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VENTRICULAR FUNCTION

Atrial and ventricular volume and function in persistent and permanent atrial fibrillation, a magnetic resonance imaging study

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Left atrial size is independently related to cardiovascular morbidity and mortality, and atrial fibrillation (AF) is strongly associated with atrial size. Our aims were to report atrial and ventricular dimensions in patients with AF evaluated with magnetic resonance imaging (MRI), and to assess the inter-study reproducibility of the measurements. Nineteen healthy volunteers, 19 patients with permanent AF, and 58 patients with persistent AF had cardiac dimensions evaluated by 6-mm cinematographic breath-hold MRI scans using a 1.5 Tesla Siemens Vision Magnetom scanner with a phased array chest coil. Intraobserver variability and inter-study reproducibility of the cardiac volumes and ejection fractions (EF) gave acceptable Bland-Altman plots, good correlations (R^2: 0.80–0.99), and low reproducibility coefficients. The mean atrial volumes were similar in the two groups with AF [systolic vol. index (SVI): 75.9–80.3 mL/m^2; diastolic vol. index (DVI): 77.4–82.1 mL/m^2] and significantly different from the healthy volunteers (SVI: 30.3 mL/m^2; DVI: 62.3 mL/m^2; $p < 0.0001$). Mean left ventricular (LV) volumes and EF were significantly different in permanent AF (SVI: 34.2 mL/m^2; DVI: 68.3 mL/m^2; EF: 50.8%) compared to persistent AF [SVI: 44.0 mL/m^2 ($p = 0.02$); DVI: 77.2 mL/m^2 ($p = 0.03$); EF: 44.9% ($p = 0.02$)], and closer to the normal values (SVI: 22.4 mL/m^2; DVI: 66.5 mL/m^2; EF: 67.0%). MRI is a highly reproducible method for measurement of atrial and ventricular dimensions in healthy volunteers and in patients with AF. Our results suggest that atrial dilatation appears within the first months of AF and stays more or less unchanged thereafter. The LV appears to dilate early as a response to AF, but later seems to adapt.

Key Words: Atrial volume; Atrial function; Ventricular volume; Ventricular function; Atrial fibrillation; Magnetic resonance imaging

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia. The prevalence goes up with increasing age of the population (1), and recently, the age-standardized prevalence has been shown to be increasing in the male population (2). AF is classified as either paroxysmal, requiring no intervention for termination (self-limited); persistent with a duration of usually more than 7 days, requiring medical or electrical cardioversion to achieve sinus rhythm; or permanent, where achieving sinus rhythm is either not possible or has not been attempted (1).

Left atrial (LA) size is independently related to cardiovascular morbidity and mortality (3–5). Moreover, it is well known that AF is strongly associated with atrial size, as atrial dilatation is both the cause and consequence of AF (1, 6).

Magnetic Resonance Imaging (MRI) of the atria has only been evaluated in few studies and never in patients with persistent or permanent AF (7, 8). For imaging of the cardiac ventricles, MRI is regarded as the gold standard, but has only been examined in a few studies in patients with AF (9). Echocardiography is the most widespread cardiac imaging technique. However, due to technical limitations, it is often difficult to accurately assess cardiac chamber volumes. Echocardiographic atrial volume measurements are dependent on correct angulations and positioning of the imaging planes and on geometric assumptions about atrial shape. Echocardiography underestimates LA volumes significantly compared to MRI (10), and is difficult in AF due to the irregular heart rhythm, causing a significant variation in ventricular filling.

Our aim was to assess the reproducibility of MRI for 1) measuring atrial volumes and ejection fraction (EF) in healthy volunteers and for 2) measuring atrial and ventricular volumes as well as EF in patients with AF. In addition, we

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report atrial measurements in healthy volunteers and atrial and ventricular measurements in patients with persistent and permanent AF.

2. Materials and methods

2.1. *Study population*

Between April 2001 and January 2003 a total of 96 participants were included: 19 healthy volunteers, 19 patients with permanent AF, and 58 patients with persistent AF. The healthy volunteers with no prior history of cardiovascular or other chronic disease were recruited by internal advertising in the hospital. They all had a normal physical examination, normal blood pressure (< 130/85 mm Hg), a normal resting electrocardiogram defined by the Minnesota Code Criteria and a normal echocardiogram (11), and were on no medication (Table 1). Patients with persistent AF were consecutively recruited as they were planned for elective cardioversion if the duration of AF was less than 8 months, and patients with permanent AF were recruited from our out-patient clinic. The patients with AF are described in Table 1. Exclusion criteria for patients with AF were contraindications to MRI (pacemaker, claustrophobia, obesity, etc.), significant valvular disease, previous cardiac surgery, severe pulmonary or renal disease, severe heart failure (NYHA III and IV), and cardiac diseases other than those listed in Table 1. The patients were in AF during the MRI examination.

