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The Impact of Race on the Prognosis of Preclinical Diastolic Dysfunction: A Large Multiracial Urban Population Study

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ABSTRACT

BACKGROUND: This study was performed to assess the impact of race on the incidence of heart failure and survival in patients with preclinical diastolic dysfunction.

METHODS: All adults during a 5-year period with grade 1 diastolic dysfunction on echocardiogram, left ventricular ejection fraction ≥50%, and no diagnosis of heart failure were included in this study. Clinical endpoints were new diagnosis of heart failure (International Classification of Diseases-Ninth Revision code 428.0) and all-cause mortality. A total of 7878 patients: 20.8% non-Hispanic White, 35.8% non-Hispanic Black, and 31.0% Hispanic individuals (mean age was 68 ± 12 years, 37% men) were included in the study. Non-Hispanic Whites were older, more frequently male, and had a higher mean socioeconomic status and more antecedent myocardial infarction.

RESULTS: Non-Hispanic Blacks and Hispanics had more hypertension, diabetes, renal disease, and cerebrovascular disease. After a median follow-up time of 6 years, 1356 patients developed heart failure and 2078 patients died. The 10-year cumulative probabilities of heart failure and all-cause mortality were 23.9% and 32.6%, respectively. Time to incident heart failure was similar among the 3 racial groups. However, non-Hispanic Blacks (hazard ratio 0.80, $P = .002$) and Hispanics (hazard ratio 0.67, $P < .001$) experienced lower mortality compared with non-Hispanic Whites, which was confirmed on a propensity-scored sensitivity analysis.

CONCLUSIONS: Time to heart failure was similar among the 3 racial groups, however, non-Hispanic Whites experienced worse survival compared with non-Hispanic Blacks and Hispanics, despite their higher burden of risk factors. The reasons for worse survival in the non-Hispanic white population need to be further explored.
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KEYWORDS: All-cause mortality; Diastolic dysfunction; Heart failure; Race; Sex

There is a heart failure epidemic in the US, with 825,000 new cases diagnosed each year and 5.1 million Americans living with the disease in 2014.[1,2] Treatment for heart failure continues to advance, but heart failure is still listed on death certificates as frequently in 2010 as it was in 1995.[3] Prevention of heart failure remains an important issue, and a better understanding of its natural history and risk factors is needed.

A well-known but poorly understood risk factor for the development of heart failure is preclinical diastolic dysfunction, defined as impaired relaxation of the left ventricle during diastole without signs or symptoms of heart failure.[4-6] Diastolic dysfunction is found in most patients with heart failure, irrespective of systolic function,[5,7] and roughly half of all heart

failure patients have heart failure with preserved ejection fraction.[8,9] Although the introduction of beta-blockers and renin-angiotensin aldosterone modulators in the past 2 decades has significantly improved the outcomes of heart failure with reduced ejection fraction, no treatment has yet been demonstrated to reduce morbidity and mortality in patients with heart failure with preserved ejection fraction.[10] Therefore, identifying which patient factors affect the progression of preclinical diastolic dysfunction to heart failure is needed.

The impact of race on the progression of preclinical diastolic dysfunction to heart failure and overall survival has been understudied. Previous studies were in mainly small, non-Hispanic White cohorts with European ancestry.[4,5,11-13] Race is known to play a key role in outcomes in patients who already have heart failure, but its role on outcomes in patients with preclinical diastolic dysfunction is unknown.[14] Therefore, this study was undertaken in a large, racially diverse urban population with preclinical diastolic dysfunction to assess the impact of race on the incidence of heart failure and overall survival.

> ## CLINICAL SIGNIFICANCE
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> - In patients with preclinical diastolic dysfunction (PDD), the 10-year cumulative probability for heart failure is 23.9%. The 10-year cumulative probability for death is 32.6%.
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> - Men and women have similar risk of developing heart failure, but men die sooner.
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> - Non-Hispanic (NH) Whites, NH Blacks, and Hispanics with PDD develop heart failure at similar rates, yet NH Whites with PDD have significantly poorer survival than NH Blacks and Hispanics.

METHODS

Patient Population

The catchment area of the authors' institution represents one of the most diverse populations in the US. According to the US Census Bureau, in 2013 the Bronx County, New York, population consisted of 10.5% non-Hispanic White, 43.3% non-Hispanic Black, and 54.6% Hispanic or Latino (Hispanic) individuals, compared with national statistics, 62.6% non-Hispanic White, 13.2% non-Hispanic Black, and 17.1% Hispanic individuals. We retrospectively reviewed our institution's electronic medical record using Clinical Looking Glass (Ver. 3.3; Montefiore Medical Center, Bronx, NY), a patented software tool that collates medical records from multiple sources for research purposes. All patients between 18 and 90 years of age who were referred for echocardiography during the period of 2003 to 2008 were screened for inclusion based on the presence of preclinical diastolic dysfunction. Patients were excluded if they had a preexisting diagnosis of heart failure, valvulopathy of any type, or atrial fibrillation. If a patient had multiple echocardiograms (echos), the first echo meeting the definition of grade 1 diastolic dysfunction was considered the index echo at time "zero" for that patient. Socioeconomic status, self-reported race, preexisting comorbidities, serologic data, and medications were gathered using Clinical Looking Glass. Socioeconomic status was measured using a summary score combined from 6 variables representing wealth and income (1. log of the median household income; 2. log of the median value of housing units; 3. the percentage of households receiving interest, dividend, or net rental income; 4. the percentage of adults 25 years of age or older who had completed high school; 5. the percentage of adults 25 years of age or older who had completed college; 6. the percentage of employed individuals 16 years of age or older in executive, managerial, or professional specialty occupations). A Z-score is computed that reflects the deviation below (negative) or above (positive) the mean socioeconomic status of the population in the state of New York.[15] This method is used by Clinical Looking Glass and has been previously validated against the US Census Bureau geocoding database.[16] Patient information was de-identified in accordance with the Health Insurance Portability and Accountability Act. The Institutional Review Board of Montefiore Medical Center and Albert Einstein College of Medicine approved this study.[15,16]

Echocardiography

Echocardiography was performed according to the guidelines of the American Society of Echocardiography using Sonos 5500, Sonos 7500, or IE-33 ultrasound systems (Philips Healthcare, Andover, MA).[17] Left ventricular ejection fractions were calculated using either biplane Simpson's method or Teichholz formula.[18] Diastolic function was measured by pulsed-wave Doppler examination of mitral inflow velocities before and during Valsalva maneuver. Preclinical diastolic dysfunction was defined as the presence of grade 1 diastolic dysfunction without a clinical diagnosis of heart failure based on the International Classification of Diseases, Ninth Revision (ICD-9) code 428.0, putting patients into stage B of the American College of Cardiology/American Heart Association stage of heart failure.[19] We measured diastolic dysfunction based on the ratio of early (E) to late (A) mitral inflow velocity and ratio of E to the lateral mitral annual velocity (E′) measured by tissue Doppler in accordance with current guidelines.[20] Grade 1 diastolic dysfunction (ie, impaired relaxation) was defined as E/A $\leq$0.75.[21] Increased volume status is a known confounder of diastolic function measurement. To ensure patients were euvolemic at the time of echocardiography, they must have had an E/E′ <10 and estimated pulmonary capillary wedge pressure <10 mm Hg based on the Nagueh formula.[22]

Clinical Endpoints

The primary endpoint of this study was the new diagnosis of heart failure and all-cause mortality. The new diagnosis of heart