Patterns of left atrial activation and evaluation of atrial dyssynchrony in patients with atrial fibrillation and normal controls: Factors beyond the left atrial dimensions

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BACKGROUND Left atrial (LA) remodeling causing slower and asynchronous conduction is crucial for the maintenance of atrial fibrillation (AF).

OBJECTIVE We propose a simple and quick method to evaluate the LA asynchrony.

METHODS One hundred thirty patients with AF (AF group) and 70 patients without a history of AF (controls) were examined prospectively using pulsed-wave tissue Doppler imaging. The time intervals from the onset of the P wave to the onset of the A′ wave (P-A′ intervals) were measured at 4 sites at the mitral annulus: septal, lateral, anterior, and posterior. To assess the LA asynchrony, the differences between the longest and the shortest P-A′ interval as well as the standard deviation of all 4 P-A′ intervals were calculated.

RESULTS Both groups were matched for the baseline characteristics. The AF group had longer differences between the longest and the shortest P-A′ than did controls (37 ± 16 ms vs 28 ± 13 ms; $P = .0001$). The standard deviation of all 4 P-A′ intervals was also higher in the AF group (17 ± 7 ms vs 13 ± 5 ms; $P = .0001$). Furthermore, distinct patterns of LA activation were observed with most patients with AF showing upward LA activation (86.5%) whereas normal controls were showing downward LA activation (65.5%). Receiver operating characteristic analysis revealed that P-A′ anterior successfully discriminated patients with AF from controls (area under the curve 0.85; $P < .0001$). Furthermore, P-A′ anterior > 55 ms discriminated between patients with AF and controls with a sensitivity of 85% a specificity of 81%, a positive predictive value of 0.898, and a negative predictive value of 0.707.

CONCLUSION Patients with AF showed greater LA asynchrony in pulsed-wave tissue Doppler imaging, upward LA activation, and a prolonged activation time at the anterior mitral annulus. Prolongation of P-A′ anterior discriminated between patients with AF and controls with high sensitivity and specificity.

KEYWORDS Atrial; Asynchrony; Atrial fibrillation; PW-TDI

(Heart Rhythm 2016;13:1829–1836)

Introduction

Earlier risk stratification for atrial fibrillation (AF) is important to prevent devastating AF-associated events such as stroke. Numerous clinical and echocardiographic parameters were found to be associated with an increased likelihood of new-onset AF. However, even the most widely used prognostic variables have low diagnostic yield, suggesting a multifactorial pathogenesis of AF.

Although pulmonary vein foci are widely accepted as drivers of paroxysmal AF, multiple mechanisms can contribute to AF maintenance. Experimental studies[1–4] showed that along with shortening of the atrial refractory period, slowing of intra-atrial conduction is a common hallmark of the AF-associated left atrial (LA) remodeling. Previous studies[5,6] suggested that the total atrial activation time (TACT) measured at the lateral mitral annulus (MA) using pulsed-wave tissue Doppler imaging (PW-TDI) is an independent predictor of AF. Some recent studies[7,8] also demonstrated that TACT is associated with an increased probability of AF recurrences after electrical cardioversion and catheter ablation (CA) of AF.

In this article, we propose a more elaborate method to assess the LA asynchronous activation and conduction delay using PW-TDI. We test whether the measurement of local atrial contraction at 4 LA sites can be useful to distinguish patients with AF from those without a history of AF (controls).

Methods

We *prospectively* studied a total of 200 patients from September 2014 to September 2015. One hundred thirty patients had documented AF (both paroxysmal and

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1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2016.06.003

persistent) and were referred for CA. All of them were in sinus rhythm at the time of admission. They were compared with a control group of 70 patients without a history of AF referred for the electrophysiology study (EPS) and CA because of other arrhythmias. Exclusion criteria were previous CA for supraventricular or ventricular arrhythmias, impaired left ventricular (LV) ejection fraction, severe valvular disorders, pacemaker stimulation or intraventricular conduction delay, overt preexcitation, history of palpitations without electrocardiographic documentation, history of electrical cardioversion within 4 weeks, and age <18 years. All patients gave a written informed consent for ablation. The study was approved by the institutional committee on human research.

