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Assessment of Left Atrial Volume by Magnetic Resonance in Patients with Permanent Atrial Fibrillation. The Short-axis Method vs. the Single Plane Area-length Method

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Abstract: *Background*: Atrial fibrillation (AF) is associated with enlargement of the left atrium (LA). The LA volume can be assessed by cardiac magnetic resonance (CMR). The standard CMR method for measuring the LA volume is the short-axis (SA) method, which is time consuming, hence little useful in the clinical setting. For this reason more simplified methods have been developed to assess the LA volume.

Objective: To compare the standard SA method and the simplified single plane area-length (AL) method for measurements of the LA volume in patients with permanent AF.

Methods and Results: CMR was performed in 34 patients with permanent AF. CMR was conducted with the steady-state free precession (SSFP) technique TrueFISP. LA volumes were measured using the single plane AL method and the SA method. A good and statistically significant correlation was found between the two methods. The Pearson's correlation coefficients for LA maximal volume (LAmax) and LA minimal volume (LAmin) were 0.92, $p<0.0001$ and 0.91, $p<0.0001$, respectively. The single plane AL method underestimated LA volumes compared to the SA method (LAmax: 143 ± 35 ml vs. 149 ml ± 38, $p=0.046$, LAmin: 124 ml ± 30 vs. 130 ml ± 34, $p=0.014$). Intra- and interobserver agreement was inferior for the single plane AL method.

Conclusion: Measurements of LA volumes by the SA method and the single plane AL methods correlate closely in patients with permanent AF. However, the single plane AL method underestimates the LA volume and the reproducibility is inferior compared to the SA method.

Keywords: Atrial fibrillation, cardiac magnetic resonance, left atrial volume, steady-state free precession, short-axis method, area-length method.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with an adverse prognosis [1, 2], and the prevalence of AF is increasing [3]. AF is associated with enlargement of the left atrium (LA), because atrial dilatation is both the cause and consequence of AF [4-6]. LA volume provides a more accurate measure of LA size than LA diameter [7]. There is strong evidence that LA volume is a predictor of cardiovascular events in subjects without arrhythmia [7-9]. However, in patients with AF it has not been possible to confirm a relationship between LA enlargement and increased risk of future cardiovascular events [10]. In patients without arrhythmia, Cardiac Magnetic Resonance (CMR) is considered the gold standard for measuring cardiac chambers due to the methods excellent reproducibility [11, 12]. Measurements obtained using CMR resemble the true LA volume obtained from post-mortem assessment [13]. The standard CMR method for measuring LA volume is the short-axis (SA) method. This method, however, is very time consuming, making it little useful in the clinical setting. In addition, the LA volume cannot always be obtained on standard CMR images by the SA method due to lack of multislice images of the LA in the SA orientation [14]. Therefore, simplified methods have been developed to assess the LA volume, among these the single plane area-length (AL) method. The single plane AL method assumes an ellipsoid geometry of the LA and because LA enlargement associated with AF may not occur in a uniform fashion, it has been argued that application of such a method may not be feasible in patients with AF [8, 15]. For this reason, the objective of our study was to assess how measurements of LA volume obtained by the single plane AL method correlate with the standard SA method in patients with permanent AF.

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MATERIALS AND METHODOLOGY

Patients

Forty patients with permanent AF were included in the study and underwent CMR from August 2009 to July 2011.

The patients were recruited from the Outpatient Clinic at the Department of Cardiology, Hvidovre University Hospital, Copenhagen, Denmark. Inclusion criteria were ECG-documented permanent AF and ability to provide written informed consent, as well as existence of a documented decision not to attempt cardioversion. Exclusion criteria included contraindications to CMR (e.g. pacemaker, noncompatible biometalic implants, known claustrophobia), severe pulmonary disease and severe renal disease. Four of the included patients had to be excluded during the study: three patients due to claustrophobia during CMR and one due to excessive abdominal obesity. For two further patients CMR images could not be analyzed due to insufficient image quality. All patients were on their routine medication, including beta-blockers and digoxin. No additional medication was given to lower heart rate prior to or during CMR. Mean duration of AF was 3.3 ± 2.8 years. Informed consent was obtained before CMR in all cases. The study was conducted according to the principles of the Helsinki Declaration. Approval from the local Research Ethics Committee was obtained before the study was initiated.

