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Prediction of Cardiovascular Outcomes With Left Atrial Size

Is Volume Superior to Area or Diameter?

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OBJECTIVES We sought to compare left atrial (LA) volume to LA area and diameter for the prediction of adverse cardiovascular outcomes.

BACKGROUND The incremental value of LA volume compared with LA area or diameter as a cardiovascular risk marker has not been evaluated prospectively for patients with sinus rhythm or atrial fibrillation (AF).

METHODS Left atrial size was assessed with biplane LA volume, four-chamber LA area, and M-mode dimension for 423 patients (mean age 71 ± 8 years, 56% men) who were prospectively followed for development of first AF, congestive heart failure, stroke, transient ischemic attack, myocardial infarction, coronary revascularization, and cardiovascular death.

RESULTS Of the 317 subjects in sinus rhythm at baseline, 62 had 90 new events during a mean follow-up of 3.5 ± 2.3 years. All three LA size parameters were independently predictive of combined outcomes (all $p < 0.0001$). The overall performance for the prediction of cardiovascular events was greatest for LA volume (area under the receiver operator characteristic curve: indexed LA volume 0.71; LA area 0.64; LA diameter 0.59). A graded association between the degree of LA enlargement and risk of cardiovascular events was only evident for indexed LA volume. For subjects with AF, there was no association between LA size and cardiovascular events.

CONCLUSIONS Left atrial volume is a more robust marker of cardiovascular events than LA area or diameter in subjects with sinus rhythm. The predictive utility of LA size for cardiovascular events in AF was poor, irrespective of the method of LA size quantitation. (J Am Coll Cardiol 2006; 47:1018–23) © 2006 by the American College of Cardiology Foundation

Left atrial (LA) volume is a more accurate measure of LA size than LA diameter (1,2), although both LA size parameters have been shown to be markers of cardiovascular risk (3–12). We are unaware of any prospective studies that compare the utility of the two LA size parameters for the prediction of cardiovascular outcomes. Additionally, although LA volume has been demonstrated to be a robust predictor of cardiovascular outcomes among patients with sinus rhythm in a number of retrospective studies (5,6,13,14), its prognostic utility for patients with atrial fibrillation (AF) is unknown. In this prospective study, we assessed the clinical and echocardiographic correlations of biplane LA volume and M-mode LA dimension and compared the utility of LA volume, area, and dimension for the prediction of age-related cardiovascular outcomes in patients with sinus rhythm and those with AF.

METHODS

Study population. This study was approved by the Mayo Foundation Institutional Review Board. Patients age ≥50 years referred for a general medical consultation were invited to participate if they had no history of congenital heart disease, treatment with pacemaker implantation, valvular surgery, or cardiac transplantation.

Clinical data. Age, gender, height, weight, brachial blood pressure, cardiac rhythm, and history of comorbid conditions were recorded at enrollment. Definitions for all covariates have been previously published (15).

Baseline cardiac rhythm was considered sinus if the patient was in sinus rhythm at the time of echocardiography and had no prior history of atrial arrhythmias. Paroxysmal AF was defined by a history of AF episodes with intervening sinus rhythm. Because of the small number of paroxysmal AF patients, we did not try to differentiate whether conversion to sinus rhythm in these patients was spontaneous or not. Permanent AF was defined by AF at baseline and the persistence of the arrhythmia without intervening sinus episodes.

Echocardiographic data. Data for all echocardiographic studies were collected prospectively, and the parameters of interest were specified a priori. Measurements were obtained at least two times for an average if the rhythm was sinus and at least three times if the rhythm was AF. M-mode LA dimension was measured as per the American Society of Echocardiography method (16). Single-plane area was evaluated from the four-chamber view of the left

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Abbreviations and Acronyms

AF = atrial fibrillation
CHF = congestive heart failure
LA = left atrial
LV = left ventricular
MI = myocardial infarction
TIA = transient ischemic attack

atrium at end-ventricular systole, ensuring that there was no foreshortening of the atrium. The area was then planimetered with the inferior LA border defined as the plane of the mitral annulus, excluding the confluence of the pulmonary veins and the LA appendage.

Maximal biplane LA volume was measured in all patients with a modified biplane area-length method (17). This method as well as the Simpson's method of disc had both been well-validated (18–20). Orthogonal apical views, most commonly apical four- and two-chamber views, were obtained for determination of LA area and length (from the middle of the plane of the mitral annulus to the posterior wall). The apical long-axis view was used instead of the two-chamber view if the left atrium in the latter view appeared foreshortened. Specifically, the maximal LA chamber area and length were measured at end ventricular systole, excluding the LA appendage and pulmonary veins. Left atrial volume was calculated on the basis of the algorithm ([0.85 × A1 × A2]/L); where A1 is the four-chamber LA area, A2 is the two-chamber or apical long axis LA area, and L is the average of the two lengths obtained from the orthogonal views) and indexed to body surface area.

