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LA Volumes and Reservoir Function Are Associated With Subclinical Cerebrovascular Disease

The CABL (Cardiovascular Abnormalities and Brain Lesions) Study

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OBJECTIVES The purpose of this study was to assess the relationship of left atrial (LA) phasic volumes and LA reservoir function with subclinical cerebrovascular disease in a stroke-free community-based cohort.

BACKGROUND An increase in LA size is associated with cardiovascular events including stroke. However, it is not known whether LA phasic volumes and reservoir function are associated with subclinical cerebrovascular disease.

METHODS The LA minimum (LAV_{min}) and maximum (LAV_{max}) volumes, and LA reservoir function, measured as total emptying volume (LAEV) and total emptying fraction (LAEF), were assessed by real-time 3-dimensional echocardiography in 455 stroke-free participants from the community-based CABL (Cardiovascular Abnormalities and Brain Lesions) study. Subclinical cerebrovascular disease was assessed as silent brain infarcts (SBI) and white matter hyperintensity volume (WMHV) by brain magnetic resonance imaging.

RESULTS Prevalence of SBI was 15.4%; mean WMHV was 0.66 ± 0.92%. Participants with SBI showed greater LAV_{min} (17.1 ± 9.3 ml/m^2 vs. 12.5 ± 5.6 ml/m^2, $p < 0.01$) and LAV_{max} (26.6 ± 8.8 ml/m^2 vs. 23.3 ± 7.0 ml/m^2, $p < 0.01$) compared to those without SBI. The LAEV (9.5 ± 3.4 ml/m^2 vs. 10.8 ± 3.9 ml/m^2, $p < 0.01$) and LAEF (38.7 ± 14.7% vs. 47.0 ± 11.9%, $p < 0.01$) were also reduced in participants with SBI. In univariate analyses, greater LA volumes and smaller reservoir function were significantly associated with greater WMHV. In multivariate analyses, LAV_{min} remained significantly associated with SBI (adjusted odds ratio per SD increase: 1.37, 95% confidence interval: 1.04 to 1.80, $p < 0.05$) and with WMHV ($\beta = 0.12$, $p < 0.01$), whereas LAV_{max} was not independently associated with either. Smaller LAEF was independently associated with SBI (adjusted odds ratio: 0.67, 95% confidence interval: 0.50 to 0.90, $p < 0.01$) and WMHV ($\beta = -0.09$, $p < 0.05$).

CONCLUSIONS Greater LA volumes and reduced LA reservoir function are associated with subclinical cerebrovascular disease detected by brain magnetic resonance imaging in subjects without history of stroke. In particular, LAV_{min} and LAEF are more strongly associated with SBI and WMHV than the more commonly measured LAV_{max}, and their relationship with subclinical brain lesions is independent of other cardiovascular risk factors. (J Am Coll Cardiol Img 2013;6:313–24) © 2013 by the American College of Cardiology Foundation

In the United States, the prevalence of stroke in the population >20 years of age is estimated at 3.0%, with 7,000,000 people having had a stroke at some point in their lifetime (1). Brain imaging studies have revealed that the prevalence of asymptomatic brain vascular lesions is substantially higher than clinically overt disease. In the general population, the prevalence of silent brain infarcts (SBI) has been estimated from 7% to 28%, with a steep increase observed with aging (2–8). Cerebral white matter hyperintensities, often expressed as percent of the brain volume (white matter hyperintensity volume [WMHV]), have also been described in asymptomatic participants in population studies (9–12). Both SBI and WMHV have been associated with future incidence of stroke, cognitive impairment, and dementia (10,11,13–15).

ABBREVIATIONS AND ACRONYMS

BMI = body mass index
CAD = coronary artery disease
CI = confidence interval
LA = left atrial
LAEF = left atrial total emptying fraction
LAEV = left atrial total emptying volume
LAV_{max} = left atrial maximum volume
LAV_{min} = left atrial minimum volume
LV = left ventricular
MRI = magnetic resonance imaging
OR = odds ratio
RT3D = real-time 3-dimensional
SBI = silent brain infarcts
WMHV = white matter hyperintensity volume

Increased left atrial (LA) size is associated with higher mortality and cardiovascular events, including stroke (16–18). Among measures of LA size, LA volume appears to provide the best prediction of adverse prognosis (19). The LA volume is usually measured in end systole, when the LA reaches maximum expansion (LAV_{max}). Growing evidence, however, suggests that the analysis of LA volume in different phases of the cardiac cycle may provide additional prognostic information. In particular, the LA minimum (end-diastolic) volume (LAV_{min}) and the LA reservoir function are better predictors of incident atrial arrhythmias than LAV_{max} (20,21). However, it is not known whether and to what extent parameters of LA size and function are associated with subclinical cerebrovascular disease. The identification of markers of cerebrovascular disease at an early subclinical stage might improve risk stratification of people at high cardiovascular risk, and allow the use of more aggressive therapeutic strategies to reduce their risk. Accordingly, the aim of this study was to investigate the relationships of LA volumes and reservoir function measured by real-time 3-dimensional (RT3D) echocardiography with the presence of subclinical cerebrovascular disease evaluated by magnetic resonance imaging (MRI) in a community-based cohort.

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METHODS

Study population. The CABL (Cardiovascular Abnormalities and Brain Lesions) study is a community-based epidemiologic study designed to investigate the cardiovascular predictors of silent cerebrovascular disease in the community. The CABL study based its recruitment on the NOMAS (Northern Manhattan Study), a population-based prospective study that enrolled 3,298 participants from the community living in northern Manhattan between 1993 and 2001. The study design and recruitment details of NOMAS have been described previously (22). Participants were invited to participate in an MRI substudy beginning in 2003 and were eligible for the MRI cohort if they: 1) were at least 55 years of age; 2) had no contraindications to MRI; and 3) did not have a prior diagnosis of stroke. From September 2005 to July 2010, NOMAS MRI participants who voluntarily agreed to undergo a more extensive cardiovascular evaluation were included in the CABL study. Participants for whom LA volume measurements by RT3D echocardiography and brain MRI information were available constitute the final sample of the present study. Written informed consent was obtained from all study participants. The study was approved by the institutional review boards of Columbia University Medical Center and of the University of Miami.

Risk factors assessment. Cardiovascular risk factors were ascertained through direct examination and interview by trained research assistants. Systolic blood pressure and diastolic blood pressure were measured at the nondominant arm in sitting position after 5 min of rest using a mercury sphygmomanometer and a proportioned arm cuff. Study participants were not asked to discontinue antihypertensive medications on the day of the visit. Two blood pressure measurements were performed and averaged. Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood