Left Ventricular Mass, Blood Pressure, and Lowered Cognitive Performance in the Framingham Offspring

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Abstract—The purpose of this study was to determine whether echocardiographic left ventricular mass is related to cognitive performance beyond casual blood pressure adjusting for the influence of other vascular risk factors. We used multivariable regression analyses to relate left ventricular mass assessed at a routine examination (1995–1998) to measures of cognitive ability obtained routinely (1998–2001) in 1673 Framingham Offspring Study participants (56% women; mean age: 57 years) free from stroke, transient ischemic attack, and dementia. We adjusted for the following covariates hierarchically: (1) age, education, sex, body weight, height, interval between left ventricular mass measurement and neuropsychological testing (basic model); (2) basic model+blood pressure+treatment for hypertension; and (3) basic model+blood pressure+treatment for hypertension+vascular risk factors and prevalent cardiovascular disease. For the basic model, left ventricular mass was inversely associated with abstract reasoning (similarities), visual-spatial memory and organization, and verbal memory. For the basic model+blood pressure+treatment for hypertension, left ventricular mass was inversely associated with similarities and visual-spatial memory and organization. For the basic+blood pressure+treatment for hypertension+risk factors+cardiovascular disease model, no significant associations were observed. Echocardiographic left ventricular mass is associated with cognitive performance beyond casual and time-averaged systolic blood pressure, but this association is attenuated and rendered nonsignificant with additional adjustment for cardiovascular risk factors and cardiovascular disease, thus suggesting that these variables play an important role in mediating the association between left ventricular mass and cognition. (*Hypertension*. 2007;49:439-445.)

Key Words: left ventricular mass ■ blood pressure ■ cognitive performance ■ cardiovascular risk factors ■ cardiovascular disease

Although there is an extensive literature on the association of blood pressure and cognitive performance, little information is available regarding the relationship of left ventricular mass (LVM) to cognition. With regard to blood pressure (BP), many studies have shown that, over a wide range of BP values and with adjustment for hypertension-related complications, both systolic and diastolic BP are inversely related to the level of cognitive performance and longitudinal decline in performance.[1–9] The most widely accepted mechanism by which high BP reduces cognitive ability is via its effect on brain structure and function.[10–16] Hypertension is associated with acceleration of atherosclerosis in the large arteries and is associated with medial thickening of the intracerebral vessels leading to cerebral white matter hypoperfusion and ischemic rarefaction.[16] A causal association between higher BP and lower cognition has been suggested because of the observation of a "dose–response" effect in studies relating BP and cognition.[1–3,7–9]

Both the duration and the magnitude of BP elevation have been related inversely to cognitive performance.[9] However, the use of the duration of hypertension as a marker of the chronic hemodynamic burden posed by high BP is challenged by the lack of precision in identifying the exact date of hypertension onset in epidemiological studies. LVM is strongly associated with long-term BP cross-sectionally[10] and is a predictor of future risk of hypertension in nonhypertensive individuals.[11] In addition, LVM is a surrogate marker of cardiovascular target organ damage and is associated with incidence of cardiovascular disease prospectively.[12–16] These findings suggest that LVM, as determined by echocardiography, should relate to levels of cognitive performance in a manner similar to, but not necessarily identical with, BP.

Because LVM is a time-integrated correlate of exposure to BP and to other cardiovascular risk factors, it may serve as a marker of the chronicity and the degree of BP elevation and an indicator of long-term burden of vascular risk factors.

Moreover, the strong association of LVM with vascular disease[12–16] leads to the hypothesis that LVM is inversely related to cognitive functioning. The finding of an association between higher LVM and lower cognitive performance may strengthen the hypothesis that long-term exposure to high BP results in subclinical brain injury, which, in turn, results in lower levels of cognitive performance.

Surprisingly, few studies have related LVM or left ventricular hypertrophy to objective measures of cognitive performance. In the Helsinki Aging Study, LVM was associated with a 5-year decline in Mini-Mental State Examination scores for 160 elderly participants.[17] For younger individuals, one would expect a similar relation between LVM and cognition if chronic BP burden affects brain function and, hence, cognition. Given previous findings of a continuous association between LVM and cardiovascular morbidity and mortality in complicated and uncomplicated hypertension,[12,18,19] our investigation focused on a range of LVM values in relation to cognitive functioning.

