Aims Reports using two-dimensional echocardiography have indicated that radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) results in a reduction in the left atrial (LA) size. Furthermore, the effect of pulmonary vein isolation (PVI) on right atrial (RA) anatomical remodelling has not been studied. Three-dimensional echocardiography (3DE) allows us to more precisely quantify atrial volume. Our aim was to assess the effect of PVI on biatrial anatomical remodelling using real-time 3DE.

Methods and results We prospectively studied 91 patients (age 59 ± 8 years, 79 males) referred for RFCA of paroxysmal (n = 79) or chronic (n = 19) AF. Left atrial and RA volumes were measured using real-time 3DE at baseline and after 6 months of follow-up. Data on AF recurrences were also collected. Left atrial volume was significantly reduced at follow-up when compared with baseline (51 ± 16 vs. 60 ± 21 mL, P < 0.001). The same occurred with RA volume (43 ± 17 vs. 50 ± 20 mL, P = 0.001). The reduction in the LA volume was more marked in patients with chronic than in those with paroxysmal AF (17 ± 16 vs. 6 ± 17 mL, P = 0.017). Patients with AF recurrence (23%) showed similar atrial volume reduction compared with those who were seemingly cured.

Conclusion Three-dimensional echocardiography shows evidence of biatrial anatomical reverse remodelling after RFCA for AF. A reduction in the atrial volume occurs despite recurrence of AF.

Introduction

Radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF) including principally pulmonary vein isolation (PVI) is now the standard therapy for selected patients with AF. Maintenance of sinus rhythm with the procedure has been shown to result in a reduction of the left atrial (LA) size assessed by two-dimensional (2D) echocardiography and magnetic resonance imaging. However, in these studies, the LA size was calculated from 2D echocardiography with formulae that make geometrical assumptions that may not apply to remodelled atria. The advent of real-time full-volume three-dimensional echocardiography (3DE) allows us to measure the chamber volume without making these assumptions, as volume is reconstructed from endocardial contours of the entire chamber. Moreover, 3DE overcomes errors due to foreshortening and off-axis image planes inherent to 2D echocardiography, which is the limitation for measuring changes in volume between subsequent studies.

There are no reports to date about the use of 3DE for evaluating atrial remodelling following AF ablation. Furthermore, it is not known whether AF ablation results in any change in the right atrial (RA) volume. Our aim was to use the 3DE for studying biatrial remodelling following AF ablation and to correlate these findings with procedural success.

Methods

Patients

Consecutive patients with paroxysmal or chronic AF undergoing RFCA were enrolled. Of 92 patients studied with 3DE, 91 (98.9%) had echographic windows that were suitable for measuring LA volume by 3DE and yielded the data for the study. Patient demographics are shown in Table 1. All patients were anticoagulated...
variable-loop circular mapping catheter (Lasso Variable, 15–25 mm cool, Biosense Webster, Diamond Bar, CA, USA) and a duo-decapolar, the coronary sinus. A 7 Fr irrigated-tip ablation catheter (Thermocatheter (Bard Electrophysiology, Lowell, MA, USA) was placed in boluses of IV midazolam and morphine. A 6 Fr multipolar diagnostic access under local anaesthesia, supplemented by sedation with procedure. Three catheters were introduced via right femoral venous thromboplastin time of 2.5 times control) until 6 h before the procedure. Radiofrequency ablation with vitamin K antagonists for a consecutive period of at least 2 years duration (AF < 2 years duration (%) 22 (24) Type of AF Paroxysmal (%) 72 (79) Persistent (%) 11 (12) Permanent AF (%) 8 (9) Ischaemic heart disease (%) 6 (7) Hypertension (%) 30 (33) Anti-arrhythmic drugs Amiodarone (%) 22 (24) Sotalol (%) 11 (12) Ic (%) 28 (31) β-Blocker (%) 39 (43) ACEI and/or ARBs (%) 28 (30) Diuretic (%) 14 (15) ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker.

with vitamin K antagonists for a consecutive period of at least 4 weeks with a target international normalized ratio (INR) of 2–3 until 48 h before the procedure. A transoesophageal echocardiogram was performed prior to the procedure to exclude the presence of LA thrombi. The study complies with the Declaration of Helsinki and was approved by the Institutional Ethics Committee. All patients gave written informed consent.

