

RESEARCH

Predictive value of various Doppler-derived parameters of atrial conduction time for successful atrial fibrillation ablation

Miriam Shanks MD PhD, Lucas Valtuille MD CEPS, Jonathan B Choy MD MBA FASE and Harald Becher MD PhD

Mazankowski Alberta Heart Institute, University of Alberta, 2C2 Walter C. Mackenzie, 8440-112 Street, Alberta, Edmonton, Canada, T6G 2B7

Correspondence
should be addressed
to M Shanks
Email
mshanks@ualberta.ca

Abstract

Various Doppler-derived parameters of left atrial electrical remodeling have been demonstrated to predict recurrence of atrial fibrillation (AF) after AF ablation. The aim of this study was to compare three Doppler-derived measures of atrial conduction time in patients undergoing AF ablation, and to investigate their predictive value for successful procedure. In 32 prospectively enrolled patients undergoing the first AF ablation, atrial conduction time was estimated by measuring the time delay between the onset of P-wave on the surface ECG to the peak of the a'-wave on the pulsed-wave Doppler and color-coded tissue Doppler imaging of the left atrial lateral wall, and to the peak of the A-wave on the pulsed-wave Doppler of the mitral inflow. There was a significant difference in the baseline atrial conduction time measured by different echocardiographic techniques. Most (88%) patients had normal or only mildly dilated left atrium. At 6 months, 12 patients (38%) had recurrent AF/atrial tachycardia. The duration of history of AF was the only predictor of AF/atrial tachycardia recurrence following the first AF ablation ($P=0.024$; OR 1.023, CI 1.003–1.044). A combination of normal left atrial volume and history of paroxysmal AF of ≤ 48 months was associated with the best outcome. Predictive value of the Doppler derived parameters of atrial conduction time may be reduced in the early stages of left atrial remodeling. Future studies may determine which echocardiographic parameter correlates best with the extent of left atrial remodeling and is most predictive of successful AF ablation.

Key Words

- ▶ tissue Doppler imaging
- ▶ atrial fibrillation
- ▶ catheter ablation
- ▶ echocardiography
- ▶ Doppler echocardiography

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice, with many patients requiring invasive treatment with catheter ablation for drug-refractory AF (1). However, long-term success rate of AF ablation is modest, with the highest risk of recurrence in the first 6–12 months, often requiring repeated procedures (2, 3, 4, 5, 6). Considering the invasive nature of the procedure with potential complications, it is important to identify the patients who are less

likely to benefit. Several clinical and imaging-based variables are currently used to define efficacy and risk of ablation in a given patient, including concomitant structural heart disease, sleep apnea, hypertension, left atrial (LA) dilatation, persistent as opposed to paroxysmal AF, and AF duration (6). Moreover, electrical alterations in the conduction of electrical stimulation of the atria themselves likely play an important role in perpetuation of arrhythmia (7, 8). Atrial dilatation and depressed intra-atrial conduction determine the total time required for atrial electrical activation (8). Various Doppler

echocardiography-derived parameters have been described that estimate atrial conduction time as a marker of electrical remodeling, including the time intervals from the onset of the P-wave on ECG to the peak of the local lateral LA signal on color-coded tissue Doppler imaging (TDI) (9), or to the peak of the lateral mitral annulus Doppler signal in pulsed wave (PW) mode (8, 10, 11, 12), or to the peak of the late transmitral diastolic velocities on PW Doppler (13). Their predictive value for recurrence of AF after AF ablation has been demonstrated in several studies (9, 10, 11, 12, 13). The aim of this study was to compare these three Doppler-derived parameters of atrial conduction time in the patients undergoing the first AF ablation, and to investigate their prognostic value to predict atrial tachyarrhythmia after the procedure.

Methods

Patient population and follow-up

The patient population consisted of prospectively enrolled consecutive patients with symptomatic drug-refractory paroxysmal AF (spontaneous termination within 7 days, or cardioversion performed within 48 h of AF onset), scheduled for the first AF ablation. All enrolled patients provided written informed consent for the study. Prior to the procedure, a medical history, 12-lead surface electrocardiogram (ECG), transthoracic and transesophageal echocardiograms were obtained from all patients. The patients who were in AF at the time of an echocardiogram were excluded from the analysis. After the ablation, patients were prospectively followed for recurrence of atrial tachyarrhythmia with 12 lead ECG at 3 and 6 months, and 24-h Holter at 6 months. In addition, patients with intermittent palpitations were instructed to obtain a 12-lead ECG at the time of the symptoms. As per 2012 HRS/EHRA guidelines, recurrence was defined as recording of AF, atrial tachycardia (AT), or atrial flutter on ECG or an episode longer than 30 s on 24-h Holter more than 3 months after the ablation (6). This study was approved by the medical ethics committee of our institution.

