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Original article

Diastolic wall strain is associated with incident heart failure in African Americans: Insights from the atherosclerosis risk in communities study

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ABSTRACT

Background: Increased left ventricular (LV) myocardial stiffness may be associated with impaired LV hemodynamics and incident heart failure (HF). However, an indicator that estimates LV myocardial stiffness easily and non-invasively is lacking. The purpose of this study was to determine whether diastolic wall strain (DWS), an echocardiographic estimator of LV myocardial stiffness, is associated with incident HF in a middle-aged community-based cohort of African Americans.

Methods and results: We investigated associations between DWS and incident HF among 1528 African Americans (mean age 58.5 years, 66% women) with preserved LV ejection fraction (EF ≥50%) and without a history of cardiovascular disease in the Atherosclerosis Risk in Communities Study. Participants with the smallest DWS quintile (more LV myocardial stiffness) had a higher LV mass index, higher relative wall thickness, and lower arterial compliance than those in the larger four DWS quintiles ($p < 0.01$ for all). Over a mean follow-up of 15.6 years, there were 251 incident HF events (incidence rate: 10.9 per 1000 person-years). After adjustment for traditional risk factors and incident coronary artery disease, both continuous and categorical DWS were independently associated with incident HF (HR 1.21, 95%CI 1.04–1.41 for 0.1 decrease in continuous DWS, $p = 0.014$, HR 1.40, 95%CI 1.05–1.87 for the smallest DWS quintile vs other combined quintiles, $p = 0.022$).

Conclusions: DWS was independently associated with an increased risk of incident HF in a community-based cohort of African Americans. DWS could be used as a qualitative estimator of LV myocardial stiffness.

Introduction

Heart failure (HF) is a global public health problem affecting about 26 million people worldwide [1]. Overall, the prognosis for HF has improved over decades due to advances in medical therapies, but 50% of people diagnosed with HF will die within 5 years [2]. Left ventricular (LV) diastolic function is an important determinant of LV end-diastolic pressure. Previous studies showed that indices of LV diastolic function are associated with incident HF [3,4]. LV myocardial stiffness is one of the components of diastolic function and has been associated with both HF with reduced ejection fraction (HFrEF) and HF with preserved EF (HFpEF) in cross-sectional studies [5,6]. However, there have been no studies to date examining the relationship between LV myocardial stiffness and incident HF mostly due to difficulty evaluating LV

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myocardial stiffness: evaluating LV myocardial stiffness requires invasive procedures and complicated computations [7].

Diastolic wall strain (DWS) is an indicator that estimates LV myocardial stiffness non-invasively using simple echocardiographic measurements [8]. DWS was developed based on the linear elastic theory, and predicts the impairment of diastolic LV wall thinning reflecting resistance to deformation in the diastolic period [9]. In animal models, DWS was correlated with the LV myocardial stiffness constant which is the gold standard measurement of the LV myocardial stiffness [8]. DWS was lower in HFpEF patients than asymptomatic patients with LV hypertrophy [8]. Furthermore, increase in LV myocardial stiffness assessed by DWS was associated with severe LV concentric remodeling and poor prognosis in HFpEF patients [9].

Racial disparities in the incidence of HF exist: African Americans have a higher incidence of HF than whites, Hispanics, and Asians [10]. Aortic stiffness is one potential mechanism that has been implicated in this racial disparity [11]. The aims of this study were two-fold: (1) to investigate the relationships among DWS, LV structure and function, and arterial stiffness, and (2) to determine whether DWS is associated with incident HF in an African American cohort of the Atherosclerosis Risk in Communities (ARIC) Study.

Methods

Study population

The ARIC Study is a prospective cohort study conducted to investigate the risks of cardiovascular disease (CVD) and atherosclerosis. The ARIC study's design and methods have been described in detail elsewhere [12]. We used data from the African American cohort from Jackson ("the Jackson cohort") at visit 3 as baseline because echocardiograms at visit 3 (1993–1995) were available only in the Jackson cohort ($n = 2623$). We excluded those with past history of CVD including coronary heart disease (CHD), stroke, and heart failure ($n = 228$), missing information of past history of CVD ($n = 43$), absence of echo M-mode image ($n = 684$), insufficient quality of M-mode image ($n = 7$), reduced LVEF or presence of wall motion abnormality ($n = 108$), and missing information of covariates ($n = 25$) (Fig. 1). Thus, a total of 1528 participants were included in the final analyses. Excluded participants were more likely to be older, male sex, had a higher body mass index (BMI), higher prevalence of hypertension, diabetes, and current smoking than those included in the study (Supplementary Table 1). Total cholesterol/high-density lipoprotein (HDL) cholesterol ratio, systolic blood pressure, and heart rate were also higher in excluded participants than included participants. These differences could be attributed to the difference of the prevalence of a history of CVD between included and excluded participants. The ARIC Study protocols were approved by the institutional review boards of each participating center, and informed consent was obtained from each study participant.

