Quantifying left atrial structure and function using single-plane tissue-tracking cardiac magnetic resonance

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Purpose: Left atrial (LA) structure and function are important markers of adverse cardiovascular outcomes. Tissue-tracking cardiovascular magnetic resonance (CMR) accurately quantifies LA volume, strain, and strain rate based on biplane long-axis imaging. We aimed to assess the accuracy of the LA indices quantification from single-plane tissue-tracking CMR.

Methods: We included 388 subjects (mean age 57 ± 13, male 70%) whose cine CMR images in sinus rhythm were available in both four-chamber and two-chamber views: 162 patients from the Prospective Observational Study of Implantable Cardioverter-Defibrillators (PROSE-ICD) Study, 208 patients from atrial fibrillation cohort, and 18 healthy volunteers. The group was divided into the training set (n = 291) and the test set (n = 97). In the training set, we compared the LA indices derived from biplane imaging and single-plane imaging (a four-chamber view), and developed regression equations. In the test set, we used the regression equations to estimate the LA indices from the single-plane imaging, and quantified the accuracy of the estimation against the LA indices from the biplane.

Results: In the training set, all the LA indices from the single-plane imaging tended to be systematically underestimated compared with those from the biplane imaging, however, the correlation coefficient was high ($r^2 = 0.73–0.90, p < 0.001$). In the test set, LA volumetric indices showed excellent reproducibility (intra-class correlation coefficient (ICC): 0.91–0.92) with relatively low variability (16.3–22.3%); For LA strain and strain rate indices, reproducibility was excellent (ICC: 0.81–0.93), however, the variability was slightly higher than that of volumetric indices (21.7–25.4%).

Conclusions: LA volumetric indices measured from single-plane tissue-tracking CMR are highly accurate and reproducible with reference to those derived from the standard biplane imaging. The reproducibility of LA strain and strain rate indices from single-plane tissue-tracking CMR is excellent but the variability is higher than that of the volumetric indices.

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1. Introduction

The structure and function of the left atrium are critical predictors of cardiovascular morbidity and mortality. For example, a larger left atrial (LA) size is a predictive marker of cardiovascular events in the general population [1–3], as well as a prognostic marker for patients with heart failure [4,5] and myocardial infarction [6,7]. A larger LA size is also a predictive marker of development of atrial fibrillation (AF) [8,9] and stroke [10]. In addition, a lower LA function is associated with cardiovascular events in the general population [11,12] as well as in patients with preserved left ventricular (LV) systolic function [13].

In routine clinical settings, the LA structure and function are most commonly measured by biplane two-dimensional (2-D) echocardiography using either the biplane area-length method or the biplane modified Simpson’s method [14]. However, echocardiography systematically underestimates the LA volume compared with computed tomography (CT) or cardiovascular magnetic resonance (CMR) [15]. Cardiac CT can measure the LA volume with high accuracy [16], however, its routine use is limited by radiation exposure, iodinated radiopaque contrast, and relatively low temporal resolution. In contrast, CMR provides accurate measurements of LA structure and function with high spatial and temporal resolution without a concern for radiation exposure [17,18].
Tissue-tracking CMR is a novel technique which estimates myocardial motion using cine CMR images for quantitative analysis of cardiac structure and function [19,20]. Recent studies demonstrate the reproducibility and the accuracy of tissue-tracking CMR measurements of LA structure and function, such as LA volume, emptying fraction, strain, and strain rate [21–23], where the LA motion was derived from biplane long-axis views, including four-chamber and two-chamber views. To optimize the workflow in daily clinical practice, single plane quantification of LA function and structure may be sufficient. However, the accuracy of measurements of LA structure and function from a single-plane tissue-tracking CMR is unknown.

The aim of this study was to assess the accuracy of LA structure and function quantification from four-chamber imaging alone using tissue-tracking CMR. We analyzed a prospective cohorts of 388 patients where both four-chamber and two-chamber views are available.

