Assessment of atrial electromechanical interval using echocardiography after catheter ablation in patients with persistent atrial fibrillation

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Abstract

We sought to investigate variation of atrial electromechanical interval after catheter ablation procedure in patients with persistent atrial fibrillation using pulse Doppler (PW) and pulse tissue Doppler imaging (PW-TDI). A total of 25 consecutive in-patients with persistent atrial fibrillation, who restored sinus rhythm after ablation procedure, were recruited in our cardiac center. Echocardiography was performed on each patient at 2 hours, 1 day, 5 days, 1 month and 3 months after the ablation therapy, and atrial electromechanical delay was measured simultaneously by PW and PW-TDI. There was no significant difference between PW and TDI in measuring atrial electromechanical delay. However, at postoperative 2 hours, peak A detection rates were mathematically but nonsignificantly greater by PW-TDI than by PW. Second, there was a significant decreasing trend in atrial electromechanical interval from postoperative 2 hours to 3 months, but only postoperative 2-hour atrial electromechanical interval was significantly greater than atrial electromechanical interval at other time. Lastly, patients without postoperative 2-hour atrial electromechanical interval had a significantly longer duration of atrial fibrillation as compared to those with postoperative 2-hour atrial electromechanical interval, by the PW or by PW-TDI, respectively. In patients with persistent atrial fibrillation, atrial electromechanical interval may decrease significantly within the first 24 hours after ablation but remain consistent later, and was significantly related to patients' duration of atrial fibrillation. Atrial electromechanical interval, as a potential predicted factor, is recommended to be measured by either PW or TDI after 24 hours, when patients had recovered sinus rhythm by radiofrequency ablation.

Keywords: atrial fibrillation, echocardiography, tissue Doppler imaging, atrial electromechanical interval

Introduction

Atrial fibrillation (AF) is a common arrhythmia. Catheter ablation is a suitable therapeutic method for atrial fibrillation[1-4]. It has been known that AF recurrence is closely related to left atrial structural and electrical remodeling. These changes are frequently seen in post catheter ablation case[5-9]. The electromechanical interval of atrium, which could be measured from onset of P wave in electrocardiogram signal to the

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top of A wave in Doppler spectrum (PA Interval), is associated with total atrial conduction time\(^{10-11}\) and can effectively reflect left atrium remodeling\(^{8,9}\). It is also an useful indicator to predict new-onset AF occurrence and AF recurrence after radiofrequency catheter ablation\(^{9,12-15}\).

The PA interval can be obtained by mitral inflow pulse Doppler (PW) and Doppler tissue imaging (TDI). Theoretically, TDI is more sensitive and more accurate on measuring PA interval than PW as TDI measures myocardium motion directly. Recently, most studies have chosen TDI to estimate atrial electromechanical delay\(^{14,16-17}\), while Chao et al. considered that the PA interval derived from PW reflected a global atrial electromechanical delay\(^{9}\). Once a persistent AF (PAF) patient recovers to sinus rhythm after catheter ablation, reverse remodeling of the atrium initiates simultaneously. Data are scarce in the literature regarding whether PA intervals remain or not during the ablation process, as well as when and how the PA interval need to be measured.

We hypothesize the PA interval of PAF patients changes after radiofrequency catheter ablation when sinus rhythm is maintained. The purpose of this study was to explore variations in atrial electromechanical delay through assessment of the PA interval using PW and TDI.

### Patients and methods

#### Patient population

Twenty-nine consecutive PAF patients who were refractory to antiarrhythmic drugs were included in the study at our hospital from August 2013 to March 2014. These cases had been confirmed as PAF by 24-h ambulatory ECG monitors, with duration ranging from 1 month to 48 months (mean duration 11.56±15.72 months). The history of selected cases included hypertension (8 cases), diabetes (3 cases), and coronary heart disease (2 cases, 1 subject underwent coronary artery PCI operation, with one stent implanted in the anterior descending branch of the coronary artery). Excluded cases comprised reversible AF caused by dysfunction thyroid, alcohol poisoning, post operation, and etc. Analogously, cases manifesting contraindications to anticoagulation, left atrial appendage thrombus on transesophageal echocardiography (TEE) and presence of valvular heart disease or various cardiomyopathies were also taken into account. All cases underwent radiofrequency ablation operation. Four patients were excluded because AF or atrial tachycardia was recurrence within 3 months after ablation. At last 25 patients completed 3 months of follow-up (containing 18 males and 7 females, mean age 55.44±11.73 years). All patients provided signed informed consent before