Echocardiography

Echocardiograms were performed with commercially available ultrasound equipment (M3S probe, Vivid 7, GE-Vingmed, Horten, Norway). All images were digitally stored for offline analysis using software package (EchoPac version BT07.0.0, GE-Vingmed, Horten, Norway). Complete Doppler and 2D images were acquired according to standard techniques (14, 15). Maximal LA volumes

were calculated using the biplane area-length formula and indexed to body-surface area (BSA) (16, 17). Severity of mitral regurgitation was determined using an integrative approach including semi-quantitative and quantitative color Doppler-based parameters as recommended by current guidelines (18). Left ventricular (LV) mass was derived from the LV linear dimensions and calculated using the Devereux formula. Left ventricular end-systolic and end-diastolic volumes were calculated using Simpson's biplane method of discs and indexed to (BSA) (16). Left ventricular ejection fraction was subsequently derived. Using pulsed-wave Doppler, transmitral early (E) and late (A) diastolic velocities and the E-wave deceleration time were measured from the apical four-chamber view placing a 2 mm sample volume at the tips of the mitral leaflets. Tissue Doppler was applied in the PW mode to record early (e') and late (a') diastolic mitral annulus velocities at septal and lateral corners, with the E' measurements being averaged to calculate E/e' ratio as a measure of LV filling pressures (19). Color-coded TDI of the LA were obtained from the apical four-chamber views, with the sector size and depth optimized for the highest frame rates possible (>140 Hz). Regional myocardial PW Doppler velocity profiles were analyzed offline by positioning the sample volume (6×6 mm) on the lateral LA wall just above the mitral annulus.

Atrial conduction time

The atrial conduction time was estimated using three different echocardiographic techniques previously described in the literature including measuring the time delay between the onset of P-wave in lead II of the surface ECG to the i) peak of the a' -wave on PW Doppler imaging in the local lateral LA wall (PA- a') (8, 11, 12), ii) to the peak of the a' -wave on the color-coded TDI of the local lateral LA wall (PA-TDI) (9) and iii) to the peak of the A-wave on the PW imaging of the late transmitral diastolic velocities (PA-A) (13) (Fig. 1A, B, and C). To correct the atrial conduction times for LA size, all three parameters were also indexed to absolute LA volume (iPA- a' , iPA-PW, iPA-A). Both absolute and indexed atrial conduction times were included in the final analysis.

Catheter ablation

All patients underwent an electrophysiological study and AF ablation after written consent was obtained. The type of the procedure (radiofrequency ablation vs cryoablation) was performed at the discretion of the operator. All patients

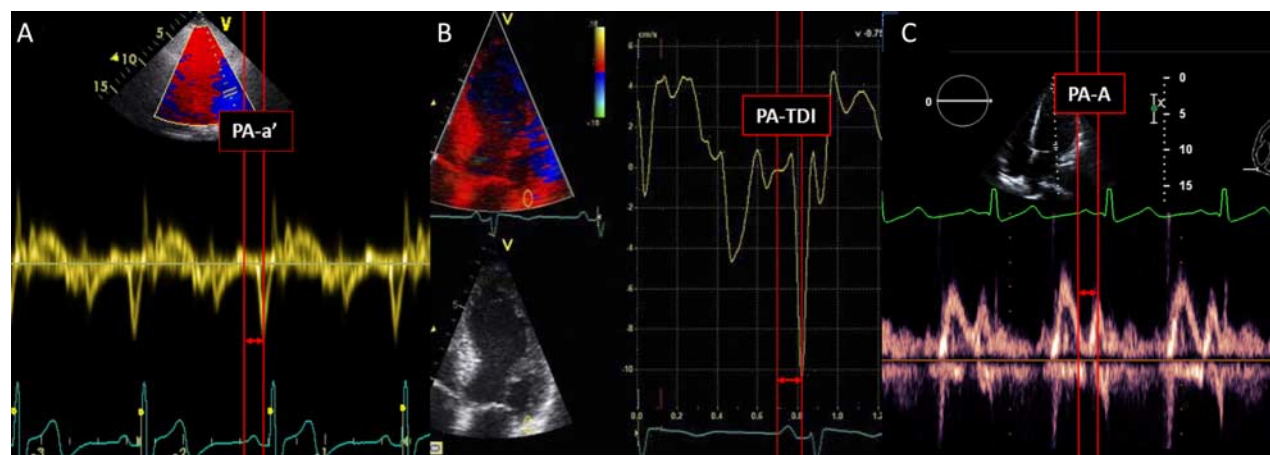


Figure 1

Examples of the atrial activation time measurements. The atrial conduction time was estimated by measuring the time delay between the onset of P-wave in lead II of the surface ECG to the peak of the a'-wave on the pulsed wave Doppler imaging (PA-a') of the lateral LA wall (A), to the peak

of the a'-wave on the color-coded tissue Doppler imaging (PA-TDI) of the LA lateral wall (B), and to the peak of the A-wave on the pulsed wave Doppler of the late trans-mitral diastolic velocity (PA-A) (C).