2. Methods

2.1. Study design

The study design is illustrated in Fig. 1. The cohort included three groups: Group 1) patients who underwent CMR before implantable cardioverter-defibrillators (ICD) implantation in the Prospective Observational Study of Implantable Cardioverter-Defibrillators (PROSE-ICD), an observational study of patients with systolic heart failure eligible for a primary prevention ICD; Group 2) patients with drug-refractory AF referred for catheter ablation at the Johns Hopkins Hospital between June 2010 and December 2015 who underwent pre-procedural CMR; and Group 3) healthy volunteers who underwent CMR. All patients underwent CMR during sinus rhythm. The protocol was approved by the institutional review board, and all participants provided informed consent.

For Group 1, the details of the design and baseline characteristics of PROSE-ICD participants were described previously [24]. Among the 1189 participants enrolled in the PROSE-ICD study, 367 patients underwent CMR before ICD implantation to assess cardiac structure and function. In this study, we included 162 patients whose CMR cine images were available in both long-axis four-chamber and two-chamber views. For Group 2, in 335 patients who underwent CMR before AF ablation, 127 patients were excluded because of AF during CMR imaging. Thus 208 patients who underwent AF ablation were analyzed.

We randomly divided the group into two sets for analysis; the training set, consisting of the three-quarters of subjects, and the test set, consisting of the one-quarter of subjects. In the training set we compared the indices of LA structure and function derived from biplane views (both four-chamber and two-chamber views) with the single-plane view (a four-chamber view alone). Based on the comparison we developed equations to estimate the indices of LA structure and function based on the single-plane view alone. In the test set, we then applied these equations to the single-plane imaging (a four-chamber view alone) to estimate the indices of LA structure and function, and quantified the accuracy of the estimated values against the indices derived from biplane views (four-chamber and two-chamber views) as the reference standard.

2.2. Imaging

Details of the CMR protocol were reported previously [25]. Patients were scanned during sinus rhythm with a 1.5-T whole-body scanner, Signa CV/I (General Electric, Milwaukee, USA) or Avanto (Siemens Medical Systems, Erlangen, Germany). Short and long-axis cine images were acquired with a steady-state free precession sequence (TR = 2.5–3.8; TE = 1.1–1.6; flip angle = 45–60°; temporal resolution 35–45 msec; average spatial resolution 1.5 × 2.4 × 8 mm). The images were acquired with 30 frames during the time interval between the R-peak of the ECG (temporal resolution, 20 to 40 ms).

2.3. Left atrial analysis by tissue-tracking CMR

Multimodality Tissue Tracking software (MTT; version 6.0, Toshiba, Japan) was used to obtain phasic LA volumes, strain, and strain rate from four-chamber and two-chamber cine images [26,27]. Briefly, LA endocardial and epicardial borders were manually traced in the biplane images, excluding pulmonary veins and LA appendage (Fig. 2). The software automatically tracks on screen pixels during the cardiac cycle.
software records a characteristic pixel pattern of each 10 × 10 mm² area in the reference frame; an area with identical pixel pattern is recognized in the next frame that maximizes the similarity evaluated by cross-correlation between the square areas. This procedure is repeated for all pixels in each image and for each frame to track the borders throughout the whole cardiac cycle [26]. The operator reviewed all contours generated by the software for quality control.

Maximum LA volume \( (V_{\text{max}}) \), minimum LA volume \( (V_{\text{min}}) \), and pre-atrial contraction LA volume \( (V_{\text{preA}}) \) were measured using the LA volume curve generated by the biplane Simpson's method (Fig. 3A). The calculation was performed as below: 1) sample equally divided into 21 short-axis planes in long-axis four-chamber view and two-chamber view, and then 21 pairs of intersection points was defined in each long axis view \( (a_i \text{ and } b_i, c_i \text{ and } d_i; i = 0, 1, 2, \ldots, 20) \), respectively; 2) in a basal plane, the midpoints of \( a_0b_0 \) and \( c_0d_0 \) are defined as \( O_0 \) and \( M_0 \), respectively. Line \( O_0P \) and \( M_0N \) were defined to be the longest line that passes point \( O_0 \) and \( M_0 \) in counter area, respectively; 3) area of each plane was calculated:

\[
\text{Area}_i = \pi \times \left( \frac{L_a b_i}{2} \times \frac{L_c d_i}{2} \right), i = 0, 1, 2, \ldots, 20
\] (1)

and 4) volume was calculated by compound Simpson formula:

\[
\text{Volume} = \left( \text{Area}_0 + \text{Area}_{20} + \sum_{k=0}^{9} 2\text{Area}_{2k} + \sum_{k=0}^{10} 4\text{Area}_{2k-1} \right) \times \frac{h}{3} \quad (2)
\]

\[
h = \frac{h_2 + h_4}{2}, h_2 = \frac{L_{O_0P}}{20}, h_4 = \frac{L_{M_0N}}{20} \quad (3)
\]

For the LA volume generated from the four-chamber view images alone, we assumed in the Simpson's method that each short axis was a precise circle instead of an ellipse. Area of each plane was calculated:

\[
\text{Area}_i = \pi \times \left( \frac{L_a b_i}{2} \right)^2 \quad (4)
\]

and volume was calculated by Eq. (2) using \( h \) which was defined as the distance between two defined short-axis plane. Although one does not need to use the tissue-tracking CMR to quantify LA volumes, we used it since it provides the contours of the LA endocardial and epicardial borders in each frame of cine CMR. All the LA volumes were indexed by the body surface area (BSA).

![Fig. 2. Tracing of left atrial endocardial and epicardial borders. A. Four-chamber view; and B. two-chamber view. Both A and B indicate the end of left ventricular systole.](image)

![Fig. 3. Left atrial (LA) measurements by tissue-tracking cardiac magnetic resonance (CMR). A. Maximum LA volume \( (V_{\text{max}}) \), minimum LA volume \( (V_{\text{min}}) \), and pre-atrial contraction LA volume \( (V_{\text{preA}}) \) were identified from the LA volume curve. The pink dotted line is the average of the values of volume in the four- and two-chamber views, and green dotted line is in only four-chamber view. B. LA maximum strain \( (S_{\text{max}}) \) and pre-atrial contraction strain \( (S_{\text{preA}}) \) were identified from global longitudinal strain curve. C. LA strain rate in left ventricular (LV) systole \( (SR_s) \), LV early diastole \( (SR_e) \), and LA contraction \( (SR_a) \) were identified from the LA strain curve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)](image)
Global longitudinal strain and strain rate curves were generated by averaging strain and strain rate in all LA segments within either the biplane or the single-plane views. LA maximum strain (Smax) and LA pre-atrial contraction strain (SpreA) were obtained using global longitudinal strain curve (Fig. 3B). LA strain rate in LV systole (SRs), LV early diastole (SRe), and LA contraction (SRa) were measured from longitudinal strain rate curve (Fig. 3C) [28].

2.4. Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) and categorical variables are expressed as frequencies and percentages. To compare groups, we used Pearson’s χ² test for categorical variables and the Student t-test or Mann-Whitney U test for parametric or nonparametric continuous variables, respectively. We used linear regression to compare the indices derived from the biplane and the single-plane imaging. The normality of residuals from the linear regression models was assessed via standardized normal probability plots as well as by plotting the quantiles of a variable against the quantiles of a normal distribution showing no deviation from normality in the middle range of data as well as near the tails. Skewed plots of residual versus fitted values from regression models did not indicate a discernible pattern or heteroscedasticity in residuals, suggesting that no important deviations from linear model assumptions had occurred. We calculated bias (mean difference) and the 95% limits of agreement (1.96 SD around the mean difference) between the two methods to measure each LA index according to Bland and Altman [29]. We calculated coefficients of variation (CV) as the SD of the differences divided by the mean. We used a one-sample t-test with two-sided alternative to determine whether the resulting mean difference was significant from zero. Moreover, we assessed the intra-class correlation coefficient (ICC) to evaluate the accuracy and the precision of the method to measure each index from the single-plane imaging compared with the biplane imaging. ICC was scored as follows: poor agreement, ICC < 0.40; fair to good, ICC 0.40–0.75, and excellent, ICC > 0.75 [30]. We used JMP® Version 11 (SAS Institute Inc., Cary, NC, USA) to perform all statistical analyses. A difference with a p value of <0.05 was considered significant.

