Assessment of left atrial volume and function in patients with permanent atrial fibrillation: comparison of cardiac magnetic resonance imaging, 320-slice multi-detector computed tomography, and transthoracic echocardiography

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Aims
Atrial fibrillation (AF) is a common cardiac arrhythmia that is associated with substantial morbidity and mortality. AF is associated with enlargement of the left atrium (LA), and the LA volume has important prognostic implications for the disease. The objective of the study was to determine how measurements of LA volume and function obtained by transthoracic echocardiography (TTE), cardiac magnetic resonance (CMR), and 320-slice multi-detector computed tomography (MDCT) correlate in patients with permanent AF.

Methods and results
Thirty-four patients with permanent AF participated in the study. TTE, CMR, and 320-slice MDCT imaging procedures were performed within 7 + 4 days. 320-slice MDCT overestimated maximal LA volume (LAmax) and minimal LA volume (LAmi) compared with CMR (LAmax: 80 vs. 73 mL/m², P = 0.0017; LAmi: 69 vs. 64 mL/m², P = 0.0217), whereas TTE underestimated these parameters compared with CMR (LAmax: 60 vs. 73 mL/m², P < 0.0001; LAmi: 50 vs. 64 mL/m², P < 0.0001), and also compared with MDCT (LAmax: 60 vs. 80 mL/m², P < 0.0001; LAmi: 50 vs. 69 mL/m², P < 0.0001). Measurements of LA volumes by MDCT and CMR closely correlated, and both MDCT and CMR had excellent intra- and inter-observer agreement with correlation coefficients of > 0.90. The correlation between TTE-derived measurements and CMR/MDCT was fair to moderate. Intra- and inter-observer agreement for LA volume measurements by TTE were inferior to CMR and MDCT.

Conclusion
Measurements of LA volumes by CMR and 320-slice MDCT correlate closely in patients with permanent AF, and both modalities improve the reproducibility of measurements of LA volumes and function compared with 2D TTE.

Keywords
atrial fibrillation • cardiac magnetic resonance • transthoracic echocardiography • multi-detector computed tomography • left atrial volume • left atrial function

Introduction
Atrial fibrillation (AF) is an increasingly common cardiac arrhythmia that is associated with substantial morbidity and mortality. AF is associated with enlargement of the left atrium (LA), and there is strong evidence that LA enlargement is an important risk factor for the development of AF. In patients with a diagnosis of AF, an increased LA volume is associated with a risk of AF relapse after electrical cardioversion and with a risk of AF recurrence after catheter ablation. Transthoracic echocardiography (TTE) is the most...
frequently used method for the assessment of LA volumes.9 Regardless, in patients without arrhythmia, cardiac magnetic resonance imaging (CMR) imaging is considered the gold standard for measurements of cardiac chamber volumes.13,14 CMR has been shown to be highly reproducible for measurements of LA dimensions both in healthy subjects and in patients with AF.9,15 In patients without arrhythmia, TTE significantly underestimates the LA volume compared with CMR.16 Due to technical advances during the last decade, cardiac multi-detector computed tomography (MDCT) now also offers a feasible alternative for cardiac imaging in patients with an irregular heart rate, since one of the most recent MDCT techniques, 320-slice MDCT, allows for image acquisition of the heart within a single heartbeat.17 LA volume measurements by CMR and MDCT are more reproducible than TTE in patients without arrhythmia and seem to provide incremental prognostic information of the LA.18,19 Due to the important clinical implications of the LA volume, the rising prevalence of AF, and the fact that CMR and MDCT are becoming more widely available, it is important to determine how measurements of LA volumes obtained by the different non-invasive methods correlate in patients with AF. The objective of our study was to evaluate the correlation between measurements of LA volume and function obtained by TTE, CMR, and 320-slice MDCT in patients with permanent AF and to assess the reproducibility of the modalities.

Methods

Materials

Between August 2009 and July 2011, 40 patients were included in the study from the Outpatient Clinic of the Department of Cardiology, Hvidovre University Hospital, Copenhagen, Denmark.