Magnetic Resonance Imaging

CMR was conducted using the steady-state free precession (SSFP) technique TrueFISP on two scanners (Siemens Magnetom Avanto 1.5 Tesla system and Siemens Magnetom Trio 3.0 Tesla system, Siemens, Erlangen, Germany). Cardiac synergy coils were used for radiofrequency signal reception. Imaging was performed with the patients in the supine position. Retrograde ECG-gating was used to achieve 25 phases per RR-interval using Siemens arrhythmia detection sequences. Each slice was obtained from an average of 12 heart beats. After localizers, SSFP end-expiratory breath-hold cine sequences were performed covering the LV and subsequently the LA in the SA orientation with an average of 8-12 slices in the LA with a slice thickness of 6 mm. In addition, SSFP cine CMR was done in 4-chamber orientation covering the whole heart in 8-10 slices. The mid-atrial slice was used for calculating the LA volume by the single plane AL method.

Scan Parameters were as Follows

For Siemens Magnetom Avanto 1.5 Tesla system: field strength: 1.5 Tesla, TR: 58.3 msec, TE: 1.12 msec, flip angle: 80º, field of view: 340 mm, matrix size: 192 x 80, slice thickness: 6 mm.

For Siemens Magnetom Trio 3.0 Tesla system: field strength: 3.0 Tesla, TR: 64.8 msec, TE: 1.43 msec, flip angle: 38º, field of view: 340 mm, matrix size: 192 x 146, slice thickness 6 mm.

Image Analysis

LA volumes were assessed offline using the commercially available software Argus (Siemens Medical Solution, Erlangen, Germany). The LA volumes were first measured by the standard SA method, where LA maximal volume (LAmax) was defined visually as the phase with the largest LA-dimension and LA minimal volume (LAmin) as the phase with the smallest LA-dimension. Manual tracing of the endocardial borders of successive SA slices was performed from the apex of the LA to the atrioventricular 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 ventricular myocardium. Care was taken to exclude the pulmonary veins from the measurements.

LAmax and LAmin were calculated from the sums of the outlined areas using a modification of Simpson's rule [17]. LA fractional change (FC) was calculated from the formula: FC = (LAmax-LAmin)/LAmax x 100%. Next, the single plane AL measurement was performed on the mid-atrial slice in the horizontal 4-chamber image. The LA area and length were assessed at LAmax and LAmin and LA volumes was calculated at the two phases using the formula: volume = 0.85 x area²/length [14, 16]. On the 4-chamber image, LAmax was identified as maximal LA volume on the phase just before mitral valve opening and LAmin as the minimal LA volume on the phase just after mitral valve closure. Similarly to the SA measurements, pulmonary veins were excluded from the measurements on the 4-chamber image. LA FC was calculated from the same formula described above. Time consumption related to LA measurements by the SA method was on average 25 minutes. Time consumption related to LA measurements by the single plane AL method was on average 3 minutes. Patient examples of measurements are given in Fig. (**1**) and Fig. (**2**).

STATISTICAL ANALYSIS

All examined parameters of atrial volumes and function were found to be normally distributed using the Kolmogorov-Smirnov test. Continuous data are expressed as mean ± standard deviation (SD). Catagorical data are summarized as frequencies and percentages. Continuous variables were compared by paired t-tests. Categorical data were analysed by χ^2 test and Fisher's exact test when appropriate. A sample size calculation was performed using a test of equivalence, where non-equivalence was taken to be the null hypothesis, since the hypothesis was that the two CMR measuring methods would provide equivalent results, In accordance, rejection of the null hypothesis would indicate equivalence, implying that the results obtained by the two methods could be considered practically indistinguishable. Based on data from a previous imaging study conducted in patients with non-permanent AF using CMR [14], we found that acceptance of an equivalence margin of 15 ml with an assumed SD of 20 ml between mean measurements of LAmax by the two methods at a two-sided alpha level of 0.05 and a power of 80%, would require a sample size of 32 patients to reject the null hypothesis (of non-equivalence).

In order to assess the correlation between measurements of LA volume by the single plane AL method and the SA method, a Pearson's correlation coefficient (r) was calculated. In addition, Bland Altman analyses were carried out to assess the limits of agreement for results obtained by the two methods.

