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Distribution and determinants of Doppler-derived diastolic flow indices in African Americans: The Jackson Heart Study (JHS)

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Abstract

Objectives—The objective of this study is to investigate the distribution and determinants of diastolic function in a middle-aged cohort of African Americans (AA).

Background—The distribution and determinants of left ventricular (LV) diastolic function in AA are not well-described despite high rates of AA with diastolic heart failure and a five-fold higher risk of death in those with diastolic dysfunction (DD) compared to normal diastolic function.

Methods—Four categories of diastolic function were defined in JHS participants undergoing echocardiograms at the first examination (2001-2004) using mitral and pulmonary vein velocities. Investigators used logistic regression to assess the independent relation of DD to traditional risk factors and LV systolic dysfunction.

Results—Of the 3,571 study participants (mean age, 56 ± 12 years; 63.9% female), 70.4% had normal diastolic function, and 18.0%, 10.6%, and 0.9% had mild, moderate, and severe DD, respectively. In the multivariable analysis, DD was significantly related to age (OR 1.2, 95% CI 1.1-1.4), male sex (OR 1.3 CI 1.0-1.5), LV systolic dysfunction (OR 1.5, CI 1.2-2.0), body mass index (OR 0.8, CI 0.8-0.9), and heart rate (OR 1.2; CI 1.1-1.2). The severity of DD was significantly related with age (OR 0.3; CI 0.3, 0.4), male sex (OR 1.6; CI 1.2-2.2), hypertension (OR 0.6, CI 0.4-0.8), and heart rate (OR 0.7; CI 0.6-0.8).

Conclusion—This is the largest community-based analysis of LV diastolic function in middle-aged AA. DD was present in 29.5% and independently related to several traditional risk factors and LV systolic dysfunction. (*Am Heart J* 2009;158:209-16.)

Doppler-based diastolic filling abnormalities of the left ventricle (LV) measured on echocardiogram is a predictor of adverse outcome in patients with heart disease. Even patients with mild forms of diastolic dysfunction (DD) and who are asymptomatic have a 5-fold greater risk of death compared to similar patients with normal LV diastolic function.¹

Several studies have shown that with careful methodical approach, Doppler flow patterns can document a progressive pattern of abnormality in many conditions affecting the myocardium.¹ This reinforces the importance of studying diastolic ventricular function in individuals using Doppler echocardiographic assessment in mild cardiac conditions or hypertension so that the abnormalities can be identified at an early stage and possibly corrected. Though a number of population-based echocardiographic studies have been performed to study the prevalence of DD in non-African American (AA) populations, no study to date has evaluated the prevalence and severity of DD in a large middle-aged to elderly AA community using both mitral and pulmonary venous Doppler patterns on echocardiography.²⁻⁵

Methods

Study population

The JHS is a longitudinal population-based observational cohort that was initiated in 2000 to investigate prospectively the epidemiology and determinants of cardiovascular disease in AA.⁶ JHS recruited 5301 (63.4% female, age range 21-94 years, mean age $\pm$ SD 55 ± 13 years) participants from the Jackson, MI, tricounty area (Hinds, Madison, and Rankin counties). Of this number, approximately 30% were prior Jackson participants in the ARIC Study. Approximately 23% of the participants that were not from the ARIC Study were recruited by random selection. An additional 23% are members of a constrained volunteer sample, in which recruitment was distributed among defined demographic cells in proportions designed to mirror those in the overall population.⁷

This study was approved by the University of Mississippi Medical Center Institutional Review Board and the participants gave written informed consent.

Echocardiography

Echocardiograms were recorded by four experienced sonographers with a commercially available ultrasound system (Sonos 4500; Hewlett Packard, Andover, MA). All measurements were performed offline by a single observer (TES, an experienced Cardiologist with Level 3 training in echocardiography), who was blinded to the participant's clinical data, and were based on the recommendations of the American Society of Echocardiography.⁸ Left ventricular diastolic function was graded into four categories by Doppler evaluation of mitral and pulmonary venous inflow. For systolic function, the participants were divided based on their LV ejection fraction (<50 , $\geq 50\%$).

Diastolic dysfunction was evaluated using standardized diagnostic criteria.^{9,10} From the apical four-chamber transmitral recordings, the following measurements were carried out: peak E velocity, peak A velocity, and deceleration time. Isovolumic relaxation time was recorded in the apical 5-chamber view with the Doppler cursor placed in between the LV outflow tract and the anterior mitral valve leaflet. The pulmonary venous flow recordings were obtained from the 4-chamber view directed at the right upper pulmonary vein. Sample volume was obtained 1 to 2 cm into the pulmonary vein, and the following measurements were carried out: peak systolic wave velocity (PVS), peak diastolic wave velocity (PVD), and peak atrial reversal wave velocity (PVA). A display speed of 100 mm/s was used for measuring mitral and pulmonary waveform durations.