received intravenous heparin to maintain an activated clotting time of 300–400 s. A transseptal puncture was performed to gain entrance to the LA. Wide antral radiofrequency ablation of the pulmonary veins was performed using a 3.5 mm quadripolar open-loop irrigated ablation catheter (7.5Fr Navistar™, Biosense Webster, Inc., Diamond Bar, CA, USA) and a three-dimensional geometric reconstruction using Ensite NavX (St Jude Medical, St Paul, MN, USA) or CARTO (Biosense Webster, Inc.) mapping. Isolation was confirmed using the Lasso catheter. Cryoablation was performed using a 23- or 28-mm Arctic Front balloon catheter (Medtronic of Canada Ltd, Brampton, Ontario, Canada) using single or multiple 240-s deliveries, with assessment of entrance block using the Achieve multipolar catheter. The procedure was considered successful when all four pulmonary veins were isolated from the left atrium. Additional radiofrequency ablation procedures, including cavo-tricuspid isthmus, continuous fragmented electrical activity, superior vena cava, coronary sinus and additional lines (mitral valve isthmus and left atrial roof) were left at the discretion of the operator.

Statistical analysis

Continuous variables are presented as mean \pm s.d. and were compared with the Student's *t*-test for normally distributed variables, and Mann-Whitney *U* test for skewed variables. Categorical variables are presented as numbers and percentages and were compared by means of the χ^2 -test. Linear regression analysis was used to calculate the correlation

between atrial conduction time measurements and LA volume index, PR interval duration on a 12-lead electrocardiogram and the number of months since the diagnosis of paroxysmal AF was made. Univariate predictors for AF/AT recurrence after AF ablation were identified. If multiple significant univariate predictors were present, further analysis with multivariate logistic regression was planned to identify independent predictors outcome. A two-tailed $P < 0.05$ was considered significant. Odds ratio (OR) and 95% CI were calculated. All statistical analyses were performed using SPSS Software (version 22.0, SPSS, Inc.).

Results

Patient characteristics

A total of 36 patients undergoing first AF catheter ablation who were in sinus rhythm during transthoracic echocardiography were prospectively enrolled in the study. The procedural end-point of pulmonary vein isolation was reached in 32 patients (21 male (66%), mean age 54 ± 9 years), all of whom were included in the final analysis. Radiofrequency ablation was performed in 21 patients (66%), while 11 patients (34%) underwent cryoablation. The baseline clinical characteristics of the patients are described in Table 1. Twenty-five patients (78%) had CHADS₂ score 0, while five patients (16%) had CHADS₂ score of 1, and 2 patients (6%) had CHADS₂ score of 2. Twenty-four (75%) patients were on antiarrhythmic medications including 14 patients on propafenone and

Table 1 Baseline clinical characteristics of patients.

Variables	All (n=32)	No recurrence (n=20)	Recurrence (n=12)	P value
Age (years)	54±9	55±9	53±10	0.660
History of paroxysmal AF (months)	59.7±46.2	43.5±33.5	85.3±53.0	0.011
Prior electrical cardioversion, n (%)	20 (63)	14 (44)	6 (19)	0.258
Cardiac risk factors, n (%)				
HTN	7 (22)	5	2	0.581
Diabetes mellitus	NA	NA	NA	
Coronary artery disease	1(3)	1 (3)	0 (0)	0.431
Prior myocardial infarction	1(3)	1 (3)	0 (0)	0.431
CVA	1(3)	0 (0)	1 (3)	0.190
Hyperlipidemia	9 (28)	5 (16)	4 (13)	0.612
Smoking	1 (3)	1 (3)	0 (0)	0.431
Medications, n (%)				
Beta blockers	15 (47)	11 (34)	4 (13)	0.183
ACE/ARB	4 (13)	3 (9)	1 (3)	0.546
Statin	12 (38)	7 (22)	5 (16)	0.788
Anticoagulation	26 (81)	17 (53)	9 (28)	0.483
Antiplatelet agents	12 (38)	11 (34)	1 (3)	0.006
Calcium channel blocker	9 (28)	4 (13)	5 (16)	0.218
Digoxin	1 (3)	0 (0)	1 (3)	0.201
Antiarrhythmic agents	24 (75)	14 (44)	10 (31)	0.129
Diuretics	2 (6)	1 (3)	1 (3)	0.735

ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

eight patients on amiodarone. Table 2 describes the baseline echocardiographic characteristics of the patients. Mean heart rate was 56 ± 10 beats/min, and mean frame rate for color-coded TDI was 176.1 ± 16.0 frames/s. Mild left atrial dilatation was present in six patients (19%), moderate in three patients (9%), and severe in one patient (3%), while 22 patients (69%) had normal left atrial volume. There was a significant correlation between the LA size and history of paroxysmal AF ($r=0.414$, $P=0.021$).

At 6-month follow-up, 12 patients (38%) had recurrent AF/AT (AF in eight patients and atrial flutter in four patients). Tables 1 and 2 describe the baseline characteristics of the patients with and without recurrence. Patients with AF/AT recurrence had a significantly longer history of paroxysmal AF (85 ± 53 months vs 44 ± 34 months, $P=0.011$) and significantly larger baseline-indexed LA volumes compared to the patients who maintained sinus rhythm (36 ± 8 ml/m² vs 30 ± 9 ml/m², $P=0.047$). There was no difference in the outcome between the patients who underwent AF ablation using radiofrequency catheter vs cryoballoon.