Intra-observer and inter-observer variability of LA volume measurements were also determined by linear regression (Pearson's correlation coefficient) and Bland Altman analyses. Intra-observer variability was assessed by making the same investigator repeat measurements of LAmax and LAmin in 20 randomly selected patients by both the SA method and the single plane AL method approximately one month after the initial assessment. Inter-

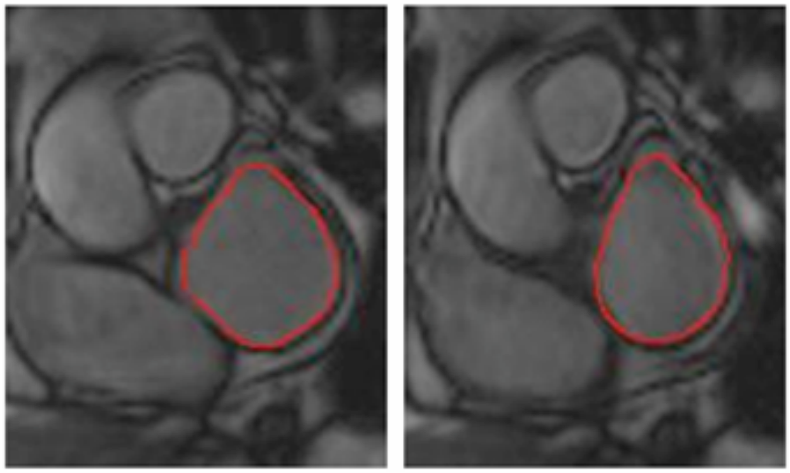

Fig. (1). Patient example.

Manual tracings of the left atrial volume using the standard short-axis (SA) method. Left: left atrial maximal volume (LAmax), Right: left atrial minimal volume (LAmin).

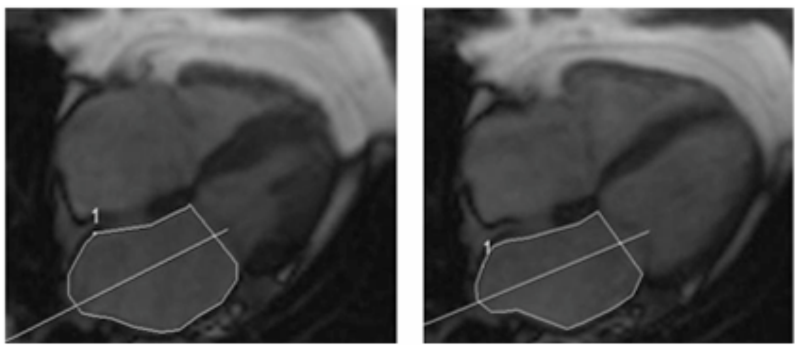

Fig. (2). Patient example.

Tracing of the left atrial volume using the single plane area-length (ALM) method in the 4-chamber view. Left: left atrial maximal volume (LAmax), Right: left atrial minimal volume (LAmin).

observer variability was assessed by a second investigator, who performed measurements of LAmax and LAmin in the same 20 patients by both the SA method and the single plane AL method. At each assessment the definition of LAmax and LAmin was reassessed visually and the measurements of LA volumes corresponding to LAmax and LAmin were repeated by the two methods.

All statistical analyses were performed with the use of a commercially available package (SAS 9.1 and 9.3, SAS System, Cary, NC, USA). A *p*-value of less than 0.05 was considered to be significant.

Table 1. Patient Characteristics

N	34
Age (years)	69 ± 6
Sex – male (%) (n)	65 (22)
Body Surface Area	2.0 ± 0.2
Body Mass Index	28 ± 6
Heart Rate	80 ± 14
Concomitant Disease	
Hypertension (%) (n)	50 (17)
Diabetes (%) (n)	21 (7)
LVEF<45% (%) (n)	32 (11)
Previous Stroke/TCI (%) (n)	9 (3)
IHD (%) (n)	29 (10)
Medication	
Beta-blocker (%) (n)	92 (31)
Digoxin (%) (n)	35 (12)
ACEi or ARB (%) (n)	68 (23)
Oral anticoagulants (%) (n)	97 (33)