3. Results

3.1. Patient characteristics

The final analysis (n = 388, mean age 57±13, male 70%) was performed in 162 patients of PROSE-ICD, 208 patients who underwent AF ablation, and 18 healthy volunteers. The training and test set included 291 and 97 patients, respectively. The patient characteristics are shown in Table 1. There was significant deference in sex between the training set and the test set (male; 74% vs 59%, p = 0.01). There was no significant difference between two sets in the other parameters compared, including age (57.4 ± 13.2 vs 57.6 ± 12.3 years, p = 0.92), history of AF (62 vs 60%, p = 0.81), left ventricular ejection fraction (LVEF; 45.2 ± 11.0 vs. 47.8 ± 16.5%, p = 0.20), and co-morbidities.

### Table 1

Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Training set</th>
<th>Test set</th>
<th>p</th>
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<tr>
<td>Age, years</td>
<td>57.4 ± 13.2</td>
<td>57.3 ± 12.3</td>
<td>0.92</td>
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<tr>
<td>Male</td>
<td>214 (74)</td>
<td>57 (59)</td>
<td>0.01</td>
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<td>Heart failure</td>
<td>143 (49)</td>
<td>41 (42)</td>
<td></td>
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<tr>
<td>Coronary artery disease</td>
<td>76 (26)</td>
<td>19 (20)</td>
<td>0.29</td>
</tr>
<tr>
<td>History of atrial fibrillation</td>
<td>180 (62)</td>
<td>58 (60)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hypertension</td>
<td>142 (49)</td>
<td>48 (49)</td>
<td>0.91</td>
</tr>
<tr>
<td>Diabetes</td>
<td>59 (20)</td>
<td>18 (19)</td>
<td>0.83</td>
</tr>
<tr>
<td>LV EF, %</td>
<td>45.2 ± 17.8</td>
<td>47.8 ± 16.5</td>
<td>0.20</td>
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<tr>
<td>Medication</td>
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<tr>
<td>ACE-I/ARB</td>
<td>155 (53)</td>
<td>50 (52)</td>
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<tr>
<td>Beta-blocker</td>
<td>189 (65)</td>
<td>58 (60)</td>
<td>0.43</td>
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<tr>
<td>Statin</td>
<td>163 (56)</td>
<td>49 (51)</td>
<td>0.41</td>
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<tr>
<td>Antiarrhythmic drugs</td>
<td>0.7 ± 0.8</td>
<td>0.8 ± 0.9</td>
<td>0.48</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation or n (%). Abbreviations: ACE-I/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers; EF, ejection fraction; LV, left ventricle.

3.2. Training set

Fig. 4 shows the correlation between each LA index derived from the single-plane (x-axis; a four-chamber view alone) and the biplane imaging (y-axis; both four-chamber and two-chamber views). The correlation coefficient was high between the single-plane and the biplane imaging for LA volumetric indices (r² = 0.90 for Vlmax, r² = 0.89 for Vlmin and r² = 0.86 for VlpreA for all p ≤ 0.001) (Fig. 4A–C), but not high for LA strain indices (r² = 0.83 for Smax, and r² = 0.78 for LA SpreA all p ≤ 0.001) (Fig. 4D–E), and for LA strain rate indices (r² = 0.73 for SRs, r² = 0.87 for SRe, and r² = 0.74 for SRa all p ≤ 0.001) (Fig. 4F–H). Bland-Altman plot analyses between the single-plane and the biplane imaging are shown in Fig. 5. The indices including VlpreA, Smax, SpreA, SRe, and SRa from the single-plane imaging were systematically underestimated compared with those from the biplane imaging (all p ≤ 0.05).