Atrial conduction time

There was a significant difference between the baseline PA-TDI, PA-a' and PA-A measurements (116.7 ± 27.6 ms, 134.7 ± 25.8 ms and 148.4 ± 25.7 ms respectively;

$P<0.001$). The largest difference in the atrial conduction time was seen between PA-A and PA-TDI, with no correlation demonstrated between these two measurements (Table 3). On the other hand, a weakly moderate correlation was seen between PA-a' and PA-TDI ($r=0.459$; $P=0.009$) and good correlation was seen between PA-A and PA-a' ($r=0.807$; $P<0.001$). When all three atrial conduction time parameters were compared to LA size, history of AF and PR interval on a 12-lead electrocardiogram, a significant although only moderate correlation was seen between PA-a' and PR interval ($r=0.550$; $P=0.001$) while no correlation was observed with the LA size and history of AF. There was no significant difference in the baseline PA-TDI, PA-A and PA-a' between the patients that were and were not on antiarrhythmic agents at the time of AF ablation. At 6 months, there was no difference in any of the baseline atrial conduction time measurements between the patients with and without recurrence of AF/AT. Similar findings were found for iPA-TDI, iPA-a' and iPA-A in terms of a significant difference between these three parameters (1.92 ± 0.78 ms/ml, 2.19 ± 0.78 ms/ml and 2.42 ± 0.84 ms/ml respectively, $P \leq 0.003$) with the largest difference seen between iPA-A and iPA-TDI (Table 3). On the other hand, there was no correlation between any of the three indexed parameters of atrial conduction time and PR interval on a 12-lead electrocardiogram.

Table 2 Baseline echocardiographic and electrocardiographic characteristics of the patients.

Variables	All (n=32)	No recurrence (n=20)	Recurrence (n=12)	P value
Echocardiography				
LAVi (ml/m ²)	32.1 ± 8.9	29.7 ± 8.8	36.1 ± 7.8	0.047
LAV absolute (ml)	66.3 ± 18.5	63.0 ± 20.0	71.8 ± 14.7	0.196
LVEDVi (ml/m ²)	54.8 ± 14.4	53.3 ± 15.0	57.2 ± 13.5	0.462
LVESVi (ml/m ²)	21.6 ± 7.6	21.2 ± 7.7	22.3 ± 7.8	0.699
LVEF (%)	61.5 ± 7.2	61.6 ± 6.8	61.2 ± 7.9	0.883
LV mass (mg/m ²)	80.9 ± 18.5	83.3 ± 16.6	77.0 ± 21.4	0.354
Deceleration time	216.8 ± 54.4	217.0 ± 48.6	215.8 ± 63.3	0.954
E (cm/s)	70.9 ± 17.1	69.3 ± 15.7	73.4 ± 19.6	0.528
A (cm/s)	52.3 ± 17.3	51.2 ± 16.3	54.1 ± 19.3	0.650
E/A	1.5 ± 0.7	1.5 ± 0.8	1.5 ± 0.5	0.749
E/e'	7.8 ± 2.7	8.0 ± 2.8	7.6 ± 2.5	0.656
Mean e' (cm/s)	9.7 ± 2.5	9.5 ± 2.5	10.0 ± 2.6	0.562
Mean a' (cm/s)	8.7 ± 2.1	8.8 ± 2.0	8.2 ± 2.5	0.440
PA-TDI lateral (ms)	116.7 ± 27.6	114.5 ± 30.5	120.3 ± 22.9	0.577
PA-a' lateral (ms)	134.7 ± 25.8	132.0 ± 28.8	139.2 ± 20.2	0.455
PA-A (ms)	148.4 ± 25.7	146.5 ± 28.0	151.7 ± 22.1	0.590
iPA-TDI lateral (ms/ml)	1.92 ± 0.78	2.01 ± 0.84	1.78 ± 0.69	0.434
iPA-a' lateral (ms/ml)	2.19 ± 0.78	2.26 ± 0.76	2.08 ± 0.84	0.527
iPA-A (ms/ml)	2.42 ± 0.84	2.52 ± 0.84	2.26 ± 0.84	0.397
Electrocardiogram				
HR (beats/min)	65 ± 16	63 ± 11	71 ± 23	0.202
PR interval (ms)	174 ± 25	173 ± 22	179 ± 25	0.525
QRS interval (ms)	95 ± 10	95 ± 10	93 ± 8	0.979
QTc (ms)	429 ± 24	432 ± 20	427 ± 30	0.601

LAVi, left atrial volume indexed to body surface area; LVEDi, left ventricular end-diastolic volume indexed to body surface area; LVESVi, left ventricular systolic volume indexed to body surface area; LVEF, left ventricular ejection fraction; HR, heart rate.

