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Relations of Left Ventricular Mass and Hypertrophy to Cognitive Function in Urban Dwelling African American and White Adults

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Objective: Evaluate the relations of left ventricular mass (LVM) and left ventricular hypertrophy (LVH) to cognitive function in midlife adults and examine potential moderating influences of self-identified race and poverty status. ***Method:*** Participants were 1,107 African American and White urban-dwelling adults (M_{age} = 52.19, 60.4% female, 56.5% African American, 34% below 125% of the poverty line) from the Healthy Aging in Neighborhoods of Diversity across the Life Span study. Multivariable linear regressions examined up to three-way interactions of LVM (and LVH), race, and poverty status to tests of attention, memory, executive function, verbal abilities, and perceptuo-motor speed. Covariates included demographic variables and cardiovascular disease risk factors. ***Results:*** There were no significant three- or two-way interactions of LVM (or LVH), race, or poverty status for any cognitive outcome. Backward elimination identified significant main effects of LVM on the Brief Test of Attention ($\beta = -0.089$, $p = .010$) and Trails Making Test (TMT)-B ($\beta = 0.072$, $p = .021$). Main effects of LVH were significant for the Brief Test of Attention ($\beta = -0.075$, $p = .017$), TMT-B ($\beta = 0.071$, $p = .012$), TMT-A ($\beta = 0.078$, $p = .009$), and Verbal Fluency ($\beta = -0.067$, $p = .027$). Both LVM and LVH were negatively associated with performance. ***Conclusions:*** In the presence of nonsignificant interactions, those with higher LVM (and LVH) displayed poorer performance on tests of divided attention, executive function, semantic verbal fluency, and perceptuo-motor speed. Findings may reflect the early emergence of neurocognitive changes associated with elevated cardiovascular risk in this largely middle-aged sample.

Key Points

Question: What is the relation of left ventricular mass/hypertrophy to cognitive function in midlife adults, and how do self-identified race and poverty status moderate that relationship? ***Findings:*** Despite nonsignificant interactions, greater left ventricular mass and presence of left ventricular hypertrophy were associated with lower performance in the domains of divided attention, executive function, semantic verbal fluency, and perceptuo-motor speed. ***Importance:*** Results indicate the effects elevated left ventricular mass and left ventricular hypertrophy are related to poorer cognitive function in several domains of function which may reflect early cognitive decline due to subclinical cardiovascular disease. ***Next Steps:*** Future work should continue to examine risks factors for accelerated cognitive aging in racially and socioeconomically diverse populations and potential mediating neurobiological changes.

Keywords: left ventricular mass, left ventricular hypertrophy, cognitive function, neuropsychology, health disparities

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After reaching a point of neurobiological and cognitive maturation, a gradual cognitive decline is often observed within individuals as they age (Anstey et al., 1993; Harada et al., 2013; Jefferson et al., 2015; Waldstein et al., 2010). Although select dimensions of cognitive performance such as vocabulary and crystallized intelligence may improve with age, domains like conceptual reasoning, memory, and processing speed tend to decline with age (Harada et al., 2013). The rate at which this decline occurs is as heterogeneous as the factors that influence these domains (Anstey et al., 1993; Jefferson et al., 2015; Waldstein et al., 2010). This is, at least in part, because aging can be divided into two distinct categories: primary and secondary aging. Primary aging involves the innate maturational processes of an individual whereas secondary aging includes the effects of environment and disease (Anstey et al., 1993). Multiple cardiovascular disease (CVD) risk factors negatively affect levels of cognitive function and trajectories of cognitive decline; they also play a role in vascular dementia (VaD) and Alzheimer's dementia (AD) pathogenesis (Waldstein & Elias, 2015). Indeed, the literature suggests the mechanisms that lead to CVD overlap with the mechanisms that influence cognitive decline and dementia (Gorelick et al., 2011). Furthermore, it appears that neurobiological and neurocognitive functional status and impairment lie on a spectrum that is associated with increasingly severe CVD manifestations across the lifespan (Jefferson et al., 2015; Waldstein et al., 2010).

With the advent of noninvasive imaging techniques and greater availability of affordable technology, it has been found that various forms of subclinical CVD—which are forms of disease intermediate to CVD risk factors and clinical CVD—are similarly associated with neuroanatomy, neurocognitive function, and impairment. Although much is known about the relations of cognitive function to select measures of subclinical CVD such as carotid intimal medial thickening which, in part, reflects carotid atherosclerosis, and pulse wave velocity which reflects arterial stiffening (W.-H. Chen et al., 2017; Palta et al., 2019; Waldstein et al., 2008; Wendell et al., 2016), relatively little is known about the relations of left ventricular mass (LVM) and left ventricular hypertrophy (LVH) with cognitive performance. As discussed below, LVM and LVH reflect distinct pathophysiological processes than these other more commonly studied measures of subclinical CVD and offer differential patterns of predictive utility for clinical CVD outcomes.

Greater LVM—a measurement of the lower left portion of the heart—predicts risk for hypertension, heart failure, and overall CVD comorbidity and mortality, and has been shown to improve CVD risk prediction when incorporated in models with traditional CVD risk factors (de Simone et al., 2008; Devereux & Alderman, 1993; Mahoney et al., 1988; Tsao et al., 2015). Higher values of LVM often progress to clinically diagnosed LVH which reflects the pathological thickening of the left ventricle and confers even greater risk for poor CVD outcomes (Devereux & Alderman, 1993; Mahoney et al., 1988). Elevated LVM and LVH can develop due to chronic strain from high blood pressure, heart conditions, or obesity (Devereux & Alderman, 1993; Mahoney et al., 1988). They are also considered sensitive biomarkers for hypertension-related end organ damage and more accurately represent cardiovascular risk from prolonged high blood pressure than single blood pressure measurements (Cameli et al., 2020; Ruilope & Schmieder, 2008). The association between LVH and other cardiovascular risk factors is strong, which ultimately compounds and predicts future incidences of disease—with hypertension, myocardial ischemia, and heart failure being the most prevalent outcomes (de Simone et al., 2008; Devereux & Alderman, 1993; Mahoney et al., 1988). Even values of LVM that are on the high-end of the normal range in normotensive children and adults can predict future elevation in blood pressure (de Simone et al., 2008; Mahoney et al., 1988). This suggests that increases in LVM early in life may be an important predictor of subsequent hypertension. In fact, the literature suggests that hypertension and LVH have a bidirectional association (de Simone et al., 2008; Devereux & Alderman, 1993; Mahoney et al., 1988).

LVH develops in two forms: concentric or eccentric, with concentric being highly associated with hypertension, mortality, and cerebral white matter disease (Patel et al., 2017; Selvetella et al., 2003; Sierra et al., 2002, 2006). Concentric hypertrophy, which is determined after calculating and indexing LVM (Devereux & Alderman, 1993; Mahoney et al., 1988), alters the amount of blood pumped by the heart, known as the left ventricular ejection fraction (LVEF). Several studies to date indicate associations between greater LVM or presence of LVH and adverse cognitive outcomes including greater risk of probable dementia (Elias et al., 2018; Moazzami et al., 2018) and lower levels of performance on various tests of cognitive function—primarily abstract reasoning, executive functioning, visual–spatial memory and organization, and verbal memory in predominantly older adults (Elias et al., 2007; Georgakis et al., 2017; Razavi et al., 2020; Restrepo et al., 2018). In fact, prior research has demonstrated significant LVM/LVH-cognition associations, independent of traditional CVD risk factors and arterial stiffness and carotid atherosclerosis, two commonly assessed forms of subclinical CVD (Scuteri et al., 2009; Zhu et al., 2023). Moreover, recent research has found that greater LVM at age 60, but not arterial stiffness or carotid atherosclerosis, was associated with poorer brain white matter integrity at age 70 (James et al., 2024). Together, these studies suggest that LVM and LVH may be particularly sensitive to risk of pathological brain changes and cognitive impairment, especially in older adults. However, to the best of our knowledge, there is little understanding of LVM/LVH-cognition associations in midlife adults. As such, more research is needed to determine whether LVM presents a risk to neurocognition at midlife or if its effects are limited to older adults. Further, to our knowledge, no prior studies have examined whether these relations vary by self-identified race and poverty status which are key dimensions of individuals' intersectional identities.

