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Multimodality imaging to guide cardiac interventional procedures

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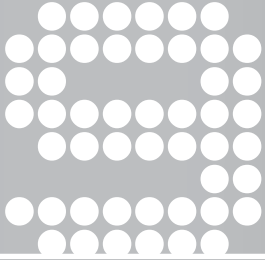
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Left atrial strain predicts reverse remodeling after catheter ablation for atrial fibrillation

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ABSTRACT

Background: The association between LA reverse remodeling and improvement in LA strain after catheter ablation has not been investigated thus far.

Objectives: The purpose of this study was to assess left atrial (LA) strain during long-term follow-up after catheter ablation for atrial fibrillation (AF), and find predictors for LA reverse remodeling.

Methods: In 148 patients undergoing catheter ablation for AF, LA volumes and LA strain were assessed with echocardiography at baseline and after a mean of 13.2 ± 6.7 months follow-up. The study population was divided according to LA reverse remodeling at follow-up: 'Responders' were defined as patients who exhibited $\geq 15\%$ reduction in maximum LA volume at long-term follow-up. LA systolic (LAs) strain was assessed with tissue Doppler imaging.

Results: At follow-up, 93 patients (63%) were classified as a responder, whereas 55 patients (37%) were non-responders. At baseline, LAs strain was significantly higher in the responders as compared with the non-responders ($19 \pm 8\%$ vs. $14 \pm 6\%$, $p=0.001$). In the responders, a significant increase in LAs strain was noted from baseline to follow-up (from $19 \pm 8\%$ to $22 \pm 9\%$, $p<0.05$), whereas no change was noted in the non-responders. LAs strain at baseline was the strongest predictor of LA reverse remodeling (Odds ratio 1.089; 95% CI 1.014-1.169, $p=0.019$).

Conclusions: In the present study, 63% of the patients exhibited LA reverse remodeling after catheter ablation for AF, with a concomitant improvement in LA strain. Left atrial strain at baseline was the strongest predictor of LA reverse remodeling.

INTRODUCTION

Left atrial (LA) enlargement is associated with cardiac morbidity and is a robust predictor of cardiovascular outcome (1,2). The relation between LA enlargement and atrial fibrillation (AF) has been well recognized. However, it still remains controversial whether LA enlargement causes AF (3), or vice versa (4).

Reversal of LA enlargement, or 'reverse remodeling', has been demonstrated with drug therapy and after restoration of sinus rhythm with cardioversion (5). In addition, it has been shown that LA reverse remodeling may occur after successful catheter ablation for AF (6).

At the same time, LA function may improve after restoration of sinus rhythm with catheter ablation (7). Using tissue Doppler imaging, it has been demonstrated that LA strain may improve at three months after successful catheter ablation for AF (8). However, it is unclear whether these changes in LA strain remain during long-term follow-up. More importantly, the association between LA reverse remodeling and the improvement in LA strain has not been investigated thus far. Accordingly, the purpose of the present study was to evaluate reverse remodeling and LA strain during long-term follow-up after catheter ablation for AF. In addition, predictors for LA reverse remodeling were studied.

METHODS

Study population and study protocol

The study population comprised 148 patients from an ongoing clinical registry (6) with symptomatic drug-refractory AF, who were referred for radiofrequency catheter ablation. Before the ablation procedure and after 12 months follow-up, an extensive echocardiographic evaluation was performed to assess LA strain. In a subgroup of patients with an available echocardiogram during sinus rhythm both at baseline and at follow-up (n=122), LA late diastolic strain (representing LA active contraction) and LV systolic strain was assessed. At long-term follow-up, the study population was divided according to reverse remodeling of the LA after the catheter ablation procedure.

Catheter ablation procedure

The protocol of the catheter ablation procedure has been described in more detail elsewhere (9). In brief, electrical isolation of all pulmonary veins from the LA was attempted using an electroanatomic mapping system with an image integration module (CARTO™ and CartoMerge™, Biosense Webster, Diamond Bar, California). Endocardial mapping and ablation was performed with a 4 mm quadripolar mapping/ablation catheter, with an open loop irrigated tip (7F Thermocool, Biosense Webster). A 6F diagnostic catheter placed in the right atrium served as a temporal reference. Radiofrequency current was applied outside the ostia of all pulmonary

veins using the following settings: irrigation rate 20 mL/min, maximum temperature 50°C, maximum radiofrequency energy 30 W. At each point, radiofrequency current was applied until a voltage <0.1 mV was achieved, with a maximum of 60 seconds per point. The procedure was considered successful when pulmonary vein isolation was confirmed by recording entrance block during sinus rhythm or pacing in the coronary sinus. All patients received heparin intravenously (activated clotting time > 300 sec) to avoid thrombo-embolic complications.

