



Three-dimensional echocardiography of the athlete's heart: a comparison with cardiac magnetic resonance imaging

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Abstract

Three-dimensional echocardiography (3DE) is the most accurate cardiac ultrasound technique to assess cardiac structure. 3DE has shown close correlation with cardiac magnetic resonance imaging (CMR) in various populations. There is limited data on the accuracy of 3DE in athletes and its value in detecting alterations during follow-up. Indexed left and right ventricular end-diastolic volume (LVEDVi, RVEDVi), end-systolic volume, ejection fraction (LVEF, RVEF) and left ventricular mass (LVMi) were assessed by 3DE and CMR in two-hundred and one competitive endurance athletes (79% male) from the Pro@Heart trial. Sixty-four athletes were assessed at 2 year follow-up. Linear regression and Bland–Altman analyses compared 3DE and CMR at baseline and follow-up. Interquartile analysis evaluated the agreement as cardiac volumes and mass increase. 3DE showed strong correlation with CMR (LVEDVi $r=0.91$, LVEF $r=0.85$, LVMi $r=0.84$, RVEDVi $r=0.84$, RVEF $r=0.86$ $p<0.001$). At follow up, the percentage change by 3DE and CMR were similar (Δ LVEDVi $r=0.96$ bias -0.3% , Δ LVEF $r=0.94$, bias 0.7% , Δ LVMi $r=0.94$ bias 0.8% , Δ RVESVi $r=0.93$, bias 1.2% , Δ RVEF $r=0.87$ bias 0.4%). 3DE underestimated volumes (LVEDVi bias -18.5 mL/m², RVEDVi bias -25.5 mL/m²) and the degree of underestimation increased with larger dimensions (Q1vsQ4 LVEDVi relative bias -14.5 versus -17.4% , $p=0.016$; Q1vsQ4 RVEDVi relative bias -17 versus -21.9% , $p=0.005$). Measurements of cardiac volumes, mass and function by 3DE correlate well with CMR and 3DE accurately detects changes over time. 3DE underestimates volumes and the relative bias increases with larger cardiac size.

Keywords Athlete's heart · Cardiac magnetic resonance imaging · Three dimensional echocardiography · Cardiac remodeling

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Introduction

High-intensity endurance exercise induces profound structural and functional cardiac alterations which includes an increase in left ventricular (LV) volume, mass and right ventricular (RV) volume accompanied by normal or low-normal systolic function [1–5]. In some cases the athlete's heart may evolve towards phenotypic mimics of cardiac disease such as a dilated, hypertrophic or arrhythmogenic cardiomyopathy. Hence, accurate and repeatable evaluation of cardiac volumes and function is essential in endurance athletes to enable early identification of potential adverse cardiac remodeling throughout their competitive career.

Several professional sports federations, such as UCI and FIFA, mandate echocardiography biannually as part of routine pre-participation cardiovascular evaluation. The low cost, widespread availability and lack of exposure to ionizing radiation of two-dimensional echocardiography (2DE) make it the most popular imaging modality in the evaluation of the athlete's heart. 2DE is however limited by potential foreshortening of the apex and geometric assumptions to obtain LV volumes. The complex shape of the RV and through-plane phenomenon limit its assessment by 2DE.

Cardiac magnetic resonance imaging (CMR) is considered the gold standard to assess cardiac morphology and function given its high spatial resolution and imaging quality regardless of body composition [6]. It is however limited by claustrophobia, the presence of implanted cardiac devices, administration of gadolinium contrast, a high financial burden and limited availability which are barriers for serial clinical follow-up and large prospective trials.

Three-dimensional echocardiography (3DE) may provide an alternative as it has the advantages of 2DE but does not rely on geometric assumptions for volume calculations and is not subject to plane positioning errors. Several studies have reported accurate comparisons between 3DE and CMR for both ventricles in healthy and diseased hearts [7–9].

To date, the accuracy of 3DE to depict longitudinal changes in cardiac volumes and function has not been evaluated. Accordingly, the aim of this study was to investigate the accuracy of 3DE compared to CMR in the quantification of biventricular volumes, EF and LV mass at baseline and during prospective follow-up in elite endurance athletes.

Methods

Subjects

Two hundred and one elite endurance athletes were recruited from the Pro@Heart trial (NCT05164328). The

Pro@Heart trial is a multicentre prospective cohort study aimed to assess the relationship between high-level endurance training and cardiac remodeling [10].

Athletes were recruited through sports federations or teams via local advertisements and were eligible for inclusion if the following criteria were met: (1) age 14–23 years at inclusion; (2) competing in an endurance sport in which aerobic conditioning is a principal component of performance—including triathlon, cycling (road, track or mountain), rowing, cross-country skiing, distance running (1500 m or longer) and swimming; (3) competing at a national or international level and (4) non-smoking. Athletes with a known cardiac or respiratory condition or with contra-indications for magnetic resonance imaging (e.g. pacemaker) were excluded.

The Pro@Heart study conforms to the Declaration of Helsinki and was approved by local ethics committees. All participants or their legal guardian provided written informed consent.

