



Left atrial volume quantification using cardiac MRI in atrial fibrillation: comparison of the Simpson's method with biplane area-length, ellipse, and three-dimensional methods

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PURPOSE

Left atrial volume is an important predictor of future arrhythmias, and it can be assessed by several different methods. Simpson's method is well accepted as a reference standard, although no standardization exists for cardiac magnetic resonance (CMR). We aimed to compare the estimations of left atrial volumes obtained by the Simpson's method with three other methods.

MATERIALS AND METHODS

Eighty-one consecutive patients referred for CMR imaging between February 2007 and May 2010 were included in the study (47 males; mean age, 59.4±11.5 years; body mass index, 26.3±3.7 kg/m²). Left atrial volume measurements were performed using the Simpson's, biplane area-length, ellipse, and three-dimensional methods. Results were correlated using a Bland-Altman plot and linear regression models and compared by two-tailed paired-sample *t* tests. Reader variability was also calculated.

RESULTS

Left atrial volume measurements using the biplane area-length technique showed the best correlation with Simpson's method ($r=0.92$; $P < 0.001$). Quantification values using the ellipse and three-dimensional methods were significantly different than values obtained using the Simpson's method ($P < 0.05$, for both). All methods showed excellent observer reliability (intra-class correlation coefficient >0.99).

CONCLUSION

The biplane area-length method can be used for left atrial volume measurement when the Simpson's method cannot be performed. If these two methods are not feasible, then all methods are highly reproducible and can be used, but should not be used interchangeably for follow-up studies.

The prevalence of atrial fibrillation is currently increasing over time and has a major impact on mortality and quality of life (1). Catheter ablation has become an effective treatment for patients with atrial fibrillation (2, 3); however, recurrent atrial fibrillation still remains a current issue after pulmonary vein isolation and has been shown to be related to both electrical and structural remodeling of the atrium (4).

Patients who have a normal or slightly increased left atrial volume (LAV) are generally considered to be the best candidates for pulmonary vein isolation. Moreover, patients with higher LAV have been shown to have a higher rate of recurrent postprocedural atrial fibrillation, thereby necessitating the continuation of antiarrhythmic medications and/or further invasive procedures, such as atrioventricular nodal ablation (2, 3, 5). Given the correlation of LAV and recurrence of atrial fibrillation, accurate assessment of LAV plays a crucial role in selecting patients who are most likely to benefit from pulmonary vein isolation (5). In addition, LAV is an important marker for other cardiac disease processes, such as diastolic heart failure, where accurate assessment is important for precisely defining the extent of the disease (1, 4).

The current standard of reference for measuring LAV is the Simpson's method by cardiovascular magnetic resonance (CMR) (6–8). However, the requirement of acquiring a stack of contiguous slices that cover the entire left atrium as well as the need to manually contour the left atrium on all slices makes it a time consuming method. It is therefore advantageous to seek methods for LAV quantification by CMR that are less time consuming in terms of acquisition and evaluation, but that still maintain procedural accuracy that is comparable to the Simpson's method.

Three-dimensional (3D) contrast-enhanced angiography by CMR is currently used for left atrial evaluation pre- and postablation and to map pulmonary vein ostia (5). Other methods currently used for left atrial evaluation include the biplane area-length and the ellipse methods (6, 7). However, there is currently a paucity of studies evaluating these methods within the same population (8). Therefore, in this study we compared the Simpson's method for LAV measurement to three other methods (biplane area-length, ellipse, and 3D) used for this same purpose.

Materials and methods

Study population

The study was approved by the Federal University of Rio de Janeiro Review Board, and all participants provided written informed consent before being included in the study. From February 2007 to May 2010, 81 consecutive patients were prospectively enrolled. The inclusion criteria for the study subjects included receiving a clinically indicated CMR within the scope of atrial fibrillation ablation and the presence of a si-

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nus rhythm before and during CMR. Exclusion criteria included a contraindication to CMR studies, such as claustrophobia, the presence of metallic implants, unable to follow instructions for breath holding, or the presence of a scar in late gadolinium enhancement imaging.

Age, gender, height, weight, heart rate, and systolic and diastolic blood pressures were obtained on the day of the CMR procedure. In addition, the history of atrial fibrillation was also recorded.