After the catheter ablation procedure, all patients were evaluated at the out-patient clinic on a regular basis. All medication, including anti-arrhythmic drugs, was continued in all patients during the first 3 months of follow-up. Afterwards, anti-arrhythmic drugs were discontinued at the discretion of the physician. A surface ECG was acquired at every follow-up visit, and 24-hours Holter monitoring was performed at 3 to 6 months intervals. Maintenance of sinus rhythm during follow-up was defined as the absence of symptomatic recurrences lasting more than 3 minutes and/or the absence of AF episodes lasting more than 30 seconds detected with 24-hour Holter monitoring or surface ECG, after a blanking period of 1 month (10).

Echocardiography

Two-dimensional echocardiography was performed within 2 days before the ablation procedure, and at 12 months follow-up. Two-dimensional images were recorded with the patient in the left lateral decubitus position using a commercially available system (Vivid 7, General Electric-Vingmed, Milwaukee, Wisconsin, USA). Images were acquired using a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard long-axis and 2- and 4-chamber images). Standard 2-dimensional images and color Doppler data were saved in cine loop format. All analyses were performed off-line using commercial software (Echopac 7.0.0, General Electric-Vingmed).

Left ventricular end-diastolic and end-systolic volumes were assessed from the apical 2- and 4-chamber images, and indexed to body surface area; LV ejection fraction (LVEF) was calculated using the biplane Simpson's rule (11). Left ventricular diastolic function was evaluated using the following Doppler measurements: ratio of early (E) to late (A) diastolic filling velocities (E/A) and deceleration time of the E wave (12). In addition, LV systolic strain and strain rate was assessed using color-coded tissue Doppler imaging in a subgroup of patients, as previously described (13).

Left atrial volumes and ejection fraction The LA anteroposterior diameter was measured at end-systole on the M-mode image obtained from the parasternal long-axis view. Furthermore, LA volumes were measured on apical 2- and 4-chamber views. Maximum LA volume (LA_{max}) was defined as the largest LA volume just prior to mitral valve opening; minimum LA volume (LA_{min}) was defined as the smallest possible LA volume in ventricular diastole. All LA volumes were indexed to body surface area, as recommended (14). Left atrial total emptying (LA_{EF}) was calculated using the biplane Simpson's rule (14).

Definition of LA reverse remodeling To study the determinants of reverse remodeling of the LA after catheter ablation, the study population was divided into 2 groups according to the extent of decrease in LA_{max} during follow-up (15). ‘Responders’ were defined as patients who exhibited $\geq 15\%$ reduction in LA_{max} at long-term follow-up. The ‘non-responders’ were patients who demonstrated a decrease in $LA_{max} < 15\%$, or an increase in LA_{max} during follow-up.

Left atrial strain analysis Left atrial deformation properties were studied using color-coded tissue Doppler imaging, by offline analysis of standard apical 2- and 4-chamber images of 3 consecutive heart beats. Frame rates were at least 115 frames/s, and the sector width was adjusted to allow the highest possible frame rate.

A sample volume (6 x 4 mm) was placed at the basal to mid parts of the LA septum and lateral wall (4-chamber view), and the LA anterior and inferior wall (2-chamber view). If necessary, Gaussian smoothing was applied to create clear strain curves. From the reconstructed strain curves, myocardial LA longitudinal lengthening or LAs strain (representing LA expansion function) was identified as the peak positive strain value during LV systole. In a subgroup of patients with an available echocardiogram during sinus rhythm both at baseline and at follow-up (n=122), myocardial LA shortening, or LAa strain (representing LA active contraction) was identified as the peak negative strain value during LV diastole occurring after the P-wave on the ECG.

Peak LAs strain and LAa strain was assessed for the 4 regions (septal, lateral, anterior, inferior), and averaged to acquire global LAs strain and LAa strain values. Similar, LAs strain rate and LAa strain rate, representing the speed at which LA deformation occurs, was assessed in the 4 regions and averaged (Figure 1).

Statistical analysis

All continuous variables had normal distribution (as evaluated by Kolmogorov-Smirnov tests). Summary statistics for these variables are therefore presented as mean \pm standard deviation (SD). Categorical data are summarized as frequencies and percentages.

Differences in clinical and echocardiographic variables between the responders and the non-responders were evaluated using unpaired Student t-tests (continuous variables), Chi-square tests or Fisher’s exact tests (dichotomous variables), as appropriate. Differences in continuous variables between baseline and follow-up were evaluated using paired Student t-test.

Intra- and inter-observer reproducibility for the assessment of LA strain and LA strain rate was determined by intraclass correlation coefficient and Bland-Altman analysis. Intra-observer reproducibility was determined by repeating the strain and strain rate measurements at 2 different time points by one experienced reader in 15 randomly selected patients. A second experienced reader performed the strain analysis in the same 15 patients, providing the inter-observer reproducibility data. Intra-class correlation coefficient and the mean bias with limits of agreement (2 SD) from Bland-Altman analysis are reported.