Predictors of AF recurrence

The only predictor of AF/AT recurrence following a single PVI procedure in the univariate analysis was the duration of history of AF ($P=0.024$; OR 1.023, CI 1.003–1.044), while statistical significance was not reached for LA size ($P=0.060$; OR 1.098, CI 0.996–1.211). We categorized the patients into four groups based on the LA size (those with normal LA volume index and those with a dilated LA), and based on the median duration of the history of paroxysmal AF (48 months). There was no significant difference in the recurrence of AF/AT between those patients with a normal vs dilated LA, or between those with AF duration of ≤ 48 months vs > 48 months. However only 2 out of 14 patients (14%) who had both normal LA volume and AF duration of ≤ 48 months experienced recurrence of AF/AT, compared to 10 out of 18 (56%) who had dilated LA and AF duration of > 48 months (Table 4).

Discussion

Our study demonstrated a significant difference in the atrial conduction time measurements obtained by three different echocardiographic techniques with the smallest

difference and the best correlation seen between PA-A and PA-a' and the largest difference and no correlation seen between PA-A and PA-TDI. The duration of history of AF was the only univariate predictor of AF/AT recurrence following first AF ablation. On subgroup analysis, a combination of a normal LA size and a history of paroxysmal AF of ≤ 48 months was associated with significantly lower likelihood of AF/AT recurrence.

Several clinical parameters have been shown to be associated with an increased recurrence of atrial arrhythmias after AF catheter ablation, including hypertension, structural heart disease, left atrial dilatation, older age, persistent as opposed to paroxysmal AF, and AF duration (6). Moreover, persistence of the substrate for maintaining AF as determined by the proliferation and differentiation of fibroblasts into myofibroblasts and by the increase of connective tissue resulting in fibrosis likely plays an important role in addition to the triggering foci. The resulting alterations in electrical intra-atrial conduction together with atrial dilatation determine total time required for atrial electrical activation, with the maximal P-wave duration as an equivalent on the 12-lead surface ECG (8). The gold standard for determination of P-wave duration is the signal-averaged ECG technique and has

Table 3 Mean difference in atrial conduction times as absolute measurements and measurement indexed to absolute left atrial volume using color-coded tissue Doppler imaging (PA-TDI and iPA-TDI), TDI in pulsed-wave Doppler mode (PA-a' and iPA-a') and pulsed-wave Doppler of the late trans-mitral diastolic velocities (PA-A and iPA-A).

Atrial conduction time	Mean difference	P value	Correlation coefficient	P value
PA-A vs PA-TDI (ms)	32.2 ± 33.9	P < 0.001	0.210	0.257
PA-a' vs PA-TDI (ms)	18.0 ± 28.0	P = 0.001	0.454	0.009
PA-A vs PA-a' (ms)	13.5 ± 16.0	P < 0.001	0.807	< 0.001
iPA-A vs iPA-TDI (ms/ml)	0.50 ± 0.58	P < 0.001	0.614	< 0.001
iPA-a' vs iPA-TDI (ms/ml)	0.27 ± 0.47	P = 0.003	0.661	< 0.001
iPA-A vs iPA-a' (ms/ml)	0.23 ± 0.27	P < 0.001	0.921	< 0.001

been shown to have a reasonable predictive power for the development of AF (20, 21). However, signal-averaged ECG has not found its way into clinical practice, mainly as it requires special hardware and is time-consuming. Recently, a novel non-invasive echocardiographic method has been developed for an easy, fast and reliable method to estimate the atrial conduction time (8). This technique measures total atrial conduction time using TDI of the atria, and has been validated against P-wave duration on signal-averaged ECG (8). Several recent studies have demonstrated an association of the atrial conduction time measured by Doppler echocardiography and AF/AT recurrence after electrical cardioversion (22, 23), and AF catheter ablation (9, 10, 11, 12, 13). However, the definitions of atrial conduction times in these studies varied. The atrial conduction times were defined as the time intervals measured from the onset of the P-wave on ECG to the peak a'-wave of the lateral LA wall motion on the color-coded TDI (9), or to the peak a'-wave of the lateral mitral annulus TDI in PW mode (8, 10, 11), or to the peak A-wave of the late transmitral diastolic velocities on PW Doppler (13). In our study, atrial conduction times were determined using all three echocardiographic definitions and the measurements were compared. The results demonstrated a significant difference in the atrial conduction times between the three methods. This is likely related to the fact that the measurements of peak atrial contraction are obtained either from different regions of the left atrium (at the lateral mitral annulus for PA-a' vs at the lateral LA wall distal to mitral annulus for PA-TDI), or from the peak velocity of the mitral inflow during atrial contraction. In addition, a significantly shorter PA-TDI compared to PA-a' could be explained by different methodologies of TDI measurements. Color-coded TDI has lower temporal resolution compared to PW Dopple, which could lead to underestimation of the timing of the peak contraction. In addition, PW Doppler traces may sometimes be challenging for timing

measurements if they do not yield distinct peaks. Lastly, in the PW TDI, the myocardial velocity is obtained from the peak value using the edge of the spectral PW envelopes, while in color-coded TDI, the value represents the mean velocity for a given myocardial segment. Therefore, based on previously published data, it appears that PW TDI yields higher velocities than color-coded TDI (24, 25). Whether this difference in the techniques is also associated with different timing of the peak velocities may need to be confirmed in future studies. Importantly, none of the atrial conduction time parameters used in our study predicted AF/AT recurrence after the first AF ablation. This is in contrast to some of the previous studies that demonstrated independent predictive value of atrial conduction time for recurrence of AF/AT after AF catheter ablation (9, 11, 12, 13). In the study by Chao *et al.*, PA-A interval of ≥160 ms was associated with a larger LA volume, longer left atrial total activation time and higher recurrence rate of AF/AT after ablation (13). Similarly, Fukushima *et al.* demonstrated that the rate of AF recurrence was significantly higher in the patients with PA-a' ≥151.3 ms compared with those with PA-a' <131.0 ms (12). On the other hand, atrial conduction time alone was not an independent predictor of AF recurrence in the study by Ejima *et al.* (10) but gained

