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

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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.

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 transmural 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 \((> 140 \text{ Hz})\). Regional myocardial PW Doppler velocity profiles were analyzed offline by positioning the sample volume \((6 \times 6 \text{ mm})\) 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 transmural 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...
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 NavistarTM, 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 ± 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 χ²-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
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, $P=0.003$) 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 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                  | 0.431     |
| Coronary artery disease            | 13 (1)       | 1 (3)                  | 0 (0)               | 0.431     |
| Prior myocardial infarction        | 13 (1)       | 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.
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 ($P=0.066$; 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 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/m²)            | 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/m²)          | 54.8 ± 14.4| 53.3 ± 15.0          | 57.2 ± 13.5       | 0.462   |
| LVESVi (ml/m²)          | 27.7 ± 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/m²)         | 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; LVEDVi, 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.
ECG to the peak a time intervals measured from the onset of the P-wave on varied. The atrial conduction times were defined as the definitions of atrial conduction times in these studies traces may sometimes be challenging for timing of the peak contraction. In addition, PW Doppler, which could lead to underestimation of the coded TDI has lower temporal resolution compared to different methodologies of TDI measurements. Color-coded TDI in PW mode (PA-a’ and iPA-a’) and pulsed-wave Doppler of the late trans-mitral diastolic velocities (PA-A and iPA-A).

**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±3.3         | 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 Doppler, 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                |         |
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’ ≥ 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 ≥ 160 ms or PA-a’ ≥ 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: radiofrequency 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.

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