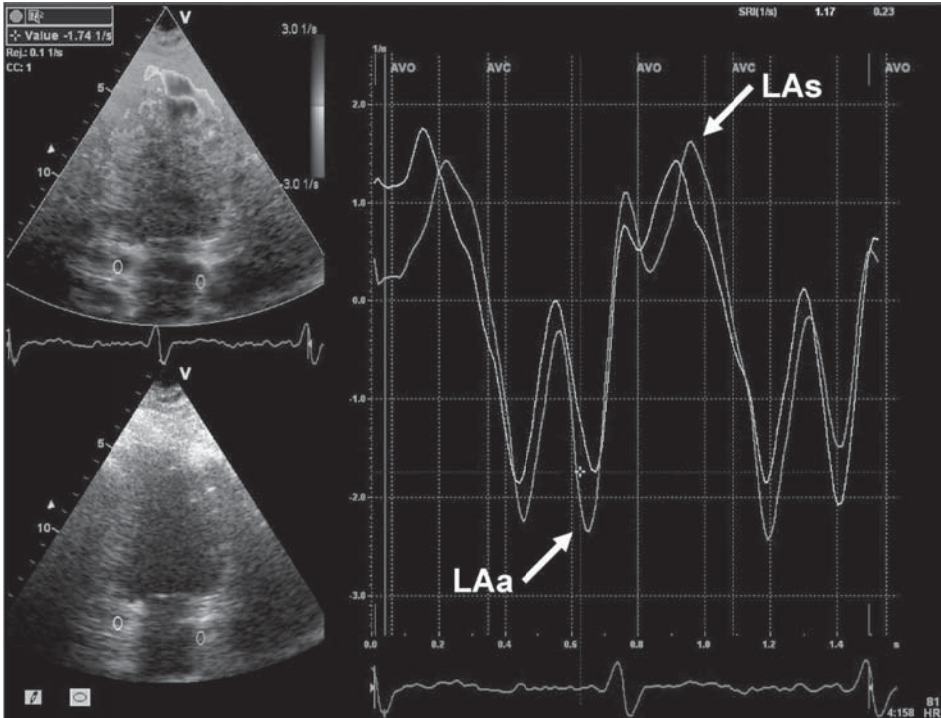


Figure 1. Strain rate imaging in the apical 2-chamber view in a patient at baseline. Samples are placed in the basal-mid atrial inferior (yellow) and anterior (green) atrial walls. With the use of the vertical green lines indicating aortic valve opening (AVO) and aortic valve closure (AVC), peak strain rate values of the different segments can be obtained (white arrows). LAa indicates peak LA strain rate during late ventricular diastole, representing the speed at which LA deformation during active contraction occurs. LAs indicates peak LA strain rate during ventricular systole, representing the speed at which LA deformation during LA expansion occurs.

To explore potential predictors of response, univariate analysis of baseline clinical and echocardiographic characteristics was performed first. Odds ratios were calculated with 95% confidence intervals as an estimate of the risk associated with each variable. Independent predictors of LA reverse remodeling were obtained by performing a multivariate logistic regression analysis based on enter model. Those variables with $p < 0.1$ at the univariate analysis were included. Statistical analyses were performed using SPSS software (version 15.0, SPSS Inc. Chicago, Illinois). All statistical tests were two-sided, and a p -value < 0.05 was considered significant.

RESULTS

Study population

A total of 148 patients were treated with radiofrequency catheter ablation. Baseline characteristics of the total study population are summarized in Table 1. Atrial fibrillation was paroxysmal in 112 patients (76%) and persistent in 36 patients (24%). Mean duration of follow-up was $13.2 \pm$

Table 1. Baseline characteristics of the study population

	All patients (n=148)	Responders (n=93)	Non-responders (n=55)	P-value *
Clinical characteristics				
Age, years	54 ± 9	55 ± 8	54 ± 10	0.5
Gender, M / F	117 / 31	75 / 18	42 / 13	0.5
Body surface area, m ²	2.1 ± 0.2	2.1 ± 0.2	2.1 ± 0.2	0.4
Type of AF				
Paroxysmal, n (%)	112 (76)	76 (82)	36 (65)	0.03
Persistent, n (%)	36 (24)	17 (18)	19 (35)	0.03
Duration of AF, years	5.3 ± 4.5	5.4 ± 4.2	5.2 ± 4.9	0.9
Previous anti-arrhythmic drugs, n	3.2 ± 1.5	3.3 ± 1.6	3.1 ± 1.3	0.4
ACE inhibitor / ATII, n (%)	72 (49)	46 (49)	26 (47)	0.9
Hypertension, n (%)	62 (42)	42 (30)	20 (36)	0.3
Coronary artery disease, n (%)	9 (6)	6 (6)	3 (5)	1.0
Echocardiographic characteristics				
LVEDV, ml/m ²	54 ± 12	54 ± 12	53 ± 12	0.4
LVESV, ml/m ²	23 ± 7	23 ± 7	23 ± 6	0.9
LVEF, %	57 ± 7	57 ± 8	56 ± 7	0.4
E/A	1.3 ± 0.4	1.3 ± 0.4	1.3 ± 0.4	0.8
Deceleration time (ms)	243 ± 70	247 ± 67	237 ± 77	0.5

* Responders vs. non-responders. ACE = angiotensin converting enzyme; AF = atrial fibrillation; ATII = angiotensin II receptor blocker; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume.