Radiofrequency ablation

Intravenous (IV) heparin was administered (with a target partial thromboplastin time of 2.5 times control) until 6 h before the procedure. Three catheters were introduced via right femoral venous access under local anaesthesia, supplemented by sedation with boluses of IV midazolam and morphine. A 6 Fr multipolar diagnostic catheter (Bard Electrophysiology, Lowell, MA, USA) was placed in the coronary sinus. A 7 Fr irrigated-tip ablation catheter (Thermocool, Biosense Webster, Diamond Bar, CA, USA) and a duo-decapolar, variable-loop circular mapping catheter (Lasso Variable, 15–25 mm diameter, 2.5–2.2 mm electrode spacing, Biosense Webster) were placed at the pulmonary vein (PV) ostia via trans-septal access under the cover of IV heparin (target activated coagulation time 200–250 s). Selective biplane PV angiography was used to define the anatomic PV ostium, and a loop mapping catheter was positioned within 5 mm distal to it. The segmental ostial PVI was performed targeting the earliest activation 5–10 mm proximal to the loop catheter. A maximum of 35 W RF energy was delivered for 45–60 s at a time during saline irrigation at 20 mL/min. Sites with sharp deflections immediately adjacent to ostial lesions were targeted so as to extend the PVI ~1 cm proximally towards the LA. Supplementary linear LA ablation was performed in patients with persistent AF or in those with AF recurrence, despite complete isolation of all the PVs. Linear LA lesions were delivered across the high posterior LA from the left superior PV ostium to the right superior PV ostium and/or from the left inferior PV ostium to the posterolateral mitral annulus. Cavo-tricuspid isthmus ablation was performed in patients with previously documented typical atrial flutter or when typical flutter, sustained for at least 2 min, was observed during the ablation procedure. Oral anticoagulation was restarted the same day after the procedure under the cover of overnight IV heparin and thereafter with subcutaneously administered low-molecular-weight heparin until the achievement of a therapeutic INR. All anti-arrhythmic drugs, including amiodarone, were stopped after the ablation, but were re-introduced, in the case of symptomatic recurrences.

Standard echocardiography and tissue Doppler imaging

Standard echocardiograms according to current guidelines were acquired in all patients within 24 h of the ablation procedure (95% of the patients had baseline images acquired before the procedure), using a transesophageal 3 MHz phased-array transducer and a Sonos 7500 echocardiograph (Phillips Medical Systems, Andover, MA, USA). We acquired several recordings from each view and performed measurements on the best images. The parasternal long-axis view was used to measure the diameter of the LA (PLAX). The apical four-chamber view was used to measure the short-axis diameter (4CH short axis), long-axis diameter (4CH long axis), and planimetry area (4CH planimetry) of the RA and LA. The LA function was assessed in patients who were in sinus rhythm. Pulsed-wave Doppler samples were placed in the apical four-chamber view at the mitral inflow to measure the velocity of E- and A-waves. Pulsed-wave tissue Doppler imaging (TDI) was also performed with samples placed on the septal and lateral mitral annulus to measure the velocity of the late diastolic velocity (A’). Doppler values were averaged for three to five cycles.

Real-time three-dimensional echocardiography and atrial volume measurement

The 3DE images were obtained during the same session as the standard echocardiograms from an apical window over four cardiac cycles during a breath hold near the end-expiratory phase, in which image quality was often the best using a matrix-array ultrasonographic transducer (X4, Sonos 7500, Philips Medical Systems, Andover, MA, USA). At least, three acquisitions were performed and the data set with the best image quality was chosen for the analysis. The measurement of 3DE RA and LA volumes was performed offline by a single observer (H.M.) using dedicated commercially available software (4D Analysis Cardio-View v1.3, Tomtec Gmbh, Unterschleissheim, Germany), which allows us to measure the volume without geometric assumptions. The RA and LA were evaluated separately. The full-volume data set was centred on the atrium being studied and split into eight equidistant slices (22.5°/slice) at ventricular end-systole. The endocardial contours of each slice were manually traced, and interpolation between the slices yielded a 3D atrial cast (Figure 1). The analysis at 6 months was blinded to the baseline measurements. We have previously reported high feasibility and good reproducibility of LA and RA 3DE volume measurements in patients with atrial arrhythmias with 95% limits of agreement of −5.9 to 8.9 and −7.5 to 11.2 mL, respectively, for intra-observer reproducibility and −12.5 to 11.3 and −10.9 to 12.9 mL, respectively, for inter-observer reproducibility. The reproducibility was comparable for patients in sinus rhythm when compared with those in AF.

Follow-up

Arrhythmia follow-up consisted of symptomatic evaluation, periodic electrocardiograms (ECGs), and at least one 24 h Holter monitoring between 3 and 6 months and additional Holters or event monitors when necessary to evaluate symptoms or suspected recurrence. Electrocardiograms and echocardiograms were repeated at 6 months. Procedural success was defined as the absence of AF recurrence or atrial flutter after a blanking period of 3 months as recommended. Re-ablation was offered to all patients with recurrent AF.

