The value of serial echocardiography in risk assessment of patients with paroxysmal atrial fibrillation

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ORIGINAL PAPER

The value of serial echocardiography in risk assessment of patients with paroxysmal atrial fibrillation

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Abstract

Progression from paroxysmal to persistent atrial fibrillation (AF) is associated with increased morbidity and mortality. We examined the association of left atrial (LA) remodeling by serial echocardiography, and AF progression over an extended follow-up period. Two-hundred ninety patients (mean age 61 ± 11 years, 73% male) who underwent transthoracic echocardiography performed at first presentation for non-valvular paroxysmal AF (PAF) and repeat echocardiogram 1-year later, were followed for progression to persistent AF. LA and left ventricular (LV) dimensions, volumes, LA reservoir, conduit and booster pump strains, LV global longitudinal systolic strain (GLS) assessed by 2D speckle tracking, and PA-TDI (time delay between electrical and mechanical LA activation– reflecting the extent of LA fibrosis) were compared on serial echocardiography. Sixty-nine (24%) patients developed persistent AF over a mean follow-up period of 6.3 years. At baseline, patients with subsequent persistent AF had larger LA dimensions (46 mm vs. 42 mm, $p < 0.001$), indexed LA volumes (41 ml/m^2 vs. 34 ml/m^2, $p < 0.001$), lower LA reservoir and conduit strain (17.6% vs. 27.6%, $p < 0.001$; 10.5% vs. 16.3%, $p < 0.001$; respectively) and longer PA-TDI (155 ms vs. 132 ms, $p < 0.001$) compared to the PAF group. Patients with subsequent persistent AF showed over time significant enlargement in LA volumes (from 37.7 ml/m^2 to 42.4 ml/m^2, $p < 0.001$), lengthening of PA-TDI (from 142.2 ms to 162.2 ms, $p = 0.002$), and decline in LA reservoir function (from 21.9% to 18.1%, $p = 0.024$) after adjusting for age, gender, diabetes and LV GLS. There were no changes in LA diameter, LA conduit or booster pump function. Conversely, the PAF group showed no decline in LA function. Patients who developed persistent AF had larger LA size and impaired LA function and atrial conduction times at baseline, compared to patients who remained PAF. Over the 1-year time course of serial echocardiographic evaluation, there was progression of LA remodeling in patients who subsequently developed persistent AF, but not in patients who remained in PAF.

Keywords Atrial fibrillation · Left atrium · Strain · Tissue Doppler imaging

Abbreviations

2D	Two-dimensional
AF	Atrial fibrillation
CHA_2DS_2-VASc	Acronym for congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and sex category (female)]
ECG	Electrocardiogram
GLS	Global longitudinal strain
IQR	Interquartile range
LA	Left atrial
LV	Left ventricular
NYHA	New York Heart Association
PAF	Paroxysmal atrial fibrillation
PA-TDI	Time interval between left atrial electrical and mechanical activation of the left atrium

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Introduction

The progression from paroxysmal to persistent atrial fibrillation (AF) is associated with increased morbidity and mortality due to consequent risk of stroke, heart failure, and death [1–4]. However, not all patients with paroxysmal AF (PAF) progress to persistent AF.

Understanding factors associated with AF progression is important for guiding management. Although previous studies have indicated that stroke rates are similar among patients with PAF and persistent AF [5–10], more recent studies suggested that increased burden of AF led to increased risk of thromboembolism, heart failure, hospital admissions and adverse cardiovascular events among both anticoagulated and non-anticoagulated patients [11–15]. In addition, identification of patients who are likely to progress to persistent AF is important in deciding whether intervention should be considered. Recent studies indicate that freedom from AF is improved if advanced atrial remodeling has not yet occurred [16, 17].

Limited studies evaluating echocardiographic predictors of AF progression demonstrated that increased left atrial (LA) diameter and volume, and reduced reservoir strain are associated with AF progression [18–20]. Reduced LA reservoir strain has also been associated with AF recurrence after catheter ablation [17], and inversely correlates with LA fibrosis burden demonstrated on late gadolinium contrast enhanced cardiac magnetic resonance imaging [21]. LA fibrosis is a major determinant of the progression to, and burden of, AF [22–24]. PA-TDI is an echocardiographic measure of total atrial activation time and a surrogate for the degree of atrial fibrosis on biopsy specimens [25]. Increasing AF burden is associated with more impaired LA reservoir strain and longer total atrial activation time (PA-TDI) [26]. However, no studies have examined the role of serial echocardiographic evaluation of LA remodeling and its relationship with AF progression over an extended follow-up period.