| Characteristics | Mean±SD |
|-----------------|---------|
| Age, years      | 55.4±11.7 |
| Male gender, n (%) | 18 (72) |
| Body mass index, Kg/m² | 25.31±3.46 |
| Diabete mellitus, n (%) | 3 (12) |
| Hypertension, n (%) | 13 (52) |
| Duration of PAF, months | 13.56±15.73 |
| CHA2DS2-VASC | 1.0±0.707 |
| Treatment | |
| ACE-I/ARB, n (%) | 8 (32) |
| β-blockers, n (%) | 6 (24) |
| Calcium channel blocker, n (%) | 7 (28) |

| Echocardiographic measurements | |
|-------------------------------|------------------|
| LAD, mm | 40.28±4.82 |
| LAVI, mL/m² | 27.04±11.19 |
| IVEDD, mm | 10.32±1.14 |
| LVEDD, mm | 47.72±3.79 |
| LVEF, % | 60.96±5.58 |

Values are means±SD for quantitative variables and numbers with percentages in parenthetic for qualitative variables. PAF: persistent atrium fibrillation; LAD: left atrial diameter; LAVI: left atrial volume index; IVEDD: inter ventricular end-diastolic diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular eject fraction.
participating in the study. The protocol was approved by the local institutional board at the authors' affiliated institution. Patients' characteristics and echocardiographic measurements are presented in Table 1.

**Electrophysiological evaluation and ablation**

TEE was performed to rule out any intracardiac thrombi. Then, the patients underwent an electrophysiological study in a mildly sedated and local anesthetized state. After transseptal punctures, intravenous heparin was administered to maintain an activated clotting time of 250 to 300 seconds. After catheter placement, a three dimensional (3D) anatomical shell of the LA and PVs was constructed using a circular mapping and/or ablation catheter with an electroanatomical mapping system (EnSite-NavX, St. Jude Medical, Inc., St. Paul, Minnesota, USA). Catheter ablation was performed using an irrigation catheter (IBI, St. Jude Medical, Inc., St. Paul, Minnesota, USA), following a sequential ablation strategy. If AF was organized into an atrial tachycardia (AT) or sinus rhythm was directly restored during ablation, complex fractionated electrogram (CFE) mapping and ablation were omitted. Any AT during the procedure was mapped and ablated accordingly. If AF was persisted after finishing the predesigned ablation strategy, electrical cardioversion was performed to restore sinus rhythm. Postoperative regimens included administration of amiodarone intravenously for 48 hours, then orally for 3 to 6 months, and simultaneous anticoagulation therapy comprising combined administration of low molecular weight heparin and warfarin for 3 or 5 days, afterwards heparin was withdrawn and oral warfarin anticoagulation was maintained by INR for 2-3.

**Instruments and methods**

All subjects received preoperative echocardiography with IE33 ultrasound system using a 1-5 MHz transducer (Philips Medical Systems, Bothell, WA, USA) through investigation of the parameters such as LA diameter (LAD), left ventricular end-diastolic diameter (LVEDD), and interventricular end-diastolic diameter (IVEDD) of the parasternal long axis plane. LAEF and LVEF were assessed in apical four chamber by Simpson's method. The measured time point was set at 2 hours, 1 day (average 25.76±1.79 h), 3 days, 1 month, and 3 months after catheter ablation. The subjects, whose posture containing supine or left lateral position with calm breathing, were connected with synchronous ECG leads. During echocardiography, in the apical four chamber view, the sampling volume box was placed in the mitral inflow tract and Doppler spectrum speed was set to 100 mm/second for acquiring Doppler spectrum (MV-PW). Measurement of ECG P wave was evaluated from the starting point to peak A point with the MV-PW spectrum in lead II (PW-PA interval), as described in Fig. 1. TDI was performed by adjusting the spectral pulsed Doppler signal filters until a Nyquist limit of 15 to 20 cm/second was reached using the minimal optimal gain. The sweep speed was set at 100 mm/second to optimize the spectral display of myocardial velocities. The pulsed Doppler sample volume (5 mm) was placed at the levels of the lateral mitral annulus. The late diastolic annular velocities (A' wave) of the lateral mitral annulus were measured. In the same view, TDI-PA interval was measured from the P wave starting point to the peak A' wave in PW-TDI spectrum (Fig. 1). All indicators were measured repeatedly for three times. The average value was subsequently calculated.

