Supplemental Material
SUPPLEMENTAL METHODS

Data Collection & Clinical Covariates

Detailed descriptions of data collection, methodology, specimen collection and processing have been previously described.\(^1\,^2\) Age, sex, and education level were obtained by self-report using standardized interviewer-administered questionnaires. Current smoking was defined by affirmative responses to the questions “Have you smoked more than 400 cigarettes in your lifetime?” and “Do you now smoke cigarettes?” Antihypertensive medication use in the two weeks prior to the study visit was self-reported. Participants were asked to bring any medications taken within 2 weeks prior to the baseline examination to the clinic visit and were transcribed verbatim. Medication coding was performed by a pharmacist using the Medispan dictionary and classified into categories according to the Therapeutic Classification System. The number of medications were also recorded. Alcohol consumption was categorized None (no drinks per week), Moderate (1-7 drinks per week for women and 1-14 drinks per week for men), or Heavy (≥8 drinks per week for women or ≥14 drinks per week for men). Using a modified Baecke questionnaire, validated in the Jackson Heart Study (JHS) using pedometers and accelerometers, the weekly duration and annual frequency of participation in sports/exercises during the previous year were recorded and summed to calculate the total number of minutes per week spent in moderate or vigorous physical activity.\(^3\,^4\) Physical activity was categorized according to American Heart
Association Life’s Simple 7 categories: Poor (0 mins of moderate physical activity and 0 minutes of vigorous physical activity), Intermediate (1-149 minutes of moderate physical activity or 1-74 minutes of vigorous physical activity or 1-149 minutes of combined moderate and vigorous physical activity), and Ideal (≥150 minutes of moderate physical activity or ≥75 minutes of vigorous physical activity or ≥150 minutes of combined moderate and vigorous physical activity).^5^ Height, weight, and blood pressure were measured and blood samples were collected by trained staff during the study visit. Body mass index was calculated as weight in kilograms divided by height in meters squared. Total and high-density lipoprotein cholesterol were quantified by an oxidase method.^1^ Serum glucose was measured using a glucose oxidase method on a Vitros 250 or 950, Ortho-Clinical Diagnostics analyzer.^1^ Hemoglobin A1c was measured using a TOSOH high performance liquid chromatography system. Diabetes was defined as a fasting (≥8 hours) serum glucose ≥126 mg/dL or hemoglobin A1c ≥6.5% or self-reported use of insulin or oral hypoglycemic medications within 2 weeks prior to the study visit. Serum creatinine was measured using a multi-point enzymatic spectrophotometric assay on a Vitros 950 Ortho-Clinical Diagnostic analyzer.

Blood pressure was measured according to a standardized protocol. Participants were asked to avoid heavy physical activity, caffeine, eating, smoking and alcohol intake for 12 hours prior to their study visit. Two blood pressure measurements were obtained using an appropriately sized cuff, determined from a measurement of arm circumference, and a random-zero sphygmomanometer (Hawksley and Sons Ltd).^6^,^7^ Participants were seated in an upright position with their back and arms supported, feet flat on the floor and legs uncrossed for at least five minutes after which trained staff
conducted the two blood pressure measurements, separated by one minute, in the right arm. The average of these two blood pressure measurements was used as the reported blood pressure. As previously described, random-zero blood pressure measurements were calibrated to an oscillometric device using robust regression.\textsuperscript{8} Pulse pressure was defined as the difference between average systolic blood pressure and average diastolic blood pressure.

**Outcomes**

Detailed description of cardiovascular disease (CVD) and all-cause mortality event adjudication have been previously described.\textsuperscript{9} JHS participants or their proxies were contacted annually via telephone to assess potential CVD events and vital status. Hospital discharge lists with specific diagnosis criteria were also obtained from the Jackson, Mississippi, tri-county area hospitals. Death certificates were requested from the Mississippi State Department of Health for JHS participants as needed. When a potential CVD-related hospitalization or death was identified, medical records were retrieved and abstracted. Trained clinicians adjudicated events following published guidelines using the information available about the circumstance surrounding each event.\textsuperscript{9}
Table S1. Percentage of missing data among Jackson Heart Study participants included in the analytic sample.