In this study we related LVM to cognitive performance in the large community-based Framingham Offspring Study sample (mean age: 57 years; SD=9). Our hypotheses were as follows: (1) LVM is inversely related to cognitive performance; (2) the significant association between LVM and cognitive performance is partially but not completely explained by time-averaged BP; (3) adjustment of relations between LVM and cognitive performance for time-averaged BP, cardiovascular risk factors, and cardiovascular disease (CVD) will further attenuate relations between LVM and cognitive performance. If hypothesis 3 is confirmed, it would suggest that cardiovascular risk factors and CVD play an important role in the relation between LVM and cognition.

Methods

Study Sample

The design and sampling procedures for the Framingham Offspring Study have been described previously.[20] Using a standardized medical interview and physical examination, participants are examined for CVD risk factors and CVD every 4 years. Participants who attended examination 6 (referred to as the index examination), received echocardiograms, and participated in neuropsychological testing (N=2208) were eligible for the present investigation. Of these, participants were excluded for the following reasons: history of clinical stroke or transient ischemic attack (n=43); diagnosed dementia (n=4); inadequate or nonavailable data on LVM (n=459); and missing data on relevant clinical risk factors (n=29). After these exclusions, 1673 participants (943 women) remained. The persons missing data on LVM were, on average, older and in generally poorer health than persons for whom LVM was available.[21]

Details of stroke and dementia surveillance methods have been published previously.[22–24] Stroke was defined as a focal neurologic deficit of acute onset persisting >24 hours and transient ischemic attack as an episode of focal neurologic dysfunction of abrupt onset lasting <24 hours, presumably secondary to focal cerebral ischemia. The study protocol was approved by the institutional review board at Boston University Medical Center, and all of the subjects gave written informed consent.

Echocardiographic Measures

At examination cycle 6, participants underwent routine transthoracic M-mode, 2D and Doppler color flow echocardiographic imaging. M-mode left ventricular measurements were obtained using the leading edge-to-leading edge technique.[25] Interventricular septum thickness, posterior left ventricular wall thickness, and left ventricular end-diastolic diameter were measured at end diastole, and LVM was calculated using a validated formula [LVM (g)=0.8 [1.04 (interventricular septum thickness+left ventricular end-diastolic diameter+posterior left ventricular wall thickness)^3−(left ventricular end-diastolic diameter)^3]+0.6 g].[26]

We related LVM measures obtained at examination cycle 6 (January 1995–1998) to the cognitive performance measures obtained an average of 3.5 years later (range: 1.3 to 6.6 years) at examination 7 (1998–2001). Data with respect to LVM were not available at examination 7, but previous studies have reported prospective relations between BP and cognition when BP was measured many years before the measurement of cognition.[8,9] Thus, we anticipated that LVM would be related prospectively to cognitive performance.

Covariates

Education in years was determined at the time of neuropsychological examination. Systolic BP and diastolic BP, based on the average of 2 physician measurements, were determined at examination 6 and also as a mean of all of the available BP values between examination cycles 1 through 6. All of the other covariates (including age, height in centimeters, and weight in kilograms) were obtained at examination cycle 6 unless otherwise noted. The number of cigarettes smoked per day and alcohol consumed (milliliters per week) were classified based on self-report at the index examination. Total cholesterol (milligrams per deciliter) and high-density lipoprotein (milligrams per deciliter) were expressed as a total/high-density lipoprotein cholesterol ratio. Diabetes was considered present if a participant had a fasting blood sugar of ≥126 mg/dL, a previous diagnosis of diabetes, or used a hypoglycemic agent or insulin. Fasting plasma homocysteine concentrations (micromoles per liter) were obtained in the manner described previously.[27] Treatment for hypertension was defined as the proportion of examinations for which the participants were treated with antihypertensive medications. Depressed mood was defined as a score >16 on the Center for Epidemiologic Studies Depression Scale, a self-report instrument.[28] We used the Center for Epidemiologic Studies Depression Scale as a categorical variable for 2 reasons: the Center for Epidemiologic Studies Depression Scale distribution was highly skewed, and we wished to use a clinically relevant index of depressed mood.[27,28] Prevalent CVD included the presence of ≥1 of the following: coronary heart disease (myocardial infarction, angina pectoris, and coronary insufficiency), intermittent claudication, and heart failure. Prevalence or history of CVD was established by a panel of 3 physicians using the relevant clinical data.[29]

Because there was variation among individuals in the time between measurements of LVM and neuropsychological testing, an LVM−neuropsychological testing interval (LVM-NT) variable was constructed by calculating for each participant the years (and fractions of a year) between measurement of LVM and neuropsychological testing.

