

## ● Original Contribution

# 3-D ECHOCARDIOGRAPHY IS FEASIBLE AND MORE REPRODUCIBLE THAN 2-D ECHOCARDIOGRAPHY FOR IN-TRAINING ECHOCARDIOGRAPHERS IN FOLLOW-UP OF PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

SORINA MIHAILA BALDEA,<sup>\*,1</sup> ANDREEA ELENA VELCEA,<sup>\*,1</sup> ROXANA CRISTINA RIMBAS,<sup>\*</sup> ANCA ANDRONIC,<sup>\*</sup> LAVINIA MATEI,<sup>†</sup> SIMONA IONELA CALIN,<sup>\*</sup> DENISA MURARU,<sup>‡,§</sup> LUIGI PAOLO BADANO,<sup>‡,§</sup> and DRAGOS VINERANU<sup>\*</sup>

<sup>\*</sup> University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; <sup>†</sup> Emergency Hospital Elias, Bucharest, Romania;

<sup>‡</sup> Istituto Auxologico Italiano, IRCCS, Department of Cardiac, Neural and Metabolic Sciences, San Luca Hospital, Milan, Italy; and

<sup>§</sup> University of Milano-Bicocca, Department of Medicine and Surgery, Milan, Italy

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**Abstract**—Left ventricular volumes (LVVs) and ejection fraction (LVEF) are key elements in the evaluation and follow-up of patients with heart failure with reduced ejection fraction (HFrEF). Therefore, a feasible and reproducible imaging method to be used by both experienced and in-training echocardiographers is mandatory. Our aim was to establish if, in a large echo lab, echocardiographers in-training provide feasible and more reproducible results for the evaluation of patients with HFrEF when using 3-dimensional echocardiography (3-DE) versus 2-dimensional echocardiography (2-DE). Sixty patients with HFrEF (46 males, age:  $58 \pm 17$  y) underwent standard transthoracic 2-D acquisitions and 3-D multibeam full volumes of the left ventricle. One expert user in echocardiography (expert) and three echocardiographers with different levels of training in 2-DE (beginner, medium and advanced) measured the 2-D LVVs and LVEFs on the same consecutive images of patients with HFrEF. Afterward, the expert performed a 1-mo training in 3-DE analysis of the users, and both the expert and trainees measured the 3-D LVVs and LVEF of the same patients. Measurements provided by the expert and all trainees in echo were compared. Six patients were excluded from the study because of poor image quality. The mean end-diastolic LVV of the remaining 54 patients was  $214 \pm 75$  mL with 2-DE and  $233 \pm 77$  mL with 3-DE. Mean LVEF was  $35 \pm 10\%$  with 2-DE and  $33 \pm 10\%$  with 3-DE. Our analysis revealed that, compared with the expert user, the trainees had acceptable reproducibility for the 2-DE measurements, according to their level of expertise in 2-DE (intra-class coefficients [ICCs] ranging from 0.75 to 0.94). However, after the short training in 3-DE, they provided feasible and more reproducible measurements of the 3-D LVVs and LVEF (ICCs ranging from 0.89–0.97) than they had with 2-DE. 3-DE is a feasible, rapidly learned and more reproducible method for the assessment of LVVs and LVEF than 2-DE, regardless of the basic level of expertise in 2-DE of the trainees in echocardiography. In echo labs with a wide range of staff experience, 3-DE might be a more accurate method for the follow-up of patients with HFrEF. (E-mail: [sorinamihaila1981@gmail.com](mailto:sorinamihaila1981@gmail.com)) © 2020 The Author(s). Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Key Words:** Heart failure with reduced ejection fraction, Left ventricular volumes and ejection fraction, Reproducibility, 3-D echocardiography, Trainees in echocardiography.

## INTRODUCTION

Echocardiography is the most useful and available imaging technique in patients with suspected heart failure and

is pivotal in diagnosis, classification and establishment of appropriate treatment (Ponikowski et al. 2016). Reliable measurements of left ventricular volumes (LVVs) and left ventricular ejection fraction (LVEF) are essential in patients with heart failure with reduced ejection fraction (HFrEF), to decide the proper pharmaceutical and interventional treatment, especially when the LVEF is below 35%. Moreover, sequential measurements of LVVs and LVEF are important for the follow-up of

Address correspondence to: Sorina Mihaila Baldea, University of Medicine and Pharmacy Carol Davila, Emergency University Hospital of Bucharest, Splaiul Independentei no 169, Sector 5, Bucharest. E-mail: [sorinamihaila1981@gmail.com](mailto:sorinamihaila1981@gmail.com)

<sup>1</sup> These authors contributed equally.

patients (Ponikowski et al. 2016) and for establishing patient prognoses (St. John Sutton et al. 1994; Dickstein and Kjekshus 2002; Packer et al. 2002; Pfeffer et al. 2003).

Even though several imaging methods may also be used in clinical practice with good results (Wood et al. 2014), the main imaging technique used for the assessment of LVVs and LVEF in patients with HFrEF is 2-dimensional echocardiography (2-DE) because of its wide availability, good reproducibility and cost-effectiveness (Popescu et al. 2009). Therefore, the majority of trials that recommend specific pharmacologic and device therapies in patients with HFrEF are based on 2-DE studies (CONSENSUS Trial Study Group 1987; Yusuf et al. 1991; Pitt et al. 1999; Bardy et al. 2005; Zannad et al. 2011). However, 2-DE measurements are based on the estimation of LVVs and LVEF using biplane Simpson's disc formula (Lang et al. 2015). Two-dimensional echocardiography algorithms rely on geometric assumptions about the LV shape and have limitations in asymmetric or aneurysmal left ventricles (Badano et al. 2012), often encountered in patients with HFrEF. Two-dimensional measurements are also vulnerable errors related to the foreshortening of apical views, and take into account only a limited amount of LV myocardium, reducing both the reproducibility and the accuracy of these calculations (Chukwo et al. 2008), with possible biases for clinical practice.

Conversely, 3-dimensional echocardiography (3-DE) overcomes these limitations and provides a true measurement of the LVVs, with increased reproducibility and accuracy (Dorosz et al. 2012). Therefore, the recent guideline for cardiac chamber quantification with echocardiography, published by the American Society of Echocardiography and the European Association of Cardiovascular Imaging recommends, whenever feasible, the 3-DE measurement of LVVs and LVEF (Lang et al. 2015). Despite all this evidence, the use of 3-DE for the assessment of left ventricle size and function is not widespread in the clinical arena yet. The time curve necessary for learning the method, and its uncertain feasibility, accuracy and reproducibility when inexperienced trainees use it, were important reasons related to the limited use of 3-DE in clinical practice.