CMR protocol

All studies were performed using a 1.5 Tesla magnetic resonance imaging (MRI) scanner (GE Signa Horizon®, GE Medical Systems, Milwaukee, Wisconsin, USA and Achieva system®, Philips Medical Systems, Best, The Netherlands) with high performance gradients (amplitude, 32 mT; slew rate, 150 T/m/s). All sequences were electrocardiography (ECG)-triggered and taken during breath holding. Scout images were taken in axial, coronal, and sagittal orientations. A retrospectively ECG-gated cine-MRI stack was acquired in the short axis orientation,

which covered the entire left ventricle and left atrium with contiguous slices for the assessment of left ventricle end-diastolic volume and left ventricle end-systolic volume to calculate the left ventricle ejection fraction and LAV (the Simpson's method).

Cine-MRI in the four- and two-chamber orientations using steady-state free precession (SSFP) pulse sequences was used to assess LAV (biplane area-length and ellipse methods) (9). Typical imaging parameters were as follows: TR, 3.1 ms; TE, 1.55 ms; flip angle, 55°; field of view, 350–420 mm; matrix, 192×128; number of cardiac phases, 20; number of acquisitions, 1; number of slices, 10–12; and slice thickness, 8 mm with a 2 mm interval (gap-range).

In addition, 3D, non-gated, breath-hold, gradient echo magnetic resonance (MR) angiography was acquired during intravenous infusion of a bolus of gadoterate meglumine contrast agent (Dotarem®, Gd-DOTA, Guerbet, Villepinte, France) at a dose of 0.2 mmol/kg with a flow rate of 2.5 mL/s. Briefly, the 3D sequence parameters were as follows: thickness, 2.4 mm (range, 2.2–2.6 mm); matrix size, 256×192 (1.5–2.0 mm in-plane); inter-

polated to a 512 matrix with zero-fill interpolation ×2 in the z-direction; echo time, 1.0 ms; repetition time, 4.6 ms; flip angle, 40–45°; receiver bandwidth, 31.25 or 62.5 kHz; number of excitations, 1.

As part of the routine protocol, phase sensitive inversion recovery late gadolinium enhancement imaging at 15 min postinjection was used to assess for myocardial scars. Inversion times were individually adjusted to suppress normal myocardium (10).

CMR analysis

All images were transferred to commercially available workstations (ADW 4.3, GE Medical Systems, Waukesha, Wisconsin, USA; Brilliance, Philips Medical Systems) for random order evaluation. One blinded reader conducted the quantitative analysis of LAV. Measurements were performed twice by the same reader (M.S.N.), and mean values were reported. Measurements were taken from approximately 40% (30/81) of randomly chosen studies to assess for intra- and inter-observer variability. The intra-observer variability evaluation was assessed by the same reader after two weeks, while a second blinded observer (R.O.F.) provided the inter-observer evaluation.

Four methods were used to measure atrial volume by CMR: the Simpson's, biplane area-length, ellipse, and 3D. The quantitative measurements of LAV were performed following very strict and precise rules. The left atrium maximal area, which was visually detected by the reader, was used to assess the maximal volumes.

Simpson's method

The Simpson's technique is based on Simpson's rules, which for our purposes were essentially the sum of the cross-sectional areas of each slice accounting for slice thickness and the interval between slices (7, 11). This was measured at short axis views of the cine-MR using SSFP sequences and anatomical landmarks, and exclusion of the pulmonary vein was applied (Fig. 1).

Biplane area-length method

The biplane area-length technique is based on the following formula: volume=0.85×four-chamber area×two-chamber area/perpendicular axis, in which LAV excludes the left atrium appendage and the confluence of the pul-

Table 1. Patients' demographic and clinical characteristics (n=81)

	Mean±SD or n (%)
Demographics	
Age (years)	59.4±11.5
Male gender	47 (58)
Height (cm)	165.1±10.7
Weight (kg)	72.3±15.0
Body mass index (kg/m ²)	26.3±3.7
Heart rate (bpm)	65.7±12.8
Systolic blood pressure (mmHg)	135.2±20.4
Diastolic blood pressure (mmHg)	81.1±10.1
Medical history	
Paroxysmal atrial fibrillation	37 (45.6)
Persistent atrial fibrillation	44 (54.4)
Left ventricular global function by CMR	
End-diastolic volume (mL)	106.1±31.0
End-systolic volume (mL)	42.7±20.7
Ejection fraction (%)	60.4±9.4
Mass (g)	131.3±38.8

CMR, cardiac magnetic resonance; SD, standard deviation.