The present study aimed to evaluate whether LA structure and function and progression of LA remodeling over 1 year follow-up differ between PAF patients who developed persistent AF and those who remained in PAF on extended follow-up.

Methods

Patients

The present retrospective observational study included patients who presented with their first episode of PAF to the Leiden University Medical Centre (The Netherlands) between 28th May 1996 and 6th August 2015. Patients who had a transthoracic echocardiogram performed around the time of their admission documenting non-valvular PAF and with 1-year follow-up echocardiogram (requested at the discretion of the treating cardiologist) were considered for inclusion. Patients with moderate or severe mitral or aortic valvular regurgitation or stenosis, mechanical or bioprosthetic heart valves, previous valvuloplasty, or congenital heart disease were excluded. The Institutional Review Board approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

AF was diagnosed in accordance with the European Society of Cardiology Guidelines for the Management of Atrial Fibrillation [27, 28]. PAF was defined when AF was self-terminating, with paroxysms continuing for up to a maximum of 7 days [27, 28]. A total of 290 patients were included. At the time of first presentation with AF, clinical information including demographic data, medications, cardiovascular risk factors, comorbidities including coronary artery disease, heart failure and New York Heart Association (NYHA) functional class, pulmonary disease, sleep apnea, thyroid disease, and previous stroke or transient ischemic attack (TIA) were collected. The CHA_2DS_2-VASc score was additionally calculated for each patient based on a point system in which 2 points were assigned for a history of stroke or TIA, or age $\geq$ 75 years; and 1 point each was assigned for age 65–74 years, a history of hypertension, diabetes, cardiac failure, vascular disease (myocardial infarction, peripheral artery disease, complex aortic plaque), and female sex [29].

Echocardiography

The first transthoracic echocardiogram performed immediately after the diagnosis of AF was selected for analysis. Preference was given to select the echocardiogram performed while the patient was in sinus rhythm to enable assessment of sinus rhythm-specific echocardiographic parameters. Transthoracic echocardiography was performed in the left lateral decubitus position using a commercially available ultrasound transducer and equipment. All images were digitally stored on hard disks for off-line analysis (EchoPAC, BT13, GE-Vingmed). Standard 2-dimensional (2D) echocardiographic and Doppler parameters of LV systolic and diastolic function were measured. The LV ejection fraction was calculated using the Simpson's biplane method of discs [30]. Maximal LA volume was calculated using the Simpson's single plane method of discs in the apical 4-chamber view.

The mitral inflow velocities were recorded using conventional pulsed-wave Doppler echocardiography in the apical 4-chamber view using a 2-mm sample volume.

Transmitral early (E-wave) and late (A-wave) diastolic velocities, as well as the deceleration time, were recorded at the mitral leaflet tips. The septal E/e' ratio was measured using pulse-wave tissue Doppler with the sample volume placed at the basal septum.

Strain imaging

Left ventricular peak global longitudinal strain (LV GLS) was measured with 2D speckle tracking echocardiography in the apical 4-, 2-chamber and long-axis views and calculated as the average of the global longitudinal strain curves of the 3 apical views. LA reservoir, conduit and booster pump strain were also evaluated using 2D speckle tracking on images obtained in the apical 4-chamber view. The electrocardiogram (ECG) was referenced to the onset of the QRS complex, and the region of interest was adjusted to the thickness of the LA wall. LA reservoir strain (εs) was measured as the peak positive longitudinal strain during ventricular systole (Fig. 1), whilst LA strain during early and late diastole (εe and εa, respectively) correspond to the LA conduit and booster pump function [31]. Care was taken to avoid images with LA or LV foreshortening.

PA—TDI

The time delay between electrical and mechanical activation of the LA, the so-called PA-TDI duration, was measured on colour-coded TDI images of the LA obtained in the apical 4-chamber view. The sector width and depth were minimized to obtain the highest possible frame rate. A fixed 8 × 8 mm region of interest was placed on the lateral LA wall, just above the mitral annulus, to obtain the tracing of mechanical activation in that area. The PA-TDI duration was obtained by measuring the time delay between the onset of the P-wave on the surface ECG and the peak of the A'-wave on the tissue Doppler tracing (Fig. 1) [16].

