

Reference Right Atrial Function Determined by Steady-State Free Precession Cardiovascular Magnetic Resonance

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ABSTRACT

Background: There is agreement that measurements of atrial volumes and ejection fraction (EF) are superior to atrial diameters for accurate determination of atrial size, follow up studies and prognosis. However, reference values for right atrial volumes and EF for cardiovascular magnetic resonance (CMR) have not been established but are crucial to identify patients with impaired right atrial function. **Methods and Results:** Atrial function was studied in 70 healthy subjects (52 ± 16 years, 38 male) with both the standard short axis method (SA) and the area-length method (AL) using steady-state free precession gradient-echo cine imaging (SSFP). Intraobserver, interobserver ($n = 70$) and interstudy ($n = 10$) variability was assessed for both methods. Maximal volumes, minimal volumes and EF for SA and AL were 101.0 ± 30.2 mL, 50.3 ± 19 mL and $47.2 \pm 8.3\%$, and 103.2 ± 32.6 mL, 50.8 ± 20.2 mL and $51.4 \pm 9.2\%$, respectively. Maximal volumes, minimal volumes and EF were higher with AL than with SA (mean difference: 2.2 ± 4.6 mL, 3.5 ± 3.5 mL and $2.8 \pm 2.8\%$, respectively). Atrial function measurements were not related to gender ($p \geq 0.387$) and age ($\rho \leq 0.16$) with either method. Intraobserver, interobserver and interstudy variability for volumes and EF was lower for SA compared to AL, with narrower limits of agreement. Analysis was faster with AL than with SA (62 ± 18 s versus 7 ± 2 minutes). **Conclusion:** Normal ranges for right atrial function vary significantly between methods. AL is faster, but less reproducible than SA. Appropriate reference ranges should be used to differentiate normal from abnormal right atrial function.

INTRODUCTION

There is growing consensus that measurements of atrial volumes and ejection fraction (EF) are superior to diameters for accurate determination of atrial size, follow up studies and prognosis (1, 2). A recently published state-of-the-art paper by

Abhayaratna et al (3) suggested that left atrial volumes should be incorporated into routine clinical evaluation.

The utility of right atrial volume and function for monitoring cardiovascular risk and for guiding therapy may also prove to have an important clinical impact, especially in patients with right heart disease, such as pulmonary hypertension, congenital heart disease, and valvular disease. There is evidence that the degree of right atrial remodeling with therapy and the regression of the right atrial size translates into improved cardiovascular outcomes (4–6). However, future studies are warranted to improve the understanding of right atrial remodeling, the extent of reversibility of right atrial enlargement with therapy, and the impact of these changes on outcomes.

In current clinical practice, right atrial function is usually visually estimated or assessed based on diameter measurements. Right atrial volume and EF measurements are not routinely performed (7). Cardiovascular magnetic resonance (CMR) is an accurate and reproducible method for follow up studies of patients and has become the gold standard method for the assessment of ventricular function (8–12). It offers excellent visualization

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of the right heart and is considered the technique of choice for non-invasive assessment of right heart function and the detection of right heart disease. The current standard technique for image acquisition is steady-state free precession (SSFP) cine imaging. Compared to spoiled gradient-echo sequences, the SSFP technique yields significantly improved blood-myocardium contrast, acquisition speed, and the ability to greatly improve the temporal resolution of the cines with improved image quality (13, 14). The evaluation of right atrial function with CMR has not yet become clinical routine. One reason might be that the acquisition and analysis of a full stack of atrial short-axis slices is time-consuming. The additional time for image acquisition and analysis might not be applicable in clinical practice. Although it is known that the standard short axis method provides accurate and reproducible volume and EF measurements, the area-length method is being widely used because it requires no additional time for image acquisition and little time for analysis. It has previously been demonstrated that the biplane area-length method for ellipsoid bodies is a rapid and reproducible alternative method for the assessment of left atrial function in both healthy subjects and patients (15). Measurements to assess right atrial function, however, are usually obtained from a single image plane, the horizontal long axis orientation. Thus, volumes and EF may differ significantly from those calculated by the sum of the outlined areas using the standard short axis method due to the geometric simplification inherent in the single-plane area-length method calculation.

Therefore, we aimed to establish CMR reference values for right atrial volumes and EF in normal subjects, for both the standard short axis method and the area-length method; to evaluate differences in the results between the standard short axis method and the area-length method; and to study the reproducibility of right atrial function measurements with both methods.