Inclusion criteria were ECG-documented sustained AF and ability to provide written informed consent, as well as a documented decision not to attempt cardioversion. The exclusion criteria included severe renal disease (S-creatinine > 125 μm/L), severe pulmonary disease, and contraindications to CMR (i.e. pacemaker, non-compatible bimetallic implants, and known claustrophobia). The patients underwent CMR (1.5 or 3.0 T), 320-slice MDCT, and TTE.

Main characteristics of the three applied methods are given in Table 1. Patient examples of imaging by the three modalities are given in Figure 1.

A written informed consent was obtained from all subjects before enrolment in the study. Approval from the local research ethics committee was obtained before the study was initiated. The study was conducted in accordance with the Declaration of Helsinki.

Cardiac magnetic resonance imaging

CMR was performed using steady-state free precession (SSFP) sequences (Siemens TrueFISP sequences; Siemens Magnetom Avanto 1.5 T or Trio 3.0 T; Siemens, Erlangen, Germany). Cardiac synergy coils were used for radio-frequency signal reception. Imaging was performed with the patient in the supine position with retrospective ECG-gating. Twenty-five phases were used for radio-frequency signal reception. Imaging was performed with the patient in the supine position with retrospective ECG-gating. Twenty-five phases were used for radio-frequency signal reception. Imaging was performed with the patient in the supine position with retrospective ECG-gating.

Image analysis

LA volumes were assessed offline using the commercially available semiautomatic software Argus (Siemens Medical Solutions, Erlangen, Germany). LA volumes were measured by the standard SA method, with the largest LA dimension and minimal LA volume (Lamin) as the phase with the smallest LA dimension. Manual tracing of the endocardial borders of successive slices was performed from the apex of the LA to the atroventricular junction in LAmax and Lamin. At the base of the LA, slices were considered to be in the atrium if the blood was less than half surrounded by the ventricular myocardium. The first slice that with certainty was located in the LA was considered reference for the visual definition of LAmax and Lamin. LAmax and Lamin were calculated from the sums of the outlined areas using a modification of Simpson’s rule.20 The left atrial appendage (LAA) was included in the LA volume, whereas pulmonary veins were carefully excluded at their ostia. LA fractional change (FC) was calculated from the formula: FC = (LAmax – Lamin)/LAmax × 100%. Analysis time was ~25 min.

Multi-detector computed tomography

Retrospective ECG-gated, contrast-enhanced 320-slice MDCT, using 0.5 × 320 mm detector collimation, tube voltage of 120 kV and a tube current between 450 and 550 mA (depending on body mass), was performed recording images of the entire cardiac cycle (Aquilion One, Toshiba Medical, Tochigi, Japan). The scanning procedure was conducted with the subject in the supine position. A dose of 70 or 100 mL of intravenous contrast agent (Visipaque 320, GE Healthcare) was infused (flow rate 5 mL/s). Patients with a heart rate of >70 bpm were given
50–100 mg metoprolol succinate orally 1 h prior to the imaging procedure unless contraindicated. Nitroglycerine was administered sublingually prior to the scanning procedure. Real-time beat control technology with arrhythmia rejection was used to monitor the heart rate. Heart beats lasting <80% of the ‘standard heart rate’ were rejected. The ‘standard heart rate’ was calculated as the average of the prior five normal beats. The imaging procedure lasted ~20 min. Radiation dose averaged 18.5 mSv.

**Image analysis**

MDCT images were reconstructed in 5% intervals of the RR interval. In each phase, the LA volume was measured by automatic tracing of the endocardial contours and subsequent manual correction. The software (Vitrea 6.0, Vital Imaging Inc.) calculated a time–volume curve, where LAmax and LAmín were determined from the maximal and minimal peaks on the curve, respectively. LA FC was calculated from the formula: $FC = (\text{LAmax} - \text{LAmín})/\text{LAmax} \times 100\%$. The LAA was
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...included in the LA volume, while pulmonary veins were carefully excluded at their ostia. Analysis time was ~10 min.