Data are presented as mean ± standard deviation or as % (n) unless otherwise stated. LVEF: left ventricular ejection fraction, TCI: transitory cerebral ischemia, IHD: ischemic heart disease, ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker

Results

Patient characteristics are shown in Table **1**. The single plane AL method underestimated LAmax and LAmin compared to the SA method (LAmax: 143 ± 35 ml vs. 149 ±

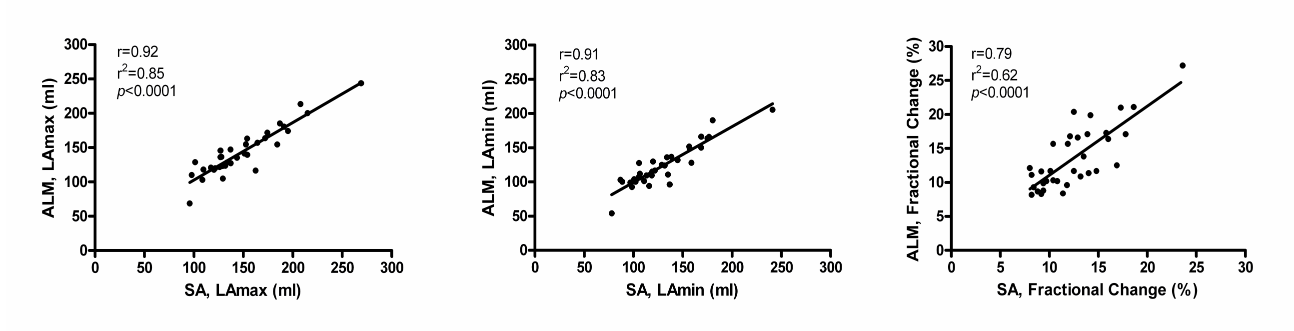

Fig. (3). Correlation between methods.

Correlation between the short-axis method (SA) and the single plane AL method (ALM) for LAmax, LAmin and LA fractional change (FC).

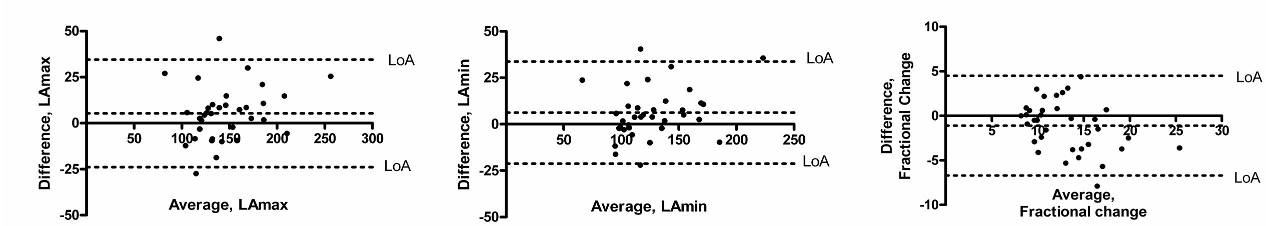

Fig. (4). Mean difference between methods.

Bland Altman plots showing agreement between measurements of LAmax, LAmin and LA fractional change (FC) performed with the short-axis (SA) method and the single plane AL method. LoA; limits of agreement.

Table 2. Intraobserver Reproducibility of LAmax and LAmin

	Short-Axis Method		**Area-Length Method**	
	r	**Mean Difference ± SD**	**r**	**Mean Difference ± SD**
LAmax	0.97*	6.9 ± 11.3 ml	0.86*	6.1 ± 15.9 ml
LAmin	0.97*	4.8 ± 9.4 ml	0.87*	8.6 ± 13.8 ml

SD: standard deviation
*$p<0.0001$

Table 3. Interobserver Reproducibility of LAmax and LAmin

	Short-Axis Method		**Area-Length Method**	
	r	**Mean Difference ± SD**	**r**	**Mean Difference ± SD**
LAmax	0.94*	1.6 ± 11.1 ml	0.87*	-6.8 ± 16.1 ml
LAmin	0.96*	2.0 ± 8.1 ml	0.92*	-2.5 ± 10.1 ml

SD: standard deviation
*$p<0.0001$

38 ml, $p=0.046$; LAmin: 124 ± 30 ml vs. 130 ± 34 ml, $p=0.014$). FC was larger when assessed by the single plane AL method compared to the SA method (FC; 13.6 ± 4.7% vs. 12.5 ± 3.6%, $p=0.040$).