MATERIALS AND METHODS

Patients

Seventy asymptomatic subjects (38 men, mean age 51.8 ± 15.6 years, range 25–73 years) with no history of cardiac and pulmonary disease, no cardiac risk factors (hypertension, diabetes, hyperlipidemia), normal physical examination, normal left and right ventricular function (EDV 147 ± 30 mL, EDV 49 ± 16 mL, EF $66 \pm 7\%$ and EDV 168 ± 34 mL, EDV 63 ± 23 mL, EF $62 \pm 6\%$, respectively), and no evidence of heart valve disease, atrial and ventricular shunting, defined by CMR, were recruited. These subjects were generally normal volunteers as part of the control arm of research studies, were referred for preventive check-up examinations as part of the cardiovascular prevention program or for insurance purposes, or were referred for clinically suspected cardiac disorders such as mitral valve prolapse, which were ruled out by the CMR exam. Ventricular function was assessed by CMR. Baseline characteristics are given in Table 1. Body surface area (BSA) was calculated according to the Mosteller formula (16). All subjects had a normal baseline electrocardiogram (ECG) and regular sinus rhythm.

Table 1. Baseline characteristics

(n = 70)	Mean \pm SD
Age (years)	51 ± 13
Height (cm)	173 ± 8
Weight (kg)	72.2 ± 11.6
Body surface area (m ²)	1.9 ± 0.2
Heart rate (beats/minute)	68 ± 11
Systolic blood pressure (mm Hg)	126 ± 16
Diastolic blood pressure (mm Hg)	79 ± 18

Subjects with contraindications to CMR were not enrolled. Informed consent was obtained before the CMR examination in all cases. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the institutional ethics committee.

Image acquisition

CMR was performed with a 1.5 Tesla magnet (Sonata, Siemens, Erlangen, Germany), using a front and rear surface coil (CP Body Array Flex, CP Spine Array, Siemens) and retrospective electrocardiographic triggering. A fast imaging sequence with steady-state free precession (SSFP) and constant radiofrequency pulsing was used. The parameters for SSFP were as follows: repetition time = 3.2 ms, echo time = 1.6 ms, bandwidth 930 Hz/pixel, flip angle = 60°, in-plane pixel size = 2.3×1.4 mm, matrix 164×256 pixel, temporal resolution ~ 38 ms, trigger pulse 1, trigger delay 0, acquisition time = 7 heartbeats, breathhold duration per slice = 6–12 s, depending on the heart rate, acceleration factor 2 (parallel image acquisition) (17).

On the basis of scout images, cine images were acquired in the short axis and the horizontal long axis view. To cover the left ventricle, short-axis images were acquired from the base of the heart (atrioventricular ring) to the apex with a 6 mm slice thickness and a 4 mm gap during breathholding. Atrial slices were planned parallel to the atrioventricular groove, and perpendicular to the interatrial septum on the horizontal long axis image. Care was taken that the entire right atrium was covered from the base (atrioventricular ring) to the roof.

Analysis

The images were evaluated with a commercially available computer software program (Argus, Siemens) by two experienced investigators (5 and 2 years experience in CMR).

Short-axis method:

Manual tracing of the endocardial borders of successive short-axis slices at ventricular end-diastole (maximal atrial volume) and ventricular end-systole (minimal atrial volume) was performed (Fig. 1A). Right atrial maximal volume was defined as the slice with the largest right atrial dimension, just prior to right atrial contraction and at ventricular end-systole. Right atrial minimal volume was defined as the slice with the smallest right atrial dimension at ventricular end-diastole. Volumes were included as atrial if less than half of the blood volume