Three-dimensional echocardiography acquisition

3DE was performed using commercially available ultrasound systems (Vivid E9 or Vivid E95, GE Healthcare, Horton, Norway). Images were acquired with subjects in left-lateral decubitus position for an apical and dedicated RV view using a 1.5–4 MHz matrix-array transducer (GE 4Vc-D Matrix 4D cardiac probe, GE Healthcare, Horton, Norway). The depth and field of view were adjusted to a minimal level still encompassing the entire ventricular volume and allowing the highest temporal resolution. 3D full-volume data sets were acquired in real time, during breath-hold and using several consecutive cardiac cycles (4–6 beats).

Three-dimensional echocardiography analysis

3DE analysis was performed off-line on a commercially available workstation (Echo PAC version 203, GE Healthcare, Horton, Norway) using a validated semiautomatic analysis software (4D Auto LVQ & 4D Auto RVQ) by experienced investigators (RDB and GC for inter-observer variability).

LV analysis by 3DE is illustrated in Online resource 4. Cine-loops of three apical views (4-chamber, 2-chamber, 3-chamber) and one short-axis view derived from the 3D full-volume dataset were displayed on a quad-screen with manual alignment when necessary. The end-diastolic frame was automatically defined by R peak on the ECG and the end-systolic frame was estimated from the R-R interval. Automatic endocardial border delineation of the whole LV cavity was processed at end-diastole and end-systole after positioning a landmark on the LV apex and mid-base on any apical view. Manual correction was performed at

end-diastole and end-systole to ensure optimal LV delineation and rendered LV end-diastolic (LVEDV) and end systolic volumes (LVESV). The papillary muscles and trabeculae were considered as part of the ventricular cavity. LVEF was computed as followed: $LVEF (\%) = (LVEDV - LVESV) / LVEDV$. Automatic epicardial border delineation of the LV was processed at end diastole rendering LV mass (LVM). Manual correction was performed to ensure optimal epicardial delineation.

RV analysis by 3DE is illustrated in Online resource 5. Cine-loops of 2 apical views (4-chamber and RV 4-chamber orthogonal) and two short-axis (apical and basal) derived from the 3D full-volume data set were displayed on a quad-screen with manual alignment when necessary. Automatic endocardial border delineation of the whole RV was processed at end diastole and end systole after positioning six landmarks. On the apical 4-chamber view landmarks were placed on the free wall and septal tricuspid annulus and at the RV apex. In a short-axis view landmarks were placed on the LV/RV posterior insertion point, LV/RV anterior insertion point and at the RV free-wall. Manual correction was performed at end diastole and end systole to ensure optimal RV delineation and rendered RV end-diastolic (RVEDV) and end-systolic volumes (RVESV). RVEF was computed as followed: $RVEF (\%) = (RVEDV - RVESV) / RVEDV$.

Biventricular volumes and LVM were divided by body surface area (BSA) rendering indexed LVEDV (LVEDVi), LVESV (LVESVi), RVEDV (RVEDVi), RVESV (RVESVi) and LVM (LVMi).

Cardiac magnetic resonance imaging acquisition and analysis

On the same day, CMR was acquired using a 1.5 or 3 T MRI scanner (Magnetom Aera—Siemens Healthineers, Erlangen, Germany; Ingenia, Achieva or Ambition—Philips Medical Systems, Best, The Netherlands), A steady-state free precession dynamic echo-gradient sequence was used to obtain cine-loops during breath-hold in short axis and four chamber views, a slice thickness of 8 mm with no slice gap, covering base to apex, rendering 14–18 slices with 30 phases per cardiac cycle and a target field of view of 320×313 mm, a target matrix size of 192×172 , with target a voxel size of 1.67×1.68 mm.

Biventricular volumes and function and LVM were quantified by experienced investigators (RDB and MC for inter-observer variability) using customised analysis software (RightVol, Leuven, Belgium). The software allowed manual tracing of the endocardial and epicardial boundaries at end-diastole and end-systole in all slices, and the papillary muscles and trabeculations were considered as part of the ventricular cavity. Disk summation was used to calculate LVEDV, LVESV, RVEDV and RVESV. LVM

was calculated as the difference between the epicardial and endocardial volumes at end-diastole multiplied by myocardial density (1.05 g/mL). [11] Similar to 3DE, volumes and LVM were indexed by BSA. CMR analysis is illustrated in Online resource 6.

Two-year follow-up

In 64 athletes, measurements were repeated at 2 year follow-up.

Statistical analysis

Data were analysed using SPSS Statistics version 26 (IBM Corporation, Amonk, NY, USA). Normality was ensured using the Shapiro–Wilk test. Continuous variables are presented as means (\pm standard deviation) or as medians (with 25% and 75% percentiles) accordingly and categorical variables as proportions. Categorical variables were compared using a χ^2 test (or Fisher's exact test) and continuous data by either a paired T-test or a Wilcoxon test as appropriate.