**Statistical analysis**

Measurement data were analyzed with software SPSS.17.0. Mean±SD was used for quantitative variables and numbers with percentages in parenthesis were used for qualitative variables. The difference of values between each corresponding time point detected by PW-TDI modes was compared with one-way analysis of variance (ANOVA), and Duncan method was applied to calculate the interclass differences. Students’ t test and Fisher' exact test were applied to compare differences in cardiovascular risk factors and echocardiographic measurements between patients with and without 2-hour-AEI for quantitative and qualitative variables, respectively. P < 0.05 was considered to be statistically significant.

**Table 2** Atrial electromechanical delays by pulse Doppler and tissue Doppler at different time points after ablation therapy

| Follow-up          | PW-PA interval, ms | TDI-PA interval, ms |
|--------------------|--------------------|---------------------|
| 2h after operation | 183.49±43.93       | 170.13±37.98        |
| 1 day after operation | 145.69±20.87     | 146.72±18.62        |
| 3 days after operation | 144.89±22.40    | 147.48±19.74        |
| 1 month after operation | 148.03±20.67    | 147.97±22.26        |
| 3 months after operation | 148.76±19.17   | 148.75±21.80        |

Values are means±SD. Students’ t test was applied to compare the atrial electromechanical delays measured by pulse Doppler and tissue Doppler at different time after ablation therapy. P values for the comparison between two methodology are all > 0.05.
Results

The atrial electromechanical intervals at different time after ablation, such as 2 hours, 1 day, 3 days, 1 month and 3 months, were compared between the Pulse Doppler group and the tissue Doppler group, but there was no significant difference (P ≥ 0.51, Table 2).

As shown in Fig. 1, there were 14 out of 25 patients with available postoperative 2-hour AEI measurements by the pulse Doppler methods, whereas 20 out of 25 patients with available postoperative 2-hour AEI measurements by the tissue Doppler methods. Herein, at postoperative 2 hours, peak A detection rates were mathematically but nonsignificantly greater in the tissue Doppler group than in the pulse Doppler group (80% vs. 56%, P = 0.07). Second, using the pulse Doppler methods, there was a significant decreasing trend in AEI from postoperative 2 hours to 6 months (P < 0.001), and in the subgroup interclass analysis, only postoperative 2-hour AEI was significantly greater than AEI at other time points (P < 0.05). Similarly, using the tissue Doppler methods, a significant decreasing trend was detected in AEI from postoperative 2 hours to 6 months (P = 0.002), and in the subgroup interclass analysis, only postoperative 2-hour AEI was significantly greater than AEI at other time points (P < 0.05). Moreover, in subjects without available postoperative 2-hour AEI, there was no significant change in AEI from postoperative 1 day to 3 months neither by the pulse Doppler (P = 0.92) nor by the tissue Doppler (P = 0.93).

In Table 3, cardiovascular risks and echocardiographic measurements were compared between patients with and without postoperative 2-hour AEI, identified either by the pulse Doppler or by the tissue Doppler. Notably, patients without postoperative 2-hour AEI had a significantly longer duration of PAF as compared by those with postoperative 2-hour AEI, by the pulse Doppler (20.5 ± 10.8 vs. 8.1 ± 10.6 months, P = 0.0497) or by the tissue Doppler (29.6 ± 16.6 vs. 9.6 ± 13.0 months, P = 0.008), respectively. Patients without postoperative 2-hour AEI also had a significantly greater LAD than those with 2-hour AEI (44.6 ± 4.8 vs. 39.2 ± 4.3 mm, P = 0.02).