Accordingly, the main objective of our study was to assess the feasibility and reproducibility of 3-DE measurements of LVVs and LVEF, when used by trainees with different levels of experience in 2-DE and after just 1 mo of training in 3-DE measurements, performed by an expert user in the field of 3-DE. The second objective of the study was to analyze if the LVEF threshold for the initiation of device therapy is interchangeable when it is measured by both 2-DE and 3-DE, by trainees with different levels of training in 2-DE, but at a beginning level of training in 3-DE.

## METHODS

### *Study design and patient selection*

We performed a single-center, prospective study in 60 consecutive patients with HFrEF, hospitalized in the Cardiology Department of the Emergency University Hospital of Bucharest, Romania, between October 2015 and December 2016. The ethics committee of the hospital approved the study, and all patients provided informed consent before the study. Inclusion criteria were (i) hospitalization for decompensated HFrEF (signs and symptoms of HF, increased pro-brain natriuretic peptide levels and an LVEF <50%); (ii) presence of a regular rhythm, to allow 3-DE full-volume multibeam acquisitions of the LVVs; and (iii) good apical window. Exclusion criteria were (i) inability to hold one's breath during the 3-D image acquisition; (ii) acute coronary syndrome, severe valvular disease or infective endocarditis; and (iii) a very poor apical window that prevented 2-DE or 3-DE acquisitions for LVVs and LVEF quantification.

### *Clinical findings*

Clinical information and cardiovascular risk factors at the time of the echocardiographic study were obtained from the clinical records of our hospital and included age, sex, weight, height, body surface area, dyslipidemia, hypertension, diabetes, chronic kidney disease, anemia and history of ischemic heart disease.

### *Echocardiography*

All 2-D and 3-DE acquisitions were obtained by one expert user (S.M.B.), with more than 5 y of experience in both 2-D and 3-D echocardiography, during the same echocardiographic study, using a commercially available echo machine (Vivid E9, GE Vingmed, Horten, Norway), equipped with both standard 2-D (M5 S) and 3-D (4 V) probes. The expert user who acquired the data sets had more than 10 y of experience in 2-DE and more than 3 y of experience in 3-DE, and used pre-defined recommendations for all acquisition modalities, according to current guidelines (Lang et al. 2012, 2015). Two-dimensional acquisitions were obtained from the apical four- and two-chamber views, with care, to encompass all endocardial contours in the images and to avoid LV foreshortening (Lang et al. 2015). Three-dimensional data sets of the left ventricle were obtained from the apical four-chamber view by using multibeam full-volume acquisition during breath hold and taking care to encompass the entire LV cavity in the data sets (Fig. 1). The expert user in echocardiography customized settings to ensure the best image quality for both 2-D and 3-DE acquisitions of the left ventricle and to avoid stitching artifacts for the 3-DE data sets. All data sets were stored in a digital archive and subsequently exported to be

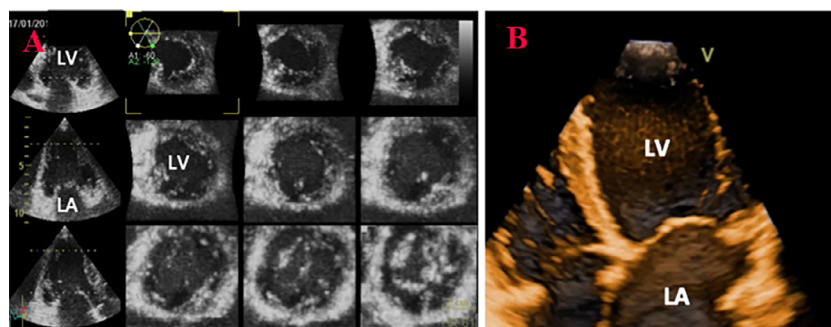


Fig. 1. (a) This multislice 3-D view of the left ventricle (LV) and left atrium (LA) was used to check that the entire endocardial surface of the LV is encompassed in the data set. (b) Three-dimensional rendering of the left heart chambers, with a focus on the left ventricle.

analyzed offline using commercially available software (Echopac BT 12, GE Vingmed).

Three cardiologists from our echocardiography laboratory, with different levels of training in 2-DE, were named beginner (6 mo of experience in 2-DE, with 300 echocardiograms performed), medium (1 y of experience in 2-DE, with 600 echocardiograms performed) and advanced (>2 y experience in 2-DE, with more than 1000 echocardiograms performed) (Popescu *et al.* 2009). The expert user (S.M.B) performed a 1-mo training in 3-DE of the beginner, medium and advanced users, by focusing on how to measure the LVVs and LVEF from the 3-DE data sets. Theoretical and practical notions were delivered to the trainees, to align their workflow with the general recommendations and to obtain results as similar as possible to those of the gold standard, cardiac magnetic resonance (CMR) (Muraru *et al.* 2012, 2013).

At the end of the training, the expert user and the beginner, medium and advanced cardiologists measured the same LVVs and LVEF acquired with 2-DE, in a blinded fashion, by using the Echopac software (BT12, GE Healthcare, Horton, Norway). For measurement of the LVVs, the end-diastolic frame was selected as the frame before mitral valve closure, whereas the end-systolic frame was identified at the time of the smallest LV cavity (Lang *et al.* 2015). Care was taken to encompass the papillary muscles inside the volume (Lang *et al.* 2015). The software derived the LVEF using the biplane method of disc summation (modified Simpson's rule).

At the end of the training in 3-DE, the expert, beginner, medium and advanced users measured the 3-DE LVVs and LVEF using dedicated software for LV analysis (4 D Auto LVQ, GE Vingmed Ultrasound) and in a blinded fashion, as well. Measurement workflow started with semi-automated detection of LV endocardial borders, followed by a phase of manual editing, to optimize the endocardial contours. The same criteria used for defining the end-systolic and end-diastolic frames were also used for the 3-DE analysis. Care was taken to

encompass the papillary muscles and trabeculae inside the volume, to obtain volumes as close as possible to CMR measurements (Fig. 2) (Muraru *et al.* 2012, 2013).