Statistical analysis

Analysis was performed using SPSS for Windows (Chicago, IL, USA). Data were normally distributed according to the Kolmogorov-Smirnoff
Paired-sample Student's $t$-test was used for evaluating changes in echographic parameters at follow-up. Unpaired $t$-test was used for comparing means between unrelated groups. Pearson's correlation was used for relating changes in RA and LA volumes. A $P$-value of $<0.05$ was considered statistically significant. Values are expressed as mean ± SD.

Results

The isolation of the four PVs was obtained in all patients. Cavo-tricuspid isthmus ablation was performed in 16/91 (18%) patients. Atrial fibrillation recurrence after ≥3 months of follow-up was documented in 21/91 (23%) patients. Of the 21 patients, 6 underwent a redo procedure before the 6-month follow-up (and 15 others thereafter).

The echographic results for the entire population are shown in Table 2.

Standard echocardiography

Data were available for all patients for the LA; two patients did not have data on the RA because of insufficient image quality. There was a significant decrease at 6 months in 4CH planimetry area and in 4CH long-axis diameters for both the atria. The 4CH short-axis diameter decreased significantly for the RA, but not for the LA.

Left atrial function

Seventy-nine patients (87%) were in sinus rhythm at both baseline and follow-up image acquisition. Complete data for the LA function were available in a subset of 51 (56%) patients at both time points. There were no significant changes in mitral Doppler or mitral annulus TDI parameters at follow-up, compared with baseline.

Three-dimensional echocardiography volumes

Eighty-three patients (91%) were in the same rhythm at the time of the initial image acquisition and the 6-month follow-up echo (79 in sinus rhythm and 4 in AF or flutter). Data were available at baseline and follow-up in all patients for LA volumes. Right atrial volumes were not available at one or both time points in 25 (27%) patients due to dropout of the RA free wall on the 3D full-volume data.
set. There was a significant decrease in the LA volume of 8.7 ± 17.5 mL ($P < 0.001$) and in the RA volume of 7.1 ± 17.0 mL ($P = 0.001$). Changes in LA and RA volumes were moderately correlated ($R = 0.53$, $P < 0.001$).

**Atrial volumes and procedural success**

Left atrial volumes were slightly larger at baseline in patients with AF recurrence than in those with primary procedural success. However, LA volumes were significantly reduced at follow-up in both subgroups ($P = 0.11$ for comparison of patients with AF recurrence and primary success). Right atrial volume was also reduced in patients with primary success and showed a non-significant reduction in patients with AF recurrence ($P = 0.64$ for comparison of changes in the RA volume in patients with primary success vs. AF recurrence) (Figure 2).

**Atrial volumes and type of atrial fibrillation**

For the purpose of this study, patients with persistent and permanent AF were grouped together as chronic AF and compared with those with paroxysmal AF. Patients with chronic AF had a significantly larger atria at baseline compared with those with paroxysmal AF. Both subgroups showed a significant reduction in the atrial volumes at follow-up, although patients with chronic AF had a greater reduction in LA volume (16.9 ± 15.7 vs. 6.5 ± 17.4 mL, $P = 0.017$) (Figure 3).

**Atrial volumes and cavo-tricuspid isthmus ablation**

There were no significant differences in reduction in the LA volume in patients with ($n = 16$) or without ($n = 73$) cavo-tricuspid isthmus ablation (reduction of 10.5 ± 19.6 vs. 8.5 ± 17.2 mL, $P = 0.72$). There was a trend in greater reduction in the RA volume in patients with cavo-tricuspid isthmus ablation compared with those without (reduction of 12.8 ± 5.6 vs. 5.6 ± 17.1 mL, $P = 0.18$).

**Atrial volumes and drug therapy**

As cardiac remodelling may be influenced by angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs), and cardiac chamber volume may be affected by diuretic therapy, we analysed the effect of these drugs on changes in the atrial volume. There were no significant differences in reduction in atrial volumes at follow-up in patients under ACEI or ARBs at baseline, compared with those without treatment (reduction in the LA volume of 10.9 ± 18.4 vs. 7.5 ± 17.2 mL, respectively, $P = 0.35$ and reduction in the RA volume of 7.9 ± 21 vs. 6.2 ± 15.0 mL, respectively, $P = 0.27$). The same held true for patients with or without diuretic therapy (reduction in the LA volume of 8.3 ± 18.5 vs. 8.7 ± 17.4 mL, $P = 0.79$ and reduction in the RA volume of 9.4 ± 24.1 vs. 6.8 ± 16.2 mL, $P = 0.50$).