In the primary analysis, the CVD risk factors and CVD were determined at examination cycle 6. In a set of secondary analyses, these were determined at the time of neuropsychological testing (examination cycle 7).

Neuropsychological Test Performance

The neuropsychological test battery has been described in detail previously[30] and is briefly described in Table 1. The battery has been predictive of future stroke in a previous investigation in the Framingham offspring cohort.[31] A detailed description of each test may be found in Lezak et al.[32] For each test score, the distribution of original (raw) test scores was standardized to z scores by subtracting the mean of the distribution of raw scores from each individual raw score and dividing by the sample SD. This linear transformation does not change the distribution of scores but allows all of the scores to be expressed in SD units.

After confirmatory factor analyses, we used composite scores derived previously from the application of principal components analysis and orthogonal (Varimax) rotation to the multiple individual

TABLE 1. Description of the Cognitive Tests Administered to the Participants of the Framingham Offspring Study (1971–2005)

Neuropsychological Test (1998–2001)	Latent Cognitive Ability Tested
From the Wechsler Adult Intelligence Scale	
Similarities	Abstract reasoning
From the Wechsler Memory Scale	
Paired associates learning	New verbal learning and memory
Logical memory–immediate recall	Immediate recall of verbal passages
Logical memory–delayed recall	Delayed recall of verbal passages
Logical memory–delayed recognition	Delayed recognition of verbal passages
Visual reproductions–immediate recall	Immediate recall of visual/spatial stimuli
Visual reproductions–delayed recall	Delayed recall of visual/spatial stimuli
Visual reproductions–delayed recognition	Delayed recognition of visual/spatial stimuli
From the Hooper Visual Organization Test	Visual organization with some demands on executive function
From the Halstead–Reitan Battery	
Trail-making A	Attention, concentration, visual scanning, and speed of tracking
Trail-making B	Attention, concentration, visual scanning, and speed of tracking; demands on executive function

test scores in the NP battery.[31,33] The resulting composite scores meet the following criteria: (1) outcome variable reduction; (2) each score is constructed from tests indexing a common cognitive factor; (3) no cognitive test is included in >1 composite; and (4) the composites are theoretically meaningful.

Three independent factors were identified and, for consistency among studies, recommended for use in Framingham offspring studies of cognitive performance[33]: (1) factor 1, visual-spatial memory and organization: visual reproduction–immediate recall, visual reproductions–delayed recall, visual reproductions–delayed recognition, and Hooper visual organization; (2) factor 2, verbal memory: logical memory–immediate recall, logical memory–delayed recall, and logical memory–delayed recognition; and (3) factor 3, scanning and tracking: trails A and trails B. Similarities (a measure of abstract reasoning) and paired associates learning loaded on all 3 of the factors, and, thus, they were included in the analysis as separate test scores.

Statistical Analyses Plan

Descriptive statistics were generated for each LVM measure for demographic characteristics and covariates (including means and SDs for continuous variables and percentages for categorical variables). Multivariable regression models with linear and categorical variables were used to examine the associations between the LVM measures (independent variable) and cognitive performance (dependent variable).

The multivariable regression coefficients relating LVM and LVM-z (standardized LVM) to cognition were adjusted for 3 sets of covariates (defined at examination 6): (1) basic: age, height, weight, education, sex, and interval between the measurement of LVM and neuropsychological testing (LVM-NT interval); (2) basic+BP+treatment for hypertension; and (3) basic+BP+treatment for hypertension+risk factors (diabetes mellitus, total cholesterol/high-density lipoprotein cholesterol, alcohol consumed per week, cigarettes smoked per day, plasma homocysteine concentration, and depressed mood)+prevalent CVD. A separate regression analysis

was performed for each measure of BP, systolic BP at examination cycle 6, mean systolic BP, diastolic BP at examination cycle 6, and mean diastolic BP.