The study conformed with the principles outlined in the Declaration of Helsinki, and was approved by the local ethics committee. Written informed consent was obtained from the patients and healthy volunteers.

2.2. *MR imaging technique*

MRI was performed using a 1.5 Tesla Siemens Vision Magnetom (Siemens Medical Systems, Erlangen, Germany) with high performance gradients (maximum amplitude 20

Table 1. Demographics and patient characteristics

	Healthy volunteers	Persistent AF	Permanent AF
Number	19	58	19
Age years	56 (51–69)	65 (34–84)[a]	67 (44–83)[a]
Sex male/female	69%/31%	78%/22%	64%/36%
Weight kg	75 (48–90)	84 (54–118)[a]	82 (52–120)
Height cm	175 (162–192)	176 (155–196)	175 (155–195)
Systolic BP mmHg	135 (110–170)	144 (72–200)	148 (111–186)[a]
Diastolic BP mmHg	83 (70–92)	89 (58–124)[a]	86 (61–117)
Heart rate	66 (50–89)	77 (39–110)[a]	82 (57–109)[a]
Smoking	5 (26%)	16 (28%)	3 (16%)
Medication			
Digoxin	0	10 (17%)[a]	11 (58%)[a,b]
Verapamil	0	16 (28%)[a]	4 (21%)[a]
Beta blocker (other than Sotalol)	0	12 (21%)[a]	3 (16%)
Sotalol	0	20 (35%)[a]	2 (11%)[b]
Flecainide	0	1 (2%)	0
Propafenone	0	41 (71%)[a]	1 (5%)[b]
Amiodarone	0	3 (5%)	0
ACE Inhibitors	0	17 (29%)[a]	9 (47%)[a]
Angiotensin II antagonists	0	2 (3%)	1 (5%)
Cardiac history			
Ischemic heart disease (by historgy)	0	8 (14%)[a]	3 (16%)
Previous myocardial infraction	0	7 (12%)[a]	1 (5%)
Hypertension (on medication)	0	23 (40%)[a]	7 (37%)[a]
LV systolic dysfunction (EF < 60%)	0	10 (17%)[a]	5 (26%)[a]
EF % at baseline echo (if EF < 60%)		42% (35–55%)	35% (30–40%)
Days since last in sinusrhytm	0	107 (14–240)[a]	1022 (311–4745)[a,b]
Days with AF in total	0	146 (35–440)[a]	1154 (360–4745)[a,b]
Lone atrial fibrillation	0	24 (41%)[a]	9 (47%)[a]

Note: Values are either mean (range) or total number (%).
[a]Significantly different compared to the group with healthy volunteers.
[b]Significantly different compared to the group with persistent AF.

mT/m; maximum slew rate 66 T/m/s). Imaging was performed with patients in the supine position using a phased array chest coil. Localizing scans were followed by breath hold (in expiration) cine acquisitions. Each slice was obtained over 15 heart beats with an electrocardiographically gated fast low angle shot (FLASH) cinematographic pulse sequence, with echo sharing to improve the temporal resolution. The time resolution between images was 50 ms (TR = 9.9 ms; TE = 4.8 ms; flip angle = 20°; field of view = 350 × 350 mm, and matrix size = 128 × 256 interpolated to 256 × 256). Atrial slices were planned parallel to the axis going from the tip of the mitral valve to the apex of the left ventricle on the cinematographic four-chamber image at ventricular end diastole (0 ms), creating vertical long-axis atrial images. The vertical long axis was chosen, as Järvinen (7) showed that the definition of the atrioventricular borders (atrioventricular valve annulus) is optimal in this position. Both atria were covered by 20–25 6-mm slices with no inter-slice gaps. The same sequence was used to visualize both ventricles with a stack of short-axis images. The short-axis images were positioned according to the protocol suggested by Pennell (12), although we used 6-mm slices with no inter-slice gaps. In all, we had 18–25 slices covering both ventricles. The healthy volunteers only had atrial scans, and consequently we used ventricular data from Lorenz et al. (13) as our normal reference intervals.

2.3. *Image analysis*

Image analysis was performed off-line using CMR tools (CMR tools, Evaluation Version 1, Imperial College, London, UK). All atrial and ventricular volumes were analyzed blindly in one batch by the same examiner with manual tracing of the systolic and diastolic endocardial borders, see Fig. 1. For each slice, atrial and ventricular systole and diastole were defined.