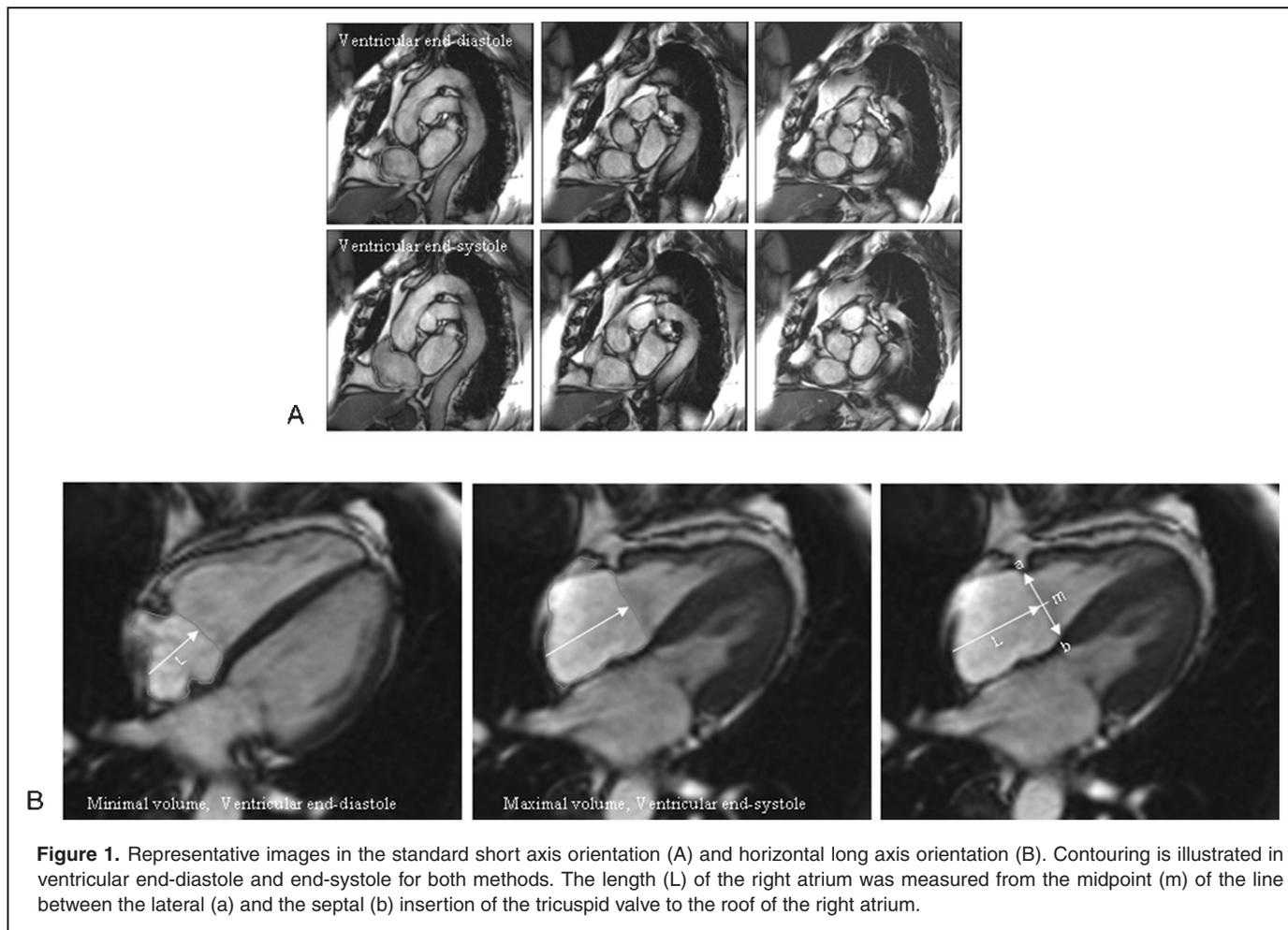


Figure 1. Representative images in the standard short axis orientation (A) and horizontal long axis orientation (B). Contouring is illustrated in ventricular end-diastole and end-systole for both methods. The length (L) of the right atrium was measured from the midpoint (m) of the line between the lateral (a) and the septal (b) insertion of the tricuspid valve to the roof of the right atrium.

was surrounded by ventricular myocardium. Slices below the level of the tricuspid and mitral valves were considered ventricular. Care was taken that the cava veins were excluded for volume measurements. The right atrial appendage was included in the atrial volumes. Both observers were blinded to the patient's history and clinical information. The frame with the maximal and minimal volume was selected independently by each observer. Maximal and minimal right atrial volumes were used to calculate atrial stroke volumes and EF: Maximal volume-minimal volume = stroke volume (mL); (Stroke volume/maximal volume) x 100 = EF (%).

Area-length method:

Maximal and minimal right atrial areas were traced using the horizontal long axis image (15). In addition, the length from the midpoint of the line between the septal and lateral insertion of the tricuspid valve to the roof of the right atrium was measured on both the frame with the maximal and the minimal right atrial area (Fig. 1B). Right atrial volumes and EF were then calculated using the area length method for ellipsoid bodies as previously described (15, 18). Briefly, the following formula was used: $8 \times (\text{Area})^2 / 3\pi \text{Length}$.