### Statistics

Continuous data are expressed as the mean  $\pm$  standard deviation, whereas categorical data are expressed as the frequency or percentage (%). Measurements of LVVs and LVEF performed with different echocardiographic methods were compared using Student's *t*-test analysis. Pearson correlations were used to compare the measurements performed by the expert, beginner, medium and advanced users. The intra-observer reproducibility of the measurements was assessed using intra-class coefficients (ICCs), while agreements between methods and trainees were expressed using Bland–Altman plots. A *p* value <0.5 was considered to indicate significance. Data analysis was performed using statistical software analysis (SPSS 20, IBM, Armonk, NY, USA) and MedCalc (MedCalc Software, Ostend, Belgium).

## RESULTS

Sixty patients were enrolled in the study. Six of them were excluded because of the very poor quality of the 2-DE or 3-DE images, which prevented reliable measurements. The expert, beginner, medium and advanced users performed measurements of LVVs and LVEF on the same echocardiography images of the remaining 54 patients (46 males, age:  $58 \pm 17$ ). The average resolutions of the 2-DE and 3-DE data sets were  $70 \pm 8$  frames/s and  $34 \pm 7$  volumes/s, respectively.

The expert user measured both 2-DE and 3-DE data sets in all 54 patients. Mean LV end-diastolic volume (LVEDV) was  $214 \pm 75$  mL when calculated with 2-DE and  $233 \pm 77$  mL when measured with 3-DE ( $p < 0.05$ ). Mean LV end-systolic volume (LVESV) was  $144 \pm 64$  mL when calculated with 2-DE and  $161 \pm 66$  mL when measured with 3-DE ( $p < 0.05$ ). Meanwhile, mean

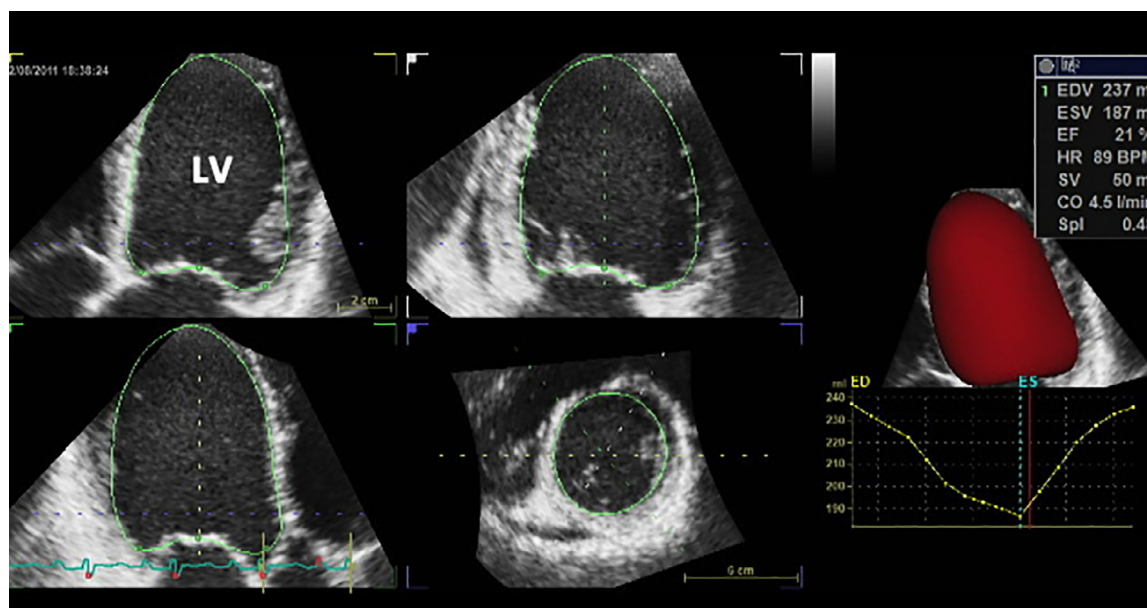


Fig. 2. Measurements of left ventricle (LV) volumes and ejection fraction using a dedicated software package. In red is a beutel of the left ventricle, obtained after contouring the endocardial surface of the left ventricle in end-diastole and end-systole. Below is the volumetric curve of the left ventricle during the cardiac cycle.

LVEF was  $35 \pm 10\%$  when calculated with 2-DE and  $33 \pm 10\%$  when measured with 3-DE ( $p > 0.05$ ).

The beginner, medium and advanced users succeeded in measuring the 2-DE data sets in 49, 51 and 53 patients (feasibility = 91%, 94% and 98%, respectively, for the 2-DE measurements). Conversely, the beginner, medium and advanced users succeeded in measuring the 3-DE data sets in 49, 51 and 53 patients (feasibility = 91%, 94% and 98%, respectively, for the 3-DE measurements).

The time spent measuring the 2-D data sets was  $138 \pm 25$  s for the beginner and  $115 \pm 32$  s for the expert user ( $p = 0.04$ ). The time spent measuring the 3-D data sets was  $182 \pm 30$  s for the beginner and  $150 \pm 27$  s for the expert user ( $p = 0.03$ ).

#### *Comparison between 2-DE and 3-DE measurements of LVVs and LVEF provided by trainees in 3-D echocardiography*

The beginner, medium and advanced users provided 2-DE measurements of LVVs and LVEF that correlated with the measurements provided by the expert user (Fig. 3). Moreover, the beginner, medium and advanced users provided 3-DE measurements of LVVs and LVEF that highly correlated with the measurements provided by the expert user (Fig. 4).

Compared with the 2-DE measurements performed by the expert user, the trainees in echocardiography exhibited good reproducibility of LVVs, but lower reproducibility of LVEF (Table 1). However, after only a

1-mo training in 3-DE, the trainees provided more reproducible results for LVVs and LVEF measured by 3-DE, as compared with the measurements performed by the expert user in echocardiography (Table 1).

Agreement analysis using Bland–Altman plots revealed no systematic biases for the measurements of LVEDVs performed with 2-DE (Table 1, Fig. 5). However, the trainees exhibited a tendency to underestimate LVESVs when using 2-DE. Therefore, trainees tended to “overestimate” LVEF calculated with 2-DE (Table 1, Figs. 6 and 7), by comparison with the LVEFs calculated with 3-DE. Conversely, there were no systematic biases between the measurements of LVVs and LVEF provided by the expert user and the trainees when using 3-DE (Table 1, Figs. 5–7).