3.3. Test set

We used the regression equations derived from the training set to estimate the LA indices from the single-plane imaging in the test set. Bland-Altman plot analyses between the estimated indices from the single-plane imaging and the measured indices from the biplane imaging are shown in Fig. 6. There was no significant difference in the mean difference from zero for all the LA indices between the single-plane and biplane imaging, and 94.7 ± 0.02% of measurements were within 95% limits of agreement in Bland-Altman analysis. The mean differences ± 1.96 SD (Bland-Altman analysis), ICC, and CV for all the LA indices are summarized in Table 2. The inter-study reproducibility was excellent for LA volumetric indices with relatively low variability; Vlmax (ICC 0.91, CV 16.3%), Vlmin (ICC 0.91, CV 22.3%), and VlpreA (ICC 0.92, CV 16.8%). Reproducibility was excellent for LA strain and strain rate indices, however, the variability was slightly higher than that of LA volumetric indices; LA Smax (ICC 0.87, CV 19.1%), SpreA (ICC 0.87, CV 23.7%), SRs (ICC 0.81, CV 25.0%), SRe (ICC 0.93, CV 21.7%), and SRa (ICC 0.86, CV 25.4%).

4. Discussion

4.1. Main findings

First, we found that LA volumetric indices derived from the single-plane imaging were highly correlated with indices measured by a standard method using the biplane imaging, with high reproducibility and low variability. Second, we found that LA strain and strain rate indices derived from the single-plane imaging were also highly correlated with indices measured by the standard method. The level of reproducibility was excellent, equivalent to that of LA volumetric indices; however, the variability was higher than that of LA volumetric indices.

4.2. LA volume

Since larger LA volumes predict adverse cardiovascular events and development of AF [1–9], accurate LA volume quantification have become increasingly important in routine clinical settings. The American Society of Echocardiography guidelines recommend the quantification of LA volume by 2-D echocardiography using either the biplane area-length method or the biplane modified Simpson’s method [14]. Previous
Fig. 4. Linear regression analysis of indices of left atrial (LA) structure and function in the training set (n = 291). The x-axis indicates the single-plane imaging (four-chamber view alone) and the y-axis indicates the biplane imaging (four-chamber and two-chamber views). The red dotted lines represent the 95% prediction intervals. A. LA maximum indexed volume (VImax); B. LA minimum indexed volume (VImin); C. LA pre-atrial contraction indexed volume (VIpream); D. LA maximum strain (Smax); E. LA pre-atrial contraction strain (Spream); F. LA strain rate during LV systole (SRs); G. LA strain rate during LV early diastole (SRe); H. LA strain rate at LA contraction (SRa). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Echocardiographic studies report that LA volumetric measurements between the single-plane area-length method and the biplane modified Simpson’s method are highly correlated[31]. Therefore, quantification of the LA volumes from single-plane imaging may have a role in clinical settings as a simpler yet accurate method. However, echocardiography often cannot visualize the LA borders due to the limitation in

**Fig. 5.** The Bland-Altman plots in the training set (n = 291). The y-axis indicates the difference between the value from bi-plane imaging and that from single-plane imaging. The red dotted lines represent the 95% confidence intervals and the blue dot lines represent limits of agreement (mean ± 1.96 SD). All indices were systematically underestimated in the single-plane imaging compared to the biplane imaging. A. LA maximum indexed volume (VI_max); B. LA minimum indexed volume (VI_min); C. LA pre-atrial contraction indexed volume (VI_preA); D. LA maximum strain (S_max); E. LA pre-atrial contraction strain (S_preA); F. LA strain rate in left ventricular (LV) systole (SR_s); G. LA strain rate in LV early diastole (SR_e); H. LA strain rate in LA contraction (SR_a). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Echocardiographic views. This limitation dampens the reliability of echocardiography as a clinical tool for LA volume assessment.