6.7 months. During follow-up, 99 patients (67%) remained in sinus rhythm, whereas 49 patients (33%) had recurrence of AF. None of the patients underwent a repeat procedure during follow-up.

Left atrial volumes and strain analysis

In the overall study population, LA diameter decreased from 43 ± 5 mm to 42 ± 5 mm ($p=0.003$) during follow-up. In addition, LA_{max} decreased significantly from baseline to follow-up (from 30 ± 7 ml/m² to 25 ± 7 ml/m², $p<0.001$). In parallel, LA_{min} decreased from 18 ± 6 ml/m² to 15 ± 7 ml/m² ($p<0.001$). Finally, there was a modest but statistically significant improvement in LA_{Ef} from baseline to follow-up in the overall study population (from $41 \pm 13\%$ to $45 \pm 14\%$, $p=0.002$).

Left atrial strain and strain rate measurements were feasible in 2078 of 2160 attempted segments (96%). In 15 randomly selected patients, reproducibility data for LA strain and LA strain rate measurements was assessed. Intra-observer agreement for the assessment of LA strain and LA strain rate was good. Intra-class correlation coefficients were: 0.8 for LA strain and 0.6 for LA strain rate. For LA strain, mean bias was 0.98 (limits of agreement: -4.39 – 6.34) without significant trend. For LA strain rate, mean bias was -0.02 (limits of agreement: -0.34 – 0.31) without significant trend. Similar, inter-observer agreement for LA strain and LA strain rate was good. Intra-class correlation coefficients were: 0.7 for LA strain and 0.8 for LA strain rate. For LA strain, mean bias was -0.14 (limits of agreement: -5.91 – 5.64). For LA strain rate, mean bias was -0.10 (limits of agreement: -0.21 – 0.42).

In the overall study population, LA deformation properties showed a significant improvement during follow-up. LAs strain increased from $17 \pm 7\%$ to $19 \pm 9\%$ ($p=0.001$), and LAs strain rate increased from 1.1 ± 0.4 1/s to 1.2 ± 0.5 1/s ($p=0.001$). Similar, LAa strain improved from

$-4 \pm 3\%$ to $-6 \pm 6\%$ ($p=0.03$), and LAa strain rate improved from -1.4 ± 0.7 1/s to -1.6 ± 0.7 1/s ($p=0.03$).

Left atrial reverse remodeling

Based on the cut-off value ($\geq 15\%$ decrease in LA_{max}), 93 patients (63%) were classified as a responder, whereas 55 patients (37%) were non-responders. Baseline characteristics of the two groups are listed in Table 1. The proportion of patients with paroxysmal AF was significantly higher among the responders compared with the non-responders (82% vs. 65%, $p=0.03$).

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Responders vs. non-responders Mean follow-up duration was comparable in the 2 groups (responders 12.7 ± 5.2 months vs. non-responders 13.8 ± 8.6 months, $p=0.3$). Importantly, 69% ($n=38$) of the non-responders experienced recurrence of AF, as compared to 12% ($n=11$) of the responders ($p<0.001$). At follow-up, 34 responders (37%) and 17 non-responders (31%) were off anti-arrhythmic drugs ($p=0.6$). The majority of the patients were on either beta-blockers or class IC anti-arrhythmic drugs. There were no differences between the 2 groups regarding the use of beta-blockers (27% vs. 22%, respectively, $p=0.6$) and class IC anti-arrhythmic drugs (32% vs. 31%, $p=1.0$) at follow-up.

Left ventricular systolic strain significantly improved in the responders during follow-up (from $-20 \pm 5\%$ to $-22 \pm 4\%$, $p<0.05$), whereas it decreased in the non-responders (from $-20 \pm 5\%$ to $-18 \pm 5\%$, $p<0.05$). Similar, an improvement in LV systolic strain rate was noted in the responders, and an impairment was noted in the non-responders (Table 2).