**Transthoracic echocardiography**

All patients underwent 2D TTE (Philips i-E33, Philips Medical Systems, Andover, MA, USA) with simultaneous ECG recording. Imaging was conducted according to the guidelines from the American Society of Echocardiography (ASE). Images in standard parasternal and apical views were obtained with the patients in the left lateral decubitus position. Approximately 10 beats were recorded in each view. The TTE imaging procedure lasted ~30 min.

**Image analysis**

Images were analysed offline using the commercially available software (Xcelera, Philips Health Care, Andover, MA, USA). In order to assess LAmax and Lamin from a representative cardiac cycle, the beat following two cardiac cycles with an equal or nearly equal RR interval was chosen for analysis, since this approach of selecting an ‘index beat’ following two equal preceding cardiac cycles has previously been validated in patients with persistent and permanent AF. LAmax was defined visually as the frame just prior to mitral valve opening on the four-chamber view and Lamin as the frame just after mitral valve closure. LA endocardial contours were manually traced at LAmax and Lamin in the apical four- and two-chamber views. LA volumes were assessed using the modified Simpson’s method and calculated as the average of the measurements from the apical four- and two-chamber views. LA FC was calculated from the formula: $FC = (LAMax - Lamin) / LAMax \times 100%$. Analysis time was ~2 min.

**Statistical analysis**

All examined parameters of atrial volumes and function were found to be normally distributed using the Kolmogorov–Smirnov test. Summary data for continuous variables are presented as mean ± standard deviation (SD). Categorical variables are reported numerically and as percentages. As comparisons of LA volume measurements by the three methods have not previously been performed in patients with permanent AF, sample size calculations had to be based on the assumption that the relationships between measurements by the three different methods would be similar to previously observed results in patients with sinus rhythm. Since the primary hypothesis was that CMR and MDCT would provide equivalent results, sample size calculations were performed by a test of equivalence, where non-equivalence was taken to be the null hypothesis and equivalence was considered the alternative hypothesis. Rejection of the null hypothesis would thus indicate equivalence, meaning that results obtained by the three methods are not statistically significant, whereas omission of a correction could, in fact, reveal statistically significant differences. Measurements and analyses for all three modalities were performed by the same investigator with a time interval of ~1 month between measurements by the different modalities. The correlations between CMR/MDCT, CMR/TTE, and MDCT/TTE were determined by calculating Pearson’s correlation coefficients ($r$). In addition, bias and limits of agreement (LoA) were assessed by Bland–Altman analyses. Pearson’s correlation coefficients and Bland-Altman analyses were also used to evaluate the reproducibility of the three methods. Intra-observer variability was assessed by the same investigator repeating measurements of LAmax and Lamin, and inter-observer variability was assessed by another investigator, who performed additional measurements of LAmax and Lamin. For CMR, intra- and inter-observer agreement were evaluated by repeating measurements in 20 patients. For MDCT and TTE, intra- and inter-observer agreement were evaluated by repeating measurements in 30 patients. Statistical analyses were performed using the Statistical Analysis System (SAS 9.3, SAS Institute, Inc., Cary, NC, USA). A two-sided $P$-value of <0.05 was considered significant.

**Results**

A total of 40 patients were enrolled in the study. Of these, six had to be excluded during the study due to issues related to CMR: three were excluded due to claustrophobia during CMR and one due to obesity that prevented conduction of CMR. Another two patients were excluded due to insufficient image quality of the recorded CMR images (one of these patients was scanned with 1.5 T and the other with 3.0 T). Patient characteristics of the remaining 34 patients are given in Table 2. Furthermore, two patients did not have MDCT performed due to unexpectedly high S-creatinine prior to the MDCT procedure. For this reason, the comparison of measurements obtained by CMR and TTE was evaluated in 34 patients, whereas the

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**Table 2 Patient characteristics**