3DE and CMR measurements at baseline were compared using linear regression with Pearson's correlation and Bland–Altman analyses to assess the mean inter-modality differences (bias) and limits of agreement (LOA) (\pm 2 SDs of the mean difference). For RV and LV volumes and LVM the relative bias of 3DE was calculated as followed: $3DE \text{ bias} / \text{CMR volume or mass}$ accordingly. An interquartile comparison was performed using one-way analysis of variance (ANOVA) with a Tukey post-hoc correction or a Kruskal–Wallis test with a Dunn's post-hoc correction as appropriate. Quartiles for LV and RV measurements were respectively based on LVEDVi and RVEDVi as measured by CMR.

The change in volumes and mass at 2 year follow-up was expressed as a percentage difference from baseline using the following calculation: $(\text{volume or mass at follow-up} - \text{volume or mass at baseline}) / \text{volume or mass at baseline}$. The change in EF was expressed as the difference between follow-up and baseline. The changes measured by 3DE and CMR were compared using linear regression with Pearson's correlation and Bland–Altman analyses.

Inter-observer and intra-observer variability of 3DE and CMR measurements of biventricular volumes, EF and LVM were analyzed by the reliability statistics from 20 randomly selected athletes. At least one month after initial measurements, the first operator repeated the analysis for the intra-observer variability. The second operator was blinded to the measurements of the first operator for the inter-observer variability.

A two-tailed P-value < 0.05 was considered statistically significant.

Results

Population characteristics

3DE was performed in 207 athletes. In six athletes 3DE of the RV was not feasible due to the interference of the lungs with the acoustic window. Thus 201 endurance athletes, 158 males and 43 females, comprising 116 cyclists, 47 runners, 22 triathletes, 11 rowers and 5 cross-country skiers were assessed for this study. The median age was 18 years (17–20 years) and the mean VO₂max was 63 mL/min/kg (57–67 mL/min/kg), highlighting high athletic performance. Baseline characteristics are summarized in Table 1.

The accuracy of 3DE at baseline as compared to CMR

LVEDVi and LVESVi by 3DE showed excellent correlation with CMR ($r=0.91$ and $r=0.93$ respectively) with a negative bias and good LOA (Bias -18.5 mL/m² and -7.7 mL/m²; LOA ± 15.2 mL/m² and ± 8 mL/m² respectively). LVEF by 3DE showed strong correlation with CMR ($r=0.85$) with a negative bias of -0.2% and LOA of $\pm 5.6\%$. LVMi by 3DE and CMR correlated well ($r=0.84$). Bland–Altman analysis showed a small positive bias (4.9 g/m², LOA ± 16.3 g/m²).

RVEDVi and RVESVi by 3DE showed strong correlation with CMR ($r=0.84$ and $r=0.86$ respectively) with a negative bias and good LOA (Bias -25.5 mL/m² and -12.8 mL/m²; LOA ± 24 mL/m² and ± 15.1 mL/m²

respectively). RVEF by 3DE showed strong correlation with CMR ($r=0.86$) with a positive bias of 0.4% and LOA of $\pm 5.9\%$.

The correlation between cardiac volumes, EF and mass by 3DE and CMR is illustrated in Figs. 1, 2.

The accuracy of 3DE in follow-up as compared to CMR

The percentage change between baseline and 2 year follow-up for LVEDVi and LVESVi by 3DE showed excellent correlation with CMR ($r=0.96$ and $r=0.95$, Bias -0.3% and -1.5% ; LOA $\pm 5.9\%$ and $\pm 9.6\%$ respectively). The difference in LVEF during follow-up by 3DE showed excellent correlation with CMR ($r=0.94$) with a bias of 0.7% and LOA of $\pm 3.1\%$. 3DE and CMR correlated well for changes in LVMi ($r=0.94$, Bias 0.8% , LOA $\pm 8.5\%$).

Alterations in RVEDVi and RVESVi by 3DE compared very well with CMR ($r=0.93$ and $r=0.95$, Bias -1.2% and -1.7% ; LOA $\pm 7.4\%$ and $\pm 9.2\%$ respectively). The difference in RVEF between baseline and follow-up by 3DE showed strong correlation with CMR ($r=0.87$) with a bias of 0.4% and LOA of $\pm 5.1\%$.

The changes in cardiac volumes, EF and mass by 3DE and CMR at baseline and follow-up are illustrated in Figs. 3, 4.

The bias between 3DE and CMR relative to cardiac size

The absolute bias between 3DE and CMR for LVEDVi and LVESVi increases per quartile (Q1–Q4 -13.8 mL/m² versus -16.3 mL/m² versus -19.6 mL/m² versus -24.5 mL/m² and -6.2 mL/m² versus -6.8 mL/m² versus -8.1 mL/m² versus -9.6 mL/m², $p<0.001$, respectively). The relative bias for LVEDVi increased per quartile (Q1–Q4 -14.5% versus -14.8% versus -15.8% versus -17.7% , $p=0.013$) but was equal for LVESVi. LVEF by 3DE and CMR was similar between quartiles. The absolute and relative bias was similar between quartiles for LVMi.