Left atrial volume and strain analysis By definition, LA_{max} decreased significantly in the responders (from 31 ± 7 ml/m² to 22 ± 6 ml/m², $p<0.001$), whereas a small increase was observed in the non-responders (from 29 ± 5 ml/m² to 31 ± 6 ml/m², $p=0.002$). Left atrial diameter and LA_{min} were comparable in the 2 groups at baseline. However, a significant decrease was observed in the responders during follow-up, resulting in significant differences between the two groups at follow-up (Table 2). Finally, LA_{EF} increased significantly in the responders, whereas no change was noted in the non-responders (Table 2).

Left atrial deformation properties demonstrated different trends during follow-up according to the presence of LA reverse remodeling. LAs strain was significantly higher at baseline in the responders, as compared to the non-responders (Table 2). In addition, a significant increase in LAs strain was noted in the responders, whereas no change was observed in the non-responders (Figure 2). Similarly, LAs strain rate at baseline was significantly higher in the responders, as compared with the non-responders (Table 2). During follow-up, LAs strain rate increased significantly in the responders, whereas no change was observed in the non-responders (Table 2). Similar trends were noted for LAa strain and LAa strain rate. Whereas LAa strain and strain rate improved significantly in the responders, LAa strain remained similar and LAa strain rate decreased in the non-responders (Table 2 and Figure 2).

Table 2. Echocardiographic results of the study population at baseline and follow-up

	Responders	Non-responders	P-value *
LA diameter, mm			
Baseline	43 ± 4	43 ± 5	0.6
Follow-up	40 ± 4 †	45 ± 6 †	<0.001
LA _{max} ^r , ml/m ²			
Baseline	31 ± 7	29 ± 5	0.04
Follow-up	22 ± 6 †‡	31 ± 6 †	<0.001
LA _{min} ^r , ml/m ²			
Baseline	19 ± 6	17 ± 5	0.2
Follow-up	12 ± 5 †	19 ± 8	<0.001
LA _{EP} ^r %			
Baseline	41 ± 14	41 ± 12	0.9
Follow-up	46 ± 11 †	42 ± 18	0.1
LAs strain, %			
Baseline	19 ± 8	14 ± 6	0.001
Follow-up	22 ± 9 †	15 ± 8	<0.001
LAs strain rate, 1/s			
Baseline	1.2 ± 0.4	1.0 ± 0.4	0.02
Follow-up	1.4 ± 0.4 †	1.0 ± 0.4	<0.001
LAa strain, % §			
Baseline	-4 ± 3	-4 ± 3	0.4
Follow-up	-6 ± 6 †	-4 ± 3	0.03
LAa strain rate, 1/s §			
Baseline	-1.4 ± 0.7	-1.3 ± 0.9	0.3
Follow-up	-1.7 ± 0.7 †	-1.1 ± 0.7	<0.001
LV strain, % §			
Baseline	-20 ± 5	-20 ± 5	0.6
Follow-up	-22 ± 4 †	-18 ± 5 †	<0.001
LV strain rate, 1/s §			
Baseline	-1.2 ± 0.4	-1.1 ± 0.3	0.1
Follow-up	-1.4 ± 0.5 †	-1.0 ± 0.3	<0.001

* Responders vs. non-responders; † p<0.05 baseline vs. follow-up; ‡ by definition; § data available in 76 responders and 46 non-responders.

LA = left atrial; LA_{EP}^r = left atrial total emptying fraction; LA_{max}^r = maximum left atrial volume; LA_{min}^r = minimum left atrial volume; LV = left ventricular.

Prediction of LA reverse remodeling

Univariate and multivariate logistic regression analysis was performed to determine the predictors of LA reverse remodeling. The results of the logistic regression analysis are shown in Table 3. At multivariate analysis, the strongest predictors of LA reverse remodeling after catheter ablation were LAs strain at baseline (Odds ration 1.089; 95% CI 1.014-1.169, p=0.019) and LA_{max}^r (Odds ration 1.086; 95% CI 1.018-1.159, p=0.012).

DISCUSSION

In the present study, LA reverse remodeling and LA strain were studied in 148 patients undergoing catheter ablation for AF. In 93 patients (63%), LA reverse remodeling was noted at long-term follow-up. In these patients, LA systolic and late diastolic strain and strain rate increased significantly from baseline to follow-up. In patients without LA reverse remodeling, no significant