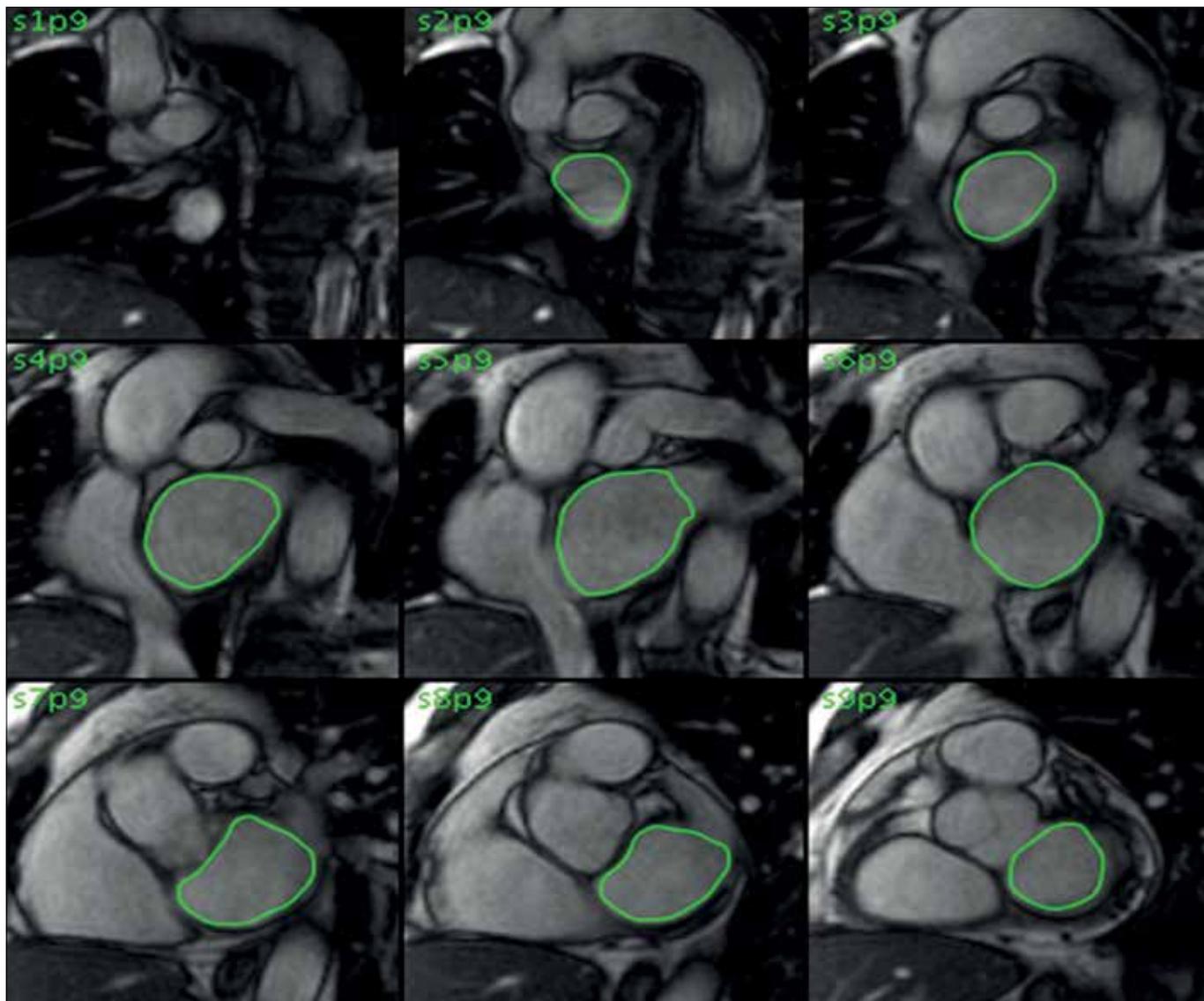


Figure 1. The Simpson's method for volume calculation. Examples of a stack of sequential images of the left atrium, acquired with a steady-state free precession (SSFP) cine sequence are seen.

monary veins at its ostium. The length is measured perpendicular between the ring plane of the mitral valve and the upper portion of the left atrium. Furthermore, the border definition of the left atrium on SSFP sequences was clear, and areas were measured on the perpendicular planes of the two-chamber and four-chamber views (Fig. 2a, 2b) (12, 13).