Due to various forms of structural racism, African American individuals have endured distinct hardships compared with the experience of their White counterparts. Studying the social construct of self-identified race, at least in part, provides a proxy for an amalgam of unique and chronic environmental and interpersonal stressors reflecting the experiences of a marginalized community that ultimately contributes to poorer cardiovascular health and cognitive outcomes (D. R. Williams et al., 2010). Similarly, lower socioeconomic position is another dimension of intersectional identity that confers additional marginalized status. In that regard, simultaneously belonging to more than one disenfranchised group has been shown to confer greater risk for disease onset and severity (Allana et al., 2021; McClain et al., 2022). Thus, it is important to examine whether LVM or LVH exert a disproportionately negative influence on cognitive function among those with more than one marginalized intersectional identity.

LVH and other CVD risk factors are especially prevalent in historically disenfranchised groups, particularly African American persons and those of lower SES (Drazner et al., 2005; East et al., 2003; Gump et al., 1999; Kizer et al., 2004; Lewis et al., 2020; Okwuosa et al., 2015; Rodriguez et al., 2004). Because African Americans are more prone to LVH and adverse events from CVD, it has been postulated that LVH could improve CVD risk prediction beyond the traditionally used Pooled Cohort and Framingham risk equations, particularly in African American samples (Okwuosa et al., 2015). Although LVH increased the goodness of fit in a logistic regression model (*C* statistic) at a lower interval than each of the other individual traditional CVD risk factors added to the base model, it still had demonstrably high predictive utility (Okwuosa et al., 2015). Greater risk for development of cognitive impairment has also been associated with self-identified African American race and lower SES (Unverzagt et al., 2011; Wang et al., 2023). African American adults and those of lower SES may be more vulnerable to LVH-cognition and LVM-cognition associations. This may not only be because LVH and elevated LVM are more prevalent among these groups, but also due to the potential compounding influences of disproportionate exposure to an aggregation of psychosocial and environmental risk factors that may potentiate the influences of subclinical CVD on cognitive function (R. Chen et al., 2022; Glymour & Manly, 2008). In this regard, prior research has demonstrated differential relations of select cardiovascular risk factors (e.g., blood pressure, carotid intima-media thickening) to disproportionately worse cognitive and brain health outcomes for Black than White adults, and for lower versus intermediate/higher SES individuals (Boots et al., 2020; Marcus et al., 2011; Nyquist et al., 2014; Singh-Manoux et al., 2008).

Importantly, most prior studies of LVM/LVH and cognitive function have solely used the minimental state examination (MMSE), a brief cognitive screening measure, instead of clinical neuropsychological tests. Using only the MMSE greatly limits the amount and specificity of information pertaining to LVM/LVH's association with cognitive performance. It is also unclear whether LVM/LVH-cognition relations are fully explained by comorbid CVD risk factors (e.g., hypertension, obesity). In a seminal study by Elias et al. (2007), relations of LVM and cognitive function were rendered nonsignificant after statistical adjustment for several traditional CVD risk factors; however, the sample was predominantly White and on average, had 14.6 years of education. In contrast, results of a recent meta-analysis suggest that LVH-cognitive function associations withstand CVD risk factor adjustment which indicates that additional candidate mediators should be examined (Georgakis et al., 2017). Decreased LVEF is a common consequence of both elevated LVM and LVH and has been independently associated with poor brain and cognitive outcomes (Devereux & Alderman, 1993; Hoth et al., 2010; Jefferson et al., 2011; Jerskey et al., 2009; Zuccalà et al., 1997) and were explored herein.

The present study extended the prior literature by examining the relations among LVM/LVH and cognition in midlife, leveraging assessment of several cognitive domains, and evaluating the potential moderating influence of race and poverty status on this relationship. As such, the purpose of the present study was twofold: (a) to examine the potential interactive relations of LVM (and LVH), race, and poverty status on cognitive performance within a sample of socioeconomically diverse, African American and White urban-dwelling adults while adjusting for traditional CVD risk factors; and (b) to evaluate via sensitivity analyses whether LVEF eliminated any noted relations of LVM/LVH and cognitive function. The neuropsychological battery used assessed multiple domains of function including attention, working memory, verbal learning and memory, nonverbal memory, verbal fluency, perceptuo-motor speed, and select executive functions.

We hypothesized that significant three-way interactions among LVM/LVH, race, and poverty status would reveal that the deleterious influence of LVM/LVH on cognitive function would be most pronounced among African American individuals living in poverty. In the absence of significant three-way interactions, it was posited that, after backward elimination, significant two-way interactions would reveal that negative LVM/LVH-cognition relations were most pronounced in African American persons and in those living in poverty. Next, in the absence of any significant two-way interactions, further backward elimination was expected to yield significant main effects of LVM/LVH whereby higher levels of LVM and presence of LVH would predict lower levels of cognitive function. It was posited that LVEF may partially mediate any noted relations of LVM/LVH and cognitive function.

As per the recommendations of Ward et al. (2019) and Whitfield et al. (2008) with respect to the study of health disparities, we further conducted exploratory multivariable regression analyses stratified by race, poverty status, and the intersection of race and poverty status to examine potential within-group associations.

Method

Participants

For the analysis of LVM-cognition associations, participants were 1,107 African American and White, urban-dwelling adults (M_{age} = 52.19, Min = 32.9, Max = 70.8, 60.4% female, 56.5% African American, 34% below 125% of the poverty line, Table 1) from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study. For the LVH-cognition association analysis, participants were 1,105 African American and White, urban-dwelling adults (M_{age} = 52.21, 60.5% female, 56.4% African American, 33.8% below 125% of the poverty line) from the HANDLS study. Data for the analyses derived from the third wave of the HANDLS study, which is a longitudinal epidemiological cohort study in Baltimore City aimed at better understanding the influence of sociodemographic, behavioral, and biological factors on age-related disease (Evans et al., 2010). The HANDLS study excluded participants outside the range of 30–64 years old during the first wave, if they were pregnant at the time of recruitment, within 6 months of receiving any cancer treatments, unable to provide a minimum of five data points on the HANDLS medical research vehicle (MRV), if they did not have a government issued I.D. with verifiable address, and if they were unable to provide informed consent due to severely impaired mental capacity. To examine the specific relations of LVM and LVH as markers of subclinical CVD and prevent introducing additional influences of clinical CVD on neurocognition (e.g., hypoxia associated with myocardial infarction, surgical complications during coronary artery bypass surgery), participants with a history of cardiac or carotid surgeries, myocardial infarction, coronary heart disease, peripheral arterial disease, heart failure, stroke, and transient ischemic attack were excluded from the present analyses; those with

Table 1
Overall, Race-, and Poverty Status-Stratified Sample Characteristics for Demographics and Cardiovascular Measures