#### *Agreement between 2-DE and 3-DE when selecting patients with an indication for device therapy, based on the LVEF cutoff of 35%*

There was substantial agreement between the 2-DE and 3-DE classifications of LVEF ( $<35\%$  and  $>35\%$ ) for all levels of training in 2-DE and 3-DE (all  $\kappa$  values  $>0.60$ , but  $<0.80$ , Table 2). However, when using 3-DE, the expert observer did not re-classify any patient as having an LVEF  $>35\%$  but did re-classify almost 15% of the patients as having an LVEF  $<35\%$  and, therefore, an indication for device implantation (Table 2). The same tendency, to re-classify patients into having an LVEF  $<35\%$  when using 3-DE, was observed for trainees as well, but in smaller percentages (Table 2).



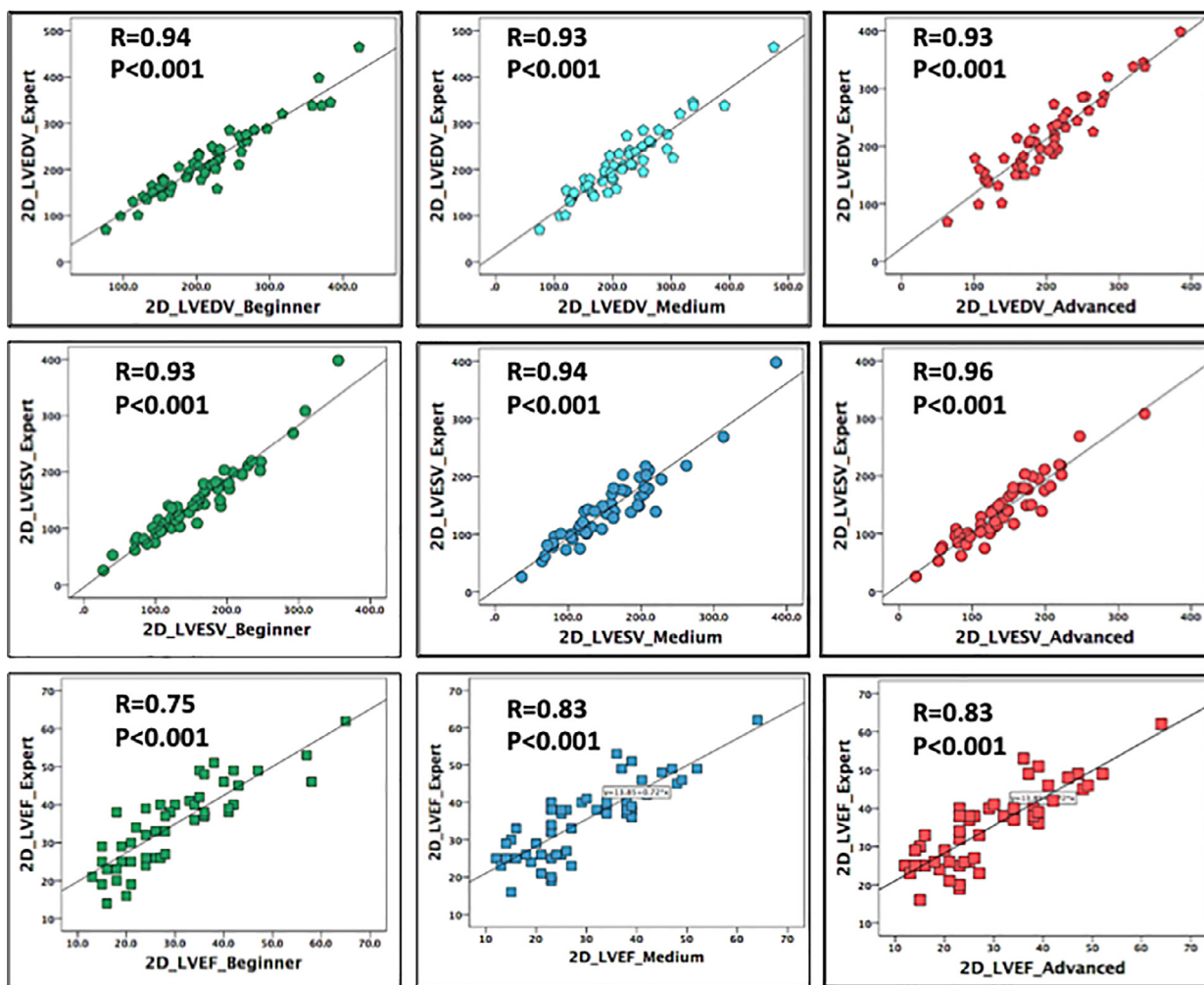


Fig. 3. Correlations between 2-D left ventricular volumes and ejection fraction measured by the expert and trainees with different levels of training in 2-D echocardiography (beginner, medium and advanced). LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVEF = left ventricular ejection fraction.

## DISCUSSION

Measurements of LVVs and LVEF are important determinants of clinical decisions in patients with HFrEF and frequently used as an endpoint in clinical trials (CONSENSUS Trial Study Group 1987; Yusuf *et al.* 1991; Pfeffer *et al.* 2003; Zannad *et al.* 2011). The most frequently used technique for assessing LV size and function is 2-DE because it is a rapid, non-invasive and cost-effective technique (Doroszi *et al.* 2012). However, measurements of LVVs and LVEF by 2-DE are limited by the geometric assumptions of left ventricle shape and by the foreshortening of the left ventricle (Lang *et al.* 2015), which reduce both the accuracy and reproducibility of the method (Chukwu *et al.* 2008). Limitations of 2-DE are more prominent in patients with dilated and aneurysmal left ventricles (Rigolli *et al.* 2016), often encountered in patients with HFrEF, in which the

decisions based on echo measurements are essential for therapeutic and interventional management. Conversely, 3-DE, which uses new matrix array probes, provides qualitative data sets of the LVVs that measure the true volumes of the LV with minimal post-processing (Dickstein and Kjekshus 2002). Yet, even if 3-DE seems to offer some advantages over 2-DE, it is considered as a method with a long learning curve, reliable only when used by experienced echocardiographers.

