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Letter to the Editor

Acute effects of atrial fibrillation on atrial and ventricular function: A simultaneous invasive-echocardiographic hemodynamic study☆

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Atrial fibrillation (AF) is the most common sustained arrhythmia in the developed world, affecting more than 2 million people in the United States alone [1,2]. AF may affect left ventricular (LV) performance in a complex fashion, with positive inotropic and lusitropic effects related to the increase in heart rate (HR) (force–frequency relationship) and diminution of LV filling from loss of atrial contraction. Evaluation of left atrial (LA) and LV function during AF and sinus rhythm thus far has relied heavily on invasive hemodynamic measurements performed in animal models [3,4], and acute hemodynamic changes during initiation of AF in humans are less well characterized. Limited studies have shown the hemodynamic changes from sinus rhythm to AF [5,6]; simultaneous volumetric assessment with hemodynamic measurements has not been studied. Echo-Doppler and tissue Doppler parameters are often employed as noninvasive measures of cardiac filling pressures, yet prior studies have been performed in sinus rhythm [7,8], and it remains unknown if the presence of AF affects the validity of these relationships.

In the current study, we sought to examine 1) the rate and rhythm-related effects of AF on LA and LV function in patients with preserved ejection fraction (EF) using simultaneous invasive pressure and echocardiographic volume assessment; 2) the effects of AF on the relationship between tissue Doppler E/e′ ratio and left heart filling pressures; and 3) the relationship between hemodynamic parameters and AF recurrence after AF ablation.

A consecutive sample of 63 patients with AF referred to the Mayo Clinic Electrophysiology Laboratory for catheter ablation of drug-refractory AF were enrolled in this prospective study between March 2007 and May 2009. Patients were excluded if they had permanent AF (AF duration >1 year), LV ejection fraction (LVEF) <50%, cardiomyopathy, valvular or congenital heart disease, and previous AF ablation. Amiodarone was discontinued 1 month prior to the procedure and all other antiarrhythmic drugs were discontinued 5 days before the procedure. The study was approved by the Mayo Clinic Institutional Review Board, and all patients provided informed consent.

All patients received general anesthesia. To minimize the effect of anesthetic agents on hemodynamics, only desflurane was used for all study patients during the study. Fentanyl and midazolam were avoided until the study is complete. Cardiac catheterization was performed from the femoral veins and right internal jugular vein using 5F to 7F catheters. Bipolar intracardiac electrograms were simultaneously recorded from the right ventricle, right atrium (RA), coronary sinus, and His bundle region, along with standard 12-lead surface electrocardiogram (ECG) (Prucka Engineering, Inc.; Houston, Texas). LA access was obtained using the double transseptal puncture technique. Intravenous unfractionated heparin was administered to maintain an activated clotting time of 300 to 400 s. The study protocol was undertaken prior to ablation. RA pacing at driving cycle lengths (CLs) of 600 ms was delivered at twice the pacing threshold (2.0 ms pulse width). Invasive hemodynamic and echocardiographic parameters (below) were assessed simultaneously during sinus rhythm, RA pacing and after induction of AF by burst RA pacing. Cardioversion was performed to resume sinus rhythm if the patient was in AF at the time of study.

Mean LA pressure (LAP) was measured using a fluid-filled 8F transseptal catheter. Continuous LV pressure tracings, including LV end-systolic pressure (LVESP) and LV end-diastolic pressure (LVEDP), were recorded using a high-fidelity 2F Millar catheter advanced through a 6F multipurpose catheter placed through the transseptal sheath. All pressure tracings were obtained at end expiration [8]. The pressure tracings were stored digitally and analyzed offline to determine the time constant of LV relaxation (Tau) and maximum (LV dP/dt_{max}) and minimum (LV dP/dt_{min}) rates of LV pressure change. Tau was determined

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with phase-plot analysis using a zero asymptote method, as described by Weiss et al. [9].

Transthoracic echocardiography was performed using a commercially available echocardiographic instrument (Vivid 7; GE Medical Systems, Milwaukee, Wisconsin) in the electrophysiology laboratory. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LVEF, LA maximum volume (LAV_{max}), LA minimum volume (LAV_{min}), and LA ejection fraction (LAEF = [LAV_{max} − LAV_{min}] / LAV_{max}) were measured by using biplane Simpson's method as recommended by the American Society of Echocardiography [10]. Mitral inflow pulsed-wave Doppler echocardiography was used to measure the peak velocities of early (E) and late diastolic flow (A), and the E/A ratio was calculated [11]. Mitral septal annulus early (e′) velocities were measured by tissue Doppler imaging [11].