Indexed LA diameter, four-chamber LA area, and indexed LA volume were categorized according to current American Society of Echocardiography guidelines (21). Additionally, we also assessed non-indexed LA diameter with 40 mm as the cut-off for normal on the basis of common clinical practice.

Other echocardiographic variables, specified a priori, included left ventricular (LV) dimension at end-systole and end-diastole; LV septal and posterior end-diastolic wall thickness; M-mode LV ejection fraction, mitral inflow filling velocities (peak E and A); mitral inflow deceleration time; mitral isovolumic relaxation time; pulmonary venous

Table 1. Baseline Characteristics of the Study Population

	Sinus Rhythm (n = 317)		Atrial Fibrillation (n = 106)	
	No CV Events (n = 255)	CV Events (n = 62)	No CV Events (n = 71)	CV Events (n = 35)
Clinical				
Men, n (%)	132 (52)	38 (61)	40 (56)	26 (74)
Age (yrs)	70 ± 8.1	73 ± 7.5	74 ± 7.5	75 ± 6.8
Body mass index (kg/m^2)	28 ± 5	28 ± 5	29 ± 6	27 ± 3
Heart rate (beats/min)	68 ± 12	67 ± 14	72 ± 16	66 ± 16
Systolic blood pressure (mm Hg)	141 ± 22	137 ± 19	133 ± 20	142 ± 22
Diastolic blood pressure (mm Hg)	78 ± 11	75 ± 11	75 ± 13	77 ± 11
Pulse pressure (mm Hg)	64 ± 20	61 ± 15	58 ± 19	45 ± 17
History of myocardial infarction, n (%)	34 (13)	18 (29)	7 (10)	9 (26)
History of coronary artery disease, n (%)	71 (28)	33 (53)	18 (25)	16 (46)
Diabetes mellitus, n (%)	40 (16)	15 (24)	11 (15)	9 (26)
Current smoking, n (%)	20 (8)	7 (11)	2 (3)	2 (6)
History of dyslipidemia, n (%)	136 (53)	42 (68)	40 (56)	18 (51)
History of systemic hypertension, n (%)	151 (59)	43 (69)	42 (59)	26 (74)
History of stroke, n (%)	16 (6)	5 (8)	7 (10)	4 (11)
History of transient ischemic attack, n (%)	11 (4)	3 (5)	10 (14)	5 (14)
History of congestive heart failure, n (%)	25 (10)	12 (19)	18 (25)	11 (31)
History of valvular heart disease, n (%)	54 (21)	24 (39)	37 (52)	16 (46)
Echocardiographic				
LV ejection fraction (%)	62 ± 10	56 ± 17	60 ± 12	50 ± 17
LV end-diastolic septal wall thickness (mm)	11 ± 2	11 ± 2	11 ± 2	11 ± 2
LV end-diastolic posterior wall thickness (mm)	10 ± 2	11 ± 2	11 ± 2	11 ± 2
M-mode LA dimension (mm)	43 ± 6	46 ± 5	52 ± 10	52 ± 8
Indexed LA diameter (mm/m^2)	23 ± 3	24 ± 3	26 ± 6	27 ± 5
LA diameter <40 mm (%)	31	4	7	3
4-chamber LA area (cm^2)	22 ± 4	24 ± 5	28 ± 6	30 ± 6
LA volume (ml)	69 ± 22	85 ± 31	126 ± 95	127 ± 77
Indexed LA volume (ml/m^2)	36 ± 10	44 ± 14	64 ± 48	65 ± 45
Indexed LA volume <28 ml/m^2 (%)	16	4	8	3
Mitral E (m/s)	0.8 ± 0.2	0.9 ± 0.3	1.0 ± 0.4	1.0 ± 0.4
Mitral A (m/s)	0.8 ± 0.3	0.9 ± 0.3	n/a	n/a
Mitral E/A	1.0 ± 0.3	1.1 ± 0.6	n/a	n/a
Mitral deceleration time (ms)	232 ± 46	226 ± 61	222 ± 85	207 ± 62

CV = cardiovascular; EF = ejection fraction; LA = left atrial; LV = left ventricular.