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Shortening of Fibrillatory Cycle Length in the Pulmonary Vein During Vagal Excitation

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OBJECTIVES The goal of the present prospective study is to evaluate the impact of vagal excitation on ongoing atrial fibrillation (AF) during pulmonary vein (PV) isolation.

BACKGROUND The role of vagal tone in maintenance of AF is controversial in humans.

METHODS Twenty-five patients (18 with paroxysmal AF, 7 with chronic AF) were selected by occurrence of vagal excitation during AF (atrioventricular [AV] block: R-R interval >3 s) produced by PV isolation. Fibrillatory cycle length (CL) in the targeted PV and coronary sinus (CS) were determined before, during, and after vagal excitation. The CL was available at PV ostium during vagal excitation in 11 patients.

RESULTS Forty-eight episodes of vagal excitation were observed. During vagal excitation, CL abruptly decreased both in CS and PV (CS, 164 ± 20 ms to 155 ± 23 ms, $p < 0.0001$; PV, 160 ± 22 ms to 143 ± 28 ms, $p < 0.0001$), and both returned to the baseline value with resumption of AV conduction. The decrease in PVCL occurred earlier (2.5 ± 1.5 s vs. 4.0 ± 2.6 s, $p < 0.01$) and was of greater magnitude than that in CSCL (16 ± 16 ms vs. 8 ± 9 ms, $p < 0.01$). A sequential gradient of CL was observed from PV to PV ostium and CS during vagal excitation (138 ± 29 ms, 149 ± 24 ms, and 159 ± 26 ms, respectively). The decrease in CL was significantly greater in paroxysmal than in chronic AF (CS, 11 ± 9 ms vs. 5 ± 7 ms, $p < 0.05$; PV, 23 ± 25 ms vs. 8 ± 14 ms, $p < 0.05$).

CONCLUSIONS Vagal excitation is associated with shortening of fibrillatory CL. This occurs earlier in PV with a sequential gradient to PV ostium and CS, suggesting that vagal excitation enhances a driving role of PV. (J Am Coll Cardiol 2006;47:774–80) © 2006 by the American College of Cardiology Foundation

The role of autonomic tone in the onset, maintenance, and termination of atrial fibrillation (AF) has been suggested in humans (1–6). In an animal model, vagal nerve stimulation decreases refractoriness and facilitates the induction and maintenance of AF (7,8), and this effect is prevented by ablation of the atrial parasympathetic nerve system (9,10). However, the mechanism of vagal excitation contributing to the maintenance of AF has not been clear in humans.

The goal of the present study is to investigate changes in AF cycle length (CL) during vagal excitation produced by radiofrequency (RF) energy delivery for pulmonary vein (PV) disconnection in patients with paroxysmal and chronic AF.

METHODS

Patient population. Among 314 consecutive patients (213 with paroxysmal AF, 101 with persistent or chronic AF) who underwent AF ablation in our institution, PV isolation was performed during ongoing AF in 272 patients (171 with paroxysmal AF, 101 with persistent or chronic AF). Twenty-five patients (9.2%; 18 with paroxysmal AF, 7 with chronic AF) were selected based on the occurrence of atrioventricular (AV) block with an R-R interval >3 s during AF produced by RF energy application for PV isolation. The occurrence of vagal excitation during sinus rhythm (sinus bradycardia or hypotension) was not included in the present study. The mean age was 55 ± 9 years, two women were included, and AF duration was 88 ± 72 months. All patients had no structural heart disease except for one with aortic valve replacement. No patient was diagnosed with vagotonic AF.

Twenty-five patients, matched for age, gender, structural heart disease, classification of AF, and duration of AF, were selected as control patients for clinical outcome (Table 1).

Catheter ablation. Anti-arrhythmic drugs were discontinued ≥5 half-lives before ablation except for amiodarone, which was taken by six patients (24%) at the time of the procedure. All patients had effective anticoagulation for > 1 month and transesophageal echocardiography before ablation. A written informed consent was obtained from all patients.