Left ventricular mass was calculated using the following formula¹¹: $LV\ mass\ (g) = 0.8 \times 1.04 [(LV\ end\ diastolic\ diameter + IVST + PWT)^3 - (LV\ end\ diastolic\ diameter)^3] + 0.6$, where IVST is interventricular septal thickness, and PWT is posterior wall thickness. Left ventricular mass was indexed to height^{2.7} to adjust for body habitus. Relative wall thickness

(RWT) was defined as $2 \text{ (PWT) / LV end-diastolic diameter}$. Left atrial diameter was measured on M-mode in the parasternal long-axis view.

Covariates

Covariates included sex, age, body mass index (BMI), LV ejection fraction, hypertension status, diabetes status, prevalent myocardial infarction (MI), current cigarette smoking, fasting low-density lipid cholesterol, ratio of fasting total cholesterol and high-density lipid cholesterol, and fasting triglycerides. Age was defined as age at the time of clinic visit. It was derived as the difference between the date of clinic visit and date of birth divided by 365.25 and rounded off to the nearest lowest integer. Body mass index was derived by the weight in kilograms divided by height in meter squared (kg/m^2). Left ventricular ejection fraction was dichotomized by $\leq 50\%$ (absent) and $\geq 50\%$ (present). The presence of type 2 diabetes mellitus (diabetes) was determined by a measured fasting glucose of $\geq 126 \text{ mg/dL}$ or use of hypoglycemic medication (self-reported or actual). The presence of hypertension was determined by systolic or diastolic values of ≥ 140 or $\geq 90 \text{ mm Hg}$, respectively, or use of antihypertensive medications (self-reported or actual). Previous MI was defined by self-report, physician-diagnosed condition, and/or electrocardiographic abnormalities. Current cigarette smoking status was defined as yes if a participant indicated that he/she had smoked at least 400 cigarettes in his/her lifetime and was smoking at the time of his/her clinic visit, and none otherwise. The lipids were classified as fasting if the derived fasting time was ≥ 8 hours prior to the drawing of blood via venipuncture.

Statistical methods

We defined four categories of diastolic function based on the mitral early to late diastolic filling velocity ratio (E/A); the deceleration time (DT); and pulmonary venous systolic, diastolic, and atrial reversal velocities (PVS, PVD, and PVA): (1) normal diastolic function (defined as $0.75 < \text{E/A} < 1.5$, $\text{DT} > 140 \text{ ms}$, $\text{PVS} \geq \text{PVD}$, and $\text{PVA} < 35 \text{ ms}$), (2) mild DD (defined as $\text{E/A} \leq 0.75$, $\text{PVS} > \text{PVD}$, and $\text{PVA} \leq 35 \text{ ms}$), (3) moderate DD (defined as $0.75 < \text{E/A} < 1.5$ and $\text{DT} > 140 \text{ ms}$, $\text{PVS} < \text{PVD}$ and $\text{PVA} \geq 35 \text{ ms}$), and (4) severe DD (defined as $\text{E/A} > 1.5$, $\text{DT} < 140 \text{ ms}$, $\text{PVS} < \text{PVD}$ and $\text{PVA} \geq 35 \text{ ms}$).

For this study, participants with atrial fibrillation and participants with mitral valve disease (those having greater than mild mitral regurgitation or any degree of mitral stenosis) were excluded from the study. Additionally, participants with missing parameters of diastolic function, missing covariate data, or who were otherwise unclassifiable based on parameters used were excluded from the analysis. The overall prevalence of DD and systolic dysfunction were estimated from participants who had the Doppler measurements to determine a dysfunction classification and had non-missing values for the clinical covariates utilized in the analysis. Descriptive statistics of clinical characteristics of the study sample by diastolic function category were performed by means of SAS PROC FREQ and MEANS (SAS Institute, Cary, NC) for categorical and continuous traits, respectively. The age- and sex-specific distribution of diastolic dysfunction was displayed by stack-bar graphs. The association between the prevalence of diastolic and systolic dysfunction and the clinical characteristics (covariates) were investigated using the χ^2 tests for univariate associations. Logistic regression via SAS PROC LOGISTIC was used to investigate age- and sex-adjusted prevalence odds ratios for the diastolic and systolic dysfunction relative to the categorical clinical characteristics.