The absolute bias between 3DE and CMR for RVEDVi and RVESVi increased per quartile (Q1–Q4 -17.6 mL/m² versus -23.8 mL/m² versus -25.6 mL/m² versus -35.2 mL/m² and -8.4 mL/m² versus -11.9 mL/m² versus -12 mL/m² versus -18.9 mL/m², $p<0.001$, respectively). The relative bias for RVEDVi and RVESVi was largest in the fourth quartile. RVEF by 3DE and CMR was similar between quartiles.

The interquartile comparisons of relative and absolute bias between 3DE and CMR are illustrated in Online resources 7 and 8.

Table 1 General characteristics of the study population

| Variable | Value |
|---------------------------------|-----------------|
| Age (years) | 18 (17–20) |
| Men, n (%) | 158 (79) |
| Height (cm) | 178 \pm 7 |
| Weight (kg) | 66.2 \pm 8.7 |
| BMI (kg/m ²) | 20.9 \pm 2.1 |
| BSA (m ²) | 1.82 \pm 0.15 |
| Sport discipline, n (%) | |
| Cycling | 116 (57.7) |
| Running | 47 (23.4) |
| Triathlon | 22 (10.9) |
| Rowing | 11 (5.5) |
| Cross-country skiing | 5 (2.5) |
| VO ₂ max (mL/kg/min) | 63 (57–67) |
| Heart rate (/min) | 56 \pm 10 |
| Systolic blood pressure (mmHg) | 122 \pm 11 |
| Diastolic blood pressure (mmHg) | 63 \pm 8 |

The general characteristics of the study population

BMI body mass index, BSA body surface area, VO₂max maximal oxygen consumption

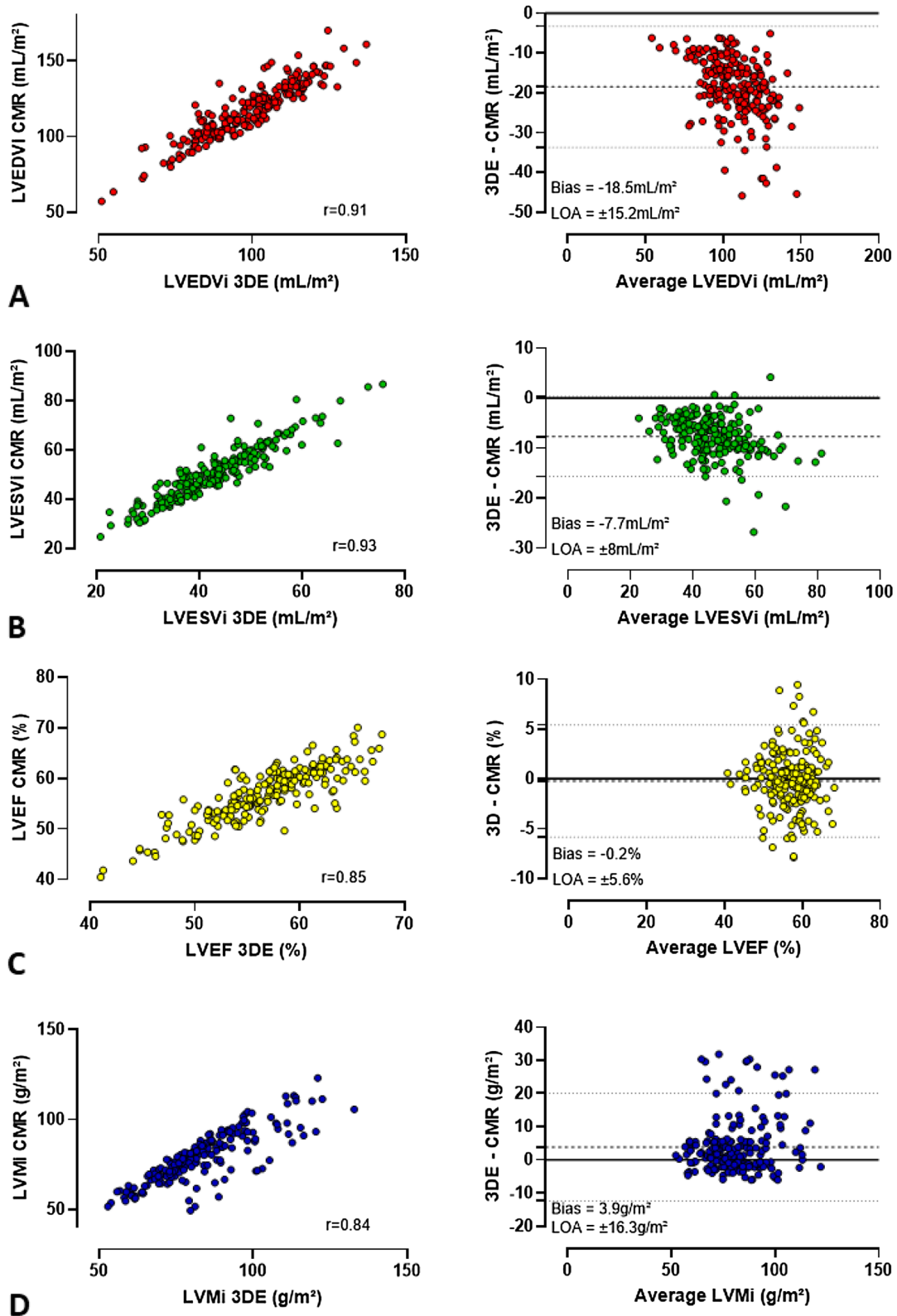


Fig. 1 Linear regression (left) and Bland–Altman analysis (right) for **A** LVEDVi, **B** LVESVi, **C** LVEF and **D** LVMI measured by 3DE and CMR. Correlation between 3DE and CMR for the left ventricle