The analysis time was defined as the time from start to finish of the tracings for both methods.

Reproducibility

The data set of all subjects was re-analyzed for both the short-axis and the area-length method by the first observer to assess intraobserver variability. The observer was blinded to the previous results. The second analysis was performed at least 1 week after the first analysis.

To provide a measure of interobserver variability a second observer analyzed the entire data set with both methods. The second observer was unaware of the results of the first observer.

To assess interstudy reproducibility, 10 subjects were scanned twice. The second scan was performed on the same day. After the first scan was completed, all subjects were taken out of the magnet for at least 30 minutes. After repositioning in the scanner, cine images were acquired on the basis of scout images in the same manner as described above.

Statistical analysis

Continuous data are expressed as mean \pm SD, except where noted. Comparisons between analysis methods (short-axis

Table 2a. Normal values (mean ± SD and range) for right atrial volumes and ejection fraction (EF), standard short axis method

	Total (n = 70)			Male (n = 38)			Female (n = 32)			p value*
	Mean	SD	Min-Max	Mean	SD	Min-Max	Mean	SD	Min-Max	
Maximal volume (mL)	101.0	30.2	36.8-170.4	104.6	31.6	45-170.4	96.7	28.3	36.8-162.8	0.273
Maximal volume index (mL/m ²)	52.8	16.3	19.7-89.2	52.1	16.6	21.6-87.5	53.7	16.3	19.7-89.2	0.786
Minimal volume (mL)	50.3	19	14.7-92	53.4	20.6	14.7-92	47.7	16.7	21-80.6	0.218
Minimal volume index (mL/m ²)	26.6	10.1	7-47.5	26.6	10.8	7-47.5	26.5	9.4	10.8-44.1	0.944
Stroke volume (mL)	50.2	15.7	14-83.7	51.2	16.4	19.3-83.7	49	15	14-82.3	0.564
Stroke volume index (mL/m ²)	26.2	8.5	7.5-45.1	25.4	8.4	8.9-44	27.2	8.7	7.5-45.1	0.409
EF (%)	47.2	8.3	32.3-64.9	46.6	8.9	32.3-64.9	47.8	7.6	33.4-64.1	0.596

(p value indicates differences between men and women).

*Two-sided Mann-Whitney-U-test.

Table 2b. Normal values (mean ± SD and range) for right atrial volumes and ejection fraction (EF), area-length method

	Total (n = 70)			Male (n = 38)			Female (n = 32)			p value*
	Mean	SD	Min-Max	Mean	SD	Min-Max	Mean	SD	Min-Max	
Maximal volume (mL)	103.2	32.6	35.5-177.2	106.6	34.4	41.1-177.2	99.2	30.3	35.5-166.7	0.383
Maximal volume index (mL/m ²)	54	17.8	19-91.3	53.1	18.2	19-90.9	55.1	17.4	19-91.3	0.715
Minimal volume (mL)	50.8	20.2	11.5-94.3	53.4	21.9	11.5-94.3	47.7	17.8	18.3-82.6	0.311
Minimal volume index (mL/m ²)	26.6	10.8	5.5-48.7	26.7	11.5	5.5-48.7	26.5	10.1	9.4-43.5	0.953
Stroke volume (mL)	52.4	16.9	15.6-87.8	53.1	17.4	17-87.8	51.5	16.6	15.6-87.3	0.814
Stroke volume index (mL/m ²)	27.4	9.2	7.9-47.8	26.4	8.9	7.9-46.2	28.6	9.5	8.3-47.8	0.311
EF (%)	51.4	9.2	31.1-73	50.7	9.3	32.7-73	52.3	9.1	31.1-72.6	0.472

(p value indicates differences between men and women).

*Two-sided Mann-Whitney-U-test.

versus area-length method) were made using the Wilcoxon matched-pairs signed-ranks test. The Mann-Whitney U Test was used to compare volumes and EF between men and women. The Spearman rank correlation coefficient was calculated to test whether changes in volume and EF are dependent on age. One-sided tolerance limits for volumes were defined as the upper bound of the 90% confidence intervals for the 90% percentiles, tolerance limits for EF as the lower bound of the 90% confidence interval for the 10% percentile. All statistical tests were 2-tailed; $p < 0.05$ was considered significant. Intraobserver, interobserver and interstudy reproducibility were assessed using the method of Bland and Altman (19). Statistical analysis was performed with Stata 8.2 (Intercooled Stata 8.2 for Windows, StataCorp LP, TX, USA).