Table 4 Recurrence of AF/AT in patient groups defined according to left atrial size and duration of history of atrial fibrillation.

Subgroups	Recurrence (n)	No recurrence (n)	P value
Normal LA and AF history ≤48 months	2	12	0.028
Enlarged LA and/or AF history >48 months	10	8	

LA, left atrium; AF, atrial fibrillation; AT, atrial tachycardia.

predictive value after combining with LA size. The study demonstrated a 10.9-fold increase in the risk of recurrent AF/AT in the patients with an enlarged LA and $PA-a' \geq 143$ ms (10). Factors that have been described to facilitate AF are LA dilatation and depressed intra-atrial conduction related to electrical and structural remodeling of LA (8). Chao *et al.* (13) reported a moderate correlation between LA volume index and $PA-a'$ ($r=0.419$, $P=0.003$), while Ejima *et al.* (10) and Park *et al.* (22) found only a weak correlation between LA volume index and $PA-TDI$ ($r=0.2585$, $P=0.0094$) and $PA-a'$ ($r=0.33$, $P=0.02$), respectively. In contrast to most of the previous studies, the majority of the patients in our study (88%) had normal or only mildly dilated left atrium. In addition, there was no correlation between the atrial conduction time and either the absolute LA volumes or LA volumes indexed to BSA. Mean $PA-TDI$, $PA-a'$ and $PA-A$ in the present study were relatively shorter compared to the previous studies. For example, in the study by Chao *et al.* (13), the mean $PA-A$ interval in the patients with recurrence of AF/AT was 171.0 ± 10.7 ms while it was 151.7 ± 22.1 ms in our study. Similarly, in the study by Mano *et al.* (11) the mean $PA-a'$ in the patients with AF/AT recurrence was 163.9 ± 11.0 ms while it was 139.2 ± 20.2 ms in our study. Lastly, the mean $PA-TDI$ interval in the patients with AF/AT recurrence in the study by DenUijl *et al.* (9) was 146 ± 20 ms while it was 120 ± 22.9 ms in our study. In all these studies, more patients were included with enlarged atria. In our study, only five out of 12 patients (42%) with recurrent AF/AT had $PA-A \geq 160$ ms or $PA-a' \geq 143$ ms which were found to indicate high recurrence of AF/AT in the previous studies. (10, 12, 13) In addition, none of the atrial conduction time parameters predicted outcome even when normalized for an absolute LA volume. This could suggest that atrial conduction time changes may be less pronounced in the earlier stages of LA remodeling. Considering also the variability of Doppler echocardiography measurements, atrial conduction time may not gain predictive value until the later stages. Interestingly, Teh *et al.* (26) demonstrated slow LA conduction without detectable structural remodeling that was more pronounced in patients with persistent than paroxysmal AF suggesting progressive electroanatomic remodeling independent of LA size in these patients. Lastly, some patients may have electrical reconnection of pulmonary veins or a primary electric disorder with the diseased atrial substrate playing a less dominant role (27, 28, 29), thus reducing the predictive value of atrial conduction time. Recent studies demonstrated that LA strain parameters that reflect the distensibility of the LA wall provided incremental predictive value

for rhythm outcomes over clinical features in patients undergoing AF ablation. This suggests that reservoir function might be preferable to contractile variables for assessing LA remodeling in clinical setting (30, 31), which will need to be determined in future studies.

Limitations

The present study evaluated a relatively small group of patients, which may have affected the precision of the results. However, the majority of patients had normal or only mildly increased LA volumes and the clinical relevance of measuring pre-ablation atrial conduction time in these patients seems to be low. Further large studies may be useful to investigate patients with the full spectrum of LA remodeling. In addition, detection of recurrent AF/AT was derived from symptom driven ECGs and 24-h Holter monitoring. This may have led to underestimation of AF/AT recurrence in patients without associated symptoms. Nevertheless, the recurrence rate of AF/AT was similar to the outcomes published in the literature. Lastly, two different techniques were used for AF ablation: radio-frequency ablation and cryoablation. However, there was no difference in our study in the rate of recurrence of AF/AT between the two AF ablation techniques.

Conclusions

The predictive value of the Doppler-derived parameters of atrial conduction time may be reduced in the patients in the early stages of LA remodeling. Future studies are required to determine which echocardiographic parameter correlates the best with the extent of LA remodeling and has the best predictive value for successful AF ablation. Larger studies are needed that would include the full spectrum of patients referred for AF ablation therapy and would be powered enough to develop scores for risk assessment.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This work was supported by the University Hospital Foundation (2010).