<table>
<thead>
<tr>
<th>Permanent atrial fibrillation ($N = 34$)</th>
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<tr>
<td>Sex, male, % ($n$)</td>
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<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Duration of AF (years)</td>
</tr>
<tr>
<td>Body surface area ($m^2$)</td>
</tr>
<tr>
<td>Hypertension, % ($n$)</td>
</tr>
<tr>
<td>Diabetes, % ($n$)</td>
</tr>
<tr>
<td>Reduced LV systolic function ($LVEF &lt; 45%$), % ($n$)</td>
</tr>
<tr>
<td>Previous stroke or TCI, % ($n$)</td>
</tr>
<tr>
<td>Ischaemic heart disease, % ($n$)</td>
</tr>
<tr>
<td>Prior PCI, % ($n$)</td>
</tr>
<tr>
<td>Baseline medication</td>
</tr>
<tr>
<td>$\beta$-blocker, % ($n$)</td>
</tr>
<tr>
<td>Digoxin, % ($n$)</td>
</tr>
<tr>
<td>ACEi or ARB, % ($n$)</td>
</tr>
<tr>
<td>Oral anticoagulants, % ($n$)</td>
</tr>
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</table>

Data are presented as mean ± SD or as % ($n$) unless otherwise stated.

LVEF, left ventricular ejection fraction; TCI, transitory cerebral ischaemia; PCI, percutaneous coronary intervention; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.
comparision between MDCT and the other modalities was evaluated in 32 patients. The patients had CMR, MDCT, and TTE performed within 7 ± 4 days. The average heart rate during the scanning procedures was 80 ± 14, 69 ± 14, and 79 ± 11 bpm for CMR, MDCT and TTE, respectively (CMR vs. MDCT: \( P = 0.021 \); CMR vs. TTE: \( P = 0.77 \), and MDCT vs. TTE: \( P = 0.025 \)). Table 3 summarizes LA volumes obtained by the three imaging techniques.

Intra- and inter-observer agreement of measurements performed by CMR, MDCT, and TTE are summarized in Tables 4 and 5.

Compared with CMR, 320-slice MDCT significantly overestimated LAmax by 10% and LAMin by 8%, whereas TTE significantly underestimated LAmax by 18% and LAMin by 22%. Compared with MDCT, TTE underestimated LAmax by 25% and LAMin by 28%. With respect to LA function, TTE significantly overestimated LA FC by 23% compared with CMR, whereas 320-slice MDCT overestimated LA FC by 8% compared with CMR. TTE also overestimated LA FC by 14% compared with MDCT. There was no clear pattern of clinical characteristics responsible for the difference of LA volume measurements between the methods, indicating that the differences were related to intrinsic properties of the methods and not to clinical characteristics.

Pearson’s correlations and Bland–Altman plots are shown in Figures 2–4 for the comparisons of CMR/MDCT, CMR/TTE, and MDCT/TTE, respectively. 320-slice MDCT had a good positive correlation with CMR for volumetric data (\( r = 0.85 \) and \( r = 0.83 \) for LAmax and LAMin, respectively, \( P < 0.0001 \)), whereas the correlation of measurements of LA FC was weaker (\( r = 0.56, P < 0.001 \)). For measurements obtained by CMR and TTE, the correlation was fair to moderate for volumetric data (\( r = 0.59 \) for LAmax and \( r = 0.59 \) for LAMin, \( P < 0.001 \)). For LA FC, the correlation was poor (\( r = 0.34, P < 0.05 \)). Similar findings were observed when TTE and MDCT were compared (\( r = 0.55 \) for LAmax, \( r = 0.55 \) for LAMin, and \( r = 0.47 \) for LA FC, \( P < 0.01 \)). Correlation coefficients, bias, and LoA between the methods are summarized in Table 6.

**Discussion**

Our data showed that 320-slice MDCT overestimated LAMax and LAMin compared with CMR in patients with permanent AF, whereas TTE significantly underestimated these parameters compared with CMR and MDCT. However, despite the presence of AF, there was a good correlation between measurements of LAFC and LAMin measured by CMR and MDCT. For measurements of LA volumes obtained by TTE and CMR/MDCT, the correlations were fair to moderate. A better correlation was found for the measurements of volume than of function in all comparisons. Intra- and inter-observer agreement between measurements of LA volumes were excellent for CMR and MDCT, with correlation coefficients of >0.90. Intra- and inter-observer agreement for LA volume measurements by TTE were inferior to CMR and MDCT.