The associations between predictive factors (clinical characteristics) and diastolic function are described for the: (1) univariate or “crude” relationships with no adjustments for other factors, (2) multivariable relationships where associations are described after adjustment for the entire set of predictive factors considered (regardless of the significance of individual

factors), and (3) in the most parsimonious model where adjustments are made for only factors found to be significant using stepwise selection using the backward method with a significant level of a variable staying in the model of 0.05. A binary logistic regression was performed dichotomizing diastolic function to normal diastolic function versus DD. For the continuous clinical characteristics, SAS PROC General Linear Models was used to obtain and compare age- and sex-adjusted estimates of the characteristics for the various classification of diastolic and systolic dysfunction. All analyses were performed using SAS version 9.1.

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Results

Of the 5,301 participants in JHS, 18 were excluded because of a lack of consent, 493 were excluded because they had at least one missing covariate, 94 were excluded because they had at least one missing parameter for defining diastolic function, and another 1,126 were excluded because they could not be classified into one of the categories of DD based on the parameters measured. In the later case, participants were excluded because they met >1 category based on parameter used. Therefore, the study population consisted of 3,571 participants (mean age 56 ± 12 years, 63.9% female). Using multiple logistic regressions, adjusted odd ratios corresponding to age, diastolic blood pressure and BMI imply that there was a significant difference in these covariates comparing participants included versus excluded in this study (age [OR 1.42, 95% CI 1.33-1.52], diastolic blood pressure [OR 1.19, 95% CI 1.10-1.28], and BMI [OR 1.14, 95% CI 1.07-1.22]).

The distribution of normal diastolic function, mild, moderate and severe DD was 70.4%, 18.0%, 10.6% and 0.9%, respectively. Participants classified as normal were approximately nine years younger than those with mild DD. The age of participants decreased with severity of DD (see Table I). There were more women than men who had normal diastolic function or had mild DD; however, the reverse was true for those with moderate or severe DD.

The percentage of the participants with low LV ejection fraction was highest in those with severe DD (21.2%) compared to mild DD (10.3%), moderate DD (7.9%), and normal diastolic function (6.1%). After indexing echocardiographic LV mass to height^{2.7}, there was minimal difference in the measure between the four groups of diastolic function. Relative wall thickness for the four diastolic function groups was similar as well.

Figure 1 provides a display of the sex and age distribution of DD in the study sample and Table II shows the association echocardiographic and clinical parameters to DD. There was a significant sex difference ($P < .0001$) in DD noted in the study population; men had a higher proportion with moderate and severe DD compared to women. Age ($P < .0001$), BMI ($P < .0001$), hypertension status ($P < .0001$), diabetes status ($P = .0002$), MI status ($P = .0016$), LV mass index ($P < .0001$), RWT ($P < .0001$), and LV ejection fraction ($P < .0001$) were all significantly associated with DD. Current smoking status was not independently associated with DD.

Table III shows a summary of the univariate, multivariable and most parsimonious models analyzing the predictive value of risk factors for the presence (abnormal vs normal) and

severity (moderate or severe vs mild) of DD. Older age, male sex, low ejection fraction, the presence of hypertension and lower BMI were all associated with the presence of DD in the univariate model. In both the multivariable and most parsimonious models, hypertension was no longer associated with the presence of DD however the other clinical variables from the univariate model remained significant. In the test for severity of DD, younger age, male sex, and the absence of both hypertension and smoking were association to moderate to severe DD. This held true for both the multivariable and most parsimonious models.

Discussion

Principal findings

This study represents the largest community-based analysis of LV diastolic function in middle-aged AA. The strength of our study is the large sample size, the community-based setting, and the comprehensive assessment of diastolic function.

In our investigation, we found that DD was present in 29.5% of participants and was significantly related to age, male sex, BMI, LV systolic dysfunction, and heart rate. The severity of DD was significantly related to male sex. Those with moderate and severe DD were younger, normotensive, and less likely to be smoker.

Predictors of the prevalence and severity of diastolic dysfunction

Diastolic dysfunction was present in approximately a third of participants. We found that age, male sex, BMI, heart rate, and echocardiographic LV systolic dysfunction were significantly related to DD and that participants with severe DD were less likely to have traditional risk factors. Because of the later finding, one may suspect that some of those participants defined as severe DD with an E/A >1.5 may actually have normal filling. However within our cohort among the participants with severe DD, 33.3% of them had hypertension, diabetes, or obesity. In addition, a higher proportion of the participants with severe DD had history of MI and/or low LV ejection fraction compared to the other groups. Strikingly, 93.9% of these participants had a left atrial diameter greater or equal to 4.0 cm. These findings suggest that the E/A >1.5 in these participants most likely represents abnormal diastolic filling induced by elevated filling pressures. These findings have been seen in previous groups analyzing diastology in population-based cohorts.¹² However, as with these other studies, interpretation of the findings should be made with caution given the small number of participants with severe DD. One may suspect that because the probable higher rates of death at younger ages in those with severe DD, this group may also have less cardiovascular risk factors compared to participants in other diastolic categories. Additionally, we cannot completely exclude a potential genetic propensity for diastolic dysfunction and/or coronary events in this small sample of participants.¹³⁻¹⁵