	Total	African American	White		Below poverty	Above poverty	
Sample characteristic	*M* (*SD*) or %	*M* (*SD*) or %	*M* (*SD*) or %	*p*	*M* (*SD*) or %	*M* (*SD*) or %	*p*
Age (years)	52.19 (9.06)	51.87 (9.12)	52.61 (8.98)	.18	51.33 (8.61)	52.63 (9.26)	.02
Female	60.4	58.4	63.1	.12	64.4	58.4	.06
AA	56.5				64.1	52.5	<.001
PovStat (below)	34.0	38.6	28.0	<.001			
Never smoker	22.5	21.3	24.0	.30	14.9	26.4	<.001
Hypertension	52.8	58.1	46.1	<.001	54.8	51.8	.35
Diabetes	35.0	34.4	35.7	.66	34.8	35.0	.95
Years of education	12.56 (2.53)	12.46 (2.19)	12.68 (2.93)	.16	11.74 (2.25)	12.99 (2.57)	<.001
BMI (kg/m^2)	30.49 (7.64)	30.57 (7.70)	30.39 (7.57)	.69	30.15 (8.13)	30.66 (7.37)	.30
LVEF	60.71 (3.96)	60.37 (4.25)	61.16 (3.52)	.001	61.01 (3.90)	60.56 (3.99)	.075
LVM (g)	157.55 (48.09)	160.49 (50.29)	153.73 (44.85)	.02	161.85 (53.87)	155.34 (44.71)	.03
LVH	6.14	7.4	4.6	.05	8.6	4.9	.02
Semantic verbal fluency	19.63 (5.52)	18.79 (4.97)	20.73 (5.98)	<.001	18.76 (4.99)	20.08 (5.72)	<.001
TMT A (seconds)	32.57 (12.56)	34.69 (12.99)	29.81 (11.42)	<.001	34.13 (12.54)	31.76 (12.50)	.003
TMT B (seconds)	105.59 (63.88)	120.24 (70.20)	86.60 (48.48)	<.001	115.69 (66.69)	100.39 (61.79)	<.001
BTA	6.70 (2.08)	6.33 (2.08)	7.18 (1.98)	<.001	6.43 (2.13)	6.84 (2.04)	.002
Digit span forward	7.47 (2.24)	7.17 (2.12)	7.86 (2.34)	<.001	7.19 (2.09)	7.61 (2.31)	.003
Digit span backward	5.83 (2.16)	5.36 (1.98)	6.45 (2.23)	<.001	5.44 (2.04)	6.03 (2.19)	<.001
CVLT list a total	20.25 (6.82)	19.07 (6.41)	21.78 (7.03)	<.001	19.22 (6.37)	20.78 (6.98)	<.001
CVLT short delay	5.88 (3.14)	5.22 (2.95)	6.73 (3.18)	<.001	5.41 (2.83)	6.12 (3.26)	<.001
CVLT long delay	5.89 (3.18)	5.17 (2.94)	6.83 (3.25)	<.001	5.42 (2.98)	6.13 (3.26)	<.001
BVRT (errors)	7.73 (4.61)	8.50 (4.59)	6.74 (4.46)	<.001	8.87 (4.68)	7.15 (4.47)	<.001

Note. $N = 1{,}107$. Independent samples *t* test were conducted for continuous variables, chi-square tests were used for categorical variables. AA = African American; BMI = body mass index; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; LVH = left ventricular hypertrophy; TMT = Trails Making Test; BTA = Brief Test of Attention; CVLT = California Verbal Learning Test; BVRT = Benton Visual Retention Test.

history of dementia or other neurological disease were also excluded ($n = 846$). Due to concerns of performance validity, participants who were tagged as performing abnormally during the Trail Making Test (TMT) and California Verbal Learning Test (CVLT) cognitive assessments due to impairment, psychiatric illness, misunderstanding directions, language difficulties, literacy problems, and/or quitting were also excluded ($n = 88$). The institutional review board of the National Institute of Environmental Health Sciences approved the HANDLS study.

HANDLS Procedure

Participants were recruited from 13 Baltimore neighborhoods that were predetermined to yield a diverse range of socioeconomic and demographic characteristics. HANDLS recruiters invited one or two eligible individuals per household to participate in the study. Those recruited consented to complete a household survey inquiring about demographic, psychosocial, and biomedical information. At the conclusion of this first visit, appointments for an examination in the HANDLS Mobile MRVs were scheduled. For the second visit, participants fasted the night before their appointment and avoided smoking and strenuous physical activity for at least 30 min before their visit on the MRVs. Participants completed a dietary recall, medical history and comprehensive physical examination, and additional biomedical, psychological, neuropsychological, and physical performance assessments on the MRVs by trained personnel. HANDLS data collection is ongoing, and participants are re-evaluated approximately every 3–4 years. The present study analyzed data from HANDLS Wave 3, which was approximately 4 years after the baseline measurements (accrual period: 2004–2009).

Measures

Health Measures

Physicians or nurse practitioners collected clinical variables and medical histories of the participants. Standard brachial artery auscultation following a 5-min rest determined seated systolic blood pressure and diastolic blood pressure. One measure was obtained for each arm and then averaged. The criteria for hypertension were self-reported history, use of hypertension medication, and/or average resting systolic pressure of ≥140 mm Hg or diastolic pressure ≥90 mm Hg (B. Williams et al., 2018). Blood samples were obtained following an overnight fast for determination of glucose levels by standard laboratory methods. The criteria for diabetes were self-reported history, use of relevant medications, and/or fasting blood glucose ≥ 126 mg/dl (American Diabetes Association Professional Practice Committee, 2022). Body mass index (BMI) was calculated by dividing participants' measured weight in kilograms over the square of their height in meters. A dichotomous variable coded the use of cigarettes, with former and current users coded as 1 and never used as 0.

Sociodemographic Variables

SES, indexed by household poverty status, was a dichotomous variable where income below 125% of the federal poverty threshold was coded as 1, and income at or above 125% of the poverty threshold was coded as 0. The 125% threshold was set due to cost of living in Baltimore, MD (Evans et al., 2010). A dichotomized poverty status variable was needed as HANDLS does not have an accurate, continuous estimate of income because many participants

were unable to accurately estimate their annual income or overall wealth, and did not have consistent employment. Sex was coded as biological sex assigned at birth (0 = female and 1 = male). Race was assessed by self-identification as White or African American (0 = White, 1 = African American), participants who identified as neither or both were excluded. Self-identified ethnicity was assessed with an open-ended response field, however, the collection and recording of ethnicity was unsystematic, limiting our ability to analyze this data. Visual inspection of available ethnicity data showed few participants with an indication of Hispanic identity. Age was a continuous variable and was self-reported. Education was a continuous variable, measured discretely by number of years of formal education and was self-reported.

Echocardiogram

A noninvasive and routine transthoracic ultrasound test measured the left ventricular systolic and diastolic function of the heart's chambers, left ventricular septal wall thickness, left ventricular posterior wall thickness, and left ventricular diastolic diameter at end diastole. LVEF is a percentage determined by the formula: ([left ventricular end diastolic volume − left ventricular end systolic volume]/left ventricular end diastolic volume). Normal LVEF ranges from 52% to 72% for men and 54% to 74% for women (Lang et al., 2015). The validated formula for LVM is: LVM (g) = 0.8 (1.04 [left ventricular septal wall thickness + left ventricular diastolic diameter at end diastole + left ventricular posterior wall thickness]^3 – [left ventricular diastolic diameter at end diastole]^3) + 0.6 g (Devereux & Alderman, 1993). Normal LVM ranges from 88 to 224 g in adult men and 67 to 162 g in adult women (Lang et al., 2015). LVM can be indexed by body height (in meters; "H") raised to allometric power of 2.7, with LVH defined as LVM/H $\geq$51 g/m$^{2.7}$ (Gosse et al., 1999). A single sonographer performed ultrasound assessments and a clinical cardiologist reviewed the validity of every scan.