In a secondary set of analyses, described later, risk factor, CVD, and BP variables were based on data gathered at the time of neuropsychological testing (examination 7). A 2-sided P value ($P<0.05$) was considered statistically significant.

Results

The primary LVM measures included LVM in grams (LVM-g) and LVM-z. LVM-z was computed by subtracting the mean LVM-g score from each LVM-g score and dividing by the SD of LVM-g. These standardized scores (z scores) were calculated separately for men and women by subtracting the respective sex-specific means and dividing by the respective sex-specific SD. This linear transformation is useful for model interpretation, because regression coefficients reflect that change in cognitive performance relative to a similar increment (1 SD change) in LVM for both men and women.

Descriptive Data

Table 2 contains descriptive statistics for the covariates used in the present study. The mean and SD values for LVM-g were 164.3 and 45.3 for the sex-pooled sample, respectively. Mean values for LVM-g were significantly lower for the women (140.8; SD=30.7) than for the men (194.6; SD=43.1; $P<0.0001$). The sex-specific LVM-z transformation resulted in a mean of z=0 and SD of z=1 for men, women, and the sex-pooled samples.

Relations Between LVM and Cognition

We examined the distributional properties of the echocardiographic and the cognitive performance measures. LVM-g was

TABLE 2. Demographic and Health Characteristics of the Study Participants (N=1673; 943 women) at Examination Cycle 6

Variable	Mean (SD)*	Range
Age, y	57 (9)	32 to 85
Education, y	14.6 (2.3)	4 to 16
Systolic BP, mm Hg	126 (19)	84 to 216
Diastolic BP, mm Hg	75 (9)	49 to 118
Mean systolic BP, mm Hg†	122 (14)	87 to 236
Mean diastolic BP, mm Hg†	76 (7)	56 to 98
Height exam 6, cm	169.6 (9.1)	132 to 193
Weight exam 6, kg	76.9 (15.7)	41 to 148
Total cholesterol/HDL	4.31 (1.52)	1.62 to 12.25
Cigarettes per day	3 (8)	0 to 60
Plasma homocysteine, μmol/L	8.1 (3.0)	3.3 to 65.21
Alcohol, mL/wk	76 (95)	0 to 1124
Diabetes mellitus, %	8.6	
Depressed mood (CESD >16), %	9.4	
Treatment for hypertension, %	23.1	
Prevalent CVD, %	6.9	

HDL indicates high-density lipoprotein; CESD, Center for Epidemiologic Studies Depression Scale.

*Percents for binary variables.

†The mean of blood pressure values from examinations 1 to 6.

TABLE 3.   Regression Coefficients (β) and SEs Expressing Associations Between 1 SD Increments in LVM (LVM-z) and Cognitive Performance in Units of SD (*z* Scores)

Cognitive Test Scores	Regression Coefficient or SE	Basic*	Basic+BP+Treatment for Hypertension		Basic+BP+Treatment for Hypertension+Risk Factors+CVD	
			With Exam 6 SBP	With Mean SBP	With Exam 6 SBP	With Mean SBP
Similarities	β	−0.062†	−0.058†	−0.055†	−0.033	−0.031
	SE	0.026	0.026	0.026	0.028	0.028
Visual–spatial memory and organization	β	−0.071‡	−0.063§	−0.061§	−0.033	−0.032
	SE	0.020	0.021	0.021	0.022	0.022
Verbal memory	β	−0.047†	−0.045	−0.042	−0.034	−0.033
	SE	0.023	0.024	0.024	0.025	0.025
Scanning and tracking	β	−0.041	−0.034	−0.029	−0.027	−0.022
	SE	0.022	0.023	0.023	0.023	0.023
Paired associates	β	−0.003	−0.004	−0.004	−0.006	−0.006
	SE	0.026	0.026	0.026	0.028	0.028

*Basic covariate set is age, education, sex, height, weight, and LVM-NP interval.
†$P<0.05$; ‡$P<0.001$; §$P<0.01$.

skewed, so the distribution was normalized via a natural logarithmic transformation. Similarly, it was necessary to normalize 2 cognitive measures (trails A and B) using the natural logarithmic transformation.