Findings of our study are supported to an extent by other investigations evaluating DD in the AA populations however there are some differences noted. The JHS had a higher percentage of participants with DD (29.5%) compared to the AA cohort of the ARIC Study where 15.3% had DD. This study like others was limited by not having pulmonary venous Doppler indices that can aid in identifying participants with DD but with pseudonormalized mitral inflow patterns. This limitation in addition to differences in cutoffs used in defining DD between the 2 studies may contribute to the different prevalence rates.¹² Similar to our cohort, participants in the ARIC Study with severe DD were younger and had a lower prevalence of clinical risk factors compared to those with mild DD. This group, however, was noted to have lower ejection fraction and higher prevalence of MI. Also similar to our cohort, participants in the ARIC with DD were more likely to have concentric hypertrophy (RWT >4.0).¹⁶ In the Coronary Artery Risk Development in Young Adults Study,

investigators performed Doppler analysis in 3492 black and white men and women (aged 23-35 years). In this group of young adults, Doppler measures of LV diastolic filling were related to age, sex, body weight, blood pressure, and LV systolic function. These findings were similar to those in our study except that we did not find that blood pressure was significantly related to DD after adjusting for all other clinical risk factors.

There have been a number of investigations looking at diastolic function in non-AA populations. For instance, in the Framingham Heart Study, investigators looked at diastolic function in a subset of normal participants (free of coronary artery disease, diabetes, renal insufficiency, or heart failure). Investigators found that LV systolic function, sex, and systolic blood pressure were minor determinants of diastolic function; however, BMI had little or no association with DD.¹⁷ Investigators in the Cardiovascular Health Study found that in their elderly cohort, sex, age and blood pressure were most strongly related to mitral E and A filling peak velocities.¹⁸ In the Strong Heart Study, 19% of participants had DD.¹⁹ Their correlates were similar to those in our cohort particularly showing that participants with E/A >1.5 had lower BMIs and were on average 10 years younger than those with normal E/A; however, only 4% of those participants were normotensive, nonobese, nondiabetic, and free of clinical heart disease or LV hypertrophy.¹⁹

Similar to the Jackson cohort of the ARIC Study, the Cardiovascular Health Study and the Framingham and Strong Heart studies did not identify those participants with pseudonormalization on Doppler assessment of mitral inflow.¹⁹ This limitation of those studies may contribute to differences in results independent of population-based differences.

Mechanism linking clinical and echocardiographic characteristics to diastolic function

Age and Sex—It is unclear how aging is related to diastolic filling of the LV. One theory is that changes in diastolic properties may be related to increasing prevalence of factors related to diastolic function with age such as hypertension, diabetes, and coronary artery disease.²⁰ In addition, cardiac remodeling with age (such as the increase in LV wall thickness and left atrial size) may contribute to changes in diastolic filling with aging.^{17,21} Animal studies suggest that cellular hyperplasia, cell death, fibrosis, and changes in calcium sequestration that occurs with aging may result in impaired LV relaxation. Among the theories proposed to help explain sex-related differences in diastolic filling are: (1) different diastolic properties of the LV in men and women and (2) a different mitral annular area/cardiac output ratio between men and women.

Blood pressure, BMI, and diabetes—The effect of blood pressure and BMI on cardiac structure and function has been established in a number of studies. Both blood pressure and BMI are associated with changes in LV mass and compliance and thereby affect diastolic filling patterns. Compliance changes in these conditions may be due to disproportionate growth of nonmyocardial extracellular matrix.²² Disproportionate growth (as seen in those with elevated blood pressure and high BMI) rather than proportional growth of the nonmyocardial matrix (as seen in other conditions) is associated with compliance changes that may result in DD. For example, ventricular remodeling that occurs with athletes results in proportional growth of myocardial and nonmyocardial matrix and is not associated with DD.²³ Diabetes may be related to DD as there is disproportionate changes in the nonmyocardial extracellular matrix in this condition similar to that seen in those with hypertension and obesity. Diabetes may result in changes in extracellular matrix through its relation to microvascular disease.