Ellipse method

The ellipse volume technique is based on the following formula: $\text{Volume} = \text{DL} \times \text{DT} \times \text{DAP} \times 0.52$, where DL=longitudinal diameter, DT=transverse diameter, and DAP=antero-posterior diameter, which are always perpendicular to each other. The

same perpendicular planes used for the biplane area-length evaluation (two-chamber and four-chamber views) were used for the ellipse method (Fig. 2c, 2d) (7).

3D method

The 3D measurement was mostly based on a semi-automatic detection method using a threshold technique with minimum operator input. The boundaries were manually corrected to avoid external tissue in the final volume dataset (Fig. 3) (14).

Statistical analysis

Statistical analysis was performed using a commercially available statistical software (STATA®, version 12.0,

StataCorp LP, College Station, Texas, USA). A P value < 0.05 was considered statistically significant. Data are presented as mean \pm standard deviation (SD) for continuous variables and as percentages for categorical variables. A paired student's two-tailed t test was used to determine significant differences between two sets of LAV methods. Linear regression analysis and Pearson's correlation were also used to examine the relationship between two methods as well as to evaluate how closely the results correlated between the two readings (Simpson's vs. biplane, Simpson's vs. ellipse, and Simpson's vs. 3D).

For intra- and inter-observer variability, Pearson's correlation coefficient was scored as follows: poor agreement,