Discussion

PA interval is a parameter which is derived from the method integrating ECG signal and echocardiography. P wave of ECG represents atrial electrical activity, while A wave of mitral inflow based in pulse Doppler and A’ wave of the left lateral wall of the mitral annulus based in TDI represent left atrium mechanical movement. PA interval is associated with LAD, LA volume, total atrial conduction time (TACT) and left atrial voltage[9]. Fuenmayor et al.[10] have demonstrated that the duration from high right atrial activation to the coronary sinus is closely related to PA interval, by means of running standard electrophysiological examination and pulse Doppler. Another study performed by Klaartje et al.[11] demonstrated that PA interval based TDI has high correlation with the duration of P wave based signal-average ECG (SA-ECG, R = 0.91, P < 0.001). Therefore, PA intervals assessed by pulse echocardiography or TDI were both reliable indicators to reflect inter-atrial
conduction of electricity. Notably, the changes of PA interval can reflect the process of left atrial electrical remodeling and reverse remodeling \([9, 10]\). TEE and TTE have been frequently used to explore atrial stunning\([18–23]\), especially after TDI technology emerged. As TEE is not easy to be accepted by patients, pulse Doppler spectrum and TDI are prevalent methods to measure PA interval. It is not clear which one of the two is better for evaluating A wave induced by atrial mechanical motion when patients maintain sinus rhythm at the early phase after PAF cardioversion. Atrial stunning can be observed in patients with chronic atrial arrhythmia when their rhythm recovered to sinus rhythm by drugs, electrical cardioversion or ablation\([24–27]\). This chronic atrial arrhythmia is linked to atrial remodeling. Its etiologies are currently considered including atrial cardiomyopathy caused by long-term rapid atrial arrhythmia\([28]\), atrial muscle cell calcium overload\([29, 30]\), and atrial myocardial hibernation\([31–32]\). Atrial reverse remodeling process begins as soon as an atrial arrhythmia recovers to a sinus rhythm. The recovery of atrial mechanical movement is also relevant to how long atrial fibrillation persists. Nevertheless, we have found few reports on atrial electrical activity recovery. Our data demonstrated that the postoperative atrial electromechanical delay (PA interval) was shortened apparently within 1-day post PAF, and with tendency to a steady-state within 3 months follow up. This phenomenon is referred to as the leap phenomenon of PA interval. Therefore, we call this “atrial electromechanical stunning.” Although the underlying mechanism remains unclear, we speculated that atrial electrical activity stayed in a turbulence state that was driven by multiple wavelets in the atrium; upon recovery to a sinus rhythm, atrial stunning attenuated intra left-atrial and reciprocal atrial electrical conductions. Thereafter, with alleviation of calcium overload and recovery of dysfunctional myocardial electrical conduction, atrial electric conduction recovers faster than the recovery of mechanical function. Accordingly, the leap phenomenon of PA interval could be detected as soon as electric conduction is recovered. Different from the restoration of electrical conduction, myocardial mechanical movement recovers much slower and is more unstable in the acute phase. To sum up, we regarded atrial slow conductance within postoperative 24 hours as atrial electromechanical stunning.

In our study, two different echocardiographic methods, PW and TDI, were addressed in measuring PA interval. Our study showed that peak A disappearing in a portion of PAF patients under both modes after conversion, probably due to the presence of atrial stunning. But our data also revealed that peak A disappearing was not recorded in all 25 subjects with PW, and peak A was detectable in 14 cases while 20 cases showed peak A with TDI. MV-PW reflects flow through the mitral valve, which is affected by several factors, such as contraction of the atrial myocardium, electric conduction of the left atrium, and pressure difference between the left atrial and left ventricle, while TDI is used to quantify the myocardium motion. Therefore, the patients after ablation procedure may

### Table 3 Comparison of cardiovascular risks and echocardiographic measurements between patients with and without 2-hour-AEI

|                      | Pulse-wave Doppler imaging | Tissue Doppler imaging |
|----------------------|----------------------------|------------------------|
|                      | Patients with 2-h-AEI (n=14) | Patients without 2-h-AEI (n=11) | P | Patients with 2-h-AEI (n=20) | Patients without 2-h-AEI (n=5) | P |
| Age, years           | 55.2±13.7                  | 55.7±9.3               | 0.92 | 57.0±12.1                  | 49.4±8.4               | 0.20 |
| Male gender, n (%)   | (78.6)                     | 7 (63.6)               | 0.41 | 14 (7.0)                  | 4 (80.0)               | 0.66 |
| Body mass index, kg/m² | 24.8±2.7                  | 25.9±4.3               | 0.44 | 25.0±3.4                  | 26.6±3.9               | 0.36 |
| Duration of PAF, months | 8.1±10.6                  | 20.5±10.8              | 0.0497 | 9.6±13.0                  | 29.6±16.6              | 0.008 |
| Hypertension, n (%)  | 7 (50.0)                   | 7 (63.6)               | 0.71 | 11 (55.0)                 | 3 (60.0)               | 0.99 |
| Diabetes, n (%)      | 2 (14.3)                   | 1 (9.1)                | 0.99 | 2 (10.0)                  | 1 (20.0)               | 0.50 |
| CHA₂DS₂-VASc         | 0.93±0.73                  | 1.09±0.70              | 0.58 | 25.4±7.9                  | 33.8±19.5              | 0.40 |
| LAVL/mL/m²           | 26.0±8.8                   | 28.4±14.0              | 0.60 | 1.00±0.73                 | 1.00±0.71              | 1.00 |
| LAD, mm              | 39.9±4.0                   | 40.7±5.9               | 0.69 | 39.2±4.3                  | 44.6±2.4               | 0.02 |
| IVSedWT, mm          | 10.2±1.2                   | 10.5±1.1               | 0.61 | 10.5±1.1                  | 9.6±0.9                | 0.12 |
| LVEDd, mm            | 47.0±3.9                   | 48.6±3.6               | 0.29 | 47.3±3.7                  | 49.6±3.6               | 0.22 |
| LVEF, %              | 61.0±5.5                   | 60.9±5.9               | 0.97 | 61.1±4.8                  | 61.1±4.8               | 0.88 |