A 6-F quadripolar catheter (Xtrem, Ela Medical, Montrouge, France) was positioned in the coronary sinus (CS). A 10-pole circumferential catheter (Lasso, Biosense-Webster, Diamond Bar, California) for PV ostial mapping and a 4-mm irrigated-tip ablation catheter (Biosense-Webster) were used. Surface electrocardiogram and intracardiac electrograms were filtered from 30 to 500 Hz and measured at a paper speed of 100 mm/s with a digital

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Abbreviations and Acronyms

AF = atrial fibrillation
AV = atrioventricular
CL = cycle length
CS = coronary sinus
CSCL = cycle length in the coronary sinus
PV = pulmonary vein
PVCL = cycle length in the pulmonary vein
RF = radiofrequency

amplifier/recording system (Bard Electrophysiology, Lowell, Massachusetts). A single bolus dose of 50 IU/kg of heparin was administered after the transseptal puncture and repeated only for procedures lasting more than four hours.

The RF application was performed at 1 cm proximal to the ostium of all PVs with a power limit of 30 W. When RF was applied at the anterior and inferior rim of the left PVs, delivered power was limited as 25 W. If ipsilateral PVs were located closely, these two PVs were isolated en bloc. Ablation catheter was dragged every 30 to 60 s during continuous RF delivery. The end point was a disappearance or dissociation of the PV potentials on a circumferential catheter. When a vagal response with an R-R interval > 5 s was observed, RF delivery was discontinued.

Study protocol. The mean CL in the CS (CSCL) and the targeted PV (PVCL) were determined at the following times: 1) before the commencement of RF application (baseline), 2) 5 s before, 3) during, and 4) 5 s after the episode of vagal excitation. The CSCL was selected because of the stability of catheter allowing reproducible serial measurement. In addition, CL was available at the PV ostium in 11 patients during vagal excitation. The mean CL was defined as an average of 30 consecutive cycles. They were measured with a dedicated system (Bard Electrophysiology), and the detection of potentials was manually checked with online calipers at a paper speed of 100 mm/s. If an R-R interval during vagal excitation was shorter than a total duration of 30 consecutive cycles, CSCL and PVCL were determined by averaging all cycles during the episode of vagal excitation. A continuous or fragmented activity or a potential interval < 50 ms was counted as a single activity. A decrease in PVCL or CSCL of ≥ 10 ms during vagal excitation was considered as a significant decrease. The timing of onset of a significant decrease in PVCL and CSCL was measured from the last QRS before vagal excitation.

Statistical analysis. All variables are reported as mean $\pm$ SD. Comparison between groups was performed with the Student *t* test. Sequential data measurements were analyzed by repeated-measures analysis of variance followed by the Tukey post hoc test for multiple comparisons. Categorical variables were compared with the Fisher exact test. $p < 0.05$ was considered to indicate statistical significance.

RESULTS

Forty-eight episodes of vagal excitation were observed, and the R-R interval during these episodes was 8.7 $\pm$ 4.1 s (range, 3.0 to 19.6 s). The targeted PV was the left superior PV in 19, the left inferior PV in 7, the right superior PV in 1, and the right inferior PV in 1 patient.

The RF site producing vagal excitation was observed at a discrete location at approximately 1 cm proximal to the ostium of each vein: the anterosuperior ostium of the left superior PV, the inferior ostium of the left inferior PV, the

Table 1. Baseline Characteristics of the Patients and Procedural Outcomes

	Study Group (n = 25)	Control Group (n = 25)	p Value
Characteristics			
Age (yrs)	55 ± 9	56 ± 8	NS
Gender (female, %)	2 (8%)	2 (8%)	NS
AF type (paroxysmal/chronic)	18/7	18/7	NS
AF duration (months)	88 ± 72	90 ± 66	NS
Persistent duration (range: months)	12–24	5–24	NS
LA diameter			
Parasternal (mm)	41 ± 9	44 ± 7	NS
Longitudinal (mm)	54 ± 9	54 ± 9	NS
Transversal (mm)	42 ± 8	41 ± 9	NS
LV ejection fraction (%)	69 ± 10	66 ± 13	NS
Structural heart disease	Aortic valve replacement (1)	Aortic valve replacement (1)	–
Procedure and outcome			
PV isolation (%)	25 (100%)	25 (100%)	NS
Substrate modification (%)	15 (60%)	15 (60%)	NS
Repeated procedure	5 (20%)	9 (36%)	NS
Anti-arrhythmics after the procedure (%)	7 (28%)	5 (20%)	NS
Overall success (%)	20 (80%)	20 (80%)	NS
Length of follow-up since the last procedure (months)	6.2 ± 5.5	7.7 ± 4.0	NS

AF = atrial fibrillation; LA = left atrial; LV = left ventricular; PV = pulmonary vein.