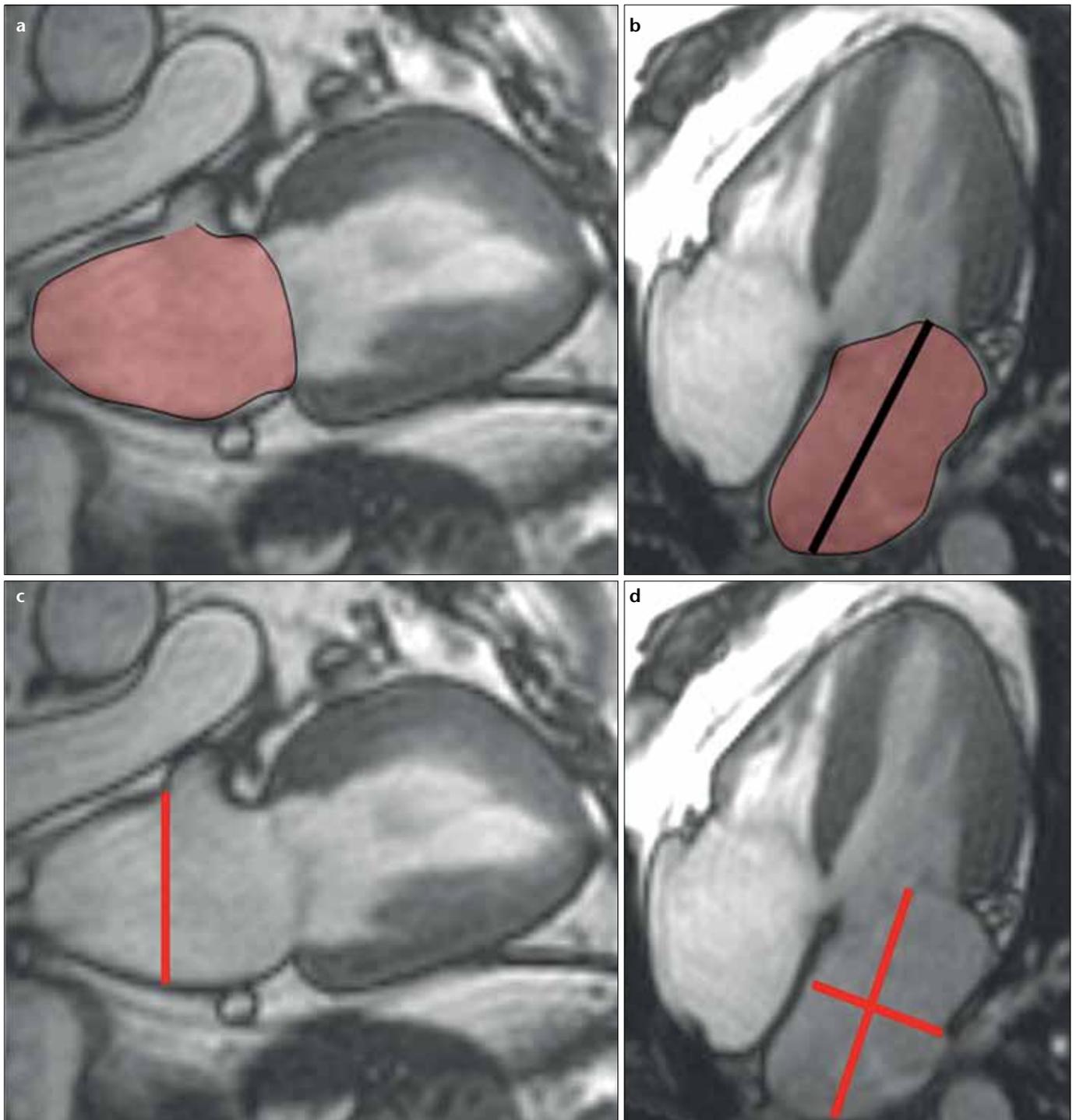


Figure 2. a–d. The biplane area-length method for volume calculation. The measurement should be performed during ventricular systole when the mitral valve is closed on a two-chamber long axis slice (a) acquired perpendicular to the long axis four-chamber view (b). The same image planes were used for the ellipse volume calculation technique, where the maximal diameter was used to assess the longitudinal diameter on the long axis two-chamber view (c) and the transverse as well as the anteroposterior diameters on the four-chamber view (d).

0; slight, 0.01–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; good, 0.61–0.80, and excellent, 0.81–1.00 agreement. In addition, a Bland-Altman analysis was calculated and the intra-class correlation coefficient (ICC) with a two-way random model (ICC <0.40, poor; ICC

≥0.40–0.75, fair to good; and ICC >0.75, excellent agreement) was evaluated.

Results

The mean CMR study duration was 36±6 min. Diagnostic image quality was obtained in all studies, which

enabled complete data analysis from all MRI datasets. Of the 81 consecutive patients, 47 (58%) were male, and mean age was 59.4±11.5 years (range, 30–84 years). Patients' characteristics are summarized in Table 1. A total of 564 LAV measurements were analyzed