Atrial image analyses: Atrial systole was defined as the first image (time = 0 ms) triggered by the R-wave, and atrial diastole as the image immediately preceding the opening of the mitral valve. Care was taken to exclude the caval veins and the pulmonary arteries from the atrial volumes.

Ventricular image analyses: Ventricular end-diastole was defined as the first image after the R-wave. Ventricular end-systole was chosen at the point where the blood pool was smallest. The contour tracing was aided by reviewing the cine scans in the movie mode. The basal slice of the ventricles was

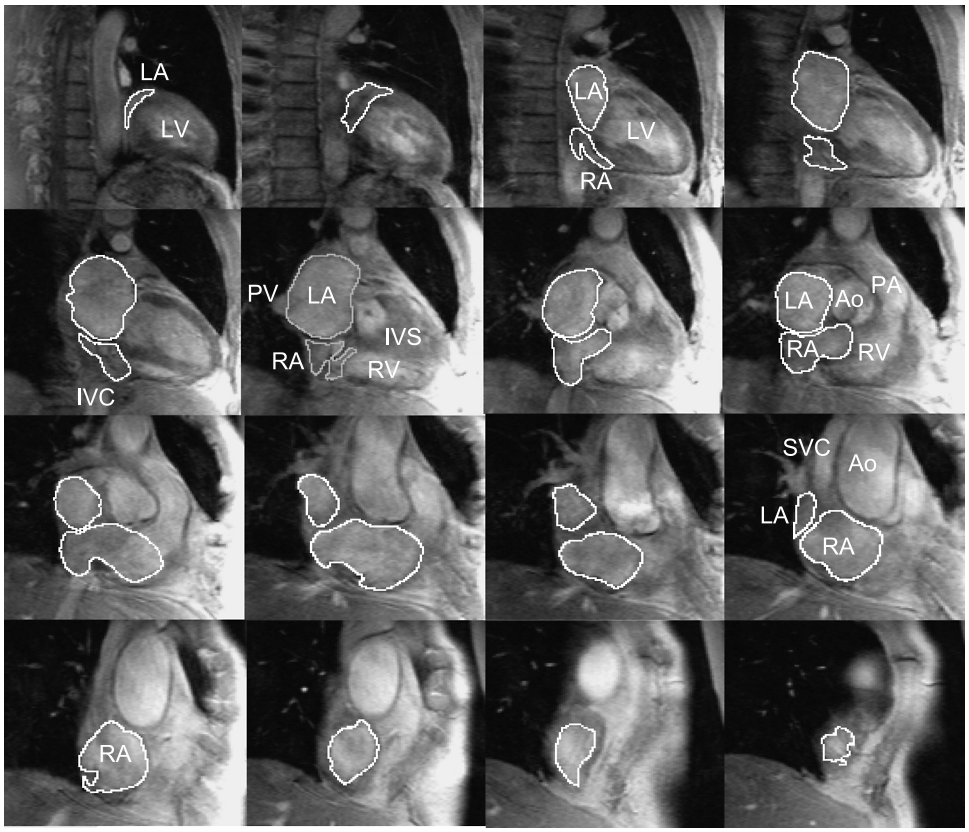

Figure 1. Examples of the atrial slices in vertical long axis with endocardial contours in atrial diastole in patients with atrial fibrillation. Contours are drawn manually on all slices in diastole and systole. LA: left atrium; RA: right atrium; LV: left ventricle; RV: right ventricle; PV: pulmonary vein; IVS: Inter-ventricular septum: Ao: Aorta; PA: pulmonary artery; IVC: inferior vena cava; SVC: Superior Vena Cava.