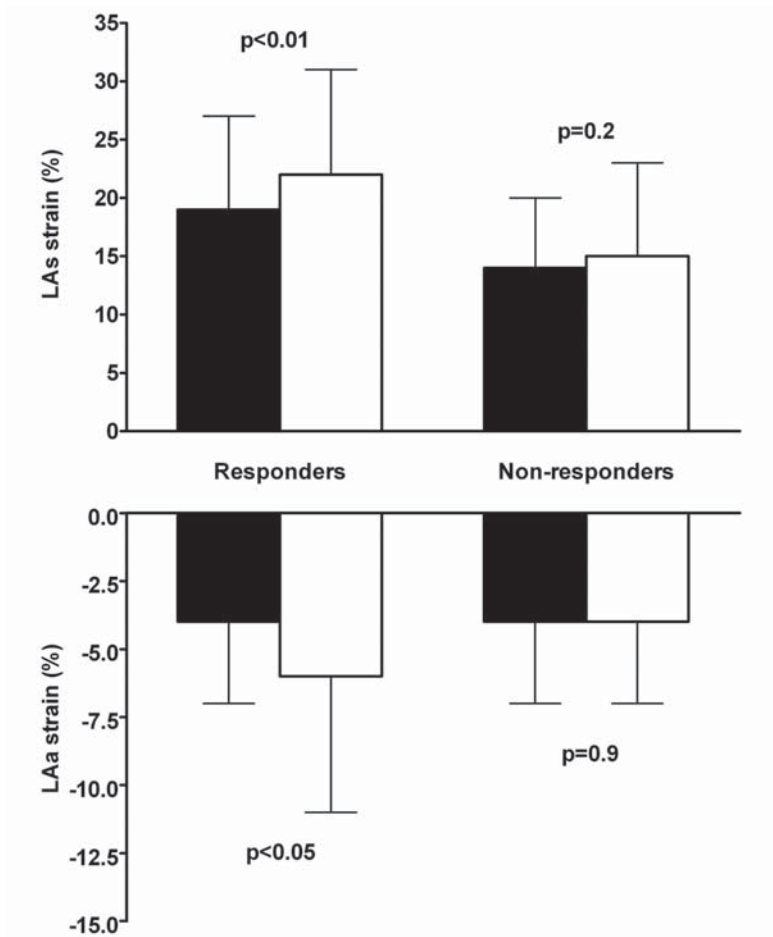


Figure 2. Changes in LAs strain and LAa strain according to LA reverse remodeling. From baseline (black bars) to follow-up (white bars), different changes in LAs strain (upper panel) and LAa strain (lower panel) were observed in the 2 groups. In the responders, a significant improvement in LAs strain and LAa strain was observed. In contrast, the non-responders did not show an improvement in LAs strain or LAa strain from baseline to follow-up.

changes in LA strain and strain rate were noted. Importantly, LAs strain at baseline was the strongest predictor of LA reverse remodeling.

Left atrial reverse remodeling

Left atrial remodeling includes structural, electrical, metabolic and neurohumoral changes, and may occur in response to several pathologic processes. Atrial dilatation is an important aspect of LA structural remodeling (1). Recently, it has been suggested that the extent of LA structural remodeling may play an important role in the success of AF ablation (16). Interestingly, several studies have demonstrated that this atrial enlargement is, at least partially, reversible. Reverse LA remodeling has been demonstrated with drug therapy (17), after mitral valve surgery (15),

Table 3. Univariate and multivariate logistic regression analysis for prediction of reverse remodeling after catheter ablation

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.015 (0.977-1.054)	0.457
Hypertension	1.441 (0.727-2.858)	0.295
Type of AF	2.359 (1.098-5.071)	0.028	1.937 (0.846-4.438)	0.118
LVEF	1.022 (0.976-1.071)	0.349
LA _{max}	1.058 (1.003-1.117)	0.040	1.086 (1.018-1.159)	0.012
LAs strain	1.102 (1.039-1.168)	0.001	1.089 (1.014-1.169)	0.019
LAs strain rate	2.996 (1.163-7.716)	0.023	1.422 (0.502-4.027)	0.508

C-statistic: 0.712; OR = Odds ratio, other abbreviations as in Tables 1 and 2.

and with cardiac resynchronization therapy (18). In addition, successful catheter ablation for AF may result in reversal of LA dilatation (6).

Although the exact underlying pathophysiology of LA reverse remodeling remains unclear, it has been suggested that reversal of LA dilatation may have prognostic implications and may reduce the risk of AF (5). Therefore, LA reverse remodeling may become a surrogate marker of success after AF ablation. Typically, maintenance of sinus rhythm during follow-up is used to define successful catheter ablation (10). However, asymptomatic AF recurrence may result in overestimation of success. Importantly, in the present study, there is an overlap between responders and patients who maintained sinus rhythm (82 out of 93 responders), and non-responders and patients with recurrence of AF (38 out of 55 non-responders). Therefore, LA reverse remodeling may be a more robust marker for successful AF ablation that can easily be quantified.

Interestingly, in the patients that exhibited LA reverse remodeling, an improvement in LA function was observed in the present study. The concordance of LA reverse remodeling and improvement in LA function has previously been demonstrated (7). In addition, predictors for LA reverse remodeling were studied in the present study. Although the proportion of patients with paroxysmal and persistent AF was different among the responders and the non-responders, the type of AF was not predictive for LA reverse remodeling at multivariate analysis. This indicates that the type of AF is not an independent determinant of LA structural changes that deteriorate LA myocardial deformation and reduce the ability of the LA to reverse remodel. Interestingly, at multivariate analysis, LA systolic strain (as a novel marker of LA reservoir function) was the strongest predictor of LA reverse remodeling during follow-up.