To our knowledge, it has not previously been attempted to compare measurements of LA volumes obtained by CMR, 320-slice MDCT, and TTE in patients with permanent AF. It has, therefore, been uncertain whether comparisons of measurements by these fundamentally different imaging modalities would yield results comparable with previously obtained measurements in patients without arrhythmia. The severe LA enlargement often observed in patients with permanent AF could potentially interfere with the measurements. Furthermore, properties inherent to the way images are acquired and analysed by the different modalities might render the comparison of the modalities invalid in patients with an irregular RR interval. MDCT images of the whole heart, for instance, were acquired in a single heartbeat, whereas CMR images had to be acquired from an average of 12 heart beats per slice. In

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**Table 3** Comparison between LA volume and function by CMR, 320-slice MDCT, and TTE

<table>
<thead>
<tr>
<th>CMR</th>
<th>MDCT</th>
<th>TTE</th>
<th>P CMR vs. MDCT</th>
<th>P CMR vs. TTE</th>
<th>P MDCT vs. TTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAmax (mL/m²)</td>
<td>73 ± 16</td>
<td>80 ± 16</td>
<td>0.0017</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LAMin (mL/m²)</td>
<td>64 ± 15</td>
<td>69 ± 15</td>
<td>0.0217</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fractional change (%)</td>
<td>13 ± 4</td>
<td>14 ± 5</td>
<td>0.0917</td>
<td>0.0054</td>
<td>0.0939</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

**Table 4** Intra-observer reproducibility of LAmax and LAMin

<table>
<thead>
<tr>
<th>CMR</th>
<th>MDCT</th>
<th>TTE</th>
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</thead>
<tbody>
<tr>
<td>r</td>
<td>Mean difference ± SD</td>
<td>r</td>
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<tr>
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<tr>
<td>LAMax</td>
<td>0.96*</td>
<td>2.9 ± 5.8 mL/m²</td>
</tr>
<tr>
<td>LAMin</td>
<td>0.96*</td>
<td>2.3 ± 4.6 mL/m²</td>
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</tbody>
</table>

*\( P < 0.0001 \).
†\( P < 0.001 \).
addition, the different strategies applied to select appropriate frames by the three methods could lead to inconsistencies in the selection of frames corresponding to LAmax and LAmin, which could potentially complicate comparisons across methods. For CMR, the selection of frames was based on visual LA appearance, and the definition of LAmax and LAmin on the short-axis CMR images was, in most cases, not straightforward and needed very careful examination. For MDCT, definition of LAmax and LAmin relied on proper identification of maximal and minimal peaks on the LA time–volume curve, and for TTE, on timing of mitral valve closure/opening. In addition, analysis of TTE images required the investigator to individually select appropriate beats for analysis. Moreover, differences in spatial and temporal resolution between modalities and utilization of different software packages for quantification could result in divergent measurements.

Nevertheless, in spite of all these impediments, our findings regarding LA volumes are consistent with previous data from patients without arrhythmias, with the exception that the patients with AF in our study had substantially larger LA volumes than previously reported normal values.

Our data show that measurements of LA volumes by CMR and MDCT are feasible in patients with permanent AF, and that the reproducibility of the two methods is superior to that of TTE-derived measurements. This is useful information, since the three imaging modalities are normally used for different clinical purposes. TTE provides readily available, first-line assessment of cardiac anatomy and pathophysiology, whereas CMR and 320-slice MDCT so far have been of limited availability. Both CMR and MDCT, however, are currently becoming more widely available to the clinician. CMR is increasingly gaining importance in the diagnosis of various structural cardiac diseases and is considered an accurate method for measuring myocardial infarction size in patients with acute and chronic myocardial infarction. MDCT yields important information about the coronary arteries, and the key feature of this technique is the ability...
to exclude the presence of obstructive coronary artery disease in patients with chest pain. For routine assessment in the daily clinical practice, a fair estimate of LA volume and function provided by TTE may be considered sufficient in most patients with AF. The improved reproducibility that CMR and 320-MDCT offer is of particular interest under circumstances, where a high level of consistency of the measurements is desirable; e.g., for serial measurements during follow-up over time. In patients not suspected of coronary
artery disease, CMR would be the method of choice, since this modality is not associated with radiation.