Echocardiography

Two-dimensional transthoracic echocardiography on the day of admission was performed using a commercially available ultrasound system (Vivid 7, General Electric, Milwaukee, WI) equipped with 3.5-MHz transducer. Recordings were done in parasternal long- and short-axis views as well as in apical 4- and 2-chamber views. All images were electrocardiogram triggered and stored as cine loops for off-line analysis.

LV wall thickness, LV dimensions, and LA diameter were measured from the gray scale images in the left parastermal long-axis view. LA diameter was corrected for the body surface area (LA diameter index). LV ejection fraction was measured in 4- and 2-chamber views using Simpson's method. LV diastolic function was evaluated using pulsed-wave Doppler recording of the mitral valve flow (E wave, A wave, and deceleration time of the E wave). LA volumes were measured from apical 4- and 2-chamber views, and the LA emptying fraction was calculated using the following formula: LA emptying fraction (%) = [(LA maximum volume – LA minimum volume)/LA maximum volume] × 100. The valvular morphology and function were assessed according to the guidelines of the American Society of Echocardiography. In addition, we performed PW-TDI in apical 4- and 2-chamber views. The sample volume was placed at the level of the septal, lateral, anterior, and posterior LA just above the MA, as well as at the lateral tricuspid annulus.

We measured time duration from the onset of the P wave to the first activation of the above-mentioned landmarks. The onset of the P wave was easily distinguishable if amplified and registered at lower rates (25 mm/s); however, the onset of the P wave was usually blurred at 200 mm/s. Therefore, we set a marker at the beginning of the P wave at 25 mm/s and changed the speed to 200 mm/s afterward to measure the distance to the A′ wave. Particular attention was paid to measure the time intervals from the onset of the surface P wave to the onset of the local A′ wave (P-A′) only of sinus beats, and P waves of different morphology were discarded. All intervals were measured in at least 3 cardiac cycles and averaged. Particular attention was paid on the quality of the image acquisitions, and patients with insufficient image quality were excluded from the study (Figure 1).

EPS and CA

All patients gave an informed consent for the EPS and CA and prepared according to the practice in our center. In all cases, a decapolar steerable catheter (2-5-2 mm) was inserted in the coronary sinus (CS). The proximal pole of the catheter (electrode pair 9-10) was placed in the vicinity of the CS ostium on the basis of its fluoroscopic position in the left anterior oblique view. The time from the onset of the sinus P wave to the local sharp CS signal was measured at the proximal CS (electrode pair 9-10) and the distal CS (electrode pair 1-2).

In patients scheduled for CA of AF, an LA access was obtained through a transseptal puncture. A circumferential pulmonary vein isolation using irrigated catheters was successfully performed in all. Electroanatomic mapping systems (CARTO 3, Biosense Webster Inc., Diamond bar, CA, or EnSite Velocity, Endocardial Solutions, Inc., St. Paul, MN) were used for the creation of pulmonary veins and LA anatomy and for the visualization of catheters. After the completion of circumferential ablation, voltage maps of the LA in sinus rhythm were constructed and the areas showing low-amplitude signals (<0.5 mV) were annotated as low-voltage areas. Additional linear ablation in these areas to connect them with electrically unexcitable hallmarks was performed as previously described.[9]

Statistical analysis

Data analysis was performed with SPSS version 21 (IBM, Armonk, NY, USA). Continuous variables are presented as mean ± SD, and categorical variables are presented as number (percentage). Differences between groups were tested using parametric (Student t test) and nonparametric (Fisher exact, χ^2, and Mann-Whitney) tests. The standard deviation of all 4 P-A′ intervals (SD-4PA′) was calculated for each patient. A bivariate Pearson correlation was performed to test for significant correlations between the proximal CS and P-A′ intervals. The predictive accuracy of the variables was evaluated using the receiver operating characteristic (ROC) curve. Sensitivity, specificity, and positive and negative predictive values were calculated. A P value of $<.05$ was considered statistically significant.

Results

Baseline characteristics

The mean age of our cohort was 58 ± 13 years, and 87 patients (43.5%) were women. Thirty patients (15%) presented with persistent AF. Both groups were matched for the baseline clinical characteristics (Table 1). Importantly, age, LV ejection fraction, LV septum thickness, LA diameter, and LA diameter index did not differ significantly between the groups.