We examined the sex×LVM-g interactions by introducing the interaction term into the multivariable regression models described previously. For each of the cognitive measures, the interaction between sex and the various measures of LVM was not statistically significant for any of the regression models (all $P>0.16$). Tests of nonlinear relations (quadratic trend) between the LVM-g and cognition test scores were also statistically nonsignificant for all of the cognitive measures (all $P>0.07$). Higher-order terms were, therefore, excluded from all further analyses. Because results were highly similar for the LVM and the LVM-z measures, we present findings for the standardized measure of LVM (LVM-z), because it takes into account the differences in LVM mass for men and women.

Relations Between LVM-z and Cognition

Table 3 summarizes associations between the LVM-z and cognitive performance with adjustment for the 3 sets of covariates defined above. With adjustment for the basic covariate set, LVM-z was inversely and significantly related to the similarities score, the visual-spatial memory and organization composite score, and the verbal memory composite score.

When either the basic+examination 6 systolic BP+treatment for hypertension or the basic+mean systolic BP+treatment for hypertension covariate set was used, relations between LVM-z and verbal memory were modestly attenuated and rendered nonsignificant. However, the significant relations between LVM-z and similarities and LVM-z and the visual–spatial memory and organization composite remained statistically significant.

When relations between LVM-z and cognitive performance were adjusted for the basic+BP+treatment for hypertension+risk factor+CVD covariate set, regression coefficients relating LVM-z to cognition were further attenuated, and no significant relations between LVM-z and cognitive performance were observed. The pattern of significant associations between LVM-z and cognitive performance was similar when mean diastolic BP was substituted for mean systolic BP in the regression models. A table describing results with mean diastolic BP in the regression models may be seen in the supplemental data (available online at http://hyper.ahajournals.org). Findings were the same when BP, treatment for hypertension, CVD risk factors, and CVD were based on data obtained at the time of neuropsychological testing.

Inspection of the regression coefficients (Table 3) expressing the relation between LVM-z and cognitive performance scores provides information with regard to the magnitude of associations. For example, with adjustment for mean systolic BP, each 1 SD increment in LVM (30.7 g in women and 43.1 g in men) was associated with a 0.06-SD decrement in performance level for the similarities score ($\beta=-0.055$) and a 0.06-SD decrement for the visual–spatial memory and organization composite score ($\beta=-0.061$). In Figures 1 and 2, we illustrate the inverse linear relation between LVM-z and similarities and for visual–spatial memory and organization adjusted for the variables in the basic+mean systolic BP+treatment for hypertension covariate set. The regression lines represent a plot of the predicted values for cognitive performance for SD increments in LVM.

Additional Analyses

Please see the online data supplement for tables summarizing each of the following additional analyses. When treatment for hypertension was deleted from the 2 models that included
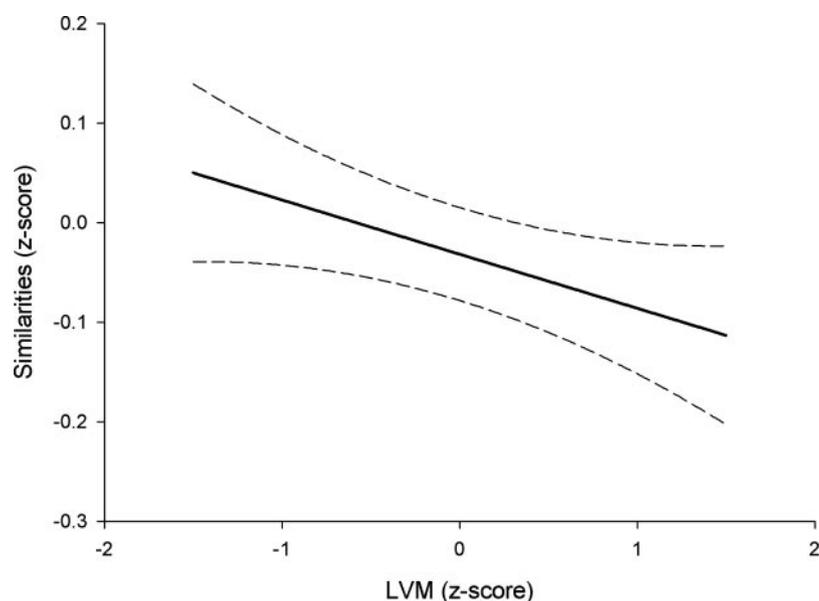
Figure 1. Illustration of the slope coefficient (with 95% CI) relating LVM to the similarities score for the basic+mean systolic BP+treatment for hypertension model.