Acknowledgements

We acknowledge the financial support from the University Hospital Foundation. We are grateful for the assistance from Sean Chiew and Joanne McGoey.

References

- Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V & Kissela B 2008 for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* **117** e25–e146. (doi:10.1161/CIRCULATION-AHA.107.187998)
- Wokhlu A, Hodge DO, Monahan KH, Asirvatham SJ, Friedman PA, Munger TM, Cha YM, Shen WK, Brady PA, Bluhm CM *et al.* 2010 Long-term outcome of atrial fibrillation ablation: impact and predictors of very late recurrence. *Journal of Cardiovascular Electrophysiology* **21** 1071–1078. (doi:10.1111/j.1540-8167.2010.01786.x)
- Stabile G, Bertaglia E, Senatore G, De Simone A, Zoppo F, Donnici G, Turco P, Pascotto P, Fazzari M & Vitale D 2006 Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation for The Cure of Atrial Fibrillation study). *European Heart Journal* **27** 216–221. (doi:10.1093/eurheartj/ehi583)
- Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Packer D & Skanes A 2005 Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* **111** 1100–1105. (doi:10.1161/01.CIR.0000157153.30978.67)
- Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F, Lellouche N, Knecht S, Wright M & Nault I 2011 Catheter ablation for atrial fibrillation. Are results maintained at 5 years of follow-up? *Journal of the American College of Cardiology* **57** 160–166. (doi:10.1016/j.jacc.2010.05.061)
- Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr, Davies DW & DiMarco J 2012 HRS/EHRA/ECAS Expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints and research trial design. *Europace* **14** 528–606. (doi:10.1093/europace/eus027)
- Wijffels MC, Kirchhof CJ, Dorland R & Allesie MA 1995 Atrial fibrillation begets atrial fibrillation: A study in awake chronically instrumented goats. *Circulation* **92** 1954–1968. (doi:10.1161/01.CIR.92.7.1954)
- Merckx KL, De Vos CB, Palmans A, Habets J, Cheriex EC, Crijns HJ & Tieleman RG 2005 Atrial activation time determined by transthoracic Doppler tissue imaging can be used as an estimate of the total duration of atrial electrical activation. *Journal of the American Society of Echocardiography* **18** 940–944. (doi:10.1016/j.echo.2005.03.022)
- Den Uijl DW, Gawrysiak M, Tops LF, Trines SA, Zeppenfeld K, Schaliij MJ, Bax JJ & Delgado V 2011 Prognostic value of total atrial conduction time estimated with tissue Doppler imaging to predict the recurrence of atrial fibrillation after radiofrequency catheter ablation. *Europace* **13** 1533–1540. (doi:10.1093/europace/eur186)
- Ejima K, Kato K, Arai K, Fukushima K, Fukushima N, Suzuki T, Yoshida K, Nuki T, Uematsu S, Hoshi H *et al.* 2014 Impact of atrial remodeling on the outcome of radiofrequency catheter ablation of paroxysmal atrial fibrillation. *Circulation Journal* **78** 872–877. (doi:10.1253/circj.CJ-13-1391)
- Mano H, Okumura Y, Watanabe I, Masakatsu O, Rikitake K, Naoko S, Toshiko N, Kimie O, Masayoshi K, Koichi N *et al.* 2014 Changes over time in echocardiographic variables and atrial electromechanical intervals after ablation for atrial fibrillation. *Journal of Arrhythmia* **30** 466–472. (doi:10.1016/j.joa.2014.01.005)
- Fukushima K, Fukushima N, Ejima K, Kato K, Sato Y, Uematsu S, Arai K, Manaka T, Takagi A, Ashihara K *et al.* 2015 Left atrial appendage flow velocity and time from P-wave onset to tissue Doppler-derived a' predict atrial fibrillation recurrence after radiofrequency catheter ablation. *Echocardiography* **32** 1101–1108. (doi:10.1111/echo.12823)
- Chao TF, Sung SH, Wang KL, Lin YJ, Chang SL, Lo LW, Hu YF, Tuan TC, Suenari K, Li CH *et al.* 2011 Association between the atrial electromechanical interval, atrial remodeling and outcome of catheter ablation in paroxysmal atrial fibrillation. *Heart* **97** 225–230. (doi:10.1136/hrt.2010.212373)
- Nishimura R, Miller FJ, Callahan M, Benassi RC, Seward JB & Tajik AJ 1985 Doppler echocardiography: theory, instrumentation technique and application. *Mayo Clinic Proceedings* **60** 321–343. (doi:10.1016/S0025-6196(12)60540-0)
- Tajik A, Seward J, Hagler D, Mair DD & Lie JT 1978 Two dimensional real-time ultrasonic imaging of the heart and great vessels: technique, image orientation, structure identification and validation. *Mayo Clinic Proceedings* **53** 271–303. (doi:10.4250/jcu.2014.22.3.127)
- Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T *et al.* 2015 Recommendations for chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography* **28** 1–39. (doi:10.1016/j.echo.2014.10.003)
- Mosteller RD 1987 Simplified calculation of body-surface area. *New England Journal of Medicine* **317** 1098. (doi:10.1056/NEJM19870223171717)
- Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, Nihoyannopoulos P, Otto CM, Quinones MA, Rakowski H *et al.* 2003 Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *Journal of the American Society of Echocardiography* **16** 777–802. (doi:10.1016/S0894-7317(03)00335-3)
- Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA & Evangelista A 2009 Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Journal of the American Society of Echocardiography* **22** 107–133. (doi:10.1016/j.echo.2008.11.023)
- Fukunami M, Yamada T, Ohmori M, Kumagai K, Umemoto K, Sakai A, Kondoh N, Minamino T & Hoki N 1991 Detection of patients at risk for paroxysmal atrial fibrillation during sinus rhythm by P wave-triggered signal-averaged electrocardiogram. *Circulation* **83** 162–169. (doi:10.1161/01.CIR.83.1.162)
- Guidera SA & Steinberg JS 1993 The signal-averaged P wave duration: a rapid and noninvasive marker of risk of atrial fibrillation. *Journal of the American College of Cardiology* **21** 1645–1651. (doi:10.1016/0735-1097(93)90381-A)
- Park SM, Kim YH, Choi JI, Pak HN, Kim YH & Shim WJ 2010 Left atrial electromechanical conduction time can predict six-month maintenance of sinus rhythm after electrical cardioversion in persistent atrial fibrillation by Doppler tissue echocardiography. *Journal of the American Society of Echocardiography* **23** 309–314. (doi:10.1016/j.echo.2009.12.019)
- Maffé S, Paffoni P, Dellavesa P, Cucchi L, Zenone F, Bergamasco L, Paino AM, Franchetti Pardo N, Signorotti F, Baduena L *et al.* 2015 Prognostic value of total atrial conduction time measured with tissue Doppler imaging to predict the maintenance of sinus rhythm after external electrical cardioversion of persistent atrial fibrillation. *Echocardiography* **32** 420–427. (doi:10.1111/echo.12702)
- Baek HK, Park TH, Park SY, Kim JH, Seo JM, Kim WJ, Nam YH, Kim MH & Kim YD 2011 Determination of diastolic dysfunction cut-off value by tissue Doppler imaging in adults 70 years of age or older: a comparative analysis of pulsed-wave and color-coded tissue Doppler imaging. *Korean Circulation Journal* **41** 137–142. (doi:10.4070/kcj.2011.41.3.137)
- McCulloch M, Zoghbi WA, Davis R, Thomas C & Dokainish H 2006 Color tissue Doppler myocardial velocities consistently underestimate spectral tissue Doppler velocities: impact on calculation peak transmitral pulsed Doppler velocity/early diastolic tissue Doppler velocity (E/Ea'). *Journal of the American Society of Echocardiography* **19** 744–748. (doi:10.1016/j.echo.2006.01.020)