Clinical endpoint and follow-up

Patients were followed by electronic chart review for subsequent progression to persistent or permanent AF documented on the cardiology department and hospital information systems (EPD-Vision and EZIS; Leiden University Medical Centre, Leiden, The Netherlands). Persistent AF was defined as recurrent AF that was not self-terminating with an episode lasting > 7 days including episodes requiring termination by either electrical or pharmacological cardioversion [27, 28]. Permanent AF was diagnosed when AF

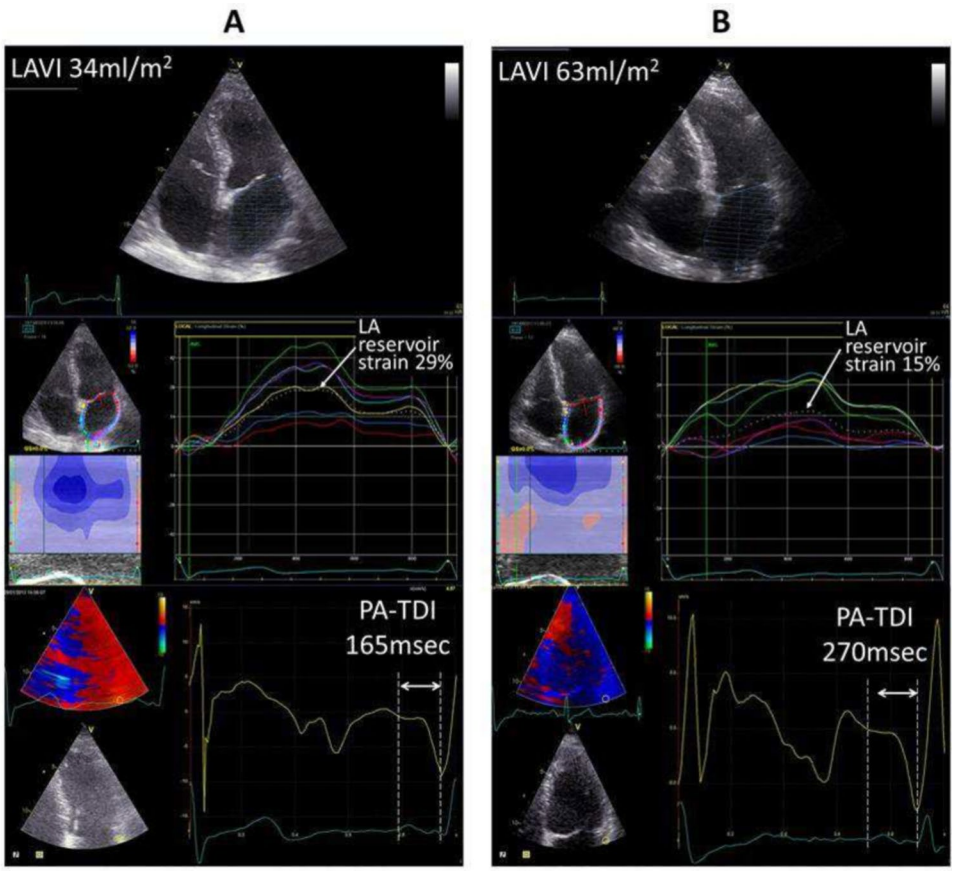

Fig. 1 Changes in LA volume, LA reservoir strain, and PA-TDI over time in a patient who developed persistent AF. Baseline LA volume indexed (LAVI), LA reservoir strain and PA-TDI are shown in Panel **A**. At 1 year follow-up (Panel **B**), there is further enlargement of LA, reduction in LA reservoir strain and prolongation of the PA-TDI

was the accepted rhythm and rhythm control strategies were no longer pursued [27, 28]. Patients with either persistent or permanent AF are hereon referred to as the "persistent AF" group. Follow-up data was complete for all patients to enable their classification as either persistent AF, or those that remained PAF.

Statistical analysis

Continuous variables were presented as mean ± standard deviation for normally distributed variables, and median (interquartile range) for non-Gaussian variables. Baseline differences between continuous variables were compared with the unpaired Student's t-test, and Wilcoxon rank sum test, as appropriate. Baseline categorical data are summarised as frequencies and percentages, and compared using the χ^2 test or Kruskal–Wallis test, as appropriate.