Left atrial strain analysis

Recent studies have demonstrated the feasibility of strain analysis to assess segmental LA function (19). In LA function, three different phases can be distinguished: 1) LA reservoir function, during ventricular systole; 2) LA conduit function, during early ventricular diastole; 3) LA booster pump function, during late ventricular diastole. In the present study, tissue Doppler imaging was used to assess LA peak systolic and late diastolic strain, which represent LA reservoir function and LA booster pump function, respectively (20). At baseline, LA strain was impaired

as compared with previously reported values for healthy controls (21,22). Left atrial reservoir function is mainly determined by LV systolic function and LA wall stiffness (23). In patients with AF and preserved LVEF, subtle changes in LV and LA myocardium may already be present (24,25). Indeed, myocardial deformation imaging techniques may reveal these subtle changes. Impaired LA strain and strain rate indicate reduced compliance of the LA, and may indirectly reflect high fibrosis content. These functional changes may therefore reflect structural changes that may determine the ability of the LA to reverse remodel after catheter ablation for AF.

Interestingly, an improvement in LA strain was observed in patients with LA reverse remodeling during follow-up. Several other studies have demonstrated improvements in LA strain in response to therapy. In a cohort of 107 heart failure patients undergoing cardiac resynchronization therapy, LA strain was assessed at baseline and after 3 months follow-up. In patients who exhibited LV reverse remodeling after cardiac resynchronization therapy, LA systolic strain improved from $16.8 \pm 9.8\%$ to $21.8 \pm 9.4\%$ ($p=0.002$), in parallel with LA reverse remodeling (26). Thomas et al. (27) noted improvements in LA strain and strain rate in 37 patients with AF who maintained sinus rhythm during 6 months after cardioversion. Similarly, it has been demonstrated that LA strain and strain rate may improve after catheter ablation for AF (8). Schneider et al. demonstrated a significant increase in LA systolic strain in patients who maintained sinus rhythm after catheter ablation, whereas it remained unchanged in patients with recurrence of AF. In addition, it was demonstrated that LA systolic strain and strain rate may predict the maintenance of sinus rhythm during 3 months follow-up (8).

In the present study, similar improvements in LA strain and strain rate were observed in 148 patients after long-term follow-up. In addition, it was demonstrated that LA strain at baseline was the strongest predictor for LA reverse remodeling during follow-up. Previously, it has been demonstrated that LA systolic strain may predict the maintenance of sinus rhythm after cardioversion (24). Although the exact mechanism remains to be elucidated, it may well be that the degree of impairment in atrial compliance (represented by LA systolic strain) plays an important role in the ability to reverse LA enlargement and maintain sinus rhythm during follow-up.

Interestingly, the improvements in LA strain and strain rate in the responders were accompanied by improvements in LV systolic strain. These findings suggest that LA and LV myocardial deformations are closely related. Restoration of sinus rhythm with catheter ablation results in an improved LA function and subsequent more efficient LV filling pattern and LV mechanics (7,28). At the same time, the improvement in LV systolic function and diastolic filling pattern due to heart rhythm normalization may result in an improved LA function, and may therefore be a determinant of LA reverse remodeling. Additional studies are warranted to elucidate whether the improvement in LV mechanics precedes the improvement in LA function or vice versa.

CONCLUSIONS

In the present study, 63% of the patients exhibited LA reverse remodeling after catheter ablation for AF. In these responders, LA strain and strain rate increased significantly from baseline to follow-up. In contrast, no changes in LA strain and strain rate were noted in the non-responders. Left atrial systolic strain at baseline was the strongest predictor of LA reverse remodeling.