Our study indicates that 3-DE can be used by cardiologists with different levels of training in 2-DE, just after a short period of training in 3-DE, with similar feasibility, but better reproducibility than 2-DE. The main results of our study indicated that, in patients with HFrEF, with a wide range of left ventricle shapes, LVVs and LVEF, (i) 3-DE provides feasible and more reproducible measurements of the LVVs and LVEF than 2-DE, when used by

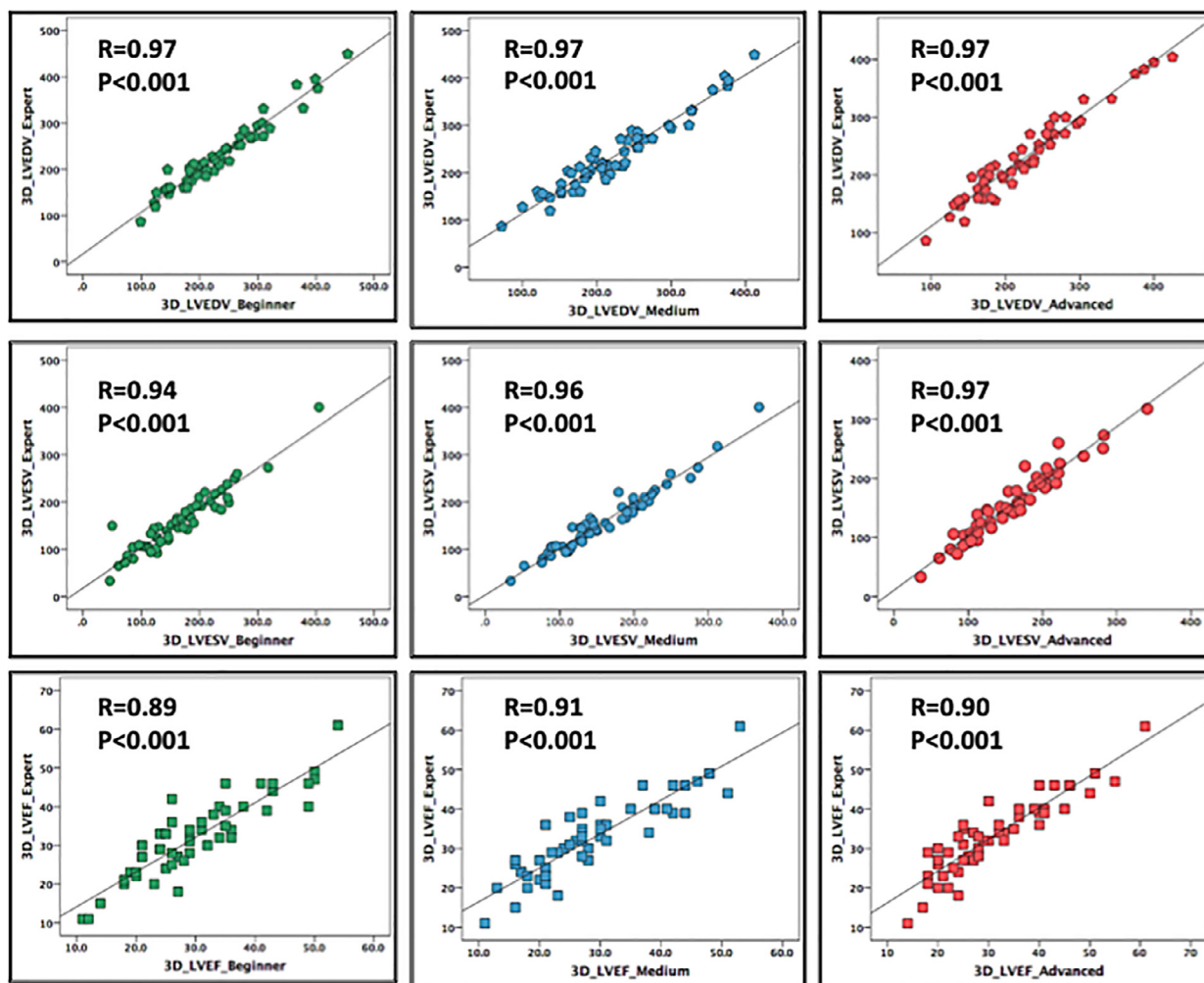


Fig. 4. Correlations between 3-D left ventricular volumes and ejection fraction measured by the expert and the trainees with different levels of training in 2-D echocardiography (beginner, medium and advanced). LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVEF = left ventricular ejection fraction;

novel trainees in 3-DE, regardless of their basic level of training in 2-DE; (ii) there is substantial agreement between 3-DE and 2-DE in measurement of LVEF, when used by trainees with different basic levels of training in 2-DE and after just 1 mo of training in 3-DE; (iii) 3-DE re-classifies more than 10% of the patients as having an LVEF <35% and, therefore, an indication for device therapy, when used by an echocardiographer experienced in both 2-D and 3-D echocardiography.

#### *Feasibility and reproducibility of 2-D and 3-DE measurements made by echocardiography trainees*

Jenkins et al. (2006), who performed a comparative study in 110 patients, obtained 99% and 97% feasibility for 2-DE and 3-DE offline measurements of LVVs and LVEF, respectively. As expected, our trainees obtained feasibilities for 2-DE measurements in line with their level of expertise in 2-DE (91%, 94% and 98% for the beginner,

medium and advanced users, respectively). However, after only 1 mo of training in 3-DE post-processing, trainees obtained similar feasibility for 3-DE measurements of LVVs and LVEF of patients with HFrEF, irrespective of their basic level of training in 2-DE.

It was reported that reproducibility is lower when measuring LVVs and LVEF with 2-DE than with 3-DE, and this limitation might be overcome by the use of contrast agents in the 2-DE techniques (Wood et al. 2014). In our study, when the 2-DE measurements provided by trainees were compared with those of the expert user, their reproducibility was in line with their basic level of training in 2-DE. However, when compared again with the expert user, the trainees had increased reproducibility in 3-DE measurements regardless of their basic training in 2-DE. Our study indicates that 3-DE might be a more accurate and reproducible method for following up patients with HFrEF after a short period of training in 3-DE.