Cognitive Measures

A neuropsychological battery assessed multiple domains of cognitive function using: the Semantic Verbal Fluency test (i.e., Animals), the Trail Making Test A (TMT-A), Trail Making Test B (TMT-B), the Digit Span Forward and Digit Span Backward subscales of the Wechsler Adult Intelligence Scale–Revised, Brief Test of Attention (BTA), Benton Visual Retention Test (BVRT), and three trials of the CVLT: total free recall, CVLT short-delay free recall, and CVLT long-delay free recall. Semantic verbal fluency assesses language and executive functions, Digit Span subscale assesses attention, concentration, and working memory; the TMT assesses attention, scanning and visuomotor tracking, cognitive flexibility, and perceptuo-motor speed; BTA assesses auditory divided attention; BVRT assesses visual perception, constructional abilities, and nonverbal memory; and CVLT assesses verbal learning and memory (Lezak et al., 2012; Strauss et al., 2006).

Overall, cognitive performance was defined by ten outcome measures from the above neuropsychological assessments: Semantic verbal fluency sum of admissible words (i.e., animals), time to completion score on TMT-A and TMT-B (longer time indicative of worse performance), successful trials on Digits Forward and Backward, number of correctly monitored lists summed across both forms of the BTA, errors score on BVRT, and CVLT total score, short free recall score, and long free recall score.

Data Analytic Approach

The Statistical Package for the Social Sciences Version 24.0 was used to compute multivariable linear regression analyses examining the interactive relations of LVM × Race × Poverty Status and then LVH × Race × Poverty Status on cognitive performance (in separate models). LVM and LVH were the predictor variables for their respective analyses, while race was the primary moderator, and poverty status was the secondary moderator. The first set of analyses examined LVM as a continuous measure, whereas the second set of analyses utilized the clinical definition of LVH with a binary variable. Cognitive performance was the outcome variable and age, sex, education, diabetes, hypertension status, BMI, and smoking status were the base covariates. Cognitive performance was defined by ten outcome measures from a series of neuropsychological assessments (Semantic verbal fluency, TMT-A, TMT-B, Digits Forward, Digits Backward, BTA, BVRT, and the CVLT total score, CVLT short free recall, and CVLT long free recall). This analysis was a three-way interaction focused on how sociodemographic variables moderate the effect of LVM/LVH on cognitive domains. Separate analyses were run for each neuropsychological test, resulting in a total of ten moderation models for LVM and another ten for the LVH analyses.

Power analyses, using $\alpha = .05$, indicated that the current analyses had statistical power of .99 to detect a small effect size ($f^2 = .02$) for each cognitive outcome in three- and two-way interaction models. Power analyses effect sizes were based on the incremental increase in R^2 from the interaction term within the full model.

Lack of interactive relations prompted backward eliminations for two-way interactions and main effects. Following computation of the initial moderation models, an additional covariate, LVEF, was entered hierarchically. It was proposed that if interactive relations for LVM/LVH-cognition associations were noted then findings would have been further queried using the Statistical Package for the Social Sciences PROCESS macro to formally evaluate the presence of mediation.

Exploratory analyses were conducted to examine the associations of LVM and LVH within specific sociodemographic groups. As such, race-, poverty status, and race-by-poverty status-stratified regression models were conducted examining associations between LVM/LVH and all cognitive outcomes.

Results

Sample characteristics are provided for the total sample, in addition to race- and poverty status-stratified groups in Table 1 while race-by-poverty status-stratified sample characteristics are presented in Table 2. Significant differences between racial and socioeconomic groups in predictor, outcome, and covariate variables were observed (see Table 1). With respect to racial groups, compared with White participants, African American participants had a significantly greater mean LVM (160.49 vs. 153.73, $p = .02$), lower mean LVEF (60.37 vs. 61.16, $p = .001$), worse performance on all cognitive outcomes (all $p < .001$), were more likely to have hypertension (58.1% vs. 46.1%, $p < .001$), and were more likely to

Table 2
Race-by-Poverty Status-Stratified Sample Characteristics for Demographics and Cardiovascular Measures

Sample characteristic	AA below poverty *M* (*SD*) or %	AA above poverty *M* (*SD*) or %	W below poverty *M* (*SD*) or %	W above poverty *M* (*SD*) or %
Age (years)	50.65 (8.60)	52.63 (9.35)	52.53 (8.51)	52.64 (9.16)
Female	61.8	56.3	68.9	60.8
Never smoker	15.2	25.1	14.4	27.9
Hypertension	58.5	57.8	48.1	45.2
Diabetes	34.9	34.1	34.8	36.0
Years of education	11.87 (2.08)	12.84 (2.18)	11.50 (2.53)	13.16 (2.95)
BMI (kg/m^2)	29.79 (8.08)	31.06 (7.43)	30.80 (8.22)	30.23 (7.30)
LVEF	61.01 (4.10)	59.97 (4.29)	61.00 (3.55)	61.22 (3.51)
LVM (g)	164.45 (55.00)	158.02 (47.00)	157.22 (51.68)	152.37 (41.89)
LVH	8.8	6.5	8.1	3.2
Semantic verbal fluency	18.62 (4.83)	18.90 (5.06)	19.01 (5.27)	21.40 (6.12)
TMT A (seconds)	35.86 (12.85)	33.96 (13.04)	31.02 (11.36)	29.33 (11.42)
TMT B (seconds)	126.06 (72.31)	116.58 (68.69)	97.18 (50.45)	82.48 (47.13)
BTA	6.17 (2.15)	6.43 (2.03)	6.88 (2.03)	7.29 (1.95)
Digit span forward	7.05 (1.99)	7.24 (2.20)	7.43 (2.25)	8.05 (2.35)
Digit span backward	5.22 (2.01)	5.45 (1.95)	5.83 (2.04)	6.70 (2.26)
CVLT list A total	18.76 (6.39)	19.26 (6.43)	20.04 (6.28)	22.45 (7.20)
CVLT short delay	5.21 (2.85)	5.23 (3.02)	5.77 (3.25)	7.10 (3.25)
CVLT long delay	5.09 (2.95)	5.22 (2.93)	6.01 (2.95)	7.15 (3.31)
BVRT	9.17 (4.67)	8.08 (4.49)	8.33 (4.67)	6.12 (4.22)

Note. N = 1,107. AA = African American; W = White; BMI = body mass index; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; LVH = left ventricular hypertrophy; TMT = Trails Making Test; BTA = Brief Test of Attention; CVLT = California Verbal Learning Test; BVRT = Benton Visual Retention Test.

live below 125% of the federal poverty line (38.6% vs. 28.0%, $p <$ .001). Further, compared with those living above 125% of the federal poverty line, participants below were significantly younger (51.33 vs. 52.63 p = .02), exhibited greater mean LVM (161.85 vs. 155.34, p = .03), had fewer years of education (11.74 vs. 12.99, $p <$ .001), had lower scores on all cognitive outcomes (all p</= .003), and had greater prevalence of LVH (8.6% vs. 4.9%, p = .02) and current or former cigarette use (85.1% vs. 73.6%, $p <$ .001). Bivariate correlations among LVM, LVH, LVEF, and all cognitive outcomes are displayed in Table 3.