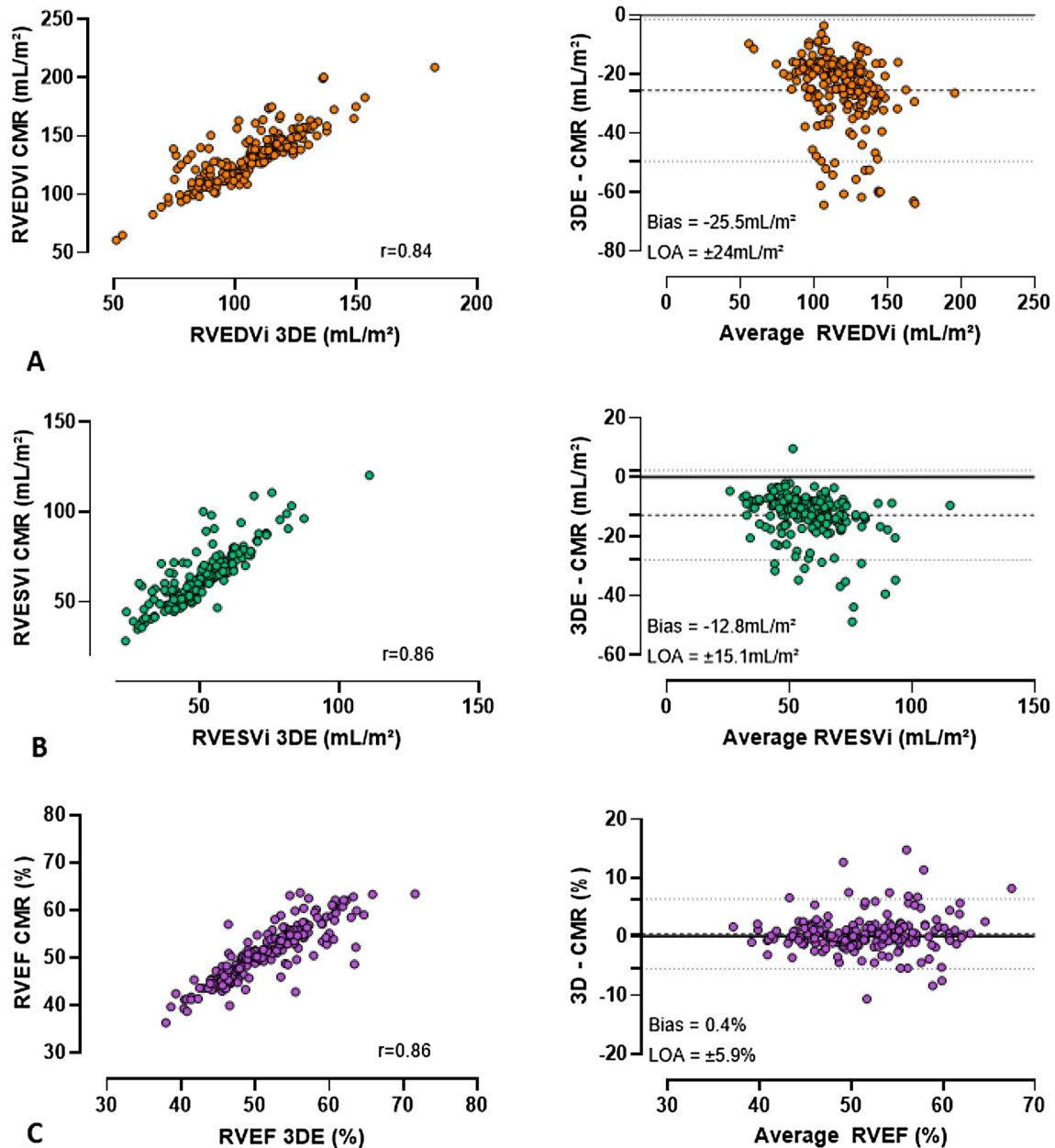


Fig. 2 Linear regression (left) and Bland–Altman analysis (right) for **A** RVEDVi **B** RVESVi and **C** RVEF measured by 3DE and CMR. Correlation between 3DE and CMR for the right ventricle

Inter-observer and intra-observer variability

3DE and CMR measures of volumes, mass and EF had excellent reproducibility with intra-class correlation coefficients ranging from 0.85 to 0.98 (Online resources 2 and 3).

