoms of heart failure and preserved LVEF may potentially explain reduced value of GLS in particular and should be interpreted with caution when extrapolated on other group of patients.

Global strain values in both modes were deliberately evaluated at the same time (AVC), which was manually entered to allow some standardization of the measured values. This step enables us to synchronise the timing of the measurements, and therefore to minimize the differences between 2D and 3D strain measurement. However, the absolute values of global strain might vary between 2D and 3D modes due to differences in the frame/volume rate. It might to a certain degree account for the differences that were observed between strain values obtained via different modes.

And finally, existing differences between vendors must be taken into consideration when results of our study are being compared with the findings presented by others using different machines.

Conclusion

Three-dimensional echocardiography is currently undergoing phase of extensive evaluation and continues to remain an area of interest and controversy. Indeed, it is the only modality that allows

simultaneous assessment of LV volumes, LVEF and all multidirectional components of strain. We have demonstrated that 3D STE provides faster and more reproducible data in the evaluation of LV function when compared with 2D STE. However, further improvements are needed to firmly establish this technology as superior to 2D in the assessment of deformation.

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Conflict of interest: none declared.

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