Finally, hypertension may be related to DD as determined by Doppler due to direct effects of hypertension on the hemodynamics of the left ventricle. Hypertension is associated with

increased afterload that may impair LV relaxation resulting in a decrease in the transmitral gradient and subsequent changes in early diastolic filling velocities and deceleration time.

LV systolic function and heart rate—In our study, LV systolic dysfunction was more prevalent in those with severe DD compared to those with normal diastolic function or mild or moderate DD. This group (those with severe DD) was also noted to have a higher percentage with MI. It is known that coronary ischemia and injury predisposes to DD. Ischemia may affect LV relaxation because during this period of the cardiac cycle there is a series of energy-consuming steps beginning with the release of calcium from troponin. An adequate supply of adenosine triphosphate is necessary for normal cardiac function.

Another explanation relating LV systolic function to diastolic function noted on echocardiogram is that changes in stroke volume may affect the transmitral pressure gradient and produce changes in the mitral diastolic filling pattern.

Finally, with faster heart rates, there is shortening of the active energy-consuming early phase of diastole that leads to an increased reliance on the later phase of diastole (atrial contraction).²⁴ These changes with heart rate result in a significant change in the diastolic filling pattern.

Study limitations

The JHS cohort is all AA therefore the findings in our study may not be generalizable to other ethnic populations. Although echocardiography is a useful and widely accepted diagnostic tool to assess diastology in the clinical setting, there are limitations to its specificity and reproducibility.¹ Assessment of diastolic function ideally requires invasive measurements. Indeed, cardiac catheterization is the gold standard to directly measure filling pressures and rate of LV relaxation.¹ In our participants, we could not justify the use of invasive methods for the assessment of active and passive diastolic LV properties. There are risks to invasive measuring and echocardiography represents an excellent noninvasive alternative to semiquantitatively estimate the hemodynamics of diastolic function.

Because of the number of exclusions due to missing covariates and missing diastolic function parameters, there were significant differences in age, blood pressure, and BMI in those included compared to those excluded in the analysis. Therefore, there may be selection bias introduced as a result of our study population being older, more hypertensive, and with lower BMI compared to the base population recruited for Examination 1.

In addition, because of concerns of participant burden and time restraint, newer less preload dependent technology including tissue Doppler for annular velocity and strain rate imaging was not used in our population. It is unclear how use of these tools to further identify diastolic abnormalities in our cohort may affect the results of our study.

Clinical implications

There is evidence that DD contributes to cardiovascular morbidity and mortality independent of systolic function. The morbidity and hospitalization associated with acute heart failure related to LV DD and LV systolic dysfunction are similar and combined account for an estimated cost of \$40 billion per year. Greater than 50% of those presenting with heart failure have normal ejection fraction and this subset of patients are more often elderly; women; AA; hypertensive; diabetic; and more often with LV hypertrophy, coronary artery disease, and renal failure. Interestingly in our population-based cohort, DD is related to male sex. Although no prevalent information on heart failure is available for the current investigation, we will be able to track the development of heart failure in participants over

time and thereby better gauge the clinical relevance in our cohort in future longitudinal studies.

Particularly for AA, the prevalence of hypertension, LV hypertrophy, and coronary artery disease is higher than in other ethnic populations. Our findings suggest that the prevalence of DD is high in AA and this prevalence may be partly due to the large number of individuals with risk factors for heart disease. Those with overt heart disease (defined as low ejection fraction and history of MI) are at greatest risk for severe diastolic dysfunction in this group underlying the importance of risk factor control and prevention.