Values are means±SD for quantitative variables and numbers with percentages in parenthetic for qualitative variables. Students’ t test and chi-square test were applied to compare the differences in cardiovascular risk factors and echocardiographic measurements between patients with and without 2-hour-AEI for quantitative and qualitative variables, respectively. LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction.
have left atrium motion detectable by TDI, but may not produce inflow through the mitral valve due to disorder in electric conduction of the left atrium, atrium-ventricle dyssynchrony, or low pressure difference between the left atrial and left ventricle. Our study showed that A wave measurement by PW-TDI was significantly higher than that by PW in the 2-hour group after ablation. On one hand, this result demonstrated the existence of atrial stunning; on the other hand, TDI showed high exhibition with atrial myocardium motion. In conclusion, TDI was more sensitive than PW in detecting postoperative peak A in 2 hours. The supposed interpretation underlies PW-PA interval reflecting atrial mechanical movement indirectly, while TDI-PA interval reflects the atrial myocardial motions directly. The complicated atrial-restarting process, involving chronic atrial reverse remodeling and recovery of currency dynamics, will not accomplish in 24 hours. Our data coincided with the principle of two ultrasonic modes.

Chao et al. observed that trans-mitral inflow Doppler pattern measurement PW-PA reflected the atrial electromechanical delay more accurately than tissue Doppler measurement (TDI-PA), because TDI measurement reflected regional myocardial motions; consequently, TDI-PA presented different values of myocardial tissue in different sites. Since there is heterogeneity in myocardial matrix or asynchronous disorder of the left atrium, TDI-PA, an indicator obtained from regional myocardial motions, cannot genuinely evaluate the mechanical motion of the left atrium as a whole. Park et al. argued that only the TDI-PA interval located in the mitral annulus of the left atrial side wall is the independent predictor of AF recurrence. Our data have also shown that there was no statistically significant difference at each corresponding time point on PA interval measured by PW and TDI. We hypothesized that the probable mechanism underlying the left lateral wall is the latest excited part of the left atrium during electrical impulse convey, and thus we referred to the left lateral wall as an alternative site in measuring PA interval, which was capable of reflecting atrial electromechanical interval precisely. Therefore, our conclusion is not contradictory to Park's inference. Theoretically, PA interval detected by PW-TDI is not as long as that by MV-PW, but our results challenged the viewpoint. We speculated that the possible causes include bias resulting from the insufficient samples, or difference beyond the detection sensitivity by means of the two methods.

Atrial electromechanical interval measured by echocardiography is usually used as an indicator to predict new-onset atrial fibrillation and atrial fibrillation after catheter ablation, cardioversion or cardiac surgery. In these studies, the measuring time of atrial electromechanical interval was not standardized. The earliest measuring time was about 6 hours after cardioversion. Most studies reported the measuring time approximately from several days to several months by either MV-Doppler or TDI. From this study's result, atrial electromechanical interval should be measured 24 hours after recovering sinus rhythm in PAF patients. There may be more sensitivity and specificity about the interval which was much valuable.

In conclusion, DI detection was more sensitive than PW detection in measuring AEI, which exhibits obvious postoperative leap phenomenon within the first 24 hours after ablation and maintains its stability later. AEI was also significantly related to the duration of atrial fibrillation.

The finding in this paper need to be interpreted within the context of limitations. First, this study is limited by the absence of the control group with paroxysmal atrial fibrillation after undergoing radiofrequency ablation. As conclusion in theory, if patients did not have continuous atrial arrhythmia, there was no atrial stunning. Therefore, this study just showed such phenomenon which was first reported in such patients, and it is limited by the relatively small sample size. Second, the 2-hour LAEI may be influenced by medication (such as amiodarone, etc.) or cardioversion. However, it is of note that every participant with PAF had both the medication and cardioversion therapy; therefore, in this case, these confounders would be balanced in those patients.

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