RESULTS

CMR was well tolerated by all subjects, and all datasets were of sufficient quality to be included in the study.

The results with differentiation into all subjects, males and females, and sub-division into absolute and BSA-normalized values are shown in Table 2. Tolerance limits are given in Table 3. Compared to men, females had smaller absolute values for maximal volumes, minimal volumes and stroke volumes with both the standard short axis method and the area-length method. EF was larger in females than in men for both methods. However, the differences were not significant for either method ($p \geq 0.22$ for all comparisons), were not gender related, and remained

insignificant after adjustment to the body surface area (BSA). There was no correlation between right atrial volumes, EF and age (Table 4).

Volumes and EF determined by the standard short axis method were smaller than those calculated by the area-length method (Table 5). Only the difference in minimal volumes was not significant between both methods ($p = 0.126$).

The time for analysis was 7 ± 2 minutes with the standard short axis method and 62 ± 18 s with the area-length method.

Intraobserver, interobserver and interstudy variability was higher for the area-length method than for the standard short axis method, with wider limits of agreement (Table 6, Fig. 2).

The heart rate was not significantly different between scan 1 and 2 (73.3 ± 8.3 versus 68.9 ± 5.2 , $p = 0.848$).

Table 3. Tolerance limits (upper limits of normal for volumes, lower limits of normal for EF) for the standard short axis method and the area-length method (absolute values, values adjusted to BSA in brackets)

	Tolerance limits			
	Short Axis Method		Area-Length Method	
	Male	Female	Male	Female
Maximal volume (mL)	164.1 (83.8)	161.1 (88.3)	170.3 (88.0)	165.3 (90.4)
Minimal volume (mL)	91.8 (47.2)	80.5 (43.7)	93.5 (48.3)	82.2 (43.5)
EF (%)	37.8 (19.1)	40.5 (21.9)	41.5 (21.1)	44.3 (23.7)

Table 4. Correlation between right atrial volumes and ejection fraction (EF) and age

	Short Axis Method		Area-Length Method	
	rho*	p-value	rho	p value
Maximal volume (mL)	0.122	0.315	0.153	0.205
Maximal volume (mL/m ²)	0.090	0.459	0.115	0.343
Minimal volume (mL)	0.159	0.189	0.150	0.217
Minimal volume (mL/m ²)	0.125	0.304	0.139	0.252
EF (%)	-0.102	0.403	-0.100	0.409

*Spearman rank correlation coefficient.

DISCUSSION

CMR has been proven to be accurate and reproducible for cardiac volume assessment and is being increasingly used as the reference standard for research trials and in clinical practise (8-10, 12). The standard acquisition of atrial volumes and EF with CMR uses the short-axis stack for which both image acquisition and post-processing is time-consuming (15). Automatic contour detection programs for rapid volume and EF assessment would be of great practical value, but they are currently only available for ventricular function assessment and have not yet been perfected (20). Manual correction of automatically detected contours often takes nearly as long as drawing the contours manually (21). The area-length method is widely used in clinical practice because it does not require additional time for image acquisition, and the analysis is significantly faster compared to the standard short axis method. However, the area-length method relies on greater geometric assumptions than the standard method, and thus, is less reproducible (Table 6).

This is the first study that provides a large database of right atrial volumes and EF in healthy subjects determined by

CMR using the standard short axis method and the less time-consuming area-length method (Table 2). We found that normal values for the standard short axis method differed from those obtained by the area-length method, and thus, CMR reference values for right atrial function are not interchangeable between methods. Volumes and EF were generally smaller with the standard short axis method compared to the area-length method. Whereas the difference in maximal volumes and EF was significant ($p < 0.0001$ for both comparisons), minimal volumes did not differ significantly between both methods ($p = 0.126$) (Table 5). The area-length method was faster (62 ± 18 s versus 7 ± 2 min), but was less reproducible (wider limits of agreement) than the standard short axis method (Table 6, Fig. 2). We did not find age- and gender-related differences in absolute right atrial volumes and EF for either method.

The main reason for the differences in volumes and EF between the two methods may rely on the geometric simplification inherent in the single-plane area-length method calculation. The greater geometric assumption may also explain the lower reproducibility of the area-length method with wider limits of agreement compared to the standard short axis method. Volumes and EF calculated from multiple orthogonal image planes reflect the actual atrial geometry more accurately than the single plane approach. Small differences in drawing contours or measuring the atrial length have a large effect on volume measurements, especially when using the area-length approach.