REFERENCES

1. Abhayaratna WP, Seward JB, Appleton CP et al. Left atrial size: physiologic determinants and clinical applications. *J Am Coll Cardiol* 2006;47:2357-63.
2. Rossi A, Cicoira M, Zanolla L et al. Determinants and prognostic value of left atrial volume in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 2002;40:1425.
3. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. *Circulation* 1994;89:724-30.
4. Sanfilippo AJ, Abascal VM, Sheehan M et al. Atrial enlargement as a consequence of atrial fibrillation. A prospective echocardiographic study. *Circulation* 1990;82:792-7.
5. Casaciang-Verzosa G, Gersh BJ, Tsang TS. Structural and functional remodeling of the left atrium: clinical and therapeutic implications for atrial fibrillation. *J Am Coll Cardiol* 2008;51:1-11.
6. Tops LF, Bax JJ, Zeppenfeld K, Jongbloed MR, van der Wall EE, Schalij MJ. Effect of radiofrequency catheter ablation for atrial fibrillation on left atrial cavity size. *Am J Cardiol* 2006;97:1220-2.
7. Marsan NA, Tops LF, Holman ER et al. Comparison of left atrial volumes and function by real-time three-dimensional echocardiography in patients having catheter ablation for atrial fibrillation with persistence of sinus rhythm versus recurrent atrial fibrillation three months later. *Am J Cardiol* 2008;102:847-53.
8. Schneider C, Malisius R, Krause K et al. Strain rate imaging for functional quantification of the left atrium: atrial deformation predicts the maintenance of sinus rhythm after catheter ablation of atrial fibrillation. *Eur Heart J* 2008;29:1397-409.
9. Tops LF, Bax JJ, Zeppenfeld K et al. Fusion of multislice computed tomography imaging with three-dimensional electroanatomic mapping to guide radiofrequency catheter ablation procedures. *Heart Rhythm* 2005;2:1076-81.
10. Calkins H, Brugada J, Packer DL et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. *Heart Rhythm* 2007;4:816-61.
11. Schiller NB, Shah PM, Crawford M et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358-67.
12. Rakowski H, Appleton C, Chan KL et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the Investigators of Consensus on Diastolic Dysfunction by Echocardiography. *J Am Soc Echocardiogr* 1996;9:736-60.
13. Abraham TP, Dimaano VL, Liang HY. Role of tissue Doppler and strain echocardiography in current clinical practice. *Circulation* 2007;116:2597-609.
14. Lang RM, Bierig M, Devereux RB et al. Recommendations for Chamber Quantification. *J Am Soc Echocardiogr* 2005;18:1440-63.
15. Westenberg JJ, van der Geest RJ, Lamb HJ et al. MRI to evaluate left atrial and ventricular reverse remodeling after restrictive mitral annuloplasty in dilated cardiomyopathy. *Circulation* 2005;112:1437-1442.
16. Oakes RS, Badger TJ, Kholmovski EG et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. *Circulation* 2009;119:1758-67.
17. Tsang TS, Barnes ME, Abhayaratna WP et al. Effects of quinapril on left atrial structural remodeling and arterial stiffness. *Am J Cardiol* 2006;97:916-20.
18. Marsan NA, Bleeker GB, Ypenburg C et al. Real-time three-dimensional echocardiography as a novel approach to assess left ventricular and left atrium reverse remodeling and to predict response to cardiac resynchronization therapy. *Heart Rhythm* 2008;5:1257-64.
19. Leung DY, Boyd A, Ng AA, Chi C, Thomas L. Echocardiographic evaluation of left atrial size and function: current understanding, pathophysiologic correlates, and prognostic implications. *Am Heart J* 2008;156:1056-64.

20. Zhang Q, Yip GW, Yu CM. Approaching regional left atrial function by tissue Doppler velocity and strain imaging. *Europace* 2008;10 Suppl 3:iii62-iii69.
21. Gulel O, Yuksel S, Soylu K et al. Evaluation of left atrial functions by color tissue Doppler imaging in adults with body mass indexes ≥ 30 kg/m² versus those < 30 kg/m². *Int J Cardiovasc Imaging* 2009;25:371-7.
22. Wang Z, Tan H, Zhong M, Jiang G, Zhang Y, Zhang W. Strain rate imaging for noninvasive functional quantification of the left atrium in hypertensive patients with paroxysmal atrial fibrillation. *Cardiology* 2008;109:15-24.
23. Barbier P, Solomon SB, Schiller NB, Glantz SA. Left atrial relaxation and left ventricular systolic function determine left atrial reservoir function. *Circulation* 1999;100:427-36.
24. Di Salvo G, Caso P, Lo PR et al. Atrial myocardial deformation properties predict maintenance of sinus rhythm after external cardioversion of recent-onset lone atrial fibrillation: a color Doppler myocardial imaging and transthoracic and transesophageal echocardiographic study. *Circulation* 2005;112:387-95.
25. Boyd AC, Schiller NB, Ross DL, Thomas L. Differential recovery of regional atrial contraction after restoration of sinus rhythm after intraoperative linear radiofrequency ablation for atrial fibrillation. *Am J Cardiol* 2009;103:528-34.
26. Yu CM, Fang F, Zhang Q et al. Improvement of atrial function and atrial reverse remodeling after cardiac resynchronization therapy for heart failure. *J Am Coll Cardiol* 2007;50:778-85.
27. Thomas L, McKay T, Byth K, Marwick TH. Abnormalities of left atrial function after cardioversion: an atrial strain rate study. *Heart* 2007;93:89-95.
28. Tops LF, den Uijl DW, Delgado V et al. Long-term improvement in left ventricular strain after successful catheter ablation for atrial fibrillation in patients with preserved left ventricular systolic function. *Circ Arrhythmia Electrophysiol* 2009;2:249-57.