After adjustment for sex, age, education, BMI, smoking status, diabetes diagnosis, and hypertension diagnosis, no significant three-way interactions among LVM, race, and poverty status were noted for any of the cognitive outcome measures (see Table 4). Initial backward elimination yielded no significant two-way interactions of LVM with race or poverty status. Further backward elimination was done to analyze main effects of LVM on cognitive outcomes and revealed significant main effects of LVM on BTA ($\beta = -0.089$, p = .010) and TMT-B scores ($\beta = 0.072$, p = .021), such that greater LVM was associated with lower scores on BTA and longer time to completion on TMT-B.

Analyses with LVH similarly revealed a lack of significant three-way or two-way interactions among LVH, race, and/or poverty status (see Supplemental Table S2). However, backward elimination similarly revealed significant main effects of LVH on BTA ($\beta = -0.075$, p = .017) and TMT-B ($\beta = 0.071$, p = .012), in addition to semantic verbal fluency ($\beta = -0.067$, p = .027), and TMT-A ($\beta = 0.078$, p = .009). These results demonstrate an association between LVH and lower scores on BTA, longer time to completion on TMT-A and TMT-B, and fewer admissible words on semantic verbal fluency.

Sensitivity analyses incorporated LVEF, a functional measure of the left ventricle, to ascertain if the significant main effects of LVM on cognition noted above were influenced by this final adjustment. All LVM- and LVH-cognition results were unchanged with the addition of LVEF (see Tables 4 and 5).

Exploratory analyses stratified all base regression models by race, poverty status, and race * poverty status to examine LVM/LVH-cognition associations within each of these sociodemographic groups. Table 6 presents all significant LVM/LVH-cognition associations for the total sample and each subgroup. First, in race-stratified models, greater LVM was significantly associated with longer TMT-B time to completion (β = .096, p = .024) and lower BTA score ($\beta = -0.127$, p = .006) for African American adults, but not Whites. In addition, greater LVH was significantly associated with lower scores for semantic verbal fluency ($\beta = -0.95$, p = .022) and BTA ($\beta = -0.094$, p = .028) among African American individuals only, while, among White participants, LVH was associated with longer TMT A time to completion ($\beta = 0.101$, p = .033). Next, in poverty status-stratified analyses, only among those above poverty, greater LVM was significantly associated with longer time to completion on TMT-B (β = 0.088, p = .021). Further, greater LVH was associated with lower Semantic Verbal Fluency score ($\beta = -0.098$, p = .008) and longer TMT-B time to completion ($\beta = 0.077$, p = .025) only among those above poverty. Last, in race by poverty status-stratified models with African American adults living above poverty, LVM was associated with longer time to completion on TMT-B (β = 0.140, p = .01) and lower BTA score ($\beta = -0.133$, p = .025). In addition, greater LVH was associated with significantly lower Semantic Verbal Fluency scores ($\beta = -0.167$, p = .002) among African Americans living above poverty. No significant relations of LVM or LVH were noted for any cognitive outcome within the subgroups of African American individuals living below the poverty line; White adults living below the poverty line; or White adults living above the

Table 3
Bivariate Correlations Among LVM, LVH, LVEF, and All Cognitive Outcomes

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. LVM	—												
2. LVH	.610***	—											
3. LVEF	−.042	−.015	—										
4. Semantic verbal fluency	.000	−.082**	−.012	—									
5. TMT-A	.108***	.112***	−.044	−.229***	—								
6. TMT-B	.106***	.103***	−.032	−.311***	.427***	—							
7. Digit span forward	−.041	−.074*	−.061*	.253***	−.286***	−.277***	—						
8. Digit span backward	−.045	−.077*	−.062*	.287***	−.296***	−.385***	.562***	—					
9. Brief test of attention	−.132***	−.116***	.015	.197***	−.274***	−.372***	.258***	.360***	—				
10. CVLT List A	−.093**	−.067*	.079**	.319***	−.290***	−.379***	−.213***	.317***	.264***	—			
11. CVLT short delay	−.085**	−.076*	.074*	.349***	−.277***	−.366***	.193***	.333***	.263***	.774***	—		
12. CVLT long delay	−.077*	−.038	.049	.347***	−.277***	−.378***	.170***	.310***	.250***	.801***	.858***	—	
13. BVRT	.029	.057	−.017	−.331***	.345***	.464***	−.261***	−.345***	−.296***	−.376***	−.366***	−.352***	—

Note. LVM = left ventricular mass; LVH = left ventricular hypertrophy; LVEF = left ventricular ejection fraction; TMT = Trails Making Test; CVLT = California Verbal Learning Test; BVRT = Benton Visual Retention Test.
* $p < .05$. ** $p < .01$. *** $p < .001$.

poverty line. Results of all stratified analyses were unchanged after additional adjustment for LVEF.

Discussion

To our knowledge, this was the first study that examined interactive relations of LVM/LVH, race, and poverty status to multiple domains of cognitive function within a socioeconomically diverse, biracial sample of urban-dwelling adults. Contrary to our expectations, we did not find any significant three-way or two-way interactions among LVM (or LVH), race, and/or poverty status with respect to cognitive outcomes. We expected to find such associations because (a) LVM varies by race and SES, such that those of marginalized races and of low-SES are at higher risk for elevated LVM values and of meeting criteria for LVH (Akintoye et al., 2018; Drazner et al., 2005; East et al., 2003; Gump et al., 1999; Kizer et al., 2004; Okwuosa et al., 2015; Rodriguez et al., 2004); (b) these disparities are also seen in the cognitive function literature, wherein disenfranchised groups tend to have lower average levels of performance on select tests than Whites (Brewster et al., 2014; R. Chen et al., 2022; Glymour & Manly, 2008); and (c) members of minoritized and marginalized groups also experience an aggregation of psychosocial and environmental risk factors that may render them more vulnerable to influences of CVD risk factors and diseases on cognitive function (Allana et al., 2021; Boots et al., 2020; Marcus et al., 2011; McClain et al., 2022; Nyquist et al., 2014). These known health disparities highlight the systemic injustices that impact the cardiovascular and cognitive health of self-identified African American individuals and those of lower SES, bolstering the hypothesis that these overlapping marginalized groups may be more vulnerable to the negative impact of LVM and LVH on cognitive performance. In addition, although the study was sufficiently powered to detect small ($f^2 = .02$) effects for three- and two-way interactions, post hoc effect size calculations indicated that none of the interaction terms effect sizes achieved this threshold. The exceedingly small effect sizes associated with the interaction terms may be due to the relatively younger age of the sample and associated limited LVH prevalence.

In the absence of significant interactive relations among LVM/LVH, race, and poverty status, the present results revealed significant main effects of LVM on the BTA, a test of complex attention, and TMT-B a test of cognitive flexibility (a dimension of executive function). Specifically, greater LVM was associated with lower levels of performance on both tests. LVH was similarly associated with lower levels of performance on these tests, in addition to semantic verbal fluency, a measure of executive function and verbal abilities, and TMT-A, a measure of perceptuo-motor processing speed. These additional finding may reflect that LVH is a more pronounced physiological state of subclinical CVD and thus perhaps more likely to incur greater cognitive consequences. In contrast, several domains of cognitive function, including working memory, verbal learning and memory, and nonverbal memory, were not associated with either LVM or presence of LVH.