LV stroke volume (SV) was determined by pulse wave Doppler of the LV outflow tract. Cardiac output (CO) was determined by the product of SV and HR. Effective arterial elastance (Ea), a lumped measure of total arterial afterload that reflects both mean resistive and oscillatory load, was calculated by the ratio of LVESP to SV [12]. Operant LA stiffness or elastance (E_{LA}) and operant LV diastolic elastance (E_{LV}) were estimated by their single beat pressure–volume quotients (E_{LA} = mean LAP/LAV_{max}; E_{LV} = LVEDP / LVEDV). Systemic vascular resistance was calculated as mean blood pressure divided by CO. To adjust for preload, LV dP/dt_{max} was scaled to LVEDV [12].

After completing the study protocol, patients underwent either 3-dimensional electroanatomic-guided mapping or circular catheter-guided pulmonary vein isolation. The endpoint was to achieve complete electrical isolation outside the 4 pulmonary vein ostia. All patients returned for follow-up 3 months after ablation. The follow-up evaluation consisted of a detailed history, physical examination, 12-lead ECG, 24-hour Holter monitoring, and computed tomographic scan of the chest. Thereafter, patients were asked to complete a survey at 12-months and then annually thereafter to collect clinical symptoms and recurrent AF. Repeat 24-hour Holter or event monitoring was provided to document symptomatic arrhythmias. AF recurrence was defined as 1 or more episodes of AF, at least 2 months after AF ablation (blanking period), documented by ECG or by Holter or event monitor.

Statistical analysis was performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina). Normally distributed continuous variables are expressed as mean ± SD and were compared using the paired Student *t* test. Categorical variables were compared using χ^2 analysis or the Fisher exact test where appropriate. Logistic regression analysis was performed for multivariate analysis. Repeated measures for analysis of variance were used to determine the effects of HR on hemodynamic parameters, and to examine whether persistent vs paroxysmal AF affected rate-responsive hemodynamic changes.

Study participants (n = 63) were 57 ± 10 years of age and predominantly male (70%, Table 1). Mean duration of AF was 6.5 ± 6.2 years, and 56 (89%) had failed antiarrhythmic drug therapy. All 63 patients completed the echocardiographic studies and complete invasive hemodynamic assessment was available in 56 patients. Failure to complete the invasive assessment in 7 patients was due to inability of obtaining stable sinus rhythm or atrial pacing (frequent episodes of AF during recording) or technical failure of hemodynamic measurements. Persistent AF was present in 30 patients and paroxysmal in 33. Patients with persistent AF had a greater body mass index and more likely to be hypertensive. Eleven patients were in AF at the onset of study and required cardioversion. Clinical and hemodynamic characteristics in these 11 patients were similar to patients in sinus rhythm at study entry (data not shown) and were included in the analysis.

Mean CL in sinus rhythm was 965 ± 171 ms or 62 ± 13 bpm (Table 2). Baseline hemodynamics and acute responses to atrial pacing at CL of 600 ms are shown in Table 2. As expected, decreasing CL was associated with enhancement in LV performance, as assessed by increased LV dP/dt_{max}, LV dP/dt_{max}/LVEDV, LV dP/dt_{min}, and shortening of Tau (positive force–frequency and rate–relaxation relationships, respectively). Arterial afterload (Ea) and blood pressure increased with pacing.

Table 1
Baseline characteristics.

Characteristic	Overall (N = 63)	Paroxysmal AF (n = 33)	Persistent AF (n = 30)	*P* value
Male, no. (%)	44 (70)	19 (58)	25 (83)	.05
Age, years	57 ± 10	56 ± 9	57 ± 11	.80
BMI, kg/m^2	31.3 ± 6.2	29.5 ± 5.9	33.3 ± 6.0	.01
Failure of ≥1 AAD, no. (%)	56 (89)	31 (94)	25 (83)	.18
Duration of AF, years	6.5 ± 6.2	6.8 ± 6.3	6.2 ± 6.3	.74
Coronary artery disease, no. (%)	9 (14)	5 (15)	4 (13)	.84
Hypertension, no. (%)	36 (57)	14 (42)	22 (73)	.03
Diabetes mellitus, no. (%)	8 (13)	2 (6)	6 (20)	.10
Cerebrovascular accident, no. (%)	6 (10)	4 (12)	2 (7)	.46
Obstructive sleep apnea, no. (%)	21 (33)	11 (33)	10 (33)	.99
β-Blocker therapy, no. (%)	42 (67)	18 (55)	24 (80)	.06
Calcium channel blocker, no. (%)	20 (32)	7 (21)	13 (43)	.11
ACEI or ARB, no. (%)	14 (22)	5 (15)	9 (30)	.27
Statin, no. (%)	17 (27)	7 (21)	10 (33)	.42