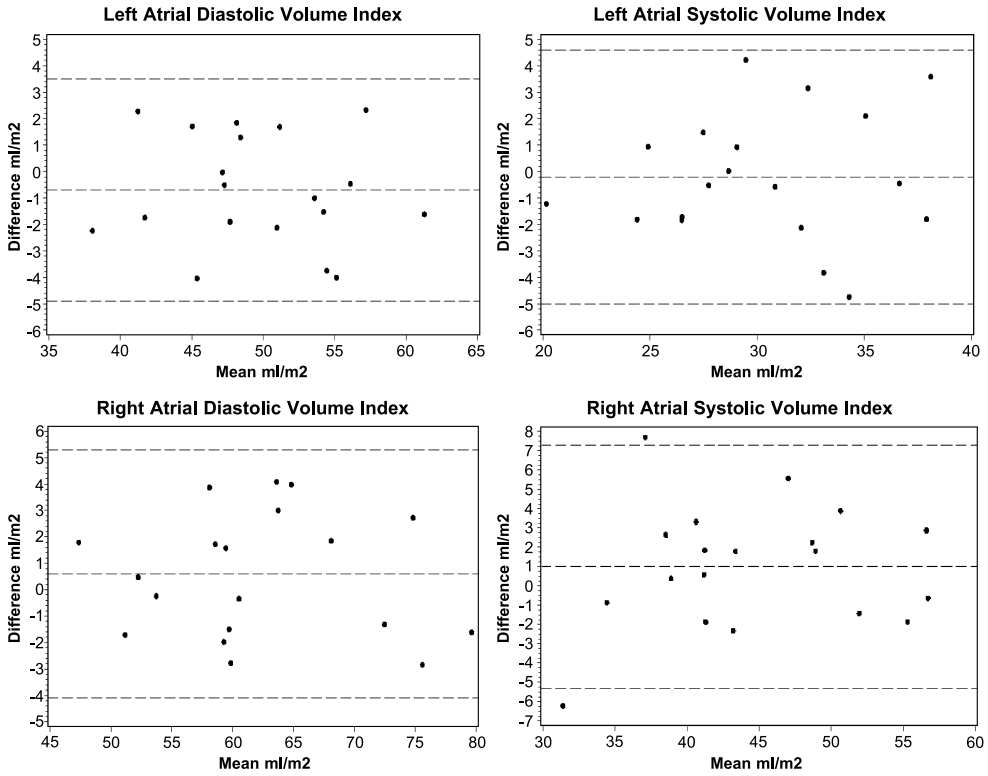

Figure 2. Intra-observer variability of the atrial volumes in the group of healthy volunteers illustrated by Bland-Altman plots. The lines indicate the mean difference + 2 SD of the difference between the two measurements. N = 19.

carefully positioned according to Pennell (12), but in case of doubt, slices were considered to be within the left ventricle if the blood volume was surrounded by 50% or more of ventricular myocardium. The papillary muscles were outlined separately and included as myocardial mass. If the pulmonary valve was evident in the basal slice, only the part of the chamber below the level of the pulmonary valve was included in the RV volume. In the inflow part of the right ventricle, the blood volume was excluded from the RV volume if the surrounding wall appeared thin and untrabeculated.

The volumes were calculated by adding the volumes of all the slices covering left and right atria and ventricles (Simpson's method). The EF was calculated as EF (%) = [End Diastolic Volume (EDV) − End Systolic Volume (ESV)]/DV × 100. LV mass was calculated as LV mass = 1.05 × (epicardial volume − endocardial volume). Body weight and body height were measured and body surface area (BSA) (14) was calculated. Subsequently, division with BSA indexed all MRI variables apart from EF.

Table 2. Intraobserver variability in healthy volunteers

	R^2	RC	Mean Δ	2SD
LA EDV index ml/m^2	0.97	1.5	−0.7	4.2
LA ESV index ml/m^2	0.94	0.7	−0.2	4.8
LA EF%	0.94	1.0	−0.4	6.1
RA EDV index ml/m^2	0.98	0.9	0.6	4.7
RA ESV index ml/m^2	0.95	2.3	1.0	6.3
RA EF%	0.88	3.2	−0.9	7.9

Note: R^2: correlation coefficient; RC: reproducibility coefficient; Mean Δ: mean difference between examination 1 and examination 2; 2SD two times the standard deviation of the mean difference. N = 19.

2.1.1. *Intraobserver variability and inter-study reproducibility*

To evaluate the intraobserver variability of atrial MRI, the 19 healthy volunteer examinations were reanalyzed at least 2 months after the initial analysis. Ten of the 19 patients with permanent AF had two MRI scans to establish the inter-study reproducibility of atrial and ventricular volume measurements in patients with AF. The two MRI scans were performed 1–5 days apart. The same 10 patients with permanent AF as above had their first MRI scan reanalyzed 7 months after the initial analyses to evaluate the intraobserver variability. The same examiner evaluated all examinations.

2.4. *Statistical analysis*

For all MRI variables, verification of normal distribution of data was accomplished using histograms, and mean values ± one standard deviation (SD) were calculated. Two-sample

