Relation of Systolic, Diastolic, and Pulse Pressures and Aortic Distensibility With Atrial Fibrillation (from the Multi-Ethnic Study of Atherosclerosis)

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Previous research suggests that elevated pulse pressure (PP) is a risk factor for atrial fibrillation (AF) independently of mean arterial pressure (MAP). PP may serve as an indirect measure of aortic stiffness (reduced distensibility), but whether directly measured aortic distensibility is related to risk for AF has not yet been studied. This analysis included 6,630 participants aged 45 to 84 years from the Multi-Ethnic Study of Atherosclerosis. At baseline, blood pressure and other relevant covariates were measured using standardized protocols. Magnetic resonance imaging−based aortic distensibility was measured in 3,441 participants. Incident AF was identified from hospitalization discharge codes and Medicare claims. Multivariate Cox models were used to estimate the association of blood pressure components and aortic distensibility with AF risk. During a mean follow-up of 7.8 years, 307 AF events (137 among those with aortic distensibility measurements) were identified. In multivariate-adjusted models simultaneously including MAP and PP, each 1-SD increase in PP was associated with a 29% increased risk of AF (95% confidence interval 5% to 59%, p = 0.02), with MAP not being associated with increased AF risk. Overall, aortic distensibility was not consistently associated with AF risk: after removing outliers, each 1-SD increase in aortic distensibility was associated with a 9% increased risk of AF (95% confidence interval −22% to 51%, p = 0.63). In conclusion, in this large community-based cohort, we found that PP, but not MAP or aortic distensibility, was a significant risk factor for AF, emphasizing the importance of PP when assessing the risk for developing AF. Our results cast doubt on the clinical utility of aortic distensibility as a predictor for the development of AF. **(Am J Cardiol 2014;114:587−592)**

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice, causing a large burden of morbidity and mortality in an increasingly aging population.[1] Studies published over the last 2 decades have consistently shown that both elevated blood pressure (BP)[2,3] and a diagnosis of hypertension[4,5] are important risk factors for AF. More recently, an analysis of the Framingham Heart Study identified pulse pressure (PP) as a better predictor for the development of AF than mean arterial pressure (MAP),[6] although these results were not confirmed in the Women's Health Study.[3] PP has also been associated with left atrial enlargement, a risk factor for AF.[7,8] Increased PP can be a consequence of aortic stiffness (reduced aortic distensibility). However, no information exists on the association between directly measured aortic stiffness and AF incidence in the general population. In the present study, we used BP and magnetic resonance imaging (MRI)−based aortic distensibility data available from the Multi-Ethnic Study of Atherosclerosis (MESA), a community-based, multi-ethnic cohort of middle-to-older aged adults. First, we assessed whether PP is more strongly associated with AF than MAP in the MESA cohort. Second, we examined the role of aortic distensibility as a risk factor for AF compared with established BP measurements.

Methods

MESA is a prospective cohort study of risk factors for subclinical atherosclerosis conducted at 6 field centers in the United States (Baltimore, Maryland; Chicago, Illinois; Saint Paul, Minnesota; Los Angeles, California; New York,

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Table 1
Baseline characteristics by AF status: Multi-Ethnic Study of Atherosclerosis, 2000 to 2002

