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Left Atrial Size is Independently Associated with Cognitive Function

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Abstract

Left atrial (LA) diameter is easily attainable from echocardiograph and sensitive to underlying cardiovascular disease severity, though its association with neurocognitive outcomes is not well understood. Fifty older adults (64.50 ± 9.41 years) recruited from outpatient cardiology clinics and local papers underwent magnetic resonance imaging (MRI), were administered the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), and completed psychosocial self-report measures. LA diameter was quantified using echocardiogram. Hierarchical regression analyses revealed greater LA size was independently associated with reduced performance on the following RBANS composites: language, delayed memory, and total index ($p < .05$ for all). Hierarchical regression analysis demonstrated no significant association between LA diameter and whole brain volume ($p > .05$). The current study suggests that greater LA size is associated with cognitive dysfunction in older adults and prospective studies are needed to validate these findings and elucidate underlying mechanisms.

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Declaration of Interest

There are no conflicts of interest.

Keywords

Left Atrial Diameter; Cognitive Function; Cardiovascular Disease; Echocardiogram; Neuroimaging; Cerebrovascular disease

1. Introduction

Cardiovascular disease (CVD) affects nearly 83 million Americans and is among the leading causes of disability, mortality, and morbidity in the United States [1]. CVD will likely remain a major public health concern due to elevated rates of common CVD risk factors within the US population, including hypertension, diabetes, obesity, lack of physical activity, smoking, among others [1].

There is a vast literature linking CVD with cognitive impairment. In fact, vascular cognitive impairment (VCI) is a term coined to describe a stage on the continuum of cognitive impairment and consists of mild impairments that do not yet meet the criteria for dementia that are secondary to vascular related pathology [2]. VCI is estimated to impact nearly 15–20% of older adults in clinical settings [3]. VCI-related deficits are most commonly found in attention, executive function, psychomotor speed, and information processing speed [2,4–6]. Such deficits appear to be a result of impaired cardiac function in CVD, resulting in cerebral hypoperfusion and subsequent cerebrovascular disease [7–9].

Cognitive impairment is also evident among individuals at risk for CVD, as past work has independently linked traditional CVD risk factors with cognitive dysfunction, including hypertension, diabetes, obesity, sedentary behaviors, and smoking [10,11]. The effects of these CVD risk factors on cardiac function may account for their impact on cognition. For instance, echocardiographic findings (i.e., left ventricular (LV) hypertrophy, LV systolic and diastolic dysfunction, mitral annular calcification, cardiac output) have been shown to uniquely contribute to cognitive impairment and neuropathological insult [7,12–19].

Left atrial (LA) diameter is also easily attainable from echocardiograph, and LA dilation is an independent predictor of cardiovascular events, including increased risk for stroke and heart failure [20–22]. Notably, LA dilation can also occur outside the context of CVD, as LA diameter increases with age and can be genetically predisposed [23,24]. Because LA dilation is a manifestation of systolic and diastolic dysfunction [25–27] there is reason to believe that it may provide key insight into cognitive function. Indeed, past work has shown LA size shares similar prognostic properties as left ventricular ejection fraction (i.e., hospitalizations and mortality)—an index of cardiac pumping efficiency associated with cognitive function [7,28,29]. Moreover, the sensitivity of LA size to the severity of cardiac dysfunction and its possible association with cerebral hemodynamics is further reason to suspect that LA diameter may serve as a useful detector of cognitive impairment [25,27,30–32].

In response to these findings, one recent study found a significant association between greater LA size with cognitive dysfunction and abnormal neuroimaging—though this relationship was demonstrated in a sample of dementia patients >80 years old without

accounting for confounding medical variables [31]. As such, it is unclear whether LA dilation may provide additive utility to the detection of cognitive impairment above and beyond other commonly used measures of cardiac function (i.e., ejection fraction) in non-demented samples. The purpose of the current study was to examine whether LA diameter independently contributes to cognitive function after adjusting for ejection fraction and other known CVD-related risk factors of cognitive impairment. We additionally sought to examine the independent relationship between LA diameter and whole brain volume.

2. Methods

2.1 Participants

The current sample consisted of 50 participants with complete neuropsychological, medical, and demographic data (64.50 ± 9.41 years of age, 58.0% female, 15.94 ± 2.49 years of education, and 92.0% Caucasian). However, analyses examining magnetic resonance imaging (MRI) consisted of 48 participants due to missing neuroimaging data for two individuals. Refer to Table 1 for further demographic and medical information of the current sample.