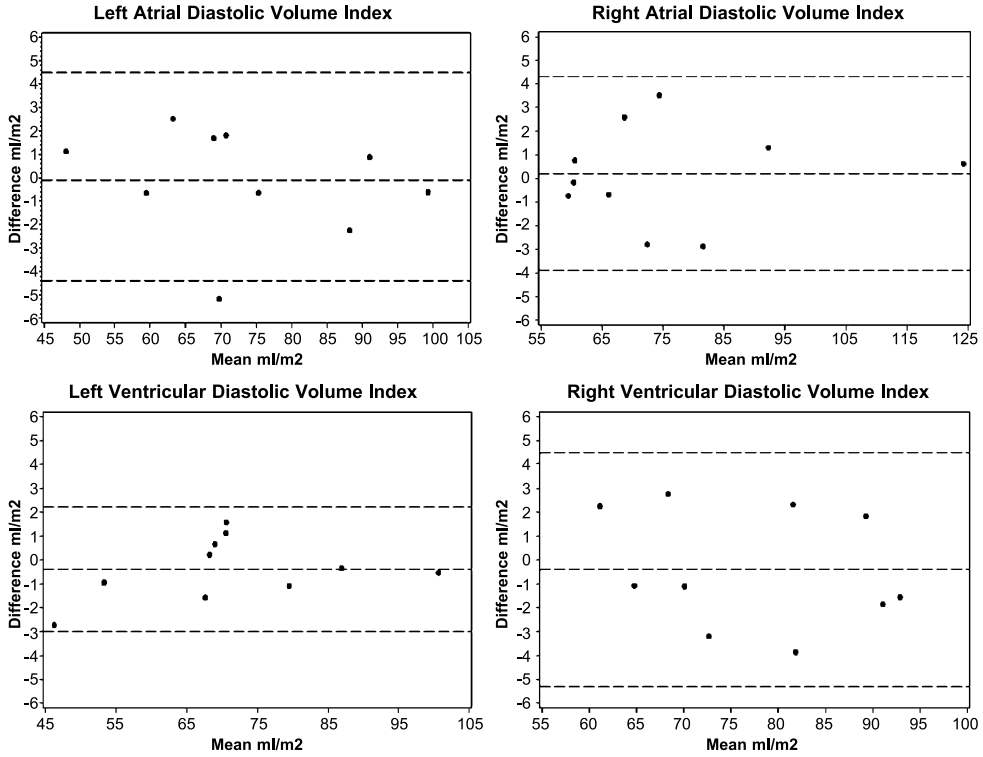

Figure 3. Intra-observer variability of the diastolic volumes in patients with permanent atrial fibrillation illustrated by Bland-Altman plots. The lines indicate the mean difference ± 2 SD of the difference between the two measurements. N = 10.

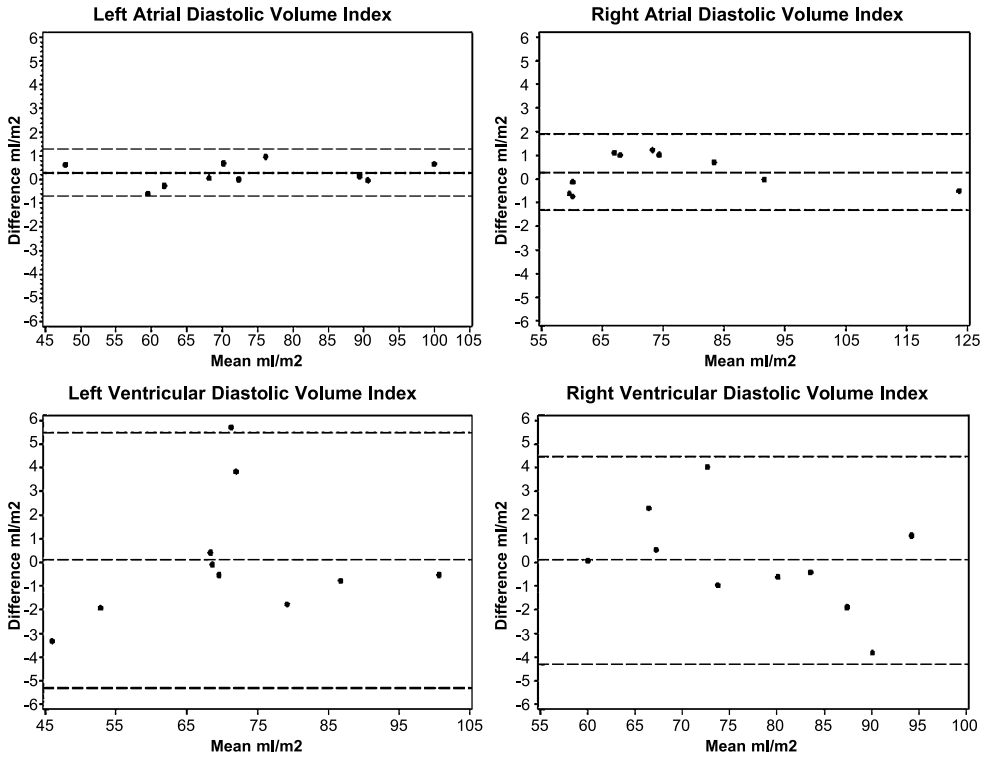

Figure 4. Reproducibility of the diastolic volumes in patients with permanent atrial fibrillation illustrated by Bland-Altman plots. The lines indicate the mean difference ± 2 SD of the difference between the two measurements. N = 10.