Comparison between patients who remain in PAF and those who progress to persistent AF at baseline and after 1-year echocardiographic follow-up was achieved using a linear mixed model with Bonferroni correction for multiple comparisons. Clinical and echocardiographic parameters were chosen a-priori based on biological plausibility and published studies [32–34]. The AF group (PAF versus persistent AF), and timing of echocardiographic measurement (baseline or follow-up) were incorporated into the model as fixed variables as well as the interaction between these two variables. An unstructured covariance matrix was applied. Non-Gaussian continuous variables such as LA reservoir strain and booster pump strain were transformed as the square root of these variables. The estimated marginal means and 95% confidence interval are presented. A 2-tailed p-value < 0.05 was considered statistically significant. Statistical analyses were performed using STATA v12 (STATA Corporation, Texas).

Results

Clinical characteristics

A total of 290 patients were followed-up over a median duration of 6.3 years (range 1–19 years), representing 20% of the total population of patients admitted to hospital with AF that met the inclusion and exclusion criteria. The mean age of the study population was 61 ± 11 years, with 73% males. There were 69 patients (24% of the study population) who developed persistent/permanent AF. The baseline clinical characteristics of the patients who developed persistent AF, compared to those who remained in PAF are presented in Table 1. Patients who developed persistent AF were older and presented more frequently with heart failure (all cases were heart failure with reduced ejection fraction) compared to PAF patients.

In terms of medication use, patients in the persistent AF group had a higher frequency of antiplatelet agent, anticoagulant and amiodarone use, compared to the PAF group. Forty-six (69%) patients in the persistent AF group had a CHA_2DS_2-VASc score ≥ 2, of which 34 (74%) were taking oral anticoagulants. Whereas 59 (50%) of the 117 (54%) patients in the PAF group with a score ≥ 2 were taking anticoagulant therapy. The use of renal-angiotensin aldosterone system inhibitors or statins did not differ between groups.

Patients with persistent AF had higher serum creatinine compared to those with PAF. The median CHA_2DS_2-VASc score in both groups was 2. The groups were otherwise similar in terms of body surface area, cardiac risk factors, and co-morbid medical conditions.

Echocardiographic characteristics at baseline

Unadjusted baseline echocardiographic parameters for the 2 groups of patients are presented in Table 2. Patients with subsequent persistent AF had larger LA dimensions and indexed LA volumes compared to the PAF group. LV GLS was impaired in both groups, but more in the persistent AF group despite normal LV dimensions, volumes, and ejection fraction. Mitral inflow parameters and LV filling pressures estimated by echocardiography were not significantly different between the two groups. However, median LA reservoir and conduit strain were significantly reduced (17.6% vs. 27.6%, p < 0.001; 10.5% vs. 16.3%, p < 0.001; respectively) and PA-TDI was significantly longer (155 ms vs. 132 ms, p < 0.001) in the group who developed persistent AF compared to those who remained in PAF.

Changes in atrial structure and function over time

At follow-up, 81% of patients were in sinus rhythm, 18% in AF, and 1% of patients had a paced rhythm at the time of echocardiography. Figure 2 demonstrates the changes in atrial structure and function over time in the 2 groups of patients, correcting for the corresponding baseline variable, age, gender, diabetes mellitus and LV GLS. There was significant enlargement in LA volumes (baseline 37.7 ml/m^2 vs. follow-up 42.4 ml/m^2, p < 0.001) and lengthening of the PA-TDI (baseline 142.2 ms vs. follow-up 162.2 ms, p = 0.002) in the persistent AF group, but not in the PAF group (Fig. 2A). There was no significant change in LA dimension for either group (persistent AF: baseline 44.2 mm vs. follow-up 45.9 mm, p = 0.064; PAF: baseline 42.1 mm vs. follow-up 42.0 mm, p = 1.000). Furthermore, there was a significant decline in LA reservoir function (baseline 21.9% vs. follow-up 18.1%, p = 0.024) without decline in conduit (14.2% vs. 14.9%,

Table 1 Baseline clinical characteristics of patients at time of first diagnosis of paroxysmal atrial fibrillation