Table 1. Comparison between echocardiography trainees with different levels of expertise in 2-D and 3-D echocardiography and the expert in both

	Level of expertise	ICC	CI	Bias*	LOA*
2-D LVEDV	Beginner	0.94	0.90–0.97	–5.3	–55; 44
	Medium	0.93	0.88–0.96	0.6	–43; 44
	Advanced	0.92	0.86–0.92	13	–35; 61
2-D LVESV	Beginner	0.91	0.85–0.95	–12	–56; 31
	Medium	0.90	0.84–0.95	–10	–44; 24
	Advanced	0.92	0.86–0.95	–1.9	–40; 36
2-D LVEF	Beginner	0.75	0.59–0.85	4.4	–10; 19
	Medium	0.82	0.71–0.90	5.1	–7.5; 18
	Advanced	0.83	0.71–0.90	5.6	–7; 18
3-D LVEDV	Beginner	0.97	0.95–0.98	22	–20; 80
	Medium	0.97	0.95–0.98	19	–33; 72
	Advanced	0.97	0.94–0.99	4.8	–30; 40
3-D LVESV	Beginner	0.97	0.94–0.98	–9.4	–46; 27
	Medium	0.96	0.94–0.98	–0.9	–30; 29
	Advanced	0.97	0.96–0.99	–1.5	–33; 30
3-D LVEF	Beginner	0.89	0.81–0.94	2	–7.4; 11
	Medium	0.90	0.83–0.94	3.8	–5.4; 13
	Advanced	0.90	0.82–0.94	2.1	–6.9; 11

CI = confidence interval; ICC = intra-class correlation coefficient; LOA = limits of agreement; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVEF = left ventricular ejection fraction.

\* Biases and LOA obtained using Bland–Altman plots.

Mor-Avi *et al.* (2008) reported that 3-DE underestimates LVVs compared with CMR in patients with a wide range of LVVs and LVEF. However, the underestimations of LVVs decrease when the trabeculae are included in the 3-DE measurements and the mitral valve plane is excluded from the CMR measurements. We acknowledge the gold standard position of CMR for the measurement of the LVVs. However, CMR is an expensive technique, with decreased availability, and the vast majority of clinical trials were based on echocardiographic measurements. Therefore, the purpose of our study was to determine whether 3-DE might be a more feasible and reproducible alternative for 2-DE measurements, even after a short period of training of the users in 3-D echocardiography.

In the study published by Mor-Avi *et al.* (2008), the reproducibility of measurements of LVVs using 3-DE decreased in parallel with the decreased experience of the centers involved in the project, mainly because of the measurement technique (inclusion vs. exclusion of LV trabeculae inside the LVVs measured from the 3-DE data set). Our purpose was to illustrate that 3-DE is a method that can be easily learned, and might be a more reproducible technique for the follow-up of patients with HFrEF. Therefore, we performed a uniform training of our cardiologist in 3-DE, which can explain the good results offered by all of them in terms of accuracy and reproducibility of the measurements.

Thavendiranathan *et al.* (2013) reported that 3-DE was the best method for sequential measurements of LVVs and LVEF in 56 patients with chemotherapy treatment and stable LV function (global longitudinal strain

>16%). The latter study was performed in patients with non-dilated left ventricles (3-D left ventricular end-diastolic volume ranged from 60–130 mL; 3-D left ventricular end-systolic volume [LVESV] ranged from 30–50 mL) and normal LVEF (3-D LVEF ranged from 56%–65%), who were assessed by a single experienced observer in echocardiography. Our study especially selected patients with HFrEF having dilated and distorted LVVs (3-D LVED ranged from 85–381 mL, and 3-D LVESV ranged from 30–293 mL) and a wide range of LVEF (3-D LVEF ranged from 13%–53%), which were measured by different observers after a short period of training in 3-DE. Moreover, we noted that even though significantly different, the measurements provided by the beginner user using both 2-D and 3-DE were not much longer than those made by the expert user.

*There is substantial agreement between 3-DE and 2-DE in measuring LVEF when used by trainees with different basic levels of training in 2-DE and beginners in 3-DE*

To the best of our knowledge, there is only one study that mentions the benefits of 3-DE when comparing its use by experienced and non-experienced observers (Hien *et al.* 2013). However, the study was performed with transesophageal echocardiography and aimed to compare how experts and beginners localize the prolapsing segments of the mitral valve in patients with organic mitral regurgitation. Our study found that trainees in echocardiography might have increased accuracy and reproducibility for 3-DE measurements of LVVs and LVEF performed in patients with dilated left ventricles and a wide range of LVEFs, by comparison with 2-DE