**Discussion**

Our study shows a significant reduction in the LA volume, and for the first time, also in the RA volume, in patients having undergone RFCA for AF, consisting predominantly of PVI. Interestingly, LA atrial volume reduction was not only seen in patients with primary procedural success, but also in those with documented AF recurrence, without any significant differences between these subgroups. This may be explained by several hypotheses. First, AF burden may have been reduced by catheter ablation despite arrhythmia recurrence, thereby leading to favourable anatomical atrial remodelling. Secondly, it is likely that undetected AF

![Figure 2](https://academic.oup.com/europace/article-abstract/10/9/1073/429834/510x510)

**Figure 2** Left (top) and right (bottom) atrial volumes at baseline and at 6 months according to primary procedural success or atrial fibrillation recurrence ≥3 months after ablation. LA, left atrial; RA, right atrial.

![Figure 3](https://academic.oup.com/europace/article-abstract/10/9/1073/429834/510x510)

**Figure 3** Left (top) and right (bottom) atrial volumes at baseline and at 6 months according to type of atrial fibrillation. Parox AF, paroxysmal AF; LA, left atrial; RA, right atrial.
recurred in some patients with a seemingly successful procedure, thus mitigating differences between the subgroups. Thirdly, radiofrequency ablation lesions in the atria may have led per se to volume reduction via a scarring process. However, this hypothesis does not explain how RA volumes are reduced in patients without cavo-tricuspid isthmus ablation (who only have radiofrequency lesions in the LA). Also, it has been shown that AF causes dilatation of both atria and that restoration of sinus rhythm (even the LA). Also, it has been shown that AF causes dilatation.

A study with canine histological specimens has shown that scarring plays an important role in the LA size reduction, but the linear lesions performed in that report covered 55% of the LA surface area. This is much more extensive ablation than typically performed in most catheter ablation procedures, including our own. Furthermore, if extensive scarring was the major cause of the LA size reduction, a reduction in the LA mechanical function would also be expected, but this was not observed.

Changes in the RA volume followed similar trends as those observed in the LA in different patient subgroups (Figures 2 and 3), and changes in the volume in both atria were significantly correlated. However, reduction in the RA volume was only statistically significant in patients with primary procedural success and in those with paroxysmal AF. This may be explained by the smaller number of patients with available RA volume data and perhaps by a lesser degree of RA dilatation at baseline compared with that of the LA.

Our data are in contrast to previous publications, which have shown the reduction in the LA size only in patients seemingly free of AF at follow-up. These discrepancies may be explained by differences in the follow-up protocols: imaging techniques (with changes being perhaps less noticeable using 2D echocardiography), and ablation technique (circular-ferential ablation vs. segmental ablation used in our centre). However, in agreement with our data, another study using segmental PVI also showed that patients with AF recurrence have a reduction in the LA size at follow-up.

As previously reported, patients with AF recurrence had larger atria at baseline when compared with those with primary procedural success, reflecting a more complex substrate for ablation. Also as expected and previously described patients with chronic AF had larger atria at baseline compared with those with paroxysmal AF, reflecting the structural changes resulting from and begetting atrial arrhythmias.

In agreement with a previous series, we did not observe any significant changes in the LA function resulting from PVI in patients with paroxysmal AF. Verma et al. showed that the LA function assessed by transthoracic echocardiography may be improved after PVI. However, the improvement seemed to be limited to patients with persistent AF, and there was no significant change in the atrial appendage emptying velocity assessed by transesophageal echocardiography. Lemola et al. found decreased LA ejection fraction measured by computed tomography (CT) in patients with paroxysmal AF after circumferential PVI. However, data were available for 10 patients only, and the findings were not confirmed by another larger series of 26 patients with LA ejection fraction also measured by CT. Therefore, our study and the majority of available data suggest that radiofrequency PVI does not have any detrimental effect on the LA transport function.

Limitations of the study

As stated previously, it is likely that undiagnosed AF was present in some patients who were considered to be free of atrial arrhythmias. It is well known that AF ablation success rate is dependent on the arrhythmia-screening protocol used for following up patients. However, the use of ECGs and Holters in our study is in line with the methodology of previous reports assessing LA remodelling after AF ablation.

Also, it is difficult to quantify changes in the arrhythmia burden in the case of AF recurrence using only 24 h Holter monitoring. Some patients had a discordant rhythm during the initial and the follow-up image acquisition, and this could possibly have influenced comparison of LA size over time. However, this applies only to a minority of patients (9%) and is unlikely to have affected the overall results.

Conclusions

Our study using real-time 3DE shows that RFCA consisting predominantly of PVI induces favourable anatomical remodelling of both atria, without having any detrimental effects on the LA contractile function. A reduction in the atrial volume occurs despite recurrence of AF, which is possibly due to a reduction in the AF burden following PVI.

Conflict of interest: none declared.

Funding

P.G. was funded by a research grant from Medtronic and Bard.

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