either systolic or diastolic BP, the same significant relations between LVM-z and similarities and LVM-z and visual–spatial memory and organization were observed with slightly larger regression coefficients. To determine whether our findings were unique to our method of adjusting for height and weight, we constructed a second measure of LVM, that is, LVM/height, and repeated the analyses above (with height removed from each of the regression models). The pattern of relations between LVM/height and cognitive performance was the same.

Although LVM is the central feature of the present study, it is important to determine whether BP, a crucial covariate in the analyses, was, in fact, related to the cognitive measures for all of the models that include LVM and treatment for hypertension. Mean systolic BP (examination cycles 1 to 6) was related to the following measures of cognitive performance with adjustment for the basic+LVM+treatment for hypertension covariate

set: visual–spatial memory and organization ($\beta=-0.042$; $P<0.05$), verbal memory ($\beta=-0.046$; $P<0.05$), and scanning and tracking ($\beta=-0.042$; $P<0.05$). It was related to the following measures of cognitive performance with adjustment for the basic+LVM+treatment for hypertension+risk factors+CVD covariate set: verbal memory ($\beta=-0.047$; $P<0.05$) and scanning and tracking ($\beta=-0.040$; $P<0.05$). The same result was obtained when mean systolic BP was calculated on the basis of BP values from examinations 1 to 7.

Discussion

Consistent with our first hypothesis, we observed an inverse association between measures of LVM and cognitive performance in our middle-aged-to-elderly community-based sample. With adjustment for the basic covariate set (age, education, sex, weight, height, and the LVM-NP interval), LVM-z was related to similarities, visual–spatial memory and orga-
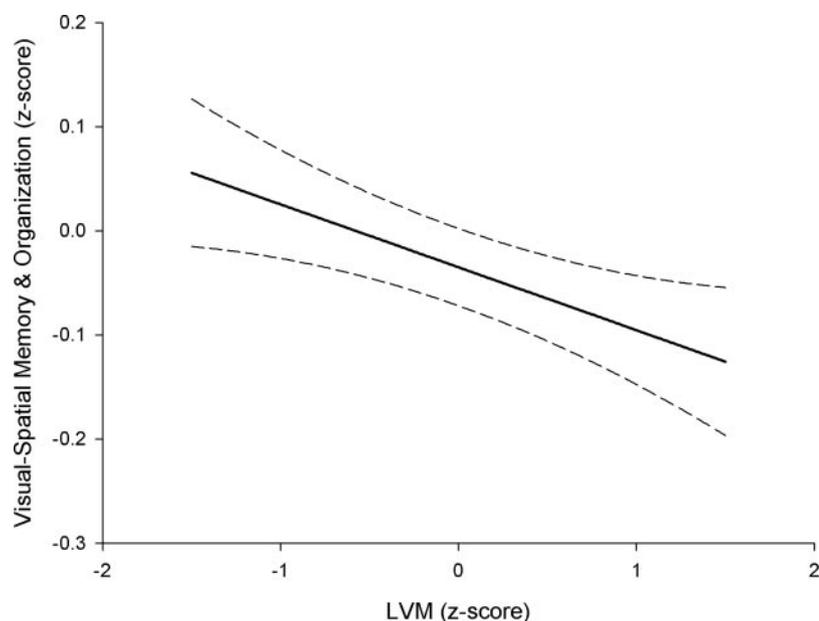

Figure 2. Illustration of the slope coefficient (with 95% CI) relating LVM to the visual–spatial memory and organization composite score for the basic+mean systolic BP+treatment for hypertension model.

nization, and verbal memory. The alternative LVM/height measure was also related to these measures and additionally to the scanning and tracking composite. Generally, our observations are consistent with the finding that LVM, adjusted for age and sex, was associated with a 5-year decline in Mini-Mental State Examination scores for a sample of persons ≥75 years of age in the Helsinki study.[17]