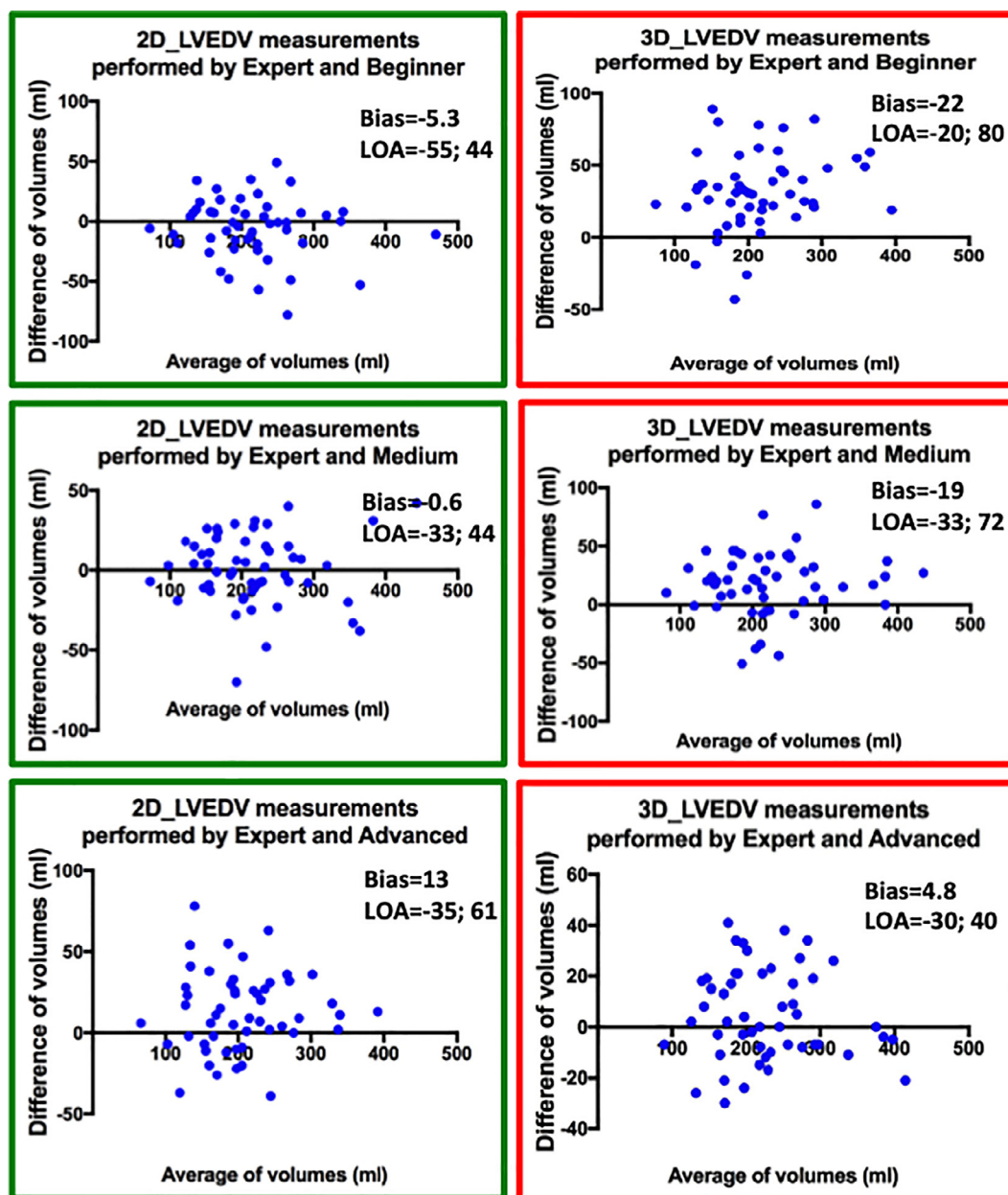


Fig. 5. Bland–Altman plots for measurements of left ventricular end-diastolic volume (LVEDV) made by the expert and beginner, medium and advanced users using 2- and 3-dimensional echocardiography.

measurements. Therefore, our study strengthens the benefit of 3-DE for the long-term follow-up of patients with HFREF, even if used by beginners in the field.

#### *3-DE reclassifies LVEF in patients with heart failure with reduced ejection fraction*

A recent meta-analysis by [Rigoli et al. \(2016\)](#) reported that 3-DE is the method with the highest accuracy in measuring LVEF, by comparison with CMR. In our study, the LVEFs measured with 3-DE by each of the echocardiographers included in the study were lower

than the LVEFs measured with 2-DE. Our results agree with a recent study published by [Rodriguez-Zanella et al. \(2019\)](#), which indicated that 3-DE usually provides lower LVEF values than 2-DE, and 3-D LVEF is an independent predictor of major arrhythmic events in patients with LV dysfunction. Moreover, in [Rodriguez-Zanella et al. \(2019\)](#), 3-DE re-assigned up to 20% of patients as having a risk for sudden cardiac death according to the LVEF and, therefore, an indication for device implantation. Our study found that more than 10% of patients are re-classified by the expert user as



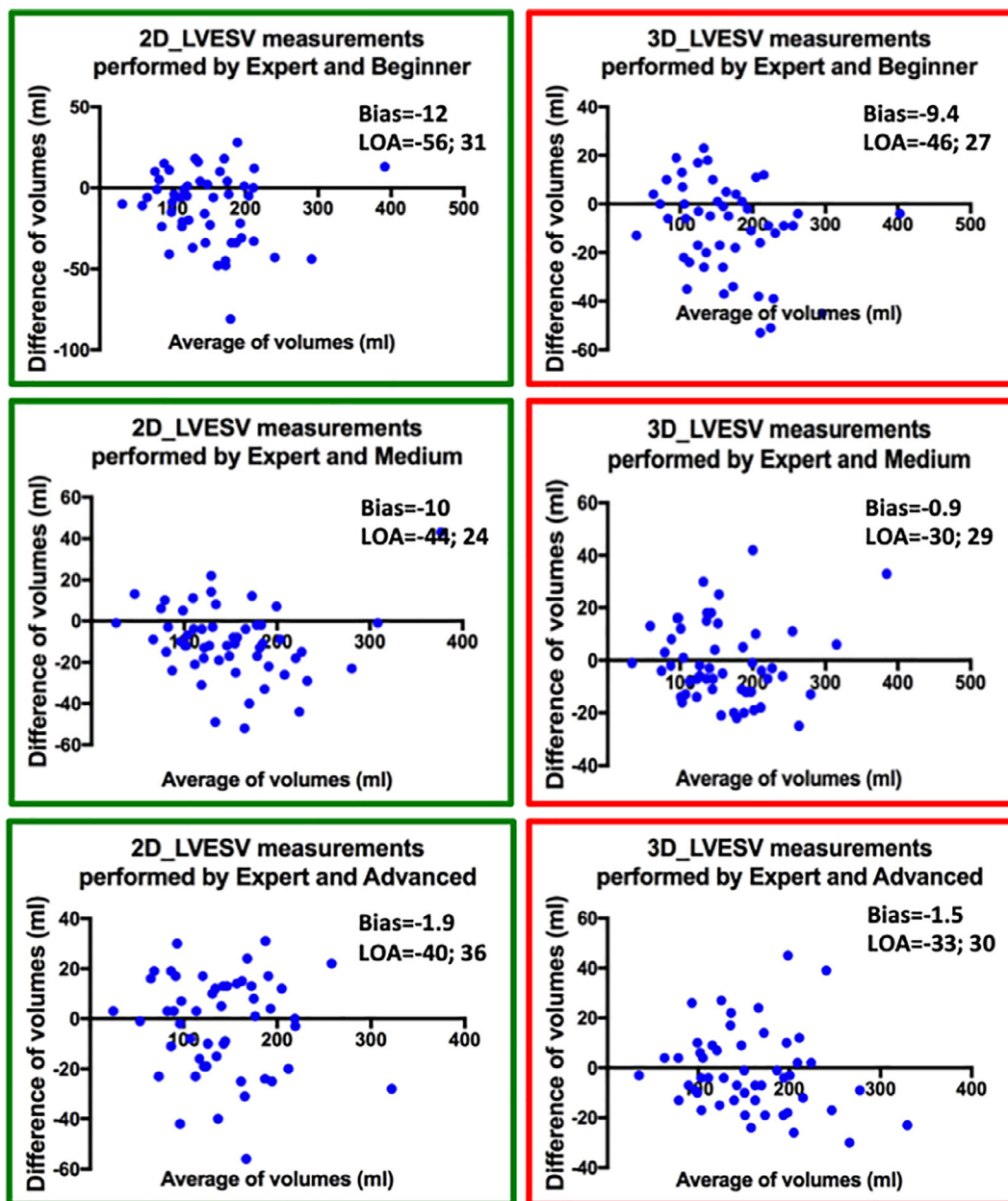


Fig. 6. Bland–Altman plots for the measurements of the end-systolic left ventricular volume using 2- and 3-dimensional echocardiography, by the Expert and Beginner, Medium, and Advanced users, respectively. LVEDV = left ventricle end-systolic volume.

having an LVEF below the threshold of 35% and, therefore, an indication for device therapy. The trainees in 3-DE also re-classified LVEF when using 3-DE, but by a lower percentage than by the expert in echocardiography.

#### Limitations

One limitation of our study is that we did not compare our measurements against the gold standard method, CMR. However, our aim was not to test the accuracy of 3-DE versus CMR, which has already been

done in previous studies (Mor-Avi *et al.* 2008), but to assess the reliability of 3-DE for the evaluation and follow-up of patients with HFrEF after a short period of training in 3-DE.

#### CONCLUSIONS

Trainees with different basic levels of expertise in 2-DE, after only 1 mo of training in 3-D echocardiography, provided more reproducible measurements of

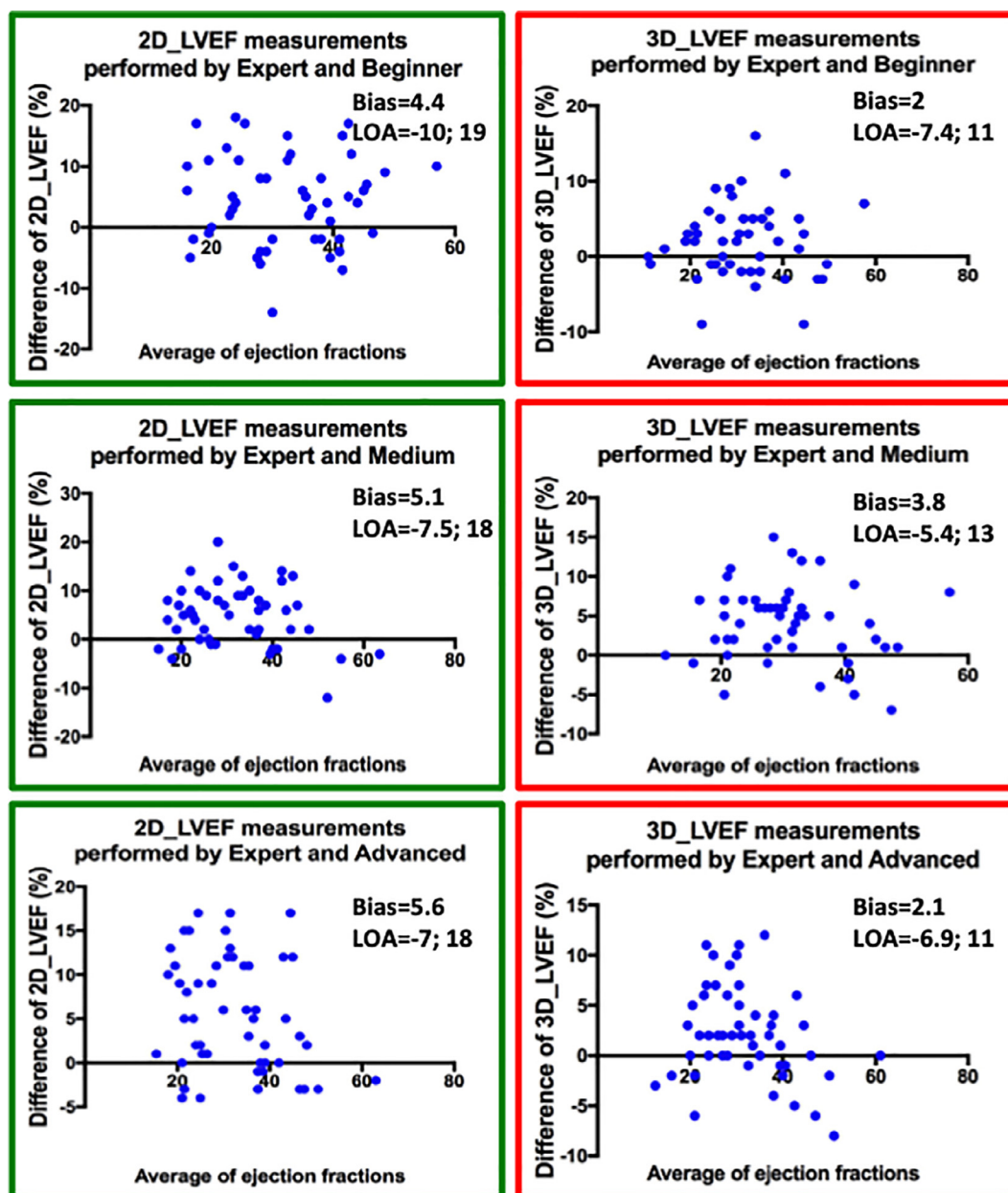


Fig. 7. Bland–Altman plots for measurements of left ventricular ejection fraction (LVEF) made by the expert and beginner, medium and advanced users with 2- and 3-dimensional echocardiography.

Table 2. Classification of LVEF (above and below 35% cutoff used for device therapy in heart failure with reduced ejection fraction) using the measurements made by the expert user on the 2-DE and 3-DE data sets

Level of expertise in echocardiography	$\kappa^*$	CI	Patients re-classified with 3-DE as having LVEF > 35%	Patients re-classified with 3-DE as having LVEF < 35%
Expert	0.73	0.63–0.83	0 (0%)	7 (14%)
Advanced	0.69	0.67–0.71	2 (4%)	5 (10%)
Medium	0.75	0.74–0.76	2 (4%)	4 (8%)
Beginner	0.79	0.70–0.88	3 (6%)	2 (4%)

2-DE (3-DE) = 2-D (3-D) echocardiography; CI = confidence interval; LVEF = left ventricular ejection fraction.

\* Cohen's  $\kappa$  inter-rater agreement test. For all inter-rater agreement tests, Cohen's  $\kappa$  was obtained with a  $p < 0.001$ .

LTVs and ejection fraction than obtained with 2-DE. The increased reproducibility of the 3-D measurements was not related to the basic level of training in 2-D echocardiography. Therefore, 3-DE might be a feasible and more reliable method for the follow-up of patients with heart failure with reduced ejection fraction, having dilated and distorted left ventricles, with a wide range of ejection fractions.

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