Characteristic	Remain PAF (n = 221)	Become persistent AF (n = 69)	p-value
Clinical features			
Age (years)	61 (16)	67 (14)	< 0.001
Male, n (%)	157 (72%)	49 (73%)	0.900
Body mass index (kg/m^2)	27 ± 4	27 ± 3	0.839
Systolic blood pressure (mmHg)	133 ± 19	135 ± 19	0.446
Diastolic blood pressure (mmHg)	81 ± 12	81 ± 12	0.916
Cardiac risk factors			
Hypertension, n (%)	133 (68%)	43 (74%)	0.326
Current smoker, n (%)	32 (15%)	7 (10%)	0.372
Dyslipidemia, n (%)	103 (47%)	35 (52%)	0.494
Diabetes mellitus, n (%)	25 (12%)	11 (16%)	0.292
Other medical conditions			
Pulmonary disease, n (%)	20 (9%)	8 (12%)	0.521
Sleep apnea, n (%)	23 (1%)	2 (3%)	0.386
Thyroid disease, n (%)	22 (10%)	7 (10%)	0.942
Coronary artery disease, n (%)	60 (28%)	24 (36%)	0.200
Coronary bypass surgery, n (%)	21 (10%)	7 (10%)	0.853
Percutaneous coronary intervention, n (%)	40 (18%)	15 (22%)	0.474
Previous myocardial infarction, n (%)	39 (18%)	15 (23%)	0.389
History of heart failure, n (%)	27 (12%)	16 (24%)	0.022
Previous TIA or stroke, n (%)	23 (11%)	9 (13%)	0.521
Valvular heart disease, n (%)	38 (18%)	16 (24%)	0.246
Implantable cardiac defibrillator, n (%)	14 (6%)	8 (12%)	0.142
Cardiac resynchronization therapy, n (%)	5 (2%)	2 (3%)	0.670
Medications			
Aspirin or clopidogrel, n (%)	59 (27%)	10 (15%)	0.041
Anticoagulant (warfarin or NOAC), n (%)	105 (48%)	47 (70%)	0.002
ACE inhibitor or ARB, n (%)	95 (44%)	35 (52%)	0.224
Calcium channel blocker, n (%)	46 (21%)	17 (25%)	0.472
Beta-blocker, n (%)	128 (59%)	47 (70%)	0.101
Amiodarone, n (%)	11 (5%)	10 (15%)	0.007
Diuretic, n (%)	44 (20%)	20 (30%)	0.101
Aldosterone antagonist, n (%)	8 (4%)	5 (7%)	0.195
Statin, n (%)	85 (39%)	28 (42%)	0.702
Laboratory parameters			
Creatinine (umol/L)	82 (23)	92 (28)	0.007
TSH (mU/L)	1.90 (1.69)	2.17 (1.55)	0.528
T4 (pmol/L)	17.1 (3.8)	17.1 (4.2)	0.534
Total cholesterol (mmol/L)	4.9 ± 1.7	5.3 ± 1.5	0.115
Triglycerides (mmol/L)	1.67 (1.26)	1.42 ± 0.94	0.154
Serum glucose (mmol/L)	6.8 (1.8)	6.9 (4.2)	0.475
Pro-brain natriuretic peptide (ng/L)	721 (0)	909 (932)	1.000
Hemoglobin (mmol/L)	9.1 (1.4)	9.2 (1.1)	0.726

Continuous variables presented as mean ± standard deviation for normally distributed variables, and median (interquartile range) for non-Gaussian variables, unless otherwise specified

ACE angiotensin converting enzyme, *ARB* angiotensin II receptor blocker, *NOAC* novel oral anticoagulant, *NYHA* New York Heart Association, *TIA* transient ischaemic attack

Table 2 Baseline echocardiographic characteristics at first diagnosis of atrial fibrillation

Characteristic	Remain PAF (n = 221)	Become persistent AF (n = 69)	p-value
Interventricular septal thickness (mm)	12 ± 3	13 ± 2	0.004
Posterior wall thickness (mm)	11 ± 2	11 ± 2	0.056
LV end diastolic diameter (mm)	49 ± 7	48 ± 7	0.924
LV end-systolic diameter (mm)	31 ± 7	32 ± 7	0.186
LV end diastolic volume (ml)	111 (44)	108 (49)	0.559
LV end systolic volume (ml)	47 (25)	48 (24)	0.758
LVEF (%)	58 (12)	56 (17)	0.241
LA dimension (mm)	42 ± 6	46 ± 7	< 0.001
LA volume (ml)	69 ± 20	83 ± 23	< 0.001
LA volume indexed (ml/m^2)	34 ± 9	41 ± 11	< 0.001
LA sphericity index	1.26 ± 0.19	1.26 ± 0.16	0.876
E (cm/sec)	70 ± 20	75 ± 21	0.110
A (cm/sec)	63 ± 19	59 ± 19	0.270
E/A ratio	1.1 (0.5)	1.1 (0.6)	0.297
Septal peak early diastolic velocity (e'), cm/sec	8 (4)	7 (0)	0.857
E/e' ratio	9 (2)	10 (0)	0.383
LV global longitudinal systolic strain (%)	−16.5 ± 4.3	−14.7 ± 4.2	< 0.001
LA reservoir strain (%)	27.6 (19.8)	17.6 (11.8)	< 0.001
LA conduit strain (%)	16.3 (12.0)	10.5 (7.5)	< 0.001
LA booster pump strain (%)	14.4 (10.0)	8.0 (7.5)	< 0.001
PA-TDI (msec)	132 ± 26	155 ± 33	< 0.001
Pulmonary artery systolic pressure (mmHg)	32 (12)	33 (15)	0.219