We now focus on findings with respect to the adjustment of LVM-z for systolic BP. When either examination 6 systolic BP or time-averaged systolic BP was added to the basic covariate set, including treatment for hypertension, relations between LVM-z and cognitive performance were attenuated, but LVM-z continued to be related significantly to similarities (an index of abstract reasoning ability) and visual–spatial memory and organization. The relation between LVM-z and verbal memory was rendered nonsignificant by adjustment for mean systolic BP and treatment for hypertension, but attenuation of the regression coefficient was minor. These observations are consistent with our second hypothesis that relations between LVM and cognition are not completely explained by time-averaged systolic BP. One possible reason why there is a residual association of LVM and cognitive performance, regardless of adjustment for time-averaged or examination-specific systolic BP, is that LVM also serves as a sensitive indicator of lifelong exposure to BP-related risk factors and CVD.[12,16,18,19]

Indeed, consistent with our third hypothesis, with adjustment for the basic+BP+treatment for hypertension+risk factors+CVD covariate set, all of the relations between LVM-z and cognition were attenuated and rendered nonsignificant. When LVM/height was substituted for LVM-z, the same results were obtained. This finding suggests that the risk factors and CVD events used in our analyses play an important role in the relation between LVM and cognition.

It seems reasonable to hypothesize that similar, although not identical, pathophysiological mechanisms may mediate the associations of lowered cognitive performance with both LVM and BP. For example, both BP and LVM may be surrogate markers of subclinical atherosclerosis in the cerebrovascular territory.[13] Yet the observation that, unlike LVM-z, mean systolic BP was related to the verbal memory and scanning and tracking composites for the LVM+BP+treatment for hypertension+RF+CVD model suggests a dissimilarity with respect to ≥1 mechanism mediating relations among LVM, systolic BP, and cognition. This is speculative and, thus, is a hypothesis for further studies involving neuroimaging methods and other cognitive domains as outcome variables.

The relations among LVM and cognition were modest and, thus, may not reflect clinically significant deficits at an individual level. For example, for the basic model, a person 2 SD above the mean of LVM-g would show a 0.24-SD decrement in performance on the visual–spatial memory and organization composite score relative to a person 2 SD below the mean of LVM-g. Nevertheless, as emphasized in the BP[1,4,5,9] and dementia[23] literature, even small decrements in cognitive ability of individuals are significant from an epidemiological and public health perspective, that is, these modest decrements may progress to more serious forms of deficit.[23]

Limitations

Several limitations of our study merit comment. Framingham Offspring Study participants are relatively well educated.[30] It is well known that education is protective with respect to cognitive performance decrement.[34] It is also possible that persons with more extreme LVM values did not participate in our study because of several factors, including early mortality, exclusion of participants with stroke, and the requirement to attend an ancillary study for neuropsychological testing. However, higher levels of education and survivorship very likely contribute to an underestimation of the association of LVM with cognition. The Framingham offspring sample consists of mostly white individuals, thereby limiting the generalizability of our findings to other ethnic/racial groups. Finally, LVM was assessed on average 3.5 years before neuropsychological performance. Hence, we cannot exclude the possibility that the LVM may have changed in the interim. Nevertheless, as has been true for previous studies of BP,[8,9] LVM exhibited a prospective association with lowered cognitive performance.

Perspectives

In stroke- and dementia-free individuals, echocardiographic LVM is associated inversely with cognitive performance, but these associations are attenuated with adjustment for mean systolic BP. They are further attenuated and rendered statistically nonsignificant with adjustment for mean systolic BP, cardiovascular risk factors, and cardiovascular events. Additional studies are warranted to confirm our findings, particularly in cohorts with longitudinal BP data collection and multiethnic samples with a wider education range. Studies identifying mediators of the relations between LVM and cognition (eg, as identified by brain imaging) are particularly important. Overall, the association of LVM with cognition suggests that lifelong exposure to vascular risk factors may adversely influence cognitive performance in later years, because LVM is regarded as an indicator of time-integrated exposure to vascular risk factors (including BP) and subclinical target organ damage as a consequence of such exposure. Although our data are observational, they are consistent with the concept that LVM is a risk marker for lower cognitive performance and that prevention and treatment of vascular risk factors throughout the life course may be associated with better cognitive performance in older age.

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