| Variable                          | N (%)     |
|----------------------------------|-----------|
| Age                              | 0 (0)     |
| Sex                              | 0 (0)     |
| Body mass index                  | 0 (0)     |
| Diabetes                         | 44 (0.99) |
| eGFR                             | 69 (1.56) |
| HDL cholesterol                  | 369 (8.34)|
| Total cholesterol                | 368 (8.32)|
| Education                        | 17 (0.38) |
| Smoking status                   | 0 (0)     |
| Physical activity category       | 3 (0.07)  |
| Alcohol use                      | 0 (0)     |
| Systolic blood pressure          | 14 (0.32) |
| Diastolic blood pressure         | 14 (0.32) |
| Antihypertensive medication use  | 82 (1.85) |

eGFR: Estimated glomerular filtration rate
HDL: High-density lipoprotein
Table S2. Echocardiographic parameters of Jackson Heart Study participants with appropriate and inappropriate left ventricular mass.

|                           | Overall Sample (n = 4,424) | aLVM (n = 3,815) | iLVM (n = 609) | p-value* |
|---------------------------|-----------------------------|------------------|----------------|----------|
| Stroke work, g-m          | 137.10 (35.90)              | 137.70 (35.25)   | 133.50 (39.53) | 0.015    |
| Stroke volume, mL         | 75.08 (16.42)               | 75.41 (16.01)    | 73.02 (18.66)  | 0.003    |
| Fractional shortening, %  | 4.93                        | 3.44             | 17.45          | <0.001   |
| Interventricular septum   | 0.88 (0.14)                 | 0.86 (0.12)      | 1.08 (0.16)    | <0.001   |
| thickness in diastole, cm | 0.84 (0.13)                 | 0.82 (0.11)      | 1.03 (0.15)    | <0.001   |
| Posterior wall thickness in diastole, cm | 0.84 (0.13) | 0.82 (0.11) | 1.03 (0.15) | <0.001 |
| RWT                       | 0.36 (0.07)                 | 0.35 (0.06)      | 0.44 (0.09)    | <0.001   |
| Left ventricular end-     | 4.84 (0.45)                 | 4.82 (0.42)      | 4.96 (0.59)    | <0.001   |
| diastolic diameter, cm    |                            |                  |                |          |
| Left ventricular end-systolic diameter, cm | 2.98 (0.47) | 2.94 (0.41) | 3.25 (0.69) | <0.001 |

The numbers in the table are mean ± standard deviation.

aLVM: Appropriate left ventricular mass; iLVM: Inappropriate left ventricular mass

Relative wall thickness (RWT) was calculated using the ASE formula; RWT = 2 x posterior wall thickness in diastole/left ventricular internal dimension in diastole. Increased RWT is defined as RWT >0.42. Normal RWT is defined as RWT ≤0.42
Table S3. Characteristics of the Jackson Heart Study participants included in the analytic sample by left ventricular mass (LVM) status for participants without left ventricular hypertrophy (LVH, left) and with LVH (right).