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References

1. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. *J Am Coll Cardiol.* 1997; 30:8–18. [PubMed: 9207615]
2. Devereux RB, Roman MJ, Paranicas M, et al. A population-based assessment of left ventricular systolic dysfunction in middle-aged and older adults: the Strong Heart Study. *Am Heart J.* 2001; 141:439–46. [PubMed: 11231443]
3. Redfield MM, Jacobsen SJ, Burnett JC Jr, et al. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA.* 2003; 289:194–202. [PubMed: 12517230]
4. Fischer M, Baessler A, Hense HW, et al. Prevalence of left ventricular diastolic dysfunction in the community. Results from a Doppler echocardiographic-based survey of a population sample. *Eur Heart J.* 2003; 24:320–8. [PubMed: 12581679]
5. Vasan RS, Larson MG, Benjamin EJ, et al. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. *J Am Coll Cardiol.* 1999; 33:1948–55. [PubMed: 10362198]
6. Taylor HA Jr, Wilson JG, Jones DW, et al. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis.* 2005; 15:S6–S17.
7. Fuqua SR, Wyatt SB, Andrew ME, et al. Recruiting African-American research participation in the Jackson Heart Study: methods, response rates, and sample description. *Ethn Dis.* 2005; 15:S6–S29. [PubMed: 16317982]
8. Sahn DJ, DeMaria A, Kisslo J, et al. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation.* 1978; 58:1072–83. [PubMed: 709763]
9. Appleton CP, Jensen JL, Hatle LK, et al. Doppler evaluation of left and right ventricular diastolic function: a technical guide for obtaining optimal flow velocity recordings. *J Am Soc Echocardiogr.* 1997; 10:271–92. [PubMed: 9109692]
10. Rakowski H, Appleton C, Chan KL, et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the Investigators of Consensus on Diastolic Dysfunction by Echocardiography. *J Am Soc Echocardiogr.* 1996; 9:736–60. [PubMed: 8887883]
11. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol.* 1986; 57:450–8. [PubMed: 2936235]
12. Fox ER, Han H, Taylor HA, et al. The prognostic value of the mitral diastolic filling velocity ratio for all-cause mortality and cardiovascular morbidity in African Americans: the Atherosclerotic Risks in Communities (ARIC) study. *Am Heart J.* 2006; 152:749–55. [PubMed: 16996852]

13. Vasan RS, Larson MG, Aragam J, et al. Genome-wide association of echocardiographic dimensions, brachial artery endothelial function and treadmill exercise responses in the Framingham Heart Study. *BMC Med Genet.* 2007; 8(Suppl 1):S2. [PubMed: 17903301]
14. Tang W, Arnett DK, Devereux RB, et al. Sibling resemblance for left ventricular structure, contractility, and diastolic filling. *Hypertension.* 2002; 40:233–8. [PubMed: 12215459]
15. Tang W, Arnett DK, Devereux RB, et al. Linkage of left ventricular early diastolic peak filling velocity to chromosome 5 in hypertensive African Americans: the HyperGEN echocardiography study. *Am J Hypertens.* 2002; 15:621–7. [PubMed: 12118910]
16. Fox ER, Taylor J, Taylor H, et al. Left ventricular geometric patterns in the Jackson cohort of the Atherosclerotic Risk in Communities (ARIC) Study: clinical correlates and influences on systolic and diastolic dysfunction. *Am Heart J.* 2007; 153:238–44. [PubMed: 17239683]
17. Benjamin EJ, Levy D, Anderson KM, et al. Determinants of Doppler indexes of left ventricular diastolic function in normal subjects (the Framingham Heart Study). *Am J Cardiol.* 1992; 70:508–15. [PubMed: 1642190]
18. Bild DE, Fitzpatrick A, Fried LP, et al. Age-related trends in cardiovascular morbidity and physical functioning in the elderly: the Cardiovascular Health Study. *J Am Geriatr Soc.* 1993; 41:1047–56. [PubMed: 8409149]
19. Bella JN, Palmieri V, Roman MJ, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults: the Strong Heart Study. *Circulation.* 2002; 105:1928–33. [PubMed: 11997279]
20. Spirito P, Maron BJ. Doppler echocardiography for assessing left ventricular diastolic function. *Ann Intern Med.* 1988; 109:122–6. [PubMed: 3289430]
21. Gerstenblith G, Frederiksen J, Yin FC, et al. Echocardiographic assessment of a normal adult aging population. *Circulation.* 1977; 56:273–8. [PubMed: 872321]
22. Slama M, Susic D, Varagic J, et al. Diastolic dysfunction in hypertension. *Curr Opin Cardiol.* 2002; 17:368–73. [PubMed: 12151871]
23. Lewis JF, Spirito P, Pelliccia A, et al. Usefulness of Doppler echocardiographic assessment of diastolic filling in distinguishing “athlete’s heart” from hypertrophic cardiomyopathy. *Br Heart J.* 1992; 68:296–300. [PubMed: 1389762]
24. Colan SD. Mechanics of left ventricular systolic and diastolic function in physiologic hypertrophy of the athlete’s heart. *Cardiol Clin.* 1997; 15:355–72. [PubMed: 9276162]

Figure 1. Age- and sex-specific distribution of diastolic dysfunction in the study population. *Values represent percentages in each category of diastolic dysfunction.