Abbreviations: AAD, antiarrhythmic drugs; ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; BMI, body mass index.

Left heart volumes (LVEDV, LAV_{max} and LAV_{min}) dropped with increasing HR, coupled with decrease in LA mean pressure. LA EF increased with pacing while LA afterload (LVEDP) remained stable. SV and E/e′ decreased, though CO increased since the elevation in HR exceeded the reduction in SV. LVEF decreased despite enhanced contractility. In contrast, E_{LA} and E_{LV} did not change with rapid atrial pacing (Table 2).

Mean CL in AF was 626 ± 127 ms (HR, 96 ± 19 bpm). Compared to sinus rhythm, AF was associated with higher LV dP/dt_{max} and LV dP/dt/LVEDV and shorter Tau (Table 3). Ea increased in AF and LVEF dropped

Table 2
Effect of heart rate on cardiac hemodynamics.

Characteristics	Sinus rhythm	Atrial pacing	*P* value
Cycle length, mean, ms	965 ± 171	600	–
Heart rate (min^{-1})	62 ± 13	100	–
Systolic BP, mm Hg	99 ± 11	103 ± 8	.008
Mean BP, mm Hg	69 ± 8	76 ± 6	<.001
Ea (=LVESP/SV), mm Hg/ml	1.31 ± 0.29	1.59 ± 0.38	.002
Left ventricular size and function			
LVEDV, ml	95 ± 19	83 ± 20	<.001
LVESV, ml	37 ± 12	35 ± 13	.15
LVEF, %	62 ± 8	60 ± 9	.02
LV dP/dt_{max}, mm Hg/s	1145 ± 227	1324 ± 243	<.001
LV dP/dt/LVEDV, mm Hg/ml	13.3 ± 3.5	17.5 ± 5.5	<.001
LV dP/dt_{min}, mm Hg/s	−1161 ± 191	−1310 ± 185	<.001
LVEDP, mm Hg	10.7 ± 8.3	9.9 ± 6.7	0.71
Tau, ms	61.0 ± 16.6	53.0 ± 13.7	<.001
E_{LV}, mm Hg/ml	0.11 ± 0.05	0.12 ± 0.06	.16
LV stroke volume, ml	76.0 ± 18	69 ± 18	.02
Cardiac output, l/min	4.7 ± 1.2	7.0 ± 1.7	<.001
E/e′	9.2 ± 3.2	7.7 ± 2.4	<.001
Left atrial size and function			
LAV_{max}, ml	77 ± 28	67 ± 25	<.001
LAV_{min}, ml	44 ± 21	35 ± 19	<.001
LAEF, %	47 ± 11	52 ± 11	.004
LA mean pressure, mm Hg	13.6 ± 5.1	11.9 ± 4.9	<.001
E_{LA} (=mean LAP/LAV_{max}), mm Hg/ml	0.20 ± 0.08	0.20 ± 0.07	.19

Abbreviations: BP, blood pressure; Ea, effective arterial elastance; E/e′, ratio of mitral velocity to early diastolic velocity of the mitral annulus; E_{LA}, left atrial elastance; E_{LV}, left ventricular elastance; LA, left atrial; LAEF, left atrial ejection fraction; LAP, left atrial pressure; LAV_{max}, maximal left atrial volume, LAV_{min}, minimal left atrial volume; LV, left ventricular; LV dP/dt_{max}, maximum value of the first derivative of LV pressure decay; LV dP/dt_{min}, minimum value of the first derivative of LV pressure decay; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESP, left ventricular end-systolic pressure; LVESV, left ventricular end-systolic volume; Tau, time constant of isovolumic LV pressure decay.