

EDITORIAL COMMENT

Diastolic Dysfunction

Does Ethnicity Matter?*

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In the U.S., 660,000 new cases of heart failure (HF) are diagnosed each year (1), a figure that has been steadily increasing. The number of prevalent HF cases is currently estimated at more than 5 million, and 1 in 5 men or women at age 40 years will have HF during their lifetime (1). After the diagnosis is made, 1-year mortality is as high as 20% (1). Racial/ethnic differences in the prevalence of HF have been reported, with African-American women having a higher prevalence than their Caucasian counterparts (1).

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Approximately 50% of patients hospitalized with symptomatic HF have normal left ventricular systolic function (2), a condition that is also referred to as HF with preserved systolic function, or diastolic HF. Although its underlying pathogenetic mechanism is different (impairment of ventricular filling as opposed to a decrease in contractile function), diastolic HF is characterized by similar mortality and rehospitalization rates as systolic HF (3,4), and the 2 conditions often coexist (5). Older age, female gender, and arterial hypertension are the main patient characteristics associated with diastolic HF (3), and the trend toward the aging of the population is likely to result in an increasing frequency of diastolic HF in the years to come.

The ability of the left ventricle to accept blood at low pressures during diastole is often referred to as diastolic "function," and its impairment, characterized by abnormal ventricular distensibility and relaxation and the consequent inability to maintain a normal ventricular filling unless the left atrial pressure rises, is therefore called diastolic dysfunction (DD). The basic mechanisms underlying DD may be intrinsic to the cardiomyocyte or the consequence of abnormalities in the extracellular matrix, especially in collagen deposition (6). Neurohormonal influences and cardiac endothelial function are also known to affect ventricular stiffness and relaxation (7). Although extracardiac factors,

and especially conditions causing volume overload, may play a role in the transition from asymptomatic DD to clinical HF (8), asymptomatic DD is considered a precursor of future HF (9), and is associated with increased mortality (10). The detection of DD is therefore important in that it provides the clinician with an opportunity to act before clinical symptoms develop (6).

The study of DD, initially confined to the cardiac catheterization laboratory, received a tremendous boost in the 1990s with the introduction of echocardiographic and Doppler-based techniques, which provided a noninvasive assessment of the diastolic performance of the left ventricle, and allowed its application to larger cohorts of patients. This effort resulted in the identification of several factors associated with DD, such as older age, female gender, arterial hypertension and left ventricular hypertrophy, diabetes mellitus, obesity, and coronary artery disease (11,12). The possibility of racial/ethnic differences in susceptibility to the development of DD has received comparatively less attention. In this issue of the *Journal*, Sharp et al. (13) report a decreased left ventricular diastolic performance in African-Caribbean hypertensive patients enrolled in the ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) study compared with their white European counterparts. The effect of African-Caribbean ethnicity on diastolic function persisted after adjustment for the most important potential confounding factors, leading the investigators to hypothesize the existence of an intrinsic difference in the diastolic performance of the left ventricle between the 2 racial/ethnic groups.

The study has important strengths, first among them the attempt to identify at a relatively early stage differences in cardiac function that may portend, at least in part, the documented excess in cardiovascular disease burden observed among persons of African heritage, an observation that is not entirely explained by differences in traditional risk factor profiles. Furthermore, the addition of tissue Doppler examination to the traditional spectral Doppler assessment of the transmitral flow provided a more accurate assessment of diastolic function than in previous studies. Finally, the circumstance that all study participants lived in the same geographic area and had similar access to health care helped minimize an important confounding factor and improve comparability between the 2 racial/ethnic groups.

The implication that the results obtained reflect intrinsic differences in ventricular diastolic performance between the 2 ethnic groups should be regarded, however, with some degree of caution. Separating genetic/ethnic differences from the effect of acquired or environmental factors may be difficult even under the best study conditions. Differences between the groups may exist in variables that were not, or were only partially, adjusted for. Arterial hypertension, one of the most potent risk factors for DD, may be a case in point. All patients in the study were hypertensive patients treated with antihypertensive medications. Although the

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degree of hypertension control in the 2 ethnic groups was similar, the duration of the hypertensive status, which was not reported, may have differed. High blood pressure is known to develop in non-Hispanic blacks at a younger age than in whites (1,14). A longer duration of the hypertensive status in the African-Caribbean subgroup might have affected the diastolic properties of the ventricle and contributed to the differences that were observed between the 2 groups. Although the investigators hypothesized a different response to the same stimulus in different ethnic groups, their observations might instead be the result of a quantitatively similar response to a stimulus acting for a longer time. Also, all patients had at least 3 of 11 pre-determined cardiovascular risk factors at entry. The effect of many of these risk factors was adjusted for in the analysis, but this adjustment was performed for each individual risk factor, and different combinations of risk factors may have been at play in the 2 ethnic subgroups with different impacts on the diastolic function of the ventricle. Finally, all study subjects had been treated for 1 year with 1 of 2 combination therapies (angiotensin-converting enzyme inhibitor plus calcium-channel blocker or beta-blocker plus diuretic) at the time the echocardiographic testing was performed. Although the effect of treatment assignment was adjusted for in the analysis, the effect of the individual drugs on the ventricular diastolic function could not be evaluated, and a different treatment effect in the 2 ethnic groups cannot be excluded.

For the preceding reasons, the results of the study by Sharp et al. (13), although valuable and relevant to the context in which they were obtained, are not conclusive regarding the existence of racial/ethnic differences in the diastolic performance of the left ventricle. Because of the characteristics of the study cohort (hypertensive subjects with several risk factors treated with combination therapy) and in view of the previous considerations, the differences observed in the study should not be extrapolated to the general population. The existence of intrinsic racial/ethnic differences in ventricular structure and function may not be entirely provable without appositely designed genomic studies. Short of that, the best chance to further clarify the possibility of racial/ethnic differences may reside in population-based studies of healthy persons, in whom any changes in ventricular structure and function may be detected at a much earlier stage and with a smaller chance of interference by confounding factors. In the few studies that have reported on the diastolic function in the general population, the prevalence of echocardiographically determined diastolic abnormalities was between 11% (11) and 21% (10) but higher than 30% among subjects older than age 60 years (12). The ethnic composition of those studies did not allow for comparisons between ethnic groups.

Similar studies in multiethnic cohorts may help clarify the existence of any independent effect of ethnicity on the diastolic properties of the left ventricle.

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