Table 3. Intraobserver variability and inter-study reproducibility in patients with permanent atrial fibrillation

	Intra obs. var				Inter-study reprod.			
	R^2	RC	Mean Δ	2SD	R^2	RC	Mean Δ	2SD
LA EDV index mL/m^2	0.98	0.2	−0.1	4.6	0.99	0.3	0.3	1.0
LA ESV index mL/m^2	0.98	1.1	−0.8	4.3	0.99	0.1	−0.1	0.7
LA EF %	0.80	48.1	1.1	3.5	0.89	23.3	0.4	1.9
RA EDV index mL/m^2	0.99	0.2	0.2	4.1	0.99	0.4	0.3	1.6
RA ESV index mL/m^2	0.99	0.2	−0.1	4.2	0.99	0.6	0.5	2.0
RA EF %	0.85	25.6	0.5	1.9	0.87	16.6	−0.2	2.7
LV EDV index mL/m^2	0.99	0.5	−0.4	2.6	0.99	0.2	0.1	5.4
LV ESV index mL/m^2	0.98	2.9	1.1	3.2	0.99	1.0	−0.4	4.1
LV EF %	0.97	3.8	−1.9	4.2	0.99	1.3	0.5	3.0
RV EDV index mL/m^2	0.96	0.5	−0.4	4.9	0.99	0.1	0.1	4.4
RV ESV index mL/m^2	0.95	0.8	0.3	3.8	0.98	0.2	0.1	3.9
RV EF %	0.89	1.7	−0.8	3.9	0.98	0.2	−0.1	2.5
LV mass index g/m^2	0.96	0.5	−0.1	8.3	0.98	2.1	−2.0	8.0

Note: Intra obs. var.: Intraobserver variability; Inter-study reprod.: Inter-study reproducibility. N = 10.

t-tests or table analyses ($\times^2$ or Fisher's exact test) were used to compare groups. All tests were two-sided, and a significance level of 5% was used. Intraobserver variability and inter-study reproducibility were evaluated in three ways: 1) by the method suggested by Bland and Altman (15), 2) by fitting a linear regression correlating the two evaluations, and 3) by calculating the reproducibility coefficient (RC) as the percentage of the absolute difference between the two measurements divided by the mean of the two measurements [(measurement 1 − measurement 2)/mean of the two measurements]. All tests were performed in the Statistical Analysis System (SAS) (SAS® Institute Inc., Cary, NC).

3. Results

The irregularity of the heart rhythm in AF can cause loss of image quality. To obtain good quality images, one to five slices in 21% of all the examinations had to be repeated, and in 8% of the examinations the trigger window had to be adjusted

Table 4. MRI variables

	Volunteers	Persistent AF	Permanent AF
Number	19	58	19
LA EDV index mL/m^2	49.7 ± 6.0	78.5 ± 18.5[a]	77.4 ± 19.1[a]
LA ESV index mL/m^2	30.3 ± 4.9	76.6 ± 18.5[a]	75.9 ± 18.6[a]
LA EF %	39.2 ± 5.9	2.6 ± 2.3[a]	2.0 ± 2.1[a]
RA EDV index mL/m^2	62.3 ± 8.7	82.1 ± 23.7[a]	78.4 ± 19.5[a]
RA ESV index mL/m^2	44.6 ± 7.4	80.3 ± 23.7[a]	77.1 ± 19.7[a]
RA EF %	28.4 ± 5.6	2.4 ± 1.9[a]	1.8 ± 2.1[a]
LV EDV index mL/m^2	66.5 ± 10.7[c]	77.2 ± 19.7	68.3 ± 13.5[b]
LV ESV index mL/m^2	22.4 ± 5.0[c]	44.0 ± 16.4	34.2 ± 11.8[b]
LV EF %	67.0 ± 5.0[c]	44.9 ± 9.2	50.8 ± 9.9[b]
RV EDV index mL/m^2	76.0 ± 12.0[c]	80.6 ± 18.2	75.9 ± 13.3
RV ESV index mL/m^2	30.0 ± 7.4[c]	46.7 ± 12.7	41.7 ± 10.5
RV EF %	61.0 ± 7.3[c]	42.3 ± 6.7	45.4 ± 6.7
LV mass index g/m^2	87.3 ± 10.0[c]	102.7 ± 22.6	94.3 ± 17.3

Note: Values are mean ± 1 standard deviation.
LA: left atrial; RA: right atrial; LV: left ventricular; RV: right ventricular; EDV: end diastolic volume; ESV: end systolic volume.
[a]Significantly different compared to the group with healthy volunteers.
[b]Significantly different compared to the group with persistent AF.
[c]Ventricular normal volumes and EF from Lorenz et al. (13).