The current findings are generally consistent with those of several prior studies that reported associations of greater LVM with lower levels of performance on tests reflecting multiple cognitive domains such as abstract reasoning, executive functioning, visual–spatial memory and organization, and verbal memory (Elias et al., 2007; Georgakis et al., 2017). More specifically, the present study results

Table 4
Hierarchical Standardized Regression Coefficients for Significant LVM Main Effects Model and Subsequent Adjustment for LVEF

Sequential step	LVM	Race	Poverty status	Sex	Age	Education	Cigarette status	BMI	Diabetes diagnosis	Hypertension status	LVEF
Brief test of attention											
Step 1	−.089**	−.185***	−.054	−.030	−.089**	.107***	.048	.002	−.004	−.052	
Step 2	−.089**	−.185***	−.054	−.030	−.089**	.107***	.048	.002	−.004	−.052	.002
Trails B test											
Step 1	.072*	.248***	.063*	.035	.255***	−.237***	−.036	−.095**	.017	.076*	
Step 2	.070*	.247***	.065*	.035	.256***	−.235***	−.035	−.094**	.017	.077*	−.014

Note. Step 1 = LVM, sex, age, education, race, poverty status, BMI, cigarette status, hypertension diagnosis, diabetes diagnosis. Step 2 = Step 1 plus LVEF. LVM = left ventricular mass; LVEF = left ventricular ejection fraction; BMI = body mass index.
* $p < .05$. ** $p < .01$. *** $p < .001$.

partially overlap with the findings of previous studies that similarly noted greater LVM associations with worse performance on tests of complex attention and processing speed (Moazzami et al., 2018; van den Hurk et al., 2011). For example, van den Hurk et al. (2011) showed that baseline LVM was negatively associated with both attention/executive function and processing speed composite scores. However, the attention/executive function composite did not include the BTA but instead was derived from the TMT-B, Verbal Fluency (animals and letters: N, A), Stroop Color–Word Test (Part III), and the Brixton Spatial Anticipation Test.

Although the present study tapped into similar and overlapping domains of cognitive function from prior literature, there was very limited overlap in terms of the specific cognitive tests administered (Georgakis et al., 2017). Of the ten cognitive outcome measures used in the present study, only four could be found in the prior LVM-cognition literature: Semantic verbal fluency (animals), Digit Span, TMT-A, and TMT-B (Elias et al., 2007; Moazzami et al., 2018; van den Hurk et al., 2011; van der Veen et al., 2015). Of these few overlapping cognitive assessments, three studies used a combination of these measures as components of a composite score to index an overarching cognitive domain of executive functioning (Elias et al., 2007; van den Hurk et al., 2011; van der Veen et al., 2015). It is possible that the results of the present study would have differed if the same measures of cognitive functioning were used or if similar cognitive composite scores were derived. It is also important to note that most studies dealing with LVM/LVH-cognition associations used cognitive screening measures such as the MMSE as opposed to clinical neuropsychological tests. Therefore, the aggregate LVH literature emphasizes the negative consequences of elevated LVM on cognitive performance; yet, due to the predominant use of global cognitive screeners the findings are not directly comparable to the present study.

The present study further differed methodologically from the majority of prior cross-sectional investigations that included samples with a mean age in the mid-70s (Haring et al., 2017; Kähönen-Väre et al., 2004; Reitz et al., 2007; Scuteri et al., 2009; Wozakowska-Kapłon et al., 2009). The current sample was substantially younger with a mean age of 52.2 years. Currently there is a paucity of data concerning midlife LVM and cognitive performance (Haring et al., 2017). However, use of a younger sample limits the likelihood of noting elevated LVM and reaching LVH cutoffs. The several LVM-cognition and LVH-cognition associations noted herein elucidate

Table 5
Hierarchical Standardized Regression Coefficients for Significant LVH Main Effects Model and Subsequent Adjustment for LVEF

Sequential step	LVH	Race	Poverty status	Sex	Age	Education	Cigarette status	BMI	Diabetes diagnosis	Hypertension status	LVEF
Brief test of attention											
Step 1	−.075*	−.183***	−.057	−.054	−.087**	.103**	.043	−.012	−.006	−.062	
Step 2	−.075*	−.183***	−.058	−.053	−.087**	.102**	.043	−.012	−.007	−.063	.005
Trails B test											
Step 1	.071*	.247***	.065*	.053	.253***	−.233***	−.032	−.086**	.020	.083**	
Step 2	.071*	.245***	.067*	.052	.254***	−.231***	−.031	−.085**	.019	.085**	−.016
Verbal fluency test											
Step 1	−.067*	−.155***	−.034	.096**	−.116***	.239***	−.018	.037	.030	−.025	
Step 2	−.067*	−.157***	−.032	.092**	−.114***	.242***	−.017	.039	.031	−.024	−.024
Trails A test											
Step 1	−.078**	.158***	.079**	.130***	.296***	−.087**	−.008	−.022	−.002	.023	
Step 2	−.077*	.154***	.083**	.126***	.298***	−.083**	−.006	−.019	−.002	.026	−.037

Note. Step 1 = LVH, sex, age, education, race, poverty status, BMI, cigarette status, hypertension diagnosis, diabetes diagnosis. Step 2 = Step 1 plus LVEF. LVH = left ventricular hypertrophy; LVEF = left ventricular ejection fraction; BMI = body mass index.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 6
Significant Associations Among LVM/LVH and Cognitive Outcomes in Total Sample and All Stratified Analyses

Cognitive outcome	Total	AA	White	Below poverty	Above poverty	AA Below poverty	AA Above poverty	White below poverty	White above poverty
LVM models									
TMT B (seconds)	X	X			X		X		
BTA	X	X					X		
LVH models									
Semantic verbal fluency	X	X			X		X		
TMT A (seconds)	X		X						
TMT B (seconds)	X				X				
BTA	X	X							

Note. "X" mark indicates significant association ($p < .05$) between LVM/LVH and cognitive outcome in multiple linear regression model. AA = African American; LVM = left ventricular mass; LVH = left ventricular hypertrophy; TMT = Trails Making Test; BTA = Brief Test of Attention.

valuable information for future studies focused on earlier points in the life span and contributes to this sparse body of work. It is possible that additional relations of LVM/LVH and cognitive function will emerge over time in the current sample, perhaps differentially among sociodemographic subgroups.

Consistent with our expectations, the current findings further indicated that the relations of LVM and LVH to cognitive performance were maintained after statistical adjustment for multiple comorbid CVD risk factors. Similarly, in a meta-analysis by Georgakis et al. (2017), LVM-cognition associations persisted following sensitivity analyses adjusting for CVD risk factors such as blood pressure levels and diabetes mellitus (Georgakis et al., 2017). However, in contrast, Elias et al. (2007) found a diminishing influence of LVM on cognitive function with additional adjustment for CVD risk factors. Ultimately, all associations were rendered nonsignificant when adjusting for blood pressure, treatment for hypertension, diabetes mellitus, total cholesterol/high density lipoprotein cholesterol, alcohol consumed per week, cigarettes smoked per day, plasma homocysteine concentration, depressed mood, and prevalent CVD (Elias et al., 2007). However, contrary to our hypothesis, results of the present study were not altered by adjustment for LVEF.