- 26 Teh AW, Kistler PM, Lee G, Medi C, Heck PM, Spence SJ, Sparks PB, Morton JB & Kalman JM 2012 Electroanatomic remodeling of the left atrium in paroxysmal and persistent atrial fibrillation patients without structural heart disease. *Journal of Cardiovascular Electrophysiology* **23** 232–238. (doi:10.1111/j.1540-8167.2011.02178.x)
- 27 Jahangir A, Lee V, Friedman PA, Trusty JM, Hodge DO, Kopecky SL, Packer DL, Hammill SC, Shen WK & Gersh BJ 2007 Long-term progression and outcomes with aging in patients with lone atrial fibrillation: a 30-year follow-up study. *Circulation* **115** 3050–3056. (doi:10.1161/CIRCULATIONAHA.106.644484)
- 28 Wyse DG & Gersh BJ 2004 Atrial fibrillation: a perspective: thinking inside and outside the box. *Circulation* **109** 3089–3095. (doi:10.1161/01.CIR.0000132611.01101.DC)
- 29 Allesie M, Ausma J & Schotten U 2002 Electrical, contractile and structural remodeling during atrial fibrillation. *Cardiovascular Research* **54** 230–246. (doi:10.1016/S0008-6363(02)00258-4)
- 30 Motoki H, Negishi K, Kusunose K, Popović ZB, Bhargava M, Wazni OM, Saliba WI, Chung MK, Marwick TH & Klein AL 2014 Global left atrial strain in the prediction of sinus rhythm maintenance after catheter ablation for atrial fibrillation. *Journal of the American Society of Echocardiography* **27** 1184–1192. (doi:10.1016/j.echo.2014.08.017)
- 31 Montserrat S, Ganrielly L, Bijmens B, Borràs R, Berrueto A, Poyatos S, Brugada J, Mont L & Sitges M 2015 Left atrial deformation predicts success of first and second percutaneous atrial fibrillation ablation. *Heart Rhythm* **12** 11–18. (doi:10.1016/j.hrthm.2014.08.032)

Received in final form 20 October 2015

Accepted 21 October 2015