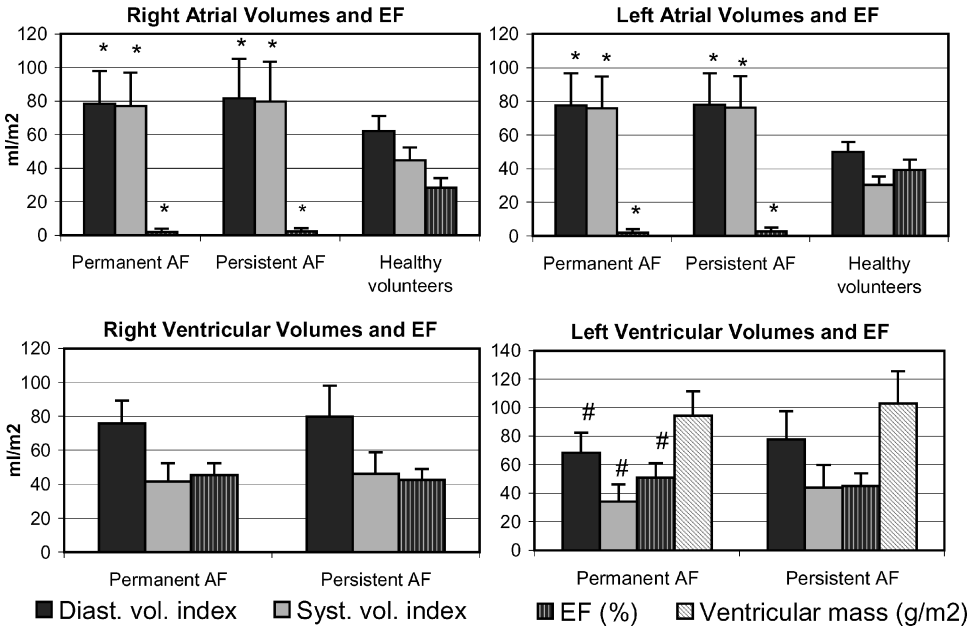

Figure 5. Mean atrial and ventricular volume indices and ejection fractions. All values are mean + 1 SD. *Significantly different from the healthy volunteers ($p < 0.0001$). #Significantly different from the group with persistent AF. (LVEDV: $p = 0.03$; LVESV and LVEF: $p = 0.02$.)

during the MRI scan. However, diagnostic quality data sets were obtained in all subjects. Figure 1 shows an example of some of the slices covering both atria in atrial diastole in the vertical long axis in a patient with atrial fibrillation.

Patients with AF were 9–11 years older than the healthy volunteers and had slightly higher blood pressure and heart rate during the MRI scan. Patients with permanent AF had a history of significantly longer duration of AF (1154 vs. 146 days), received significantly less sotalol and propafenone, and more digoxin than the patients with persistent AF. Otherwise, the groups were comparable (Table 1).

The intraobserver variability for atrial measurements in healthy volunteers is presented in Fig. 2 and Table 2. The intraobserver variability and inter-study reproducibility of the atrial and ventricular measurements for the patients with permanent AF are given in Fig. 3 and Fig. 4, respectively, and in Table 3. The agreement between the two evaluations in the healthy volunteers and in patients with AF and between the two MRI scans in patients with permanent AF was very good for all variables. Bland-Altman plots are shown for selected atrial and ventricular volume measurements (Figs. 2–4).

Table 4 and Fig. 5 show mean + 1 SD for all atrial and ventricular volumes and ejection fractions and LV mass indexed to BSA. The atrial volumes were similar in the two groups with AF. In both groups with AF there were statistically significant differences between atrial volumes and EF compared to the group of healthy volunteers. There were no differences in atrial volumes between patients with persistent AF and patients with permanent AF.

There were no differences between the two groups of patients with AF for RV volumes, RVEF, or LV mass. Compared to the reference group, RVEDV in the two AF groups were almost the same (reference group: 76.0 ± 12.0 mL/m^2; persistent AF: 80.6 ± 18.2 mL/m^2; permanent AF: 75.9 + 13.3 mL/m^2). The RVESV was 12–16 mL/m^2 higher in the AF groups, yielding a 15–19% lower EF in the AF groups.