Age- and gender-related differences in volumes and EF with CMR have been described for right and left ventricular volumes and EF (12, 22). Hudsmith et al (22) reported gender-specific differences for left atrial maximal volumes but did not find significant differences for minimal volumes and EF. In addition, left atrial function measurements were not correlated to age. In the present study, both right atrial volumes and EF were not found

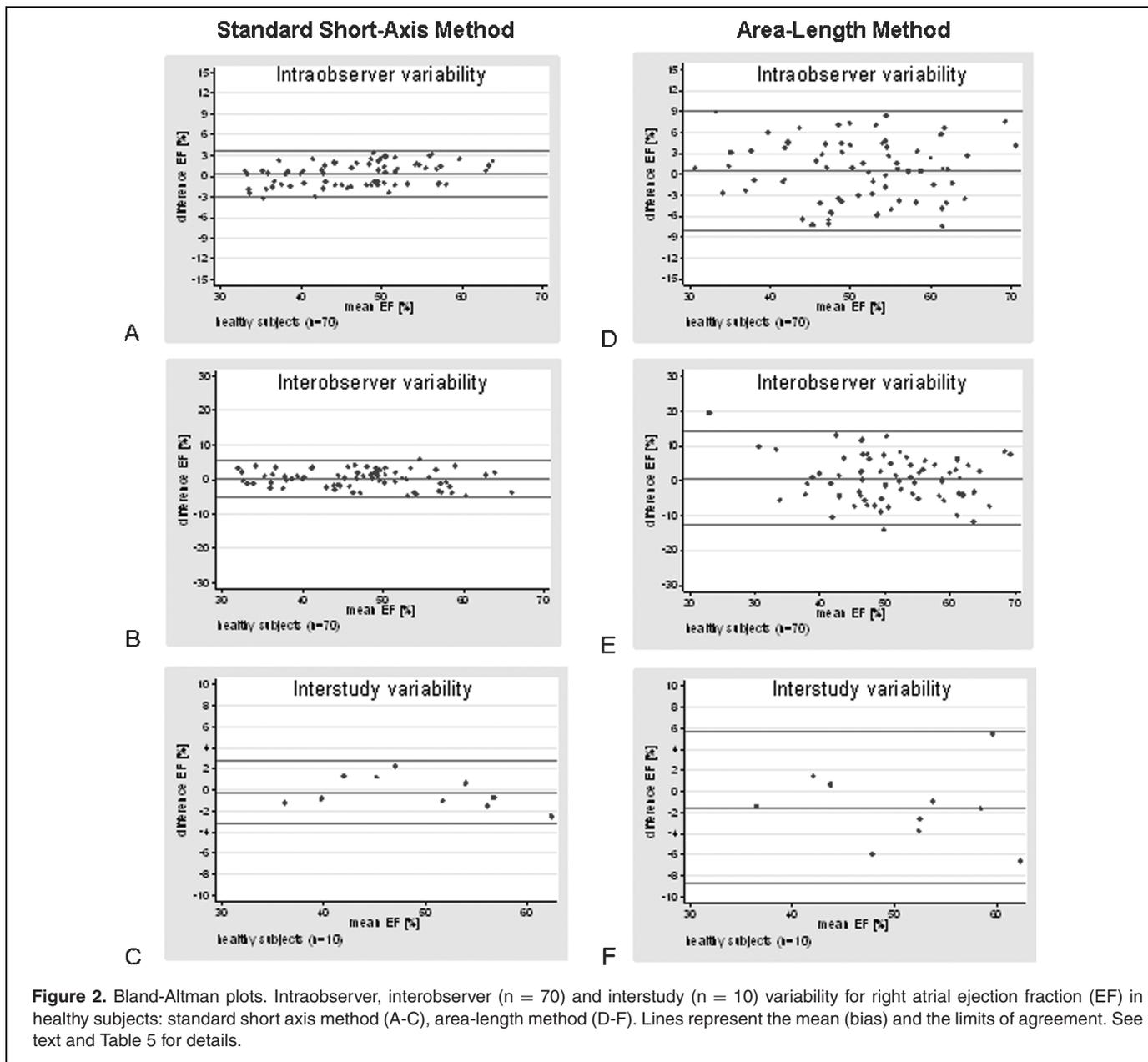
Table 5. Comparison of right atrial volumes and EF, standard short axis method versus area-length method

	Area-Length Method		Short Axis Method		Difference		p value*
	Mean	SD	Mean	SD	Mean	SD	
Maximal atrial volume (mL)	103.2	32.6	101.0	30.2	2.2	4.6	0.0001
Minimal atrial volume (mL)	50.8	20.2	50.3	19	3.5	3.5	0.126
EF (%)	51.4	9.2	47.2	8.3	2.8	2.8	0.0001

*Wilcoxon matched-pairs signed-ranks test.