Table 1

Description of clinical characteristics for each diastolic function category in the JHS study population

Clinical characteristics	Diastolic dysfunction categories			
	n (no. per category)			
	None n = 2515	Mild n = 644	Moderate n = 379	Severe n = 33
Age (mean $\pm$ SD)	55 $\pm$ 11	64 $\pm$ 11	50 $\pm$ 12	43 $\pm$ 14
% Female	66.2	64	49.9	48.5
% Ejection fraction <50% [*]	6.1	10.3	7.9	21.2
% Hypertension	64.2	81.5	50.7	33.3
% Diabetes mellitus	19.4	22.8	13.2	3.0
% Myocardial infarction	5.0	8.3	4.0	12.1
% Left atrial diameter ≥ 4.0 [†] cm	78.5	81.5	87.3	93.9
% Current smoker	13.2	12	12.1	12.1
% Renal Impairment (e-GFR <60)	5.6	12.3	2.6	9.1
% (β -Blocker therapy (%))	12.6	13.8	7.7	12.1
Ejection fraction (% [mean $\pm$ SD])	62.5 $\pm$ 7.2	61.1 $\pm$ 8.8	61.4 $\pm$ 6.7	60.0 $\pm$ 13.0
Left atrial diameter (cm [mean $\pm$ SD]) [†]	3.6 $\pm$ 0.4	3.6 $\pm$ 0.5	3.6 $\pm$ 0.4	3.9 $\pm$ 0.7
Body mass index (mean $\pm$ SD)	32 $\pm$ 7	31 $\pm$ 6	31 $\pm$ 7	31 $\pm$ 7
Total cholesterol/high-density lipoprotein (mean $\pm$ SD)	4.1 $\pm$ 1.3	4.1 $\pm$ 1.2	4.2 $\pm$ 1.4	4.3 $\pm$ 1.8
Low density lipoprotein (mean $\pm$ SD)	126 $\pm$ 36	126 $\pm$ 36	127 $\pm$ 35	117 $\pm$ 39
Triglycerides (mean $\pm$ SD)	111 $\pm$ 84	116 $\pm$ 69	102 $\pm$ 60	86 $\pm$ 45
Heart rate (in 30 s) (mean $\pm$ SD)	34 $\pm$ 5	35 $\pm$ 5	34 $\pm$ 5	33 $\pm$ 5
Left ventricular mass (mean $\pm$ SD)	147 $\pm$ 39	163 $\pm$ 44	147 $\pm$ 37	164 $\pm$ 62
Left ventricular mass index/ht ^{2.7} (mean $\pm$ SD) [*]	36 $\pm$ 9	40 $\pm$ 11	35 $\pm$ 9	37 $\pm$ 11
Relative wall thickness (mean $\pm$ SD) [*]	0.35 $\pm$ 0.1	0.37 $\pm$ 0.1	0.34 $\pm$ 0.1	0.34 $\pm$ 0.1

e-GFR, Estimated glomerular filtration rate.

^{*} n = 2420.

[†] n = 2861.

Table II

Relation of clinical and echocardiographic characteristics to diastolic dysfunction

Characteristics	Diastolic dysfunction categories				P
	Normal	Mild	Moderate	Severe	
Sex					<.0001
Men	849 (65.9)	232 (18.0)	190 (14.8)	17 (1.3)	
Women	1666 (73.0)	412 (18.1)	189 (8.3)	16 (0.7)	
Age (y)					<.0001
<45	501 (71.3)	39 (5.6)	144 (20.5)	19 (2.7)	
45-64	1465 (75.2)	283 (14.5)	188 (9.7)	12 (0.6)	
≥65	549 (60.0)	322 (35.0)	47 (5.1)	2 (0.2)	
Hypertension					<.0001
No	901 (73.3)	119 (9.7)	187 (15.2)	22 (1.8)	
Yes	1614 (68.9)	525 (22.4)	192 (8.2)	11 (0.5)	
Diabetes					.0002
No	2027 (70.3)	497 (17.2)	329 (11.4)	32 (1.1)	
Yes	488 (71.1)	147 (21.4)	50 (7.3)	1 (0.2)	
Myocardial Infarction					.0016
No	2375 (70.8)	589 (17.6)	364 (10.8)	29 (0.9)	
Yes	124 (63.3)	53 (27.0)	15 (7.7)	4 (2.0)	
Body mass index (kg/m ²)					<.0001
<25	304 (65.8)	90 (19.5)	59 (12.8)	9 (2.0)	
~30	736 (65.2)	238 (21.1)	146 (12.9)	9 (0.8)	
≥30	1475 (74.5)	316 (16.0)	174 (8.8)	15 (0.8)	
Left atrial diameter					<.0001
<4.0 cm	541 (21.5)	119 (18.5)	48 (12.7)	2 (6.1)	
≥4.0 cm	1974 (78.5)	525 (81.5)	331 (87.3)	31 (93.9)	
Smoking					NS
No	2184 (70.2)	567 (18.2)	333 (10.7)	29 (0.9)	
Yes	331 (72.3)	77 (16.8)	46 (10.0)	4 (0.9)	
LV mass index (height ^{2.7})*					<.0001