Discussion

To our knowledge, this is the first study to address the accuracy of 3DE in the assessment of biventricular volumes, function and LVM in a prospective cohort of highly trained

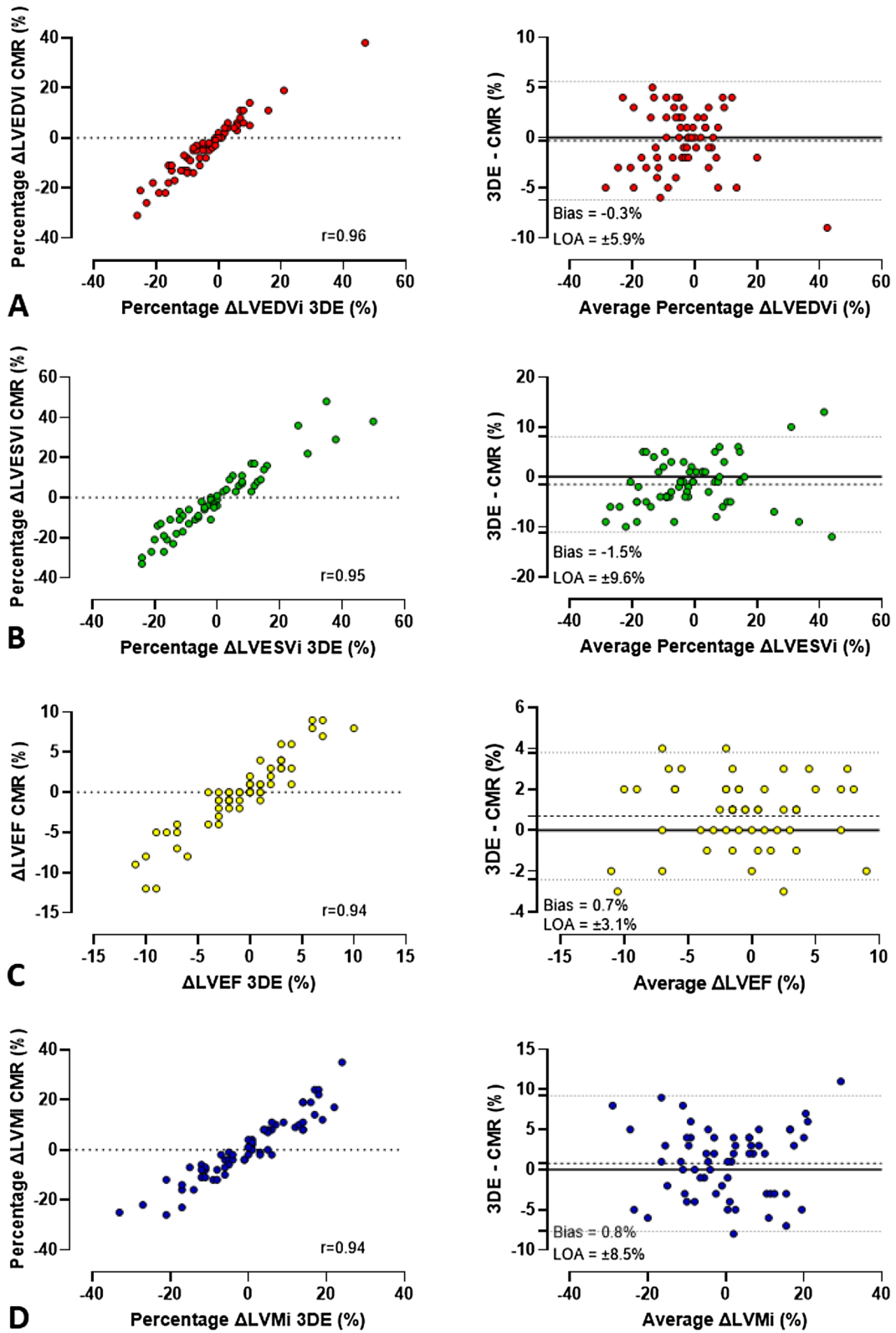


Fig. 3 Linear regression (left) and Bland–Altman analysis (right) for percentage difference in **A** LVEDVi, **B** LVESVi, **C** LVEF and **D** LVMI measured by 3DE and CMR. Correlation between 3DE and CMR to depict changes in left ventricular remodeling at 2 year follow-up