Table 6. Reproducibility

Short-Axis Method	Intraobserver Bias (limits of agreement)		Interobserver Bias (limits of agreement)		Interstudy Bias (limits of agreement)	
	CoV	CoV	CoV	CoV	CoV	CoV
Maximal volume (mL)	-0.6 (-12.0 to 10.7)	9.1	-1.7 (-13.1 to 9.6)	3.2	-0.4 (-12.6 to 11.8)	14.8
Minimal volume (mL)	-0.7 (-10.0 to 8.7)	7.1	-1.1 (-7.9 to 5.8)	3.2	-0.3 (-7.9 to 7.4)	14.4
EF (%)	0.2 (-4.9 to 5.4)	11.0	0.4 (-3.0 to 3.8)	4.7	-0.2 (-3.3 to 2.8)	6.7
Area-Length Method	Intraobserver Bias (limits of agreement)		Interobserver Bias (limits of agreement)		Interstudy Bias (limits of agreement)	
	CoV	CoV	CoV	CoV	CoV	CoV
Maximal volume (mL)	-0.2 (-23.5 to 23.1)	56.9	-0.1 (-23.3 to 23.1)	68.4	0.1 (-21.8 to 22.0)	100.2
Minimal volume (mL)	-0.7 (-16.8 to 15.4)	12.1	-0.8 (-18.6 to 17.0)	11.3	1.9 (-11.6 to 15.5)	3.5
EF (%)	0.5 (-8.1 to 9.2)	8.0	0.8 (-12.5 to 14.0)	8.6	-1.5 (-8.6 to 5.6)	2.4



to be gender-related. The reason for the differences in age and gender correlation between atria and ventricles might be due to the variable shape of the atria in normal subjects, resulting in a wide range of normal values in both men and women and across all age groups. The wide range of age in our study (25–73 years) may also account for the fact that we did not find age related differences in volumes and EF.

Only few studies with small numbers of patients ($n \leq 19$) have addressed right atrial function by CMR (23–28). The values for right atrial volumes and EF differ greatly between these studies. Discrepancies between previously published data and our results can be explained by differences in imaging sequences (25), image acquisition (25, 27), and analysis methods (23, 25–27). Thus, the comparison of the results is difficult. For instance, the vol-

umes and EF reported by Therkelsen et al (27) were smaller than ours. However, they used a prospectively gated spoiled gradient-echo sequence for image acquisition, and measurements were taken from vertical long axis images through the right atrium. In recent years, the SSFP technique has been introduced, which yields significantly improved blood-myocardium contrast, acquisition speed, and offers high temporal resolution cine imaging with improved image quality. It has been demonstrated that SSFP acquisitions lead to slightly different results to the spoiled gradient echo sequence for cardiac volumes because of superior discrimination between blood and endocardium and between epicardium and epicardial fat (14, 18, 29). Thus, previously reported values for normal right atrial function are now not ideal, and new normal ranges with SSFP are needed. In addition, it

is important to note that none of the above mentioned studies used either the standard short axis method or the horizontal long axis area-length method for right atrial function assessment. In the light of the fact that the standard short axis method is considered the gold standard for ventricular function assessment, it should also be the standard technique for atrial function evaluation. Then, both left and right atrial and ventricular function can be assessed simultaneously without changing the image orientation. Measuring volumes from different image orientations (eg, axial) (25) requires more time for image acquisition, parameter adjustment and analysis. In addition, volumes and EF may vary between different image orientations (29).

The area-length method may be used for rapid right atrial function assessment in patients in whom accurate and reproducible measurements are not the primary goal. In patients in whom therapeutic decisions are based on the results and follow up studies are required for guiding therapy, the short axis method should be preferred. The reference values for right atrial function provided by this study are of significant clinical and research utility for the interpretation of CMR studies.

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