Characteristics	Diastolic dysfunction categories				P
	Normal	Mild	Moderate	Severe	
$\geq 51 \text{ g/m}^2.7^*$	123 (64.4)	52 (27.2)	13 (6.8)	3 (1.6)	
$< 51 \text{ g/m}^2.7^*$	1580 (70.9)	325 (14.6)	298 (13.4)	26 (1.2)	
RWT [*]					<.0001
$\geq .45$	102 (64.6)	46 (29.1)	9 (5.7)	1 (0.6)	
$< .45^*$	1601 (70.8)	331 (14.6)	302 (13.4)	28 (1.2)	
Ejection fraction					<.0001
> 50	2362 (71.3)	578 (17.4)	349 (10.5)	26 (0.8)	
≤ 50	153 (59.8)	66 (25.8)	30 (7.3)	7 (0.8)	

Values in table represent the number and percentages within each dichotomized subgroup.

*
n = 2420.

Table III

Models of the presence and severity of diastolic dysfunction in the JHS population

	Prevalence: Predicting Diastolic Dysfunction (abnormal vs normal)			Severity: Predicting Severity of Abnormality (severe or moderate vs mild)		
	Univariate association	Multivariable association	Most parsimonious model	Univariate association	Multivariable association	Most parsimonious model
Age (y) (1 SD change)	1.28 (1.18-1.37)	1.24 (1.14-1.35)	1.29 (1.10-1.50)	0.29 (0.24-0.34)	0.30 (0.25-0.36)	0.30 (0.25-0.36)
Male sex	1.40 (1.21-1.62)	1.29 (1.09-1.52)	1.31 (1.12-1.53)	1.79 (1.40-2.31)	1.60 (1.16-2.21)	1.43 (1.05-2.00)
Ejection fraction b50%	1.67 (1.29-2.17)	1.54 (1.18-2.02)	1.58 (1.21-2.06)	0.86 (0.57-1.32)	0.98 (0.48-1.36)	
Ejection fraction (%)	0.83 (0.77-0.89)	0.85 (0.76-0.89)	0.85 (0.79-0.91)	1.00 (0.89-1.12)	1.07 (0.92-1.24)	
Hypertension	1.24 (1.06-1.45)	1.11 (0.94-1.32)		0.22 (0.17-0.29)	0.55 (0.38-0.79)	0.57 (0.40-0.80)
Diabetes	0.96 (0.80-1.15)	0.86 (0.71-1.06)		0.48 (0.34-0.68)	1.14 (0.75-1.75)	
Myocardial infarction	1.40 (1.04-1.90)	1.17 (0.85-1.60)		0.54 (0.31-0.92)	1.06 (0.58, 1.95)	
Current smoker	0.90 (0.73-1.12)	0.85 (0.68-1.07)		1.02 (0.70- 1.49)	0.64 (0.40- 1.00)	0.63 (0.40-0.99)
BMI (1 SD change)	0.79 (0.73-0.86)	0.82 (0.75- 0.89)	0.83 (0.76-0.90)	0.96 (0.84-1.10)	1.02 (0.86-1.22)	
Total cholesterol:HDL ratio (1 SD change)	1.02 (0.95-1.09)	1.06 (0.94-1.21)		1.11 (0.98-1.26)	1.02 (0. 78-1.33)	
LDL (1 SD change)	0.99 (0.92-1.07)	0.95 (0.85-1.05)		1.02 (0.90-1.15)	1.04 (0.84-1.29)	
Triglycerides (1 SD change)	0.99 (0.92-1.06)	0.96 (0.84-1.09)		0.73 (0.61-0.87)	1.05 (0.79-1.38)	
Heart rate (1 SD change)	1.09 (1.02-1.17)	1.15 (1.07-1.24)	1.14 (1.06, 1.23)	0.74 (0.66-0.84)	0.66 (0.56-0.77)	0.67 (0.57-0.78)
β-Blocker therapy (%)	1.09 (1.02-1.17)	0.77 (0.60-0.99)		0.54 (0.36-0.83)	1.09 (0.65-1.81)	

The 1 SD change for age is 12.2 years; for BMI, 7.1kg/m²; for ejection fraction, 7.6%; for total cholesterol:HDL ratio, 1.3 mg/dL; for LDL, 36.1 mg/dL; and for heart rate, is 10 beats/30 seconds.

Boldface items are considered statistically significant ($P < .05$).

HDL, High-density lipoprotein; LDL, low-density lipoprotein.