|                        | Without LVH (N=3,807) | With LVH (N=617) |
|------------------------|-----------------------|------------------|
|                        | aLVM (N= 3,559)       | iLVM (N= 248)    |
| Age, years             | 53.41 (12.60)         | 55.11 (12.39)    | 60.77 (11.38) | 60.11 (11.47) |
| Female, %              | 62.66                 | 64.11            | 87.89         | 71.75         | <0.001 |
| Body mass index, kg/m² | 31.18 (6.84)          | 33.61 (6.95)     | 35.73 (7.79)  | 35.37 (8.53)  | 0.592  |
| Education < high school, % | 16.09                 | 19.35            | 30.86         | 26.39         | 0.225  |
| Current smoking, %     | 11.97                 | 10.89            | 10.94         | 14.40         | 0.207  |
| Physical activity category |                        |                  | 0.207  |
| Ideal                  | 46.20                 | 50.81            | 55.08         | 56.23         | 0.950  |
| Intermediate           | 32.90                 | 32.26            | 28.91         | 28.53         |        |
| Poor                   | 20.89                 | 16.94            | 16.02         | 15.24         |        |
| Alcohol use, %         |                        |                  | 0.270  |
| Non-drinker            | 61.87                 | 66.53            | 73.83         | 75.07         |        |
| Moderate drinker       | 34.34                 | 31.05            | 24.22         | 24.38         |        |
|                          | 0          | 1          |    |    |    |
|--------------------------|------------|------------|----|----|----|
| Heavy drinker            | 3.79       | 2.42       | 1.95 | 0.55 |
| Diabetes, %              | 18.36      | 27.53      | <0.001 | 26.29 | 33.52 | 0.057 |
| eGFR <60 ml/min/m², %    | 5.82       | 9.72       | 0.013 | 16.87 | 17.18 | 0.919 |
| HDL cholesterol, mg/dL   | 51.87 (14.49) | 48.43 (12.93) | <0.001 | 54.51 (15.71) | 53.21 (15.05) | 0.325 |
| Total cholesterol, mg/dL | 199.30 (39.10) | 197.90 (43.00) | 0.627 | 204.00 (42.18) | 201.30 (42.57) | 0.458 |
| SBP, mmHg                | 125.50 (15.17) | 119.80 (15.10) | <0.001 | 141.00 (19.45) | 132.00 (18.82) | <0.001 |
| DBP, mmHg                | 75.81 (8.35) | 73.38 (8.71) | <0.001 | 77.42 (8.70) | 75.57 (10.54) | 0.018 |
| Pulse Pressure, mmHg     | 49.72 (13.04) | 46.38 (12.37) | <0.001 | 63.61 (18.53) | 56.42 (15.04) | <0.001 |
| Prevalent hypertension, %| 49.46      | 59.84      | 0.002 | 84.96 | 78.20 | 0.039 |
| Antihypertensive medication use, % | 42.81      | 56.15      | <0.001 | 70.00 | 71.80 | 0.633 |
| Number of antihypertensive medication classes | 56.53 | 43.15 | <0.001 | 30.47 | 30.19 | 0.330 |
|                          | 18.07      | 18.95      | 25.00 | 20.78 |
|                | 2     | 3+    | 22.27 | 28.25 | 22.27 | 20.78 |
|----------------|-------|-------|-------|-------|-------|-------|
| LVM, g         | 16.91 | 24.60 | 22.27 | 28.25 |
| LVMI, g/m²⁷    | 8.49  | 13.31 | 22.27 | 20.78 |
| Mean ejection fraction, % | 136.40 (28.79) | 173.10 (32.59) | 189.30 (34.27) | 228.30 (53.27) | <0.001 |
| Ejection fraction ≤ 40%, % | 32.80 (5.94) | 40.43 (4.23) | 51.42 (7.06) | 58.06 (10.72) | <0.001 |
| Stroke work, g-m | 62.01 (6.76) | 60.22 (7.75) | 64.32 (7.70) | 60.42 (10.16) | <0.001 |
| Stroke volume, mL | 0.23 | 1.22 | 0.030 | 0.78 | 4.46 | 0.007 |
| Fractional shortening, % | 134.00 (32.02) | 109.30 (23.90) | 188.80 (38.90) | 150.10 (39.61) | <0.001 |
| Interventricular septum thickness in diastole, cm | 74.14 (15.08) | 63.99 (14.26) | 93.11 (17.93) | 79.22 (18.81) | <0.001 |
| Posterior wall thickness in diastole, cm | 3.38 | 18.84 | 4.38 | 16.39 | <0.001 |
| RWT            | 0.85 (0.11) | 1.03 (0.14) | 0.98 (0.12) | 1.13 (0.16) | <0.001 |
|                | 0.81 (0.11) | 0.97 (0.13) | 0.93 (0.11) | 1.07 (0.15) | <0.001 |
|                | 0.35 (0.06) | 0.43 (0.07) | 0.37 (0.07) | 0.44 (0.10) | <0.001 |
|                                | Value 1       | Value 2       | p-value | Value 3       | Value 4       | p-value |
|--------------------------------|---------------|---------------|---------|---------------|---------------|---------|
| Left ventricular end-diastolic diameter, cm | 4.79 (0.40)  | 4.73 (0.43)  | 0.024   | 5.21 (0.45)  | 5.12 (0.63)  | 0.046   |
| Left ventricular end-systolic diameter, cm  | 2.93 (0.41)  | 3.16 (0.50)  | <0.001  | 3.06 (0.50)  | 3.31 (0.78)  | <0.001  |
| Eccentric Hypertrophy, %               | --            | --            | ---     | 83.20         | 43.21         | <0.001  |
| Concentric Hypertrophy, %              | --            | --            | ---     | 16.80         | 56.79         | <0.001  |

The numbers in the table are mean ± standard deviation or percentages.
*p-value comparing aLVM and iLVM