Continuous variables presented as mean ± standard deviation for normally distributed variables, and median (interquartile range) for non-Gaussian variables, unless otherwise specified

LA left atrial, *LV* left ventricular, *LVEF* left ventricular ejection fraction

p = 1.000; respectively) or booster pump function (10.4% vs. 8.3%, p = 0.280; respectively) in the persistent AF group (Fig. 2B). No decline in LA function was noted in the PAF group. An example of the progression in LA echocardiographic parameters in a patient with subsequent persistent AF is shown in Fig. 1.

Discussion

The present study is the first to demonstrate that in patients with their first presentation of PAF, LA structure and function, and progression of LA remodeling over 1-year follow-up differed between those who developed persistent AF versus those who remained in PAF on extended follow-up. The former group of patients had larger LA dimensions and worse LA function at baseline. Furthermore, this former group of patients had enlargement in LA volume and marked decline in LA strain and PA-TDI after just one year after the first diagnosis of PAF, whereas the latter group demonstrated no such evolutionary changes.

LA size and AF progression

To our knowledge, the temporal changes in LA structure and functional measures in relation to the progression from PAF to persistent AF have only been examined using LA dimension in the past [35]. Whilst our unadjusted study results concur with the results of Pakarsh et al., demonstrating that patients who remain in PAF have smaller baseline LA dimensions compared to those with persistent AF; and those who remain in PAF have no significant increase in LA dimension, whereas patients who develop persistent AF have larger baseline LA dimensions that significantly increase at 2 and 4 years follow up; our adjusted analysis failed to demonstrate this change. This may be related to the shorter 1 year time period between serial echocardiograms in our study, the smaller patient population in our study, and the fact that measurement of the anteroposterior LA dimension, is less sensitive to changes in LA size which occur in both the supero-inferior direction, as well as the mediolateral direction; and hence LA dimension is recommended to be used in conjunction with other measures [36]. It is now well established that LA volume is a more accurate measure of LA size