Characteristics and Risk Factors	No AF $n = 6,323$	AF $n = 307$	p-Value for AF Difference
Age (years), mean (SD)	62 (10)	70 (8)	<0.0001
Male	2942 (47%)	188 (61%)	<0.0001
Race/ethnicity			<0.0001
White	2366 (37%)	166 (54%)	
Chinese American	771 (12%)	21 (7%)	
Black	1766 (28%)	67 (22%)	
Hispanic	1420 (22%)	53 (17%)	
College degree or higher	2227 (35%)	111 (36%)	0.74
Height (cm), mean (SD)	166 (10)	169 (10)	0.0001
Body mass index (kg/m^2), mean (SD)	28 (5)	29 (6)	0.25
Systolic blood pressure (mm Hg), mean (SD)	126 (21)	135 (22)	<0.0001
Diastolic blood pressure (mm Hg), mean (SD)	72 (10)	72 (10)	0.91
Mean arterial pressure (mm Hg), mean (SD)	90 (13)	93 (13)	<0.0001
Pulse pressure (mm Hg), mean (SD)	54 (17)	63 (18)	<0.0001
Aortic distensibility ($mm\ Hg^{-1}$)*, mean (SD)	1.9 (1.2)	1.6 (1.7)	0.04
Ever-smoker	3114 (49%)	180 (59%)	0.001
Any antihypertensives	2271 (36%)	172 (56%)	<0.0001
ACE inhibitors/angiotensin receptor blockers	1107 (18%)	90 (29%)	<0.0001
Beta-blocker	566 (9%)	58 (19%)	<0.0001
Diuretics	808 (13%)	70 (23%)	<0.0001
Diabetes†	789 (12%)	46 (15%)	0.20
Left ventricular hypertrophy‡	144 (2%)	12 (4%)	0.07
Left ventricular mass (g)§, mean (SD)	144 (39)	164 (46)	<0.0001
P-R interval (msec), mean (SD)	165 (24)	174 (33)	<0.0001
Resting heart rate, mean (SD)	63 (10)	63 (11)	0.38

AF = atrial fibrillation.
* Available in 3,441 participants (137 with AF).
† Diabetes is defined as a fasting glucose level of ≥126 mg/dl or the use of glucose-lowering medication.
‡ Defined using electrocardiography by Cornell voltage criteria.
§ Measured by MRI; available in 4,885 participants (204 with AF).

New York; and Forsyth County, North Carolina).[9] At study entry, participants were aged 45 to 84 years and self-reported no history of clinical cardiovascular disease. Recruitment and baseline examination of the original 6,814 MESA participants occurred during July 2000 to August 2002. A subsample of consenting participants with no contraindications underwent a cardiac MRI, with 3,541 of the MRIs including an assessment of the ascending aorta. Four additional examinations have been completed over the follow-up (most recently in 2010 to 2012). The study was approved by the institutional review boards of all participating institutions, and all participants provided written informed consent.

AF was ascertained through study electrocardiography, hospital discharge codes, and for participants aged ≥65 years enrolled in fee-for-service Medicare (55% of the cohort), from Medicare claims data obtained from the Centers for Medicare & Medicaid Services. Annual follow-up telephone calls to study participants through February 2012 were used to identify hospitalizations, and Medicare claims data were used to ascertain inpatient AF events through December 31, 2009. Discharges showing the *International Classification of Diseases*, ninth revision (ICD-9), codes 427.31 or 427.32 were classified as AF events. The date of AF incidence was defined as the date of the first record showing a diagnosis of AF. A review of 16 validation studies determined that the use of the ICD-9 codes to identify AF events has relatively good performance.[10] At baseline, participants who self-reported AF or who had AF in the baseline electrocardiography or in a Medicare claim before study enrollment were excluded.

Measurements from physical examination and questionnaires were made at MESA baseline. Seated systolic and diastolic BPs were defined as the average of the last 2 of 3 BP measurements taken after a 5-minute seated rest using an automated oscillometric sphygmomanometer (Dinamap Pro 100; Critikon, Tampa, Florida). MAP is defined as the sum of diastolic BP and [(1/3) × systolic BP]. PP is defined as the difference between systolic and diastolic BPs. Aortic distensibility was evaluated using 1.5-T whole-body MRI systems, Signa CV/I or Signa LX (General Electric Medical Systems, Waukesha, Wisconsin), as previously described.[11] Covariate variables were measured using standard protocols, as described in Supplementary Methods.

Among the original 6,814 MESA participants, for our primary analysis, we made the following exclusions: those who were ineligible (n = 5), those with prevalent AF (n = 58), those with no follow-up information (n = 20), and those missing information on covariates (n = 101). The subgroup analysis additionally excluded MESA participants who did not receive an aortic MRI at baseline or who had invalid MRI parameters (n = 3,189).

Using restricted cubic splines, we determined that the shape of associations of BP measurements (systolic BP, diastolic BP, MAP, and PP) and aortic distensibility with