There were statistically significant differences between LVEDV, LVESV, and LVEF in the two groups with AF. Surprisingly, the volumes were higher (LVEDV + 8.9 mL/m^2 and LVESV +9.8 mL/m^2, $p = 0.03$ and 0.02, respectively) and EF was lower (LVEF − 5.9%; $p = 0.02$) in the group with persistent AF. Compared to the reference group there was only a small difference in LVEDV (−1.8 mL/m^2 compared to the group with permanent AF). LVESV was 11.8 mL/m^2 smaller in the reference group compared to the group with permanent AF and 21.6 mL/m^2 smaller compared to the group with persistent AF, which resulted in a higher EF (16.2% and 22.1%, respectively).

4. Discussion

We used MRI to describe atrial volumes and EF in healthy volunteers, and atrial and ventricular volumes and EF in patients with AF. The MRI method proved highly reproducible. The intraobserver variability was very low and inter-study reproducibility was high, indicating that MRI may be a robust method for measuring atrial and ventricular dimensions in healthy volunteers as well as in patients with AF. This is consistent with previous atrial MRI studies. Järvinen et al. (7) measured atrial volumes by MRI in healthy volunteers and compared these to the true volumes measured in cadavaric casts, and found these to be highly

comparable. Ishimoto, Ito, and Kinoshita (8) used MRI to examine patients with paroxysmal AF, while in sinus rhythm. They found no difference in atrial volumes between patients with paroxysmal AF and healthy volunteers. Hauser et al. (16) measured the LA with MRI in patients before ablation for AF, again the patients were in sinus rhythm at the time of the MRI scan. Other studies have examined atrial dimensions with MRI in healthy volunteers (17, 18) in cardiac diseases, e.g., myocardial infarction (19) and in hypertension (20).

MRI is currently considered to be the gold standard for cardiac ventricular imaging in patients without AF. A major difficulty in evaluating the LV with echocardiography in AF is that the irregular rhythm makes the contraction heterogeneous, and it is often necessary to average measurements over several heart beats. MRI inherently compensates for an irregular heart rhythm since each image slice is acquired over 15 heartbeats. This corresponds well with the findings of Hundley et al. (9), who found that MRI of the LV in AF is possible and comparable to invasive methods (ventriculography), when measuring volumes and EF. RV volumes and EF in AF have not been described with MRI before.

It is well known from previous echocardiographic studies that both atria dilate during AF. Our results indicate that the atrial dilatation appears within the first months of AF and stays unchanged afterwards. However, further studies with serial measurements are needed before any final conclusions can be drawn. The LV responded differently to the presence of AF. Patients with permanent AF had smaller ventricular volumes and higher EF than patients with persistent AF, although only statistically significant for the left ventricular measurements, indicating that the LV may dilate early as a response to AF, but later appears to adapt. LVEDV was very close to normal in permanent AF, and significantly smaller than in patients with persistent AF. Again, serial measurements are needed before definitive conclusions can be drawn.

One could speculate that the differences between the two groups of patients with AF were attributable to differences in medication. Beta blockers are known to improve LV function in patients with heart failure, and might have the same effect in patients with AF. However, patients with permanent AF received significantly less beta blockade than patients with persistent AF, making the degree of beta blockade an unlikely explanation for our findings.

Patients with permanent AF received significantly more digoxin than patients with persistent AF. Dernellis and Panaretou (21) showed that digoxin significantly decreases both LA and LV volume and increases LA and LV function evaluated by echocardiography in patients with heart failure as well as in healthy volunteers. We did not see this proposed digoxin effect on atrial volumes, but it remains a potential contributory explanation for the observed differences in LV measurements.

In recent years, large studies (22, 23) of different treatment strategies for patients with AF have been published. They have shown that mortality and quality of life are similar in patients where achieving sinus rhythm is attempted compared to patients where AF is accepted. The finding that the LV volumes and systolic function normalize over time in patients with long-term AF could be part of the explanation for these clinical findings.

5. Limitations

It is known that the turbo gradient echo sequence used in our study underestimates ventricular volumes compared to steady-state free precession sequences (SSFP) (24). It is unknown whether the use of SSFP sequences would have an influence on atrial volume measurements. Consequently, caution is required when comparing the volumes reported in our study to volumes obtained with SSFP sequences.

We used prospective gating in this study due to limitations of the MRI scanner. Retrospective gating might have allowed a more accurate determination of atrial end-systole.

We did not test for inter-observer variability.

6. Conclusions

MRI is a highly reproducible method for measurement of atrial and ventricular dimensions in healthy volunteers and in patients with atrial fibrillation.

In our study, patients with persistent AF had similar atrial volumes compared to patients with permanent AF, suggesting that atrial dilatation appears within the first months of AF and stays more or less unchanged thereafter. Our study shows that patients with persistent AF have dilated left ventricles and lower EF compared to patients with permanent AF, suggesting that the LV dilates early as a response to AF, but later appears to adapt.

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