From a biological standpoint, a diminished LVEF is known to reduce available blood supply to the brain, potentially leading to inadequate perfusion (van der Veen et al., 2015). In turn, hypoperfusion is known to be related to the development of white matter disease and associated risk for VaD, in addition to AD-related pathology (Jefferson et al., 2015; Sierra et al., 2006; van der Veen et al., 2015). That lower LVEF did not appear to drive the main effects of LVM/LVH-cognition associations suggests that the mechanisms underlying relations of LVM and LVH to brain health are perhaps more complex and uncertain. Some evidence points to the involvement of neurohormonal responses to increased LVM, or environmental and genetic interactions among factors that lead to increased LVM and LVH as underlying mechanisms of the LVM/LVH-cognition associations (Georgakis et al., 2017). A common feature of this evidence is the fact that they involve a cascade of adaptations in response to gradual hypertrophy of the left ventricle (Georgakis et al., 2017; Lazzeroni et al., 2016; Olson, 2004). This pathological hypertrophy is often caused by hypertension, congestive heart failure, poor diet, and/or inherited mutations in sarcomeric proteins (Frey & Olson, 2003; Olson, 2004; Riquelme et al., 2011). These insults lead to a transfer from lipid oxidation to glucose utilization in metabolic substrates and higher rates of fibrosis and apoptosis in cardiomyocytes (Frey & Olson, 2003; Olson, 2004; Riquelme et al., 2011). In fact, the rate of apoptotic pathways and the subsequent neurohormonal consequences seem to be the major molecular determinant for cardiac hypertrophy (Olson, 2004). Associated changes to the myocardium via fibrotic and apoptotic processes cause an accumulation of molecular changes that influences the vasculature throughout the body (Frohlich et al., 2011); this may be a key pathway through which the cerebral vasculature is altered in the context of LVH, ultimately leading to white matter disease and brain atrophy. Additionally, these physiological changes could cause endothelial dysfunction and arterial stiffness, which are pathways that could impair the mechanisms regulating cerebral perfusion (van der Veen et al., 2015) and ultimately increase the likelihood of experiencing vascular and AD-related pathology. Thus, greater

LVM or frank LVH may operate through pathways that are both similar and distinct from those of LVEF in their negative impact on brain and cognitive function.

Prior research indeed suggests linkages of elevated LVM and LVH to reduced cerebral blood flow and white matter microstructural integrity, and ultimately, the development of cerebral white matter disease (Fox et al., 2005; Haring et al., 2017; Moore et al., 2018; Selvetella et al., 2003; Sierra et al., 2002, 2006). For example, in a recent study of a midlife sample, differences in LVM as small as 25 g were associated with lower hippocampal volumes and greater white matter lesions (Haring et al., 2017). For those that met criteria for LVH, the likelihood of cerebrovascular abnormalities was even higher. Moreover, in a sample of older adults with no history of stroke, dementia, or heart failure, LVM was negatively associated with diffusor tensor imaging metrics of white matter microstructure integrity (Moore et al., 2018). In a sample of asymptomatic middle-aged hypertensive patients, 88.4% of those with white matter lesions had LVH (Sierra et al., 2002). Additionally, individuals with both hypertension and LVH were more likely to develop silent cerebrovascular lesions than those without LVH (Selvetella et al., 2003). Last, middle-aged hypertensive individuals with LVH displayed reduced regional blood flow in the striatum (Sierra et al., 2006), suggesting that elevated values of LVM impact cerebral blood flow.

The above structural and functional correlates of elevated LVM and LVEF may be proximal influences on two key aspects of executive functioning—complex attention and cognitive flexibility—and perceptuo-motor speed present in the study. It is important to note that early changes in these cognitive domains have been closely tied to the development of vascular cognitive impairment and VaD (Johansen & Gottesman, 2021). Thus, the current findings could conceivably reflect the early emergence of cognitive difficulties associated with the known vascular pathology that ultimately leads to clinically significant cognitive impairments.

Stratified Analyses

Prior work has demonstrated inherent limitations in relying on interaction terms and between-group comparisons when examining health disparities (Ward et al., 2019; Whitfield et al., 2008). Specifically, Ward and colleagues discuss how interpreting interactions without considering group-specific distributions in the predictor and outcome can obscure the extent to which a predictor contributes to a disparity in an outcome. For example, although similar regression coefficients between groups may yield a nonsignificant interaction, group-based differences in the distributions and prevalence of the predictor and outcomes can provide important evidence for the predictor's contribution to the disparity in outcome (Ward et al., 2019). Moreover, Whitfield and colleagues discuss how conclusions about between-group differences may be undermined due to measurement bias and limited measurement equivalence between racial groups, especially when using cognitive assessments, highlighting the importance of within-group analyses (Whitfield et al., 2008). Thus, given the absence of significant interactions in the present sample, and in accordance with the recommendations of Ward et al. (2019) and Whitfield et al. (2008), race-, poverty status-, and race-by-poverty status-stratified descriptive statistics and multivariate regression models were used to explore differences in distributions of LVM, LVH, and cognitive outcomes, and evaluate within-group LVM/LVH-cognition associations.

Race- and poverty status-stratified sample characteristics revealed greater LVM, lower LVEF, and lower levels of cognitive performance among African Americans and those of low SES, compared with their White and high SES counterparts, respectively. LVH prevalence was also greater in those below poverty compared with those above. These results are consistent with much of the available literature (Lewis et al., 2020; Okwuosa et al., 2015; Unverzagt et al., 2011; Wang et al., 2023) and suggest that racial and socioeconomic disparities in LVM and LVH may contribute to the observed disparities in cognitive performance.

Exploratory stratified multivariable regression analyses were then used to further examine within-group associations between LVM/LVH and cognitive performance, revealing select subgroup-specific associations. Table 6 portrays significant LVM/LVH-cognition associations for the total sample and each subgroup. Overall, stratified analyses demonstrated that among African Americans, those above poverty, and African Americans above poverty, greater LVM and presence of LVH were associated with worse performance on measures of complex attention (i.e., BTA), cognitive flexibility (i.e., TMT-B), and semantic verbal fluency, whereas among Whites, presence of LVH was associated with worse perceptuo-motor speed (i.e., TMT-A).

Taken together, the results of the main analyses, stratified descriptive statistics, and stratified multiple regression models suggest that greater LVM and presence of LVH are associated with worse performance on tests of executive function (i.e., complex attention, cognitive flexibility, semantic verbal fluency) and perceptuo-motor speed and that African Americans may be particularly susceptible to the negative effects of left ventricular dysfunction on aspects of executive function, while perceptuo-motor speed may be more affected in Whites. With respect to poverty status, although those below poverty demonstrated greater LVM, greater LVH prevalence, and worse performance on all cognitive outcomes, significant negative LVM/LVH-cognition associations were observed among those above poverty but not below. These somewhat conflicting findings may be explained by the significant difference in educational attainment between those above and below poverty. Given the influence of education on neuropsychological test performance (Tombaugh, 2004; Tombaugh et al., 1999), the relatively lower degree of education among those below poverty may obscure LVM/LVH-cognition associations for those below poverty.

It is important to note that given the numerous additional stratified analyses conducted and the associated risk of Type 1 error, these exploratory analyses should be interpreted with caution. However, it is notable that all cognitive outcomes significantly associated with LVM and LVH in the stratified analyses were also significant in the total sample, suggesting that these findings may not be spurious. Moreover, these results warrant further investigation into the between and within-group associations of LVM/LVH and cognitive function among adults as a function of self-identified race and poverty status. In addition, the current findings suggest the continued importance of examining the potential disproportionate negative influence of LVM and LVH on cognitive function in marginalized populations in other contexts (e.g., among older individuals, as a function of different SES indicators, with use of different cognitive outcome measures).