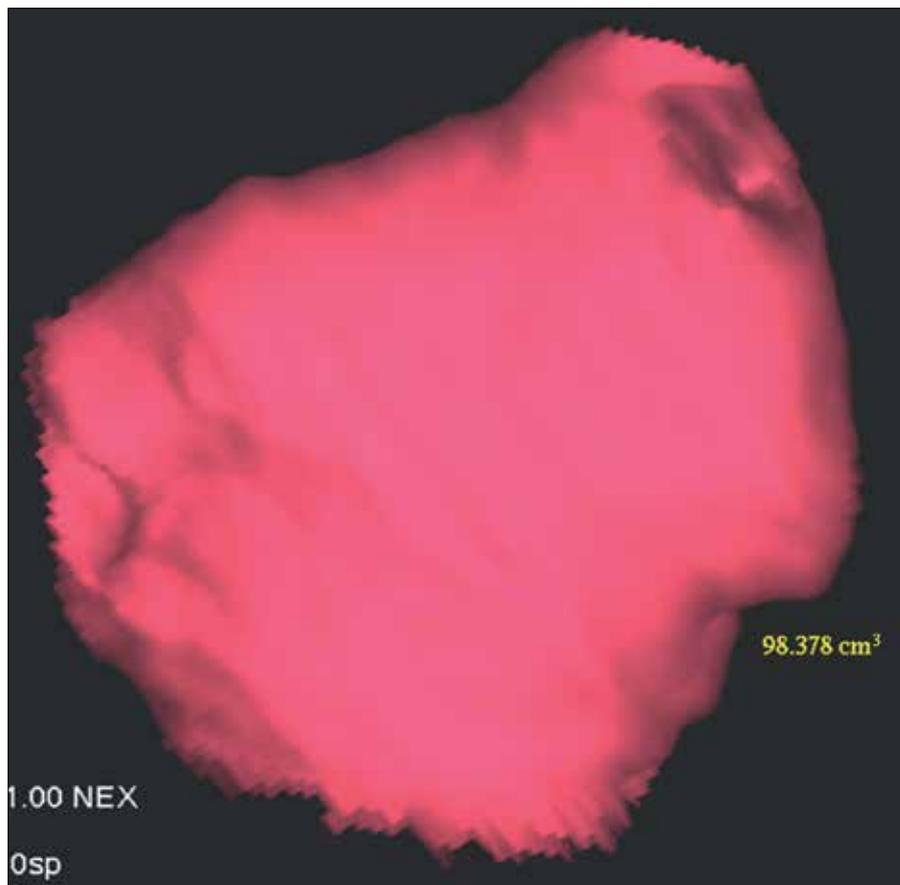


Figure 3. The 3D method for volume calculation. It is a semi-automatic detection method using a threshold technique with minimal operator input. The boundaries were manually corrected to avoid external tissue in the final volume dataset.

Table 2. Comparison between the Simpson's, biplane area-length, ellipse, and 3D methods (n=81)

Volume measuring methods	Left atrium volume (mL)			P ^a
	Mean±SD	Minimum	Maximum	
Simpson's	78.6±31.1	18.8	189.4	-
Biplane area-length	78.0±32.9	20.3	189.3	0.66
Ellipse	69.4±31.5	20.9	179	< 0.001
3D	82.1±34.2	24.9	213	0.02

^aP values are for comparison of the relevant method to the Simpson's method. SD, standard deviation; 3D, three-dimensional.

from 81 studies, which also accounted for observer variability analysis.

The comparisons between the Simpson's method and the biplane area-length, ellipse, and 3D methods are summarized in Table 2. No statistically significant difference was found in the LAV measurement between the biplane area-length (78.0±32.9 mL) than bandy Simpson's (78.6±31.1 mL) methods ($P = 0.66$). However, the ellipse (69.4±31.5 mL) and 3D (82.1±34.2 mL) methods were signifi-

cantly different from the Simpson's method (78.6±31.1 mL) ($P < 0.001$ and $P = 0.02$, respectively).

Fig. 4 shows the relationship between the Simpson's method and the biplane area-length, ellipse, and 3D methods. Despite the difference in volume, Pearson's correlation coefficient showed excellent correlation between methods (Simpson's vs. biplane area-length method, $r=0.92$; Simpson's vs. ellipse, $r=0.92$; and Simpson's vs. 3D, $r=0.91$; $P < 0.001$ for all) (Fig. 2a,

2c, and 2e). The mean difference from the Simpson's method was higher for the ellipse method (9.2 mL), followed by the 3D and biplane methods (3.4 mL and 0.6 mL, respectively) (Fig. 2b, 2d, and 2e).

Table 3 shows the inter- and intra-observer variability for all methods. The results of the Bland-Altman analysis are also shown in Table 3. An excellent inter-observer correlation (ICC >0.99) was observed, and the ellipse method had the worst mean difference of all of the methods (3.77 mL). Similar results were found for the intra-reader variability, where the ellipse method also demonstrated the worst mean difference (4.10 mL).

Discussion

The Simpson's method, which is considered to be the standard procedure for measuring LAV (15), is not routinely performed because image acquisition usually adds 6 min to the CMR protocol, which takes approximately 40 min in total. LAV methods that use the routine acquired planes are more time efficient during both image acquisition and image analysis. Therefore, the purpose of this study was to compare the Simpson's method with three different CMR-based methods to measure the LAV in atrial fibrillation subjects. Our results show that the biplane area-length technique should be used for LAV measurement when the Simpson's method cannot be performed. However, if these two methods are not feasible, all four methods assessed in this study are highly reproducible and can be used, but they should not be used interchangeably.