Limitations

A relatively small number of patients were examined, and therefore, the study does not allow for any definite conclusions. The included patients were almost all on routine beta-blocker treatment, and as a result, the average heart rate during all scanning procedures was relatively low considering the presence of the arrhythmia. Accordingly, the results may not necessarily apply to patients with a higher and more erratic heart rate, as, for example, could be the case in patients with newly diagnosed AF.

With respect to CMR, patients were scanned using two different scanners with different field strengths. Nineteen patients were scanned using the Siemens Magnetom Avanto 1.5 T scanner, and 15 were scanned using the Siemens Magnetom Trio 3.0 T scanner. It has previously been established that field strength itself has no effect on assessment of LA volume and function, therefore, the use of two different scanners does not appear to be a major limitation. However, 3.0 T may produce more artefacts than 1.5 T, and we cannot exclude the possibility that the use of two scanners with different spatial resolution might have affected the measurements. With respect to MDCT, 70–100 mL of contrast media was infused during image acquisition followed by a saline chaser. This may have contributed to the divergent measurements, as this procedure may produce a transient increase of preload. Also, the MDCT-protocol dictated that metoprolol succinate should be given if the heart rate was >70 bpm in order to optimize image quality, and for this reason, the patients had a significantly lower heart rate during MDCT than during CMR and TTE, which may have resulted in LA volume changes. The observed differences between modalities may also in part be attributed to differences in delineation of the pulmonary veins between the methods, differences in temporal and spatial resolution, use of different software packages for quantification by the different modalities, and different conventions of LA volume measurements. According to clinical imaging standards, the LAA was included in the LA volume by MDCT and CMR, but not by TTE. Since there is significant heterogeneity in LAA size and dimensions among patients with AF, this distinction could explain some of the difference between TTE and CMR/MDCT.

Comparison between CMR and MDCT with real-time 3D TTE would have been desirable in order to get a more comprehensive evaluation of the TTE technique. Unfortunately, 3D TTE was not available in our institution at the time the study was carried out.

Finally, the comparison of parameters of LA function by the three different modalities has to be interpreted with caution, since the patients in the study had severely enlarged atria with little contractile function and beat-to-beat variations inevitable occurred due to the irregularity of the RR interval.

Conclusion

Measurements of LA volumes by CMR and 320-slice MDCT closely correlate in patients with permanent AF, and both modalities improve the reproducibility of measurements of LA volumes and function compared with 2D TTE.

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Conflict of interest: None declared.

References


Table 6 Pearson’s correlation coefficients, bias, and LoA for the comparison of LAmax, LAmín, and LA FC between modalities

<table>
<thead>
<tr>
<th></th>
<th>CMR vs. MDCT</th>
<th></th>
<th></th>
<th>CMR vs. TTE</th>
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<th>MDCT vs. TTE</th>
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<tbody>
<tr>
<td></td>
<td>r</td>
<td>Bias (LoA)</td>
<td>r</td>
<td>Bias (LoA)</td>
<td>r</td>
<td>Bias (LoA)</td>
<td>r</td>
</tr>
<tr>
<td>LAmax</td>
<td>0.85*</td>
<td>−6 (−23–12) mL/m²</td>
<td>0.59†</td>
<td>14 (−12–39) mL/m²</td>
<td>0.55†</td>
<td>20 (−8–47) mL/m²</td>
<td></td>
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<tr>
<td>LAmín</td>
<td>0.83*</td>
<td>−4 (−21–13) mL/m²</td>
<td>0.59†</td>
<td>14 (−11–38) mL/m²</td>
<td>0.55†</td>
<td>18 (−8–44) mL/m²</td>
<td></td>
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<tr>
<td>LA FC</td>
<td>0.56†</td>
<td>−1 (−10–7) %</td>
<td>0.34†</td>
<td>−3 (−16–9) %</td>
<td>0.47†</td>
<td>−2 (−14–10) %</td>
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</table>

*P < 0.0001.
†P < 0.001.
‡P < 0.01.
§P < 0.05.
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