Tissue-tracking CMR using biplane imaging can quantify LA volumes accurately, and yet requires only a fraction of time for analysis compared with the Simpson’s method, the gold standard for assessment of LA volumes by CMR [22]. In addition, the biplane tissue-tracking CMR obviates the need for acquiring contiguous short-axis slices to cover the entire left atrium that is required for the Simpson’s method [32].
CI, conduce the time for both the image acquisition and off-line analysis more practical and feasible in clinical settings because it reduces the time required for both the image acquisition and off-line analysis. Our results indicate that a single-plane tissue-tracking CMR can further reduce the time for both the image acquisition and off-line analysis while maintaining the accuracy of LA volume measurements. This result is supported by the past paper that LA volumes quantified by the single plane area-length method based on a four-chamber view is highly correlated with those quantified by the 3-D reconstruction technique using multi-slice CT imaging [33]. Our findings may allow incorporation of accurate LA volume measurements based on four-chamber view imaging alone in routine clinical CMR.

4.3. LA strain analysis

The gold standard method for strain analysis by CMR is tagged MRI [34]. However, the time required for tagged MR image acquisition and off-line is so long that it is clinically impractical. Recent studies report a high accuracy and reproducibility of tissue-tracking CMR in LA strain and strain rate measurements [21–23]. Lower LA strain and strain rate measured by tissue-tracking CMR are associated with LA myocardial fibrosis [26,35], stroke/transient ischemic attack in patients with AF [28], and development of heart failure [27]. In this study, although the reproducibility of the LA strain indices was excellent, their correlation between the bi-plane and the single-plane approaches were not as high as that of volumetric indices. This result suggests that LA regional function is heterogeneous, and, in contrast to volumetric indices, it is not straightforward to estimate LA regional function by a single-plane approach alone.

One potential explanation to account for the relatively high variability in measurements between the single-plane and the biplane imaging is intrinsic regional heterogeneity in LA mechanical function. Kuklik et al. reported a greater mechanical function in the anterior, septal and lateral segments of the left atrium compared with the roof and the posterior segments [36]. Another potential explanation is a lower reproducibility of LA strain and strain rate derived from the four-chamber images than those from the two-chamber images [21]. This is most likely a consequence of the general lower reproducibility of the four-chamber view, which can be heavily affected by insufficient breath holdings as compared to the two-chamber view [21].

4.4. Limitations

We compared the single-plane approach with the bi-plane tissue-tracking CMR, instead of the gold standard such as the Simpson method for LA volume and/or tagged MRI method for strain calculation. However, recent studies demonstrate the accuracy and reproducibility of biplane tissue-tracking CMR compared to the gold standard [21–23]. Therefore, our results suggest that volumetric measurements calculated from 4-chamber images using tissue-tracking CMR is a simpler, accurate and reproducible tool for quantifying the LA volumes.

Although the cohort included patients with preserved and low EF, there remains a possibility of selection bias and it is unclear to what extent the results can be extrapolated to the general population. However, the mean LA \( V_{\text{max}} \) of 90.3 ± 36.2 ml (median; 83.6 ml [25th–75th percentile: 65.6–107.9]) and mean \( V_{\text{min}} \) of 55.1 ± 34.7 ml (median; 46.4 ml [25th–75th percentile: 33.3–65.2]) in this study are similar to those (97 ± 27 ml, 44 ± 13, respectively) in Hudsmith et al. [32] who reported normal values of LA structure and function. This finding suggests that our samples included individuals with normal LA size. A further investigation in a larger cohort including a wider spectrum of conditions will confirm our speculation. Finally, the quality of LA tissue-tracking could have been affected by the image quality, anatomy and slice orientation. In particular, the single-plane approach may be more operator-dependent than the bi-plane approach. For example, non-standard slice orientations, adjacent structures such as pulmonary veins, the LA appendage, and the aorta, could have contributed to errors in tissue tracking. Nevertheless, our results confirmed high reproducibility of the measurements by single-plane imaging, and demonstrate an excellent correlation in LA volumetric indices between the single-plane and the biplane imaging.

5. Conclusions

LA volumetric indices measured from single-plane tissue-tracking CMR are highly accurate and reproducible with reference to those derived from the standard biplane imaging. The reproducibility of LA strain and strain rate indices from single-plane tissue-tracking CMR is excellent but the variability is higher than that of the volumetric indices.

Competing interests

No authors declare any competing interests.

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