Järvinen et al. (16) and Rodevan et al. (17) previously demonstrated the ability of CMR to quantify LAV in adults. In the present study, we demonstrated that the different measurement techniques assessed lead to significantly different results for LAV. Furthermore, comparability of studies is hampered when different measurement techniques are used. We therefore recommend performing LAV measurements in a consistent and standardized manner.

In agreement with previous publications, we found that any of the methods assessed in this study for measuring the cardiac atrial cavity that assume a geometric shape for LAV quantification decrease the accuracy of the measurement; however, good

Table 3. Inter- and intra-observer variability for CMR left atrium measurements (n=30)

Volume measuring methods	Inter-observer variability			Intra-observer variability		
	Bias (mL)	Limits of agreement (mL)	ICC	Bias (mL)	Limits of agreement (mL)	ICC
Simpson's	1.52	-1.80 to +4.84	0.999	1.30	-1.18 to +3.78	0.998
Biplane area-length	1.57	-1.57 to +4.71	0.998	1.57	-2.18 to +5.32	0.997
Ellipse	3.77	-1.13 to +8.67	0.996	4.10	-0.34 to +8.54	0.999
3D	-0.79	-8.50 to +6.92	0.998	-1.19	-8.48 to +6.10	0.998

ICC, intraclass correlation coefficient; 3D, three-dimensional.