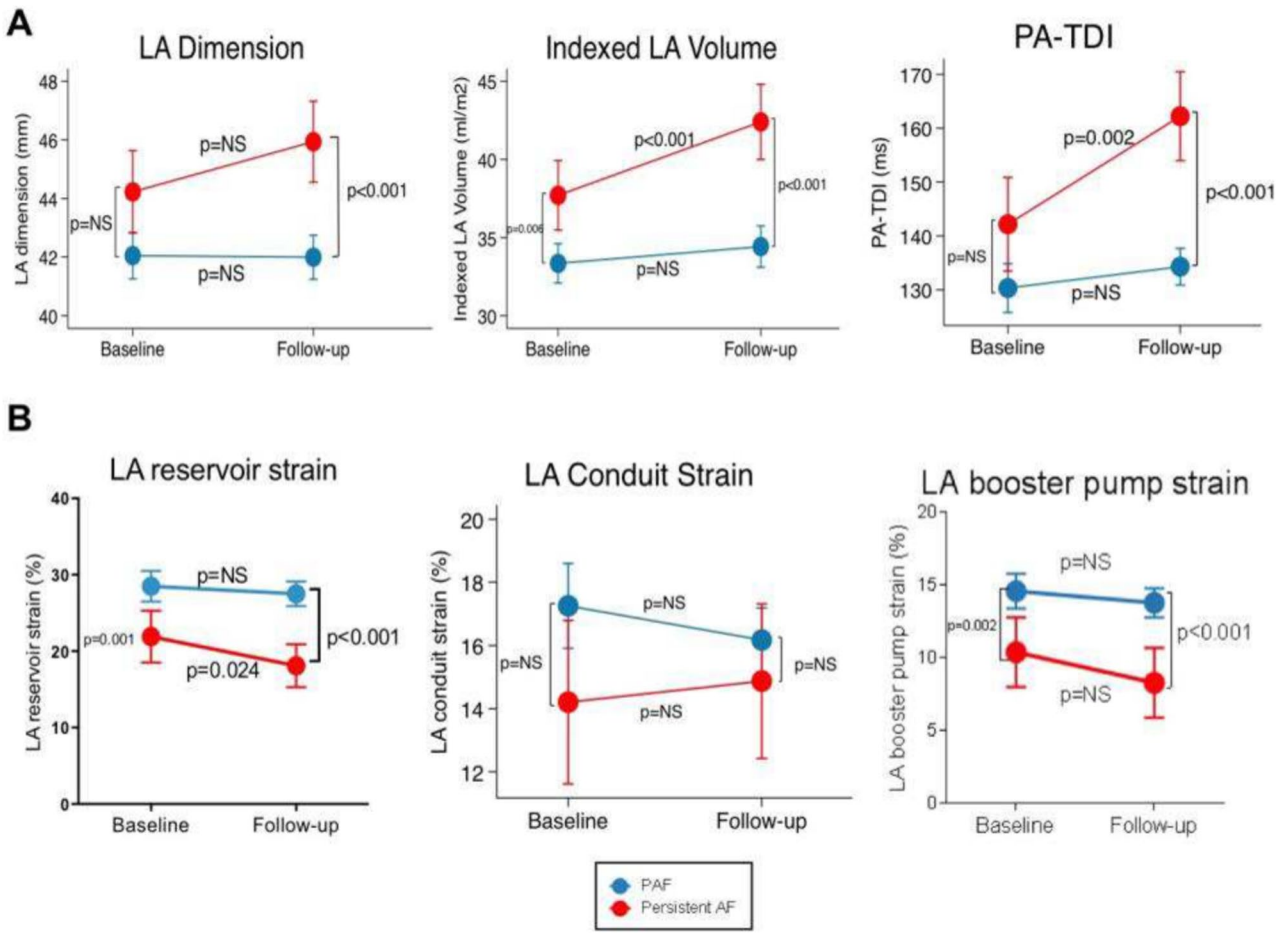

Fig. 2 Changes in LA structure and function over time in paroxysmal and persistent AF groups. An increase in LA volume, PA-TDI and reduction in LA reservoir strain can be seen in patients with persistent AF. No progression in these parameters is noted in the PAF group. Footnote: Estimates from a linear mixed model. Data are presented as estimated marginal means and 95% confidence interval. Analyses corrected for the corresponding variables: echocardiogram time point (i.e., baseline or follow up), age, gender, diabetes mellitus and LV global longitudinal strain

and the currently recommended method for assessment [30]. Despite the limitations of the LA dimension measurement and the lack of demonstration of increase over time in our persistent AF group, this measurement is easy to perform and an enlargemed LA dimension at baseline, by itself, has value for predicting AF recurrence, and the development of persistent AF [19].

The differences in baseline echocardiographic characteristics seen in the present study are also concordant with a previous study whereby patients without AF progression had smaller LA dimensions (39 mm vs 41 mm, $p=0.032$), indexed LA volumes (33.0 ml/m^2 vs. 40.4 ml/m^2, $p<0.001$), and lower LA reservoir strain (28.4% vs. 24.6%, $p=0.006$) compared to patients with AF progression [18]. In that study, echocardiographic correlates for AF progression were dichotomized based on cut-off values derived from ROC curve analysis at the time of first AF diagnosis. The investigators demonstrated that LA dimension > 39 mm, indexed LA volume > 34.2 ml/m^2, and LA reservoir strain ≤ 30.9% were associated with an increased risk of progression to persistent AF. Our study confirmed that patients who develop persistent AF already have more advanced atrial structural remodeling at baseline when they initially present with their first AF episode.

Relationship of LA size and fibrosis with AF progression

We demonstrated an increased degree of fibrosis reflected in the longer baseline PA-TDI in the persistent AF group, and progression of this fibrosis, which support the findings of previous studies that fibrosis underlies the structural remodelling in AF [22–24]. The fibrosis and atrial enlargement in AF are inextricably linked as fibrosis of atrial tissue disrupts the continuous cable-like arrangement of cardiomyocytes, thereby interfering with atrial conduction [37].

Remodeling-induced atrial dilation promotes AF by increasing the amount of atrial tissue that can accommodate reentry circuits so that larger reentry circuits can be supported and/or a larger number of circuits can be maintained; and hence are a determinant of the occurrence of multiple-circuit re-entry seen in AF [38]. Therefore, non-invasive LA structural and functional echocardiographic measures can provide all needed information to better understand and temporally monitor an individual's substrate for AF, and enable risk assessment.