Definition of co-morbidities

After a 5-minute rest, three sitting blood pressure measurements were taken with an oscillometric automated sphygmomanometer (Omron HEM-907 XL, Schaumburg, IL, USA); we averaged the last 2 measurements. Pulse pressure was calculated as systolic (SBP) – diastolic blood pressure (DBP). The information of antihypertensive medication use was obtained at visit 3. A diagnosis of hypertension was defined as prescription of antihypertensive medication use, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg. BMI was calculated as weight in kilograms divided by the square of height in meters. Blood was drawn after an 8-hour fasting period, and glucose, plasma total cholesterol, and plasma HDL cholesterol levels were measured centrally by standard enzymatic methods. Diabetes was defined as fasting glucose concentration ≥126 mg/dL, non-fasting glucose concentration ≥200 mg/dL, a self-report of a physician's diagnosis of diabetes or use of oral diabetes medication or insulin. Total cholesterol/HDL ratio was also used as a covariate in this study.

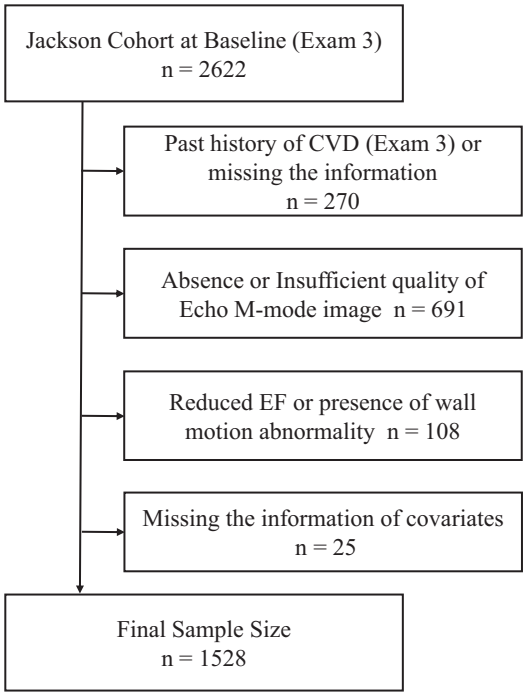

Fig. 1. Inclusion and exclusion criteria for this study. CVD, cardiovascular disease; EF, ejection fraction.

Diastolic wall strain and echocardiography

The quality control measures for echocardiography have been described previously [13]. LV internal dimension and interventricular septal and posterior wall thicknesses were measured at end-diastole and end-systole in 3 cardiac cycles according to the recommendations of the American Society of Echocardiography [14]. We used these variables measured on M-mode image. Calculations of LV mass were made using the following equation as recommended by the American Society of Echocardiography: LV mass index (g/m^2) = (0.8*{1.04*[(LVDd + IVSd + PWd)^3 − (LVDd)^3]} + 0.6)/body surface area [14], where LVDd is left ventricular diastolic dimension, IVSd is interventricular septum thickness at end-diastole, PWd is posterior wall thickness at end-diastole. Relative wall thickness (RWT) was calculated as 2*(PWd)/LVDd. DWS was calculated as (PWs − PWd)/PWs, where PWs is posterior wall thickness at end-systole, and PWd is posterior wall thickness at end-diastole [15]. LVEF was calculated by the Teichholz method. Systemic arterial compliance (SAC) was calculated as stroke volume/pulse pressure. Effective arterial elastance was calculated as 0.9*systolic blood pressure/stroke volume.

Outcomes

To obtain information regarding hospitalizations and other health issues, participants were called annually. Incident HF was the primary outcome of this study. Incident HF was defined by HF hospitalization or HF death, according to the International Classification of Diseases-Ninth Revision (ICD-9) code 410 in any position for HF, obtained by ARIC Study retrospective surveillance

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