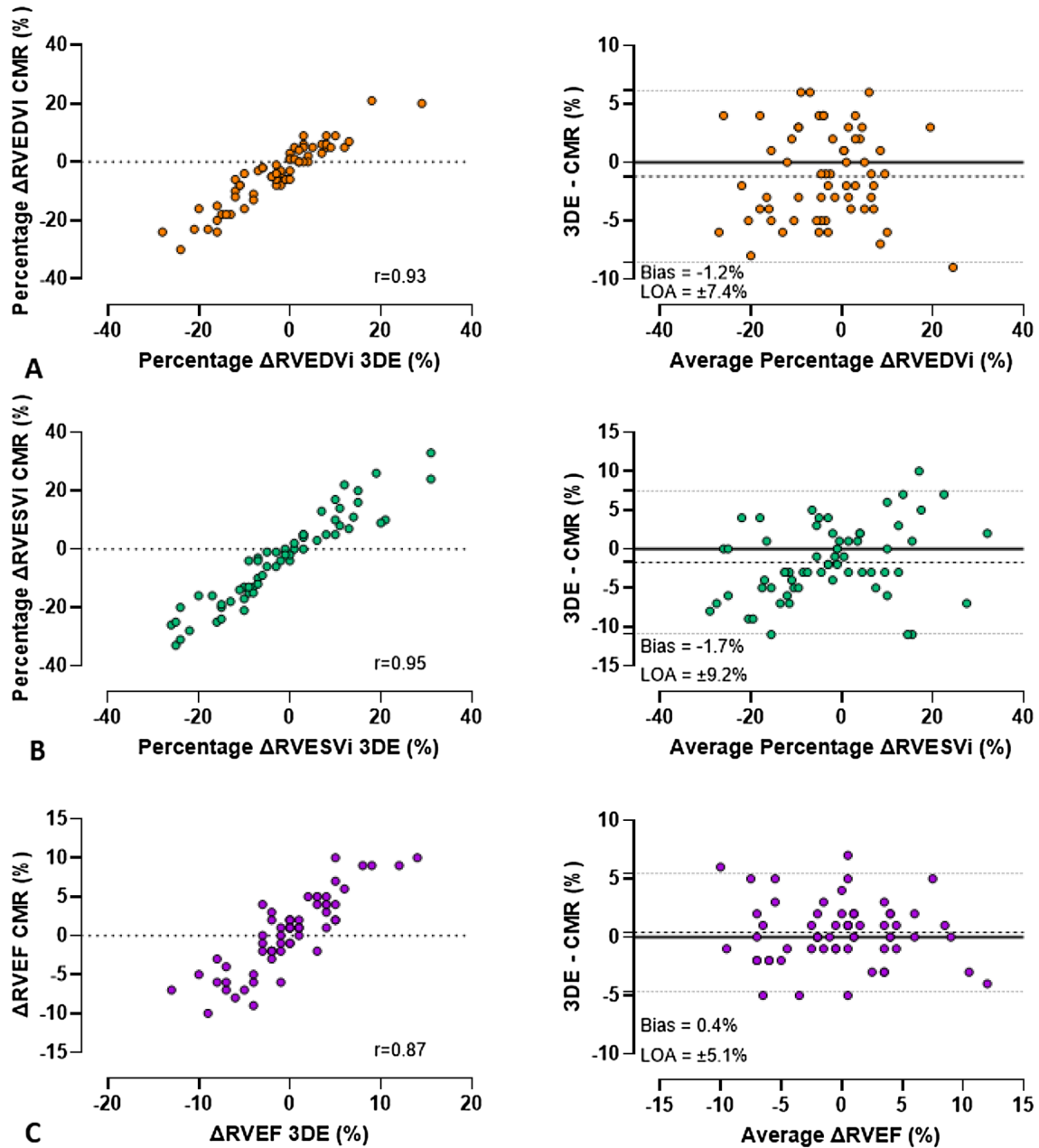


Fig. 4 Linear regression (left) and Bland–Altman analysis (right) for percentage difference in **A** RVEDVi, **B** RVESVi and **C** RVEF measured by 3DE and CMR. Correlation between 3DE and CMR to depict changes in right ventricular remodeling at 2 year follow-up

endurance athletes. The main findings of this study are: (1) biventricular volumes, function and LVM measured by 3DE compare very well with CMR as a reference; (2) although 3DE underestimates biventricular volumes EF measurements remained similar; (3) in prospective follow-up 3DE correlates strongly with CMR, accurately depicting changes in morphology and function; (4) the relative bias of 3DE for volumes increases as the athlete's heart is larger;

The strong correlation between both modalities is in line with other comparative studies in various populations,

including healthy individuals, children, dilated, hypertrophic, arrhythmogenic and ischemic cardiomyopathies, myocarditis, pulmonary hypertension and congenital heart diseases [7–9, 12–16].

Although we reported a negative bias in LV and RV volumes, measurements of EF remained similar between 3DE and CMR. LVEF and RVEF are incorporated in the diagnostic criteria for dilated and arrhythmogenic cardiomyopathy [17–19]. The athlete's heart carries features which overlap with these conditions and in the case of

arrhythmogenic cardiomyopathy, endurance exercise increases the risk of sudden death or may even cause an arrhythmogenic cardiomyopathy-like phenotype known as exercise-induced or gene-elusive arrhythmogenic cardiomyopathy [20–22]. Thus, an accurate measurement of EF in athletes is paramount to help distinguish physiologic adaptations from pathology.

Additionally the agreement between 3DE and CMR was not only strong at a single time point but was also excellent during serial follow-up. Despite slight biases between both imaging modalities, this the first trial to show that 3DE reliably depicts changes in volumes, function and mass in endurance athletes over time. Further positive remodeling, reverse remodeling and potential adverse remodeling, as measured by CMR was accurately detected by 3DE. This of particular importance as the clinical phenotype of cardiac diseases may only become apparent after years of training. Our follow-up analyses strengthen the utility of 3DE in the serial evaluation of the athletes and may alleviate the need for CMR when morphology and EF are the main parameters to follow.