Our study is novel in highlighting the disparate evolution of LA structural remodeling that occurs between these two groups of patients over time. The greater rate of LA structural remodeling and functional decline in patients who develop persistent AF compared to those who remain in PAF suggests a possible progressive atrial cardiomyopathic process for which AF may be one of the heralding arrhythmic manifestations.

Clinical implications

A clinical awareness of AF burden and the degree of atrial structural remodeling is crucial in the management of AF for several reasons. Increasing burden of AF is associated with larger degrees of LA fibrosis, independent of age [22]. When considering rhythm control therapies for AF, the efficacy of ablation procedures are crucially dependent on the extent of LA structural remodeling whereby freedom from AF is improved if advanced atrial remodeling has not yet occurred [16, 17, 39].

Since not all patients with PAF will progress to persistent AF, performing serial echocardiograms to detect a marked decline in LA structural and functional parameters may help early identification of patients most at risk of AF progression. This may also help to guide patient management such as adopting either a rate or rhythm control strategy. Furthermore, identifying patients who experience a decline in functional parameters may help guide the decision for early AF procedural intervention to reduce the burden of stroke, heart failure and death, for which patients with high AF burden are at an increased risk [1–3, 11, 40, 41].

Risk factors for AF progression include age, hypertension, diabetes mellitus, heart failure, chronic kidney and pulmonary disease, previous stroke, and LA size [42]. The current evidence relating AF burden with AF-related outcomes is currently insufficient to guide treatment and hence the current ESC Guidelines for the management of AF recommend targeting these cardiovascular risk factors to reduce AF burden [27].

Despite the technical improvements in radiofrequency catheter ablation (RFCA) such as shorter procedure time and improved safety, it has not been paralleled by a higher procedural success rate [43]. By highlighting the need for careful follow-up of patients with PAF, and understanding that timing of RFCA is linked to AF success [17], the utilization of echocardiographic guidance may help improve the long-term procedural success rates of RFCA in suppressing AF from the current range of 20% to 50% [44].

Limitations

Our study included 20% of the total population of patients admitted to hospital with their first AF presentation that met the inclusion and exclusion criteria. The majority of patients were excluded from analysis due to lack of echocardiographic baseline or follow-up data and the effect of this bias is difficult to estimate.

Assessment of 2D LA volume and LA strain is affected by maximising LA size on the apical 4- and 2- chamber views as non-maximised LA may result in an under-estimate of LA volume and an over-estimate of LA strain. Although this is the goal in image acquisition, this is often hampered by patient specific factors which are likely to be similar over time for individual patients and unlikely to result in consistent measurement bias. Furthermore, pulmonary vein Doppler velocities were not measured in this study and may have provided further insights given previously demonstrated associations of morphological changes with the frequency of AF paroxysms [45].

Classification of PAF versus persistent AF was based on chart review by medical staff and relied on an inpatient or outpatient hospital visit to record a clinical event. Patients who had asymptomatic persistent AF that did not result in re-presentation to hospital could have been misclassified as PAF. However, this misclassification would have resulted in an underestimation of the difference between the groups.

Conclusion

The current study suggests that an approach of close echocardiographic follow-up ("watchful waiting") in patients with PAF may be helpful to detect changes in atrial morphostructural parameters and guide earlier interventions before irreversible structural and functional alterations to the atrial substrate have occurred.

Authors' contributions ML: Conception and design of the study; collection, analysis and interpretation of data; drafting of the manuscript; final approval of the manuscript. PJvanR Conception and design of the study; collection, analysis and interpretation of data; final approval of the manuscript. MVR Collection, analysis and interpretation of data; final approval of the manuscript. SE van W Collection, analysis and interpretation of data; final approval of the manuscript. NAM Conception and design of the study; collection, analysis and interpretation of data; final approval of the manuscript. DYL Conception and design of the study; drafting of the manuscript; final approval of the manuscript.

VD Conception and design of the study; collection, analysis and interpretation of data; drafting of the manuscript; final approval of the manuscript. A CT N Interpretation of data; drafting of the manuscript; final approval of the manuscript. JJB Conception and design of the study; collection, analysis and interpretation of data; drafting of the manuscript; final approval of the manuscript.

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Declarations

Conflict of interest The Department of Cardiology, LUMC, received research grants from Medtronic, Biotronik, Boston Scientific and Edwards Lifesciences. VD received speaker fees from Abbott Vascular. JJB received speaker fees from Abbott and Edwards Lifesciences.

Ethical approval The Institutional Review Board approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

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