Strengths and Limitations

A major strength of this study is the use of individual neurocognitive tests rather than cognitive screening measures. Most studies have used just the MMSE—a screening measure of mental status—instead of psychometrically sound neuropsychological measures. The MMSE greatly limits the amount and specificity of information pertaining to LVM's association with cognitive performance. Furthermore, utilizing individual tests as outcome measures instead of relying on composite scores allows for a more nuanced examination of LVM-cognition associations. This is especially true when using individual tests to assess different subdomains, such as different types of executive function, which allows for a more detailed assessment of patterns of performance. This study was also the first to investigate LVM-cognition and LVH-cognition associations within a health disparities context, which is a significant strength. In that regard, this study involved a racially and socioeconomically diverse nonclinical population, a sample that is not typical of LVM/LVH research (Georgakis et al., 2017). The participants were largely middle-aged with an even distribution of men and women. These characteristics emphasize the generalizability of this study as well as highlight trends in typically understudied populations. It is particularly important to note that the effects of hypertrophy and ventricular mass were found at relatively young ages, suggesting these effects on attention and executive function may begin earlier than previously suspected. Overall, this study provided a foundation for future research in the realm of LVM and its influence on cognition from a health disparities perspective.

Although this study has many strengths, it is not without limitations. Aside from differences in cognitive outcome measures mentioned above, the present study had stricter exclusion criteria for participants. This study excluded participants with a history of cardiac or carotid surgeries, myocardial infarction, coronary heart disease, peripheral arterial disease, heart failure, stroke, transient ischemic attack, dementia, and other neurological disease; while prior literature on LVM and cognition did not exclude some or most participants with the above medical history (Georgakis et al., 2017). The current criteria may limit study generalizability and introduce selection bias. Another major limitation is the relatively low presence of participants with physiologically high values of LVM. Of the participants that were included in these analyses, only 68 participants (6.14% of the sample) met criteria for LVH. In fact, this sample presented with a mean LVM that was below the mean of prior studies (Elias et al., 2007; Gosse et al., 1999). This truncated range may have limited our ability to detect significant association of LVM and cognitive function. It is also important to recognize that many of the cognitive measures employed in this study have demonstrated biases when used with diverse populations. Most cognitive tests have been created, validated, and normed on predominantly White, middle-class, and highly educated populations. As such, they may underestimate true ability in any given cognitive domain when used with other populations (Glymour & Manly, 2008; Pedraza & Mungas, 2008).

Another limitation is the cross-sectional design of this study which only provides a snapshot of LVM-cognition associations; whereas a longitudinal model would provide a better picture of long-term influence of LVM/LVH on change in cognition over time and establish temporal associations. Moreover, the use of several cognitive outcomes for the primary LVM and LVH models, the backward elimination approach with the statistical models, and numerous additional stratified exploratory analyses increased the risk of Type 1 error, an additional limitation of this study. Relatedly, use of a Bonferroni correction for all analyses would render all associations nonsignificant. However, it is also important to consider the risk of type II error given the novelty of the interaction analyses and the diverse sample. Thus, given the novel aspects of this study, we opted to prioritize minimizing risk of false negatives. While some caution in interpreting the findings is suggested due to risk of false positives, future work can assess the persistence of the effects observed in the present study and determine stability of associated effect sizes.

Next, the use of poverty status as a proxy for SES is limited in its ability to capture the distinct hardship and stressors associated with being 125% below the poverty line. This variable determines a specific income level adjusted for household size but removes the nuance of having a continuous variable representing SES. Relatedly, the use of a dichotomous poverty status variable is another important limitation and may further obscure nuances associated with gradations in income level. Unfortunately, HANDLS does not have a continuous SES variable based on annual income, partially because many participants had difficulty computing an annual income. Use of variables that could further parse the nuance and range of SES (e.g., wealth, education, occupation) could hold utility for future work on potential interactive effects involving SES.

A broader range of neuropsychological tests that touched upon more domains of function could further expand the possibility of observing a relation between LVM/LVH and cognitive performance. Another potential improvement to the current design could include examination of other potentially important moderator variables such as hypertension status, age, and sex. Hypertension status is an especially prominent risk factor that not only elevates LVM but impacts cognitive performance on its own (Maugeri et al., 2019; Selvetella et al., 2003; Sierra et al., 2002, 2006; Yildiz et al., 2020). Age is a variable that is seen to have a distinct influence on the relation between LVM and cognitive performance, where LVM values that reach the threshold for LVH begin to lose their predictive utility in older age, especially for octogenarians (Kähönen-Väre et al., 2004). Men are also at higher risk for cognitive decline and LVM, especially as they age (de Simone et al., 2008; Devereux & Alderman, 1993; Langa & Levine, 2014; Mahoney et al., 1988).

Conclusion

Despite the absence of significant interactions among LVM/LVH, race, and/or poverty status, higher levels of LVM and/or the presence of LVH were associated with an intriguing pattern of diminished performance on select tests of executive function (e.g., divided attention, cognitive flexibility, verbal fluency) and perceptuo-motor speed after adjustment for comorbid CVD risk factors and LVEF. This pattern aligns with deficits commonly found in the emergence of vascular cognitive impairment and, ultimately, VaD (Johansen & Gottesman, 2021). Further, results of stratified analyses revealed significantly greater left ventricular dysfunction and worse cognitive performance among African Americans and those below poverty, and significant associations between greater LVM and/or presence of LVH and worse performance on measures of executive function among African Americans, those above poverty, and African Americans above poverty, while among Whites, LVH was

associated with worse perceptuo-motor speed. Overall, these stratified analyses provide some initial evidence for the contribution of LVM/LVH in racial disparities of cognition, especially executive function. The present findings suggests that one potential pathway through which such impairments ultimately emerge is through physiological changes in the heart and potential neurohormonal and vascular responses that diminish cerebral perfusion and promote subclinical cerebrovascular disease. Additionally, the present study contributed to the scarce body of literature pertaining to LVM-cognition and LVH-cognition associations and goes further by probing how sociodemographic variables may play a part in this phenomenon.

This study also laid the groundwork for justifying the examination of neural substrates that may be responsible for the LVM-cognition and LVH-cognition associations in the present study. This is especially relevant for studying frontal lobe white matter lesions or atrophy, given the predominately attentional and executive function focused deficits observed in the present study. Prior studies have highlighted the influence of other dimensions of subclinical CVD, for example, arterial stiffness, carotid intima-media thickness, on neuroanatomy (Badji et al., 2019; Devereux & Alderman, 1993; Hoth et al., 2010; Humayra et al., 2024; Jefferson et al., 2011; Jerskey et al., 2009; Thurston et al., 2023); however very few emphasize the influence LVM/LVH have on these brain regions (Fox et al., 2005; Moore et al., 2018; Selvetella et al., 2003; Sierra et al., 2002).

Ultimately, the present findings may reflect the early emergence of neurocognitive changes associated with enhanced cardiovascular risk in this largely middle-aged sample; particularly within the domain of attention and executive function. Despite the mixed findings, there is enough evidence to suggest that—however limited—LVM and LVH have an impact on cognitive aging. As highlighted by others, future work should build upon these findings by probing the possibility of neuroanatomical changes, particularly within the frontal and temporal lobes, mediating these observed associations between LVM/LVH and executive functions (Elias et al., 2018). This topic highlights the importance of CVD risk factors and their influence on cognition, while simultaneously acknowledging the sociodemographic characteristics of a population that may moderate this relation. These findings should motivate future work to continue examining racially and socioeconomically diverse populations, and their risks for accelerated cognitive aging. This area of research could identify early targets for prevention and intervention to ameliorate the long-term influence of subclinical CVD on brain and cognitive health disparities.

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