The underestimation of volumes by 3DE is in accordance with previous studies in different populations [9, 23–27]. Several factors may explain this bias. First 3DE has a lower spatial resolution with suboptimal differentiation between the trabeculae and the compact layer of the myocardium leading to less accurate contouring of the endocardial borders. This is illustrated by the improved accuracy and reproducibility in contrast-enhanced 3DE [28, 29] and when default endocardial border thresholds are increased in automated analysis software [30, 31]. In athletes the endocardium of both ventricles can be highly trabeculated, thereby decreasing contouring accuracy [32, 33]. Secondly, the lower frame rate of 3DE may cause undersampling but is likely attenuated by the lower heart rate in endurance athletes. Thirdly, despite high image quality in athletes, suboptimal visualization of certain segments still occurs, particularly at the RV anterior wall and outflow tract which may contribute to lower volumes on 3DE. [34] Finally, stitching artefacts in multi-beat 3DE acquisition may render less accurate volumes. [23, 35–37] A lower heart rate requires a longer breath-hold which may increase the potential for stitching artefacts.

The underestimation of volumes by 3DE increased with cardiac size. Similarly, other studies have reported a larger bias in volumes between 3DE and CMR in more dilated ventricles [27, 38]. A higher relative bias in larger ventricles may be due to some of the following factors: (1) more pronounced trabeculae; (2) a reduced frame rate due to an increased field of view; (3) a larger RVOT, which is challenging to entirely visualize. The latter is supported by recent research demonstrating that the infundibulum of

the RV in athletes presented the highest degree of remodeling [39].

With regard to LVM we observed a slight overestimation by 3DE with wide LOA. Our results oppose the reported underestimation of LVM by 3DE in a meta-analysis by Shimada et al. from 2012, but do reflect the heterogeneity in published data [40]. High heterogeneity and significant underestimation of LVM was seen, particularly in studies published before 2007. The accuracy and homogeneity improved as of 2008 and more recent trials demonstrated a slight overestimation of LVM by 3DE [13, 41]. Furthermore, underestimation of mass was particularly seen in cardiac disease, whereas measurements in healthy volunteers resulted in excellent accuracy [40]. In healthy endurance athletes the superior image quality enables accurate delineation of the epicardial border which along with smaller volumes derived by endocardial contouring would lead to higher LVM measurements. Additionally, in some athletes the higher echo density of the pericardium may cause overestimation of the subepicardial border, thus further increasing LVM.

Discrepancies between 3DE and CMR may also be due to technical differences analysis. 3DE measures volumes from a full-3D-volume dataset and semi-automatic border detection, whereas CMR volumes are obtained from a stack of contiguous short-axis slices obtained at end-diastole and end-systole. Although CMR is considered the gold standard for cardiac morphology and functional analysis, it also has some limitations. Firstly, identifying the border of mitral, tricuspid, pulmonary, aortic valve and endocardium can be challenging. Furthermore through-plane motion, especially at the basal segments, may cause overestimation of volumes [23].

Clinical implications

Accurate and reproducible evaluation of cardiac volumes and EF is essential in endurance athletes to differentiate between physiological exercise-induced remodeling and underlying structural heart disease such as dilated or arrhythmogenic cardiomyopathy. Our data demonstrate that, despite a small bias, 3DE can be used as a reliable modality to assess cardiac volumes and function compared to the gold standard of CMR. Our study also shows that 3DE can accurately assess changes in volumes, function and mass over time, which is essential for early identification of potentially adverse cardiac remodeling. This finding is particularly relevant given the low cost and widespread availability of echocardiography and because routine biannual echocardiography is mandated by several professional sports federations, such as UCI and FIFA, as part of routine pre-participation cardiovascular evaluation. 3DE, superior to 2DE, can therefore serve a valid alternative to CMR in the clinical follow-up of athletes and in large prospective trials in sports cardiology.

Limitations

This study has some limitations. First, as none of the athletes had arrhythmias, our results only apply to athletes in sinus rhythm. 3DE requires four to six consecutive stable heart beats for accurate measurements [42]. However endurance athletes have a higher risk of arrhythmias, particularly atrial fibrillation [43, 44]. Secondly, no exclusions were made based on image quality as all acquisitions were at least of good quality. Thirdly, we used a single vendor ultrasound system for acquisition and analysis. It is known that values of cardiac morphology vary significantly between vendors and analysis software [45]. Therefore, our results may not be extrapolated to other vendors and software packages.

Conclusion

Measurements of LV volumes, function, mass as well as RV volumes and function by 3DE correlate very well with CMR measurements in elite endurance athletes. 3DE accurately identifies morphologic and functional changes of the athlete's heart during longitudinal follow-up with equal accuracy as CMR. 3DE and CMR are not interchangeable given the underestimation of volumes by 3DE, especially with larger cardiac size.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10554-022-02726-5>.

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Data availability The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Conflict of interest The authors have not disclosed any competing interests.

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