The Pearson's correlation coefficients between measurements using the two methods were: 0.92, 0.91 and 0.79 ($p<0.0001$) for LAmax, LAmin and FC, respectively (Fig. **3**).

Bland Altman analyses showed good agreement for measurements of LAmax, LAmin and FC performed with the two methods. Bias were: 5.3 ± 14.9 ml, 6.2 ± 14.0 ml and -1.1 ± 2.9 % for LAmax, LAmin and FC, respectively (Fig. **4**).

Data on intra- and interobserver variability are summarized in Table **2** and Table **3**. For measurements performed by the standard SA method, assessment of both intra- and interobserver variability gave Pearson's correlation coefficients above 0.90 for LAmax and LAmin ($p<0.0001$). For measurements performed by the single plane AL method, correlation coefficients of intraobserver variability were 0.86 for LAmax and 0.87 for LAmin ($p<0.0001$) and correlation coefficients of interobserver variability were 0.87 for LAmax and 0.92 for LAmin ($p<0.0001$).

Bland Altman analyses showed good intra- and interobserver agreement for measurements of LAmax and

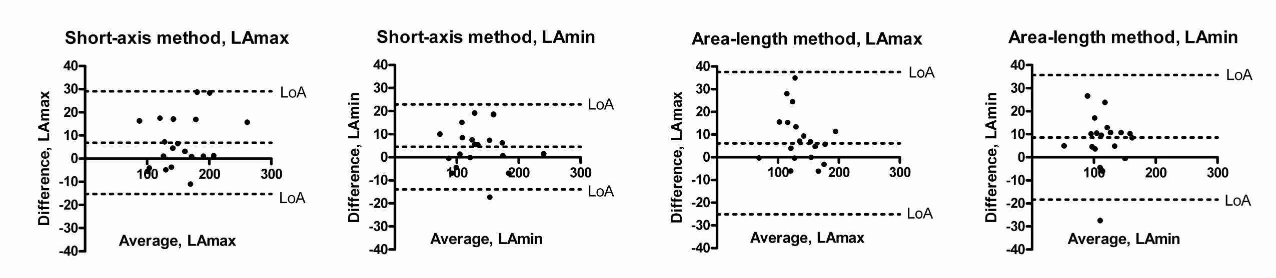

Fig. (5). Intraobserver variability.

Bland Altman plots of intraobserver variability of LAmax and LAmin using the short-axis (SA) method (left) and the single plane AL method (right). LoA: limits of agreement.

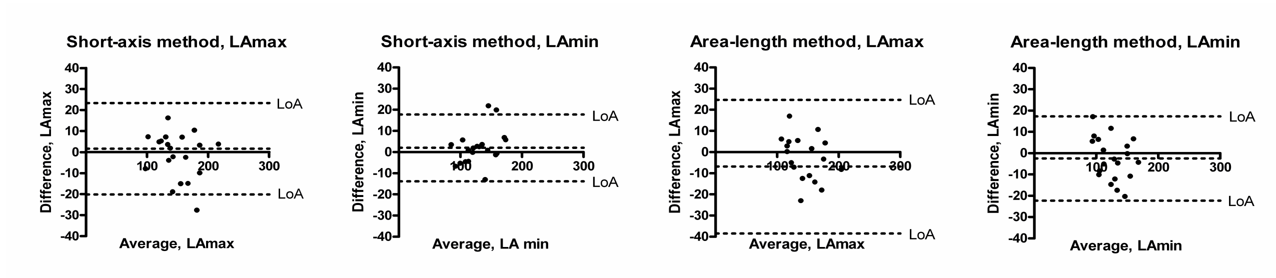

Fig. (6). Interobserver variability.

Bland Altman plots of intraobserver variability of LAmax and LAmin using the short-axis (SA) method (left) and the single plane AL method (right). LoA: limits of agreement.

LAmin by the SA method. With respect to both intra- and interobserver assessment, limits of agreement were larger for the single plane AL method than for the SA method (Fig. **5** and Fig. **6**).