Left Ventricular Hypertrophy (LVH) is defined as LVM index (LVMI) ≥45 g/m².7 in females and ≥49 g/m².7 in males
LVMI is calculated as LVM/height².7
Relative wall thickness (RWT) was calculated using the American Society of Echocardiography formula; RWT = 2 x posterior wall thickness in diastole/left ventricular internal dimension in diastole.
Increased RWT is defined as RWT >0.42. Normal RWT is defined as RWT ≤0.42
Eccentric Hypertrophy is defined as: LVH and normal Relative wall thickness
Concentric Hypertrophy is defined as: LVH and increased Relative wall thickness

aLVM: Appropriate left ventricular mass
iLVM: Inappropriate left ventricular mass
eGFR: Estimated glomerular filtration rate
HDL: High-density lipoprotein
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
LVM: Left ventricular mass
Table S4. Hazard ratios for cardiovascular disease events associated with an observed-to-predicted LVM ratio, modeled as a continuous variable, in the overall analytic sample and among participants without and with left ventricular hypertrophy.

| CVD events / n at risk | Hazard Ratios (95% CI) per one SD higher observed-to-predicted LVM ratio |
|------------------------|---------------------------------------------------------------|
|                        | Model 1 | Model 2 | Model 3 | Model 4 |
| Overall (N=4,424)      |         |         |         |         |
| 262 / 4424             | 1.35 (1.25 – 1.45) | 1.29 (1.19 – 1.40) | 1.31 (1.21 – 1.42) | 1.28 (1.16 – 1.43) |
| Without LVH (N=3,807)  |         |         |         |         |
| 184 / 3807             | 1.64 (1.37 – 1.96) | 1.52 (1.28 – 1.82) | 1.60 (1.34 – 1.91) | # |
| With LVH (N=617)       |         |         |         |         |
| 78 / 617               | 1.11 (0.96 – 1.29) | 1.05 (0.90 – 1.23) | 1.16 (0.99 – 1.37) | # |

CVD: Cardiovascular disease  
CI: Confidence Interval  
LVM: Left ventricular mass  
SD: Standard deviation. 1 SD = 0.235 = 23.5%  
LVH: Left ventricular hypertrophy  
Model 1: Adjusted for age, sex, and body mass index  
Model 2: Adjusted for the variables in Model 1 and diabetes, estimated glomerular filtration rate < 60 ml/min/1.73m², education level (less than high school), current smoking, physical activity, and alcohol use (none, moderate, heavy)  
Model 3: Adjusted for the variables in Model 2 and mean systolic blood pressure, mean diastolic blood pressure, and antihypertensive medication use  
Model 4: Adjusted for the variables in Model 3 and left ventricular hypertrophy  
# Model 4 was not performed as these analyses are stratified by left ventricular hypertrophy status  
The test for interaction between LVH and iLVM for CVD events had a $P_{interaction} = 0.004$ (on Model 4)
Table S5. Hazard ratios for all-cause mortality associated with observed-to-predicted LVM ratio, modeled as a continuous variable in the overall analytic sample and among participants without and with left ventricular hypertrophy.

|                  | Deaths / n at risk | Model 1 (Hazard Ratio) | Model 2 (Hazard Ratio) | Model 3 (Hazard Ratio) | Model 4 (Hazard Ratio) |
|------------------|--------------------|------------------------|------------------------|------------------------|------------------------|
| Overall (N=4,424)| 419 / 4424         | 1.26 (1.18 – 1.35)     | 1.21 (1.13 – 1.30)     | 1.24 (1.15 – 1.33)     | 1.18 (1.08 – 1.29)     |
| Without LVH (N=3,807) | 288 / 3807     | 1.12 (0.95 – 1.31)     | 1.06 (0.90 – 1.24)     | 1.14 (0.97 – 1.34)     | #                      |
| With LVH (N=617)  | 131 / 617          | 1.17 (1.05 – 1.30)     | 1.12 (1.00 – 1.25)     | 1.17 (1.05 – 1.32)     | #                      |

CI: Confidence Interval  
LVM: Left ventricular mass  
SD: Standard deviation. 1 SD = 0.235 = 23.5%  
LVH: Left ventricular hypertrophy

Model 1: Adjusted for age, sex, and body mass index  
Model 2: Adjusted for the variables in Model 1 and diabetes, estimated glomerular filtration rate < 60 ml/min/1.73m², education level (less than high school), current smoking, physical activity, and alcohol use (none, moderate, heavy)  
Model 3: Adjusted for the variables in Model 2 and mean systolic blood pressure, mean diastolic blood pressure, and antihypertensive medication use  
Model 4: Adjusted for the variables in Model 3 and left ventricular hypertrophy  
# Model 4 was not performed as these analyses are stratified by left ventricular hypertrophy status

The test for interaction between LVH and iLVM for all-cause mortality had a $P_{interaction} = 0.534$ (on Model 4)
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