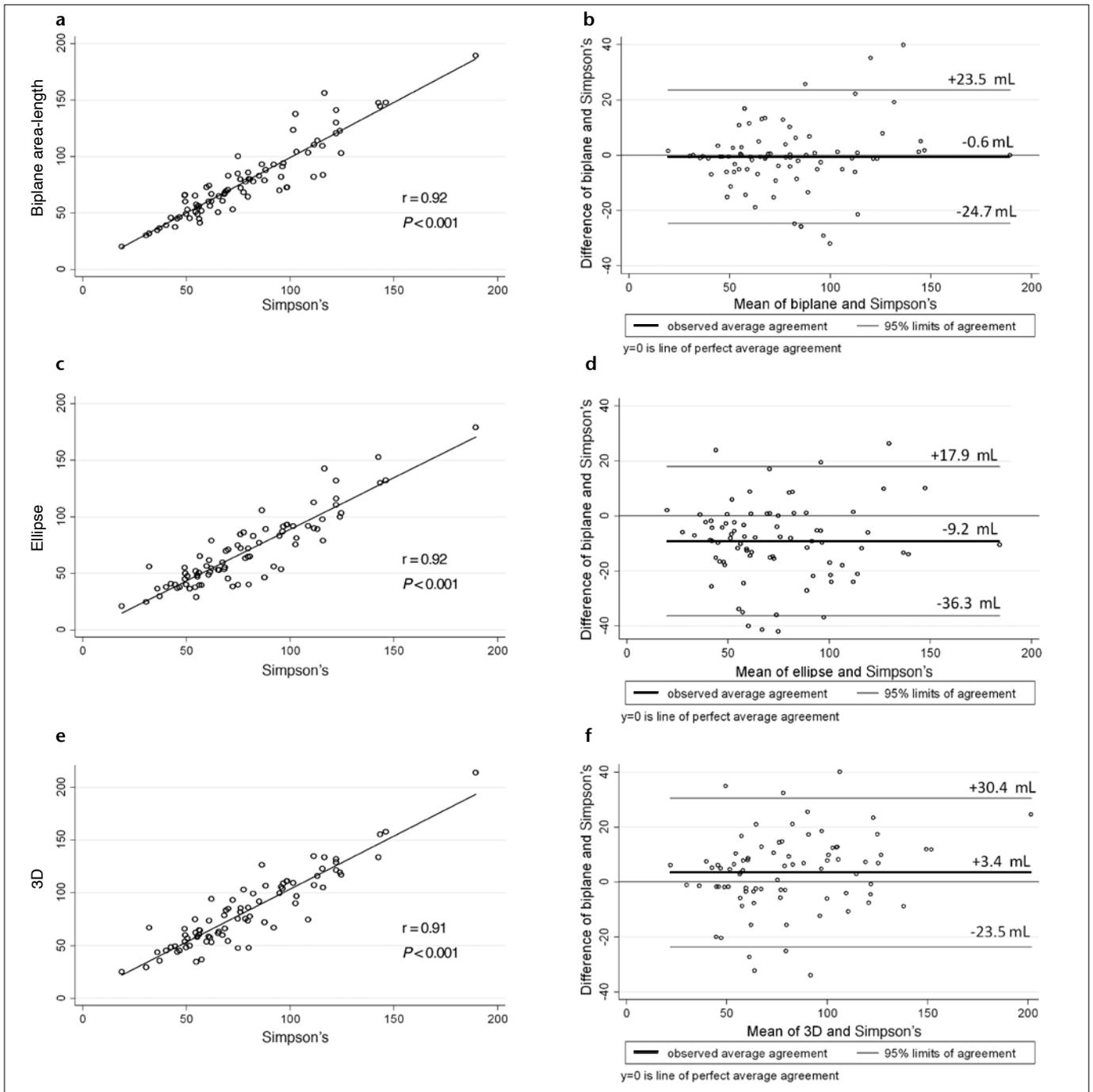


Figure 4. a-f. Linear regressions and Bland-Altman plots analysis. The Pearson's correlation coefficient (r), the mean difference, and the 95% limits of agreement are shown. Biplane area-length vs. Simpson's (a and b); ellipse vs. Simpson's (c and d); and 3D vs. Simpson's (e and f).

agreement between the procedures may be achieved (18). In addition, similar to the work of Mahabadi et al. (18), we observed excellent intra-reader agreement for all of the CMR-based methods for measuring LAV.

ECG-gated 3D methods appear to provide greater agreement in LAV estimation (12). The biplane area-length and ellipse methods depend on the accurate acquisition of the respective images in order to detect the median planes perpendicular to each other, and also depend on the correct characterization of LAV during the post-processing steps. The 3D method is non-ECG-gated, which means that the acquired image is a ratio between atrial systole and diastole. This was partially responsible for the poor agreement of this procedure in our study. Further limitations in 3D estimations of LAV include the inability to distinguish epicardial fat and adjacent tissue from the left atrium, which leads to systematic overestimation compared to the Simpson's method. Therefore, these differences should be overcome using better software and an ECG-gated 3D method with respiratory navigator (19). In addition, in several studies of normal volunteers and patients with a sinus rhythm, it has been observed that the measurement of LAV by echocardiography underestimates the results obtained by cardiac computed tomography or MRI, which is most likely due to suboptimal limited acoustic windows of the specific study (6, 7, 12).

Several limitations could have affected the results presented in this study. First, this study was designed to assess the correlations and agreement of methods for LAV assessment with CMR in patients with atrial fibrillation. The study cohort did not have normal healthy volunteers, which may be a weakness for agreement between the methods. However, to overcome gating errors, only patients with atrial fibrillation and a sinus rhythm at the time of the CMR exam were included in the study. Therefore, our results only apply to patients with previous or paroxysmal atrial fibrillation who have a sinus rhythm at the time of the CMR examination. Second, our findings may differ for patients in atrial fibrillation during the imaging acquisition or with other disease afflictions. Third, the 3D MR angiography protocol used

was not a high resolution ECG-gated, free breathing procedure with respiratory navigator, which is now available and may provide better results. Therefore, this technique may demonstrate better results in future studies that use newer pulse sequences.

In summary, our study has highlighted the advantages and limitations of each technique assessed. The Simpson's method does not have geometric shape distortions, which minimizes the mathematical assumption, but takes longer for data acquisition and analysis. In addition, the biplane area-length partially corrects the shape distortion usually seen when using the ellipse method. Both methods calculate volumes using mathematical assumptions, where the ellipse method systematically calculates smaller volumes than the biplane method; however the ellipse method is the easiest method for clinical use. Moreover, the 3D method tends to be more reproducible and independent of geometric assumptions regarding left atrial shape, but image acquisition should use gated protocols.

In this study we have demonstrated the quantification of LAV using four different techniques. The biplane area-length technique should be used for LAV measurement when the Simpson's method cannot be performed. If these two approaches are not feasible, then the other methods assessed in this study are highly reproducible and can be used, but should not be used interchangeably for follow-up studies. The different methods for LAV calculation may show significantly different results, which have to be taken into consideration for comparisons and follow-up studies. Therefore, the same method should be applied for repeated and follow-up studies.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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