DISCUSSION

Transthoracic echocardiography (TTE) is due to its wide availability the most frequently used method for assessment of the LA volume [18]. CMR, however, allows 3-dimensional measurements of the LA volume with a clear delimitation of endocardial borders, and due to the fact that CMR is increasingly gaining importance in the assessment of structural heart disease and is considered an accurate method for measuring myocardial infarction size in patients with myocardial infarction [19, 20], evaluation of the use of CMR is warranted in the growing number of patients with AF, who often have substantial cardiac co-morbidity. Until recently, patients with AF were generally excluded from CMR studies, because the reliability of measurements was impaired by the varying RR-interval that caused reduced image quality. Due to technical advances during the last decade, a number of CMR studies have now been performed including patients with AF [4, 18, 21, 22]. The currently used SSFP technique is able to produce high-quality images with clear distinction of endocardial and epicardial borders in spite of the varying cycle length in AF [21]. Due to the scarcity of CMR studies in patients with AF, it has not previously been assessed how the single plane AL method compares to the SA method for assessment of the LA volume in patients with permanent AF. Hof et al. found a good correlation between measurements of LA volume and function by the two methods in patients with paroxysmal and persistent AF, who where all in SR at the time of CMR, although the single plane AL method underestimated LA volumes and overestimated LA function and had inferior reproducibility compared to the SA method [14]. Our data confirm that this also applies to patients with permanent AF in spite of the fact that the patients in our study were scanned during AF and had substantially larger LA volumes. Even though LA enlargement is often more evident and may occur in a non-uniform fashion in patients with permanent AF, we have demonstrated that also in these patients the single plane AL method correlate well with the SA method, but underestimates LAmax and LAmin and overestimates FC compared to the SA method. However, although the difference is statistically significant, it is hardly of any clinical significance. With respect to intra- and interobserver agreement, the limits of agreement for the single plane AL method were quite wide implying that the reproducibility of this method is considerably inferior to the SA method, which to some extent limits the utility of the method. Since CMR is usually performed for other purposes than assessment of the LA volume, e.g. evaluation of ischemic heart disease, it can be argued that a fair estimate of the LA volume may be sufficient in most cases even in patients with permanent AF. For this reason use of the single plane AL method may in fact be a reasonable alternative to the SA method in the majority of patients, since the measurements correlate closely with the SA method and the trade off between reduced reproducibility and time saving may favour the latter in daily clinical practice. Also, in circumstances where multiple slices of the LA in the SA orientation are not available, it may be justified to use the single plane AL method for assessment of the LA volume, due to the close correlation between the two methods. Nevertheless, in cases where a high level of reproducibility is required, e.g. for serial assessments of LA volumes over time, use of the SA method should be encouraged. However, CMR should at this stage only be used for research in group studies in patients with permanent AF, as the feasibility of CMR need to be validated in larger studies before the method can be implemented in clinical decision making or research with serial measurements in individual patients.

LIMITATIONS

A relatively small number of patients were examined, therefore the study does not allow for any definite conclusions. Due to practical logistics, patients were scanned using two different scanners with different field strengths. Nineteen patients were scanned using Siemens Magnetom Avanto 1.5 T and fifteen patients were scanned using Siemens Magnetom Trio 3.0 T. Previously, it has been established that field strength have no effect on LA assessment of volume and function [23], hence, 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 this might have affected the measurements complicating the evaluation. Since images were only acquired in the SA orientation and 4-chamber view according to the CMR protocol, images in the 2-chamber view were not obtained, and calculations of LA volumes using a biplane AL method have not been possible. We anticipate that application of a biplane AL method would have yielded comparable results, since good agreement between measurements derived from the single- and biplane AL method has previously been reported [15], but this remains to be determined. With respect to time consumption related to measurements by the two methods, we found that the single plane AL method was associated with a substantial reduction of analysis time compared to the SA method (approx. 3 min vs. 25 min). With greater routine, however, it might be possible to shorten the time consumption associated with the SA method. Also, semi-automated software is increasingly becoming available, which will eventually allow faster volumetric analysis.

CONCLUSION

Measurements of LA volumes by the SA method and the single plane AL methods correlate closely in patients with permanent AF. However, the single plane AL method underestimates the LA volume compared to the standard SA method in patients with permanent AF and the reproducibility is inferior to the SA method.

CONFLICT OF INTERESTS

The author(s) confirm that this article content has no conflicts of interest.

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