Participants were recruited from either outpatient cardiology offices ($n = 38$) or from advertisements in local papers ($n = 12$). Although the small sample size of the community participants may preclude significant between group differences, no significant differences were found between participants recruited from cardiology clinics and those from newspapers on key medical and demographic variables, including age, sex, years of education, LA size, LV ejection fraction, or history of medical comorbidities (e.g., diabetes, hypertension, heart failure, cardiac arrhythmia, or mitral valve regurgitation; $p > .10$ for all). There were also no between group differences in cognitive function ($p > .10$). The inclusion criteria were English-speaking and normal or corrected hearing and vision at the time of testing. Potential participants were excluded for significant neurological disease (e.g., history of stroke, multiple sclerosis), moderate or severe traumatic brain injury (with loss of consciousness), diagnosis of a current psychiatric illness, history of substance abuse with subsequent hospitalization, or any contraindications for magnetic resonance imaging (MRI; e.g., some metal implants). Participants were administered a brief neuropsychological battery. Lastly, all participants scored above the cutoff for dementia (Mini Mental State Examination > 24) and no participants had a clinical diagnosis of dementia [33]. Institutional IRB approval was granted and informed consent was obtained from all participants prior to testing.

2.2 Procedures

2.2.1 Echocardiogram—A complete, transthoracic echocardiogram was obtained with two-dimensional apical views from each participant according to standards of the American Society of Echocardiography [34]. From these data three parameters were derived: degree of mitral regurgitation, left ventricular (LV) ejection fraction, and left atrial dimension. The degree of mitral regurgitation was graded as mild, moderate or severe by integration of semiquantitative visual assessment of spectral and color Doppler and quantitative measure of vena contracta as per ASE guidelines [35]. The biplane method of discs (or Simpson's

rule) calculates left ventricular volumes from the summation of areas from diameters of 20 cylinders, discs of equal height; these are apportioned by dividing the chambers longest length into 20 equal sections. Left ventricular ejection fraction is calculated based upon biplane volumes (i.e., $EF = EDV - ESV / EDV$). Left atrial dimension was measured in the anterior-posterior dimension from the parasternal long-axis view.

2.2.2 Magnetic Resonance Imaging—Anatomical reference was acquired on a Siemens 3T Tim Trio scanner by a sagittally-oriented whole-brain Magnetization Prepared Rapid Gradient Echo (MP-RAGE) acquisition with a slice thickness of 1mm; FOV 256mm; imaging matrix 256×256 ; and $TE / TR / TI / \alpha = 4ms / 9.7ms / 300ms / 12^\circ$; BW = 130 Hz/Px. For morphometric analyses, T1 volumes were normalized to the Montreal Neurological Institute geometry and compared to standard T1 templates segmented into gray, white, CSF, and non-brain tissues. These procedures are based on established techniques and procedures for the surface and subcortical reconstruction using the FreeSurfer software package and have been described previously [36–41]. The fully automated FreeSurfer v5.0 recon-all processing stream was completed for 48 participants. After preprocessing, results underwent quality control measures via manual examination to confirm absence of any for errors or defects in the segmentation.

2.2.3 Neurocognitive Assessment—All participants completed a standardized neuropsychological assessment by trained research assistants under the supervision of a licensed clinical neuropsychologist. For the purposes of the current work, the primary outcome measure came from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [42]. This brief battery consists of ten subtests that divide into five index scores (i.e., immediate and delayed memory, language, visuospatial processing/construction, and attention). Subtests are similar to other popular standardized batteries; language consists of tasks assessing confrontation naming and semantic fluency, attention taps digit span and a coding task, and visuospatial/construction abilities are measured from production of a complex figure and a modified judgment of line orientation. The memory subtest consists of immediate memory of verbal information from a list learning procedure and a prose passage. Delayed memory includes these verbal tasks as well as incidental recall of the complex figure. In addition, a total index score is derived from the summation of the index scores representing a global score of functioning.

2.2.4 Depressive Symptomatology—Depression was assessed using the Beck Depression Inventory-II (BDI-II). The BDI-II is a commonly used check-list of depressive symptoms that demonstrates good psychometric properties in persons with medical conditions (i.e., test-re-test reliability of $r = .93$ to $r = .96$, and an internal consistency of $r = .54$ to $r = .74$) [43,44]. BDI-II scores range from 0–63 with higher scores indicative of greater symptomatology.

2.2.5 Physical Activity—The Rapid Assessment of Physical Activity (RAPA) was administered to all participants to assess physical activity levels in the current sample. It is a validated measure [45] that asks participants to indicate ‘yes’ or ‘no’ to 9-items assessing

participation in intensity varying levels of physical activity. The first seven questions are scored and a value below six is considered suboptimal participation in physical activity [46].

2.2.6 Estimated Premorbid Intelligence—To assess premorbid intelligence, the Wechsler Test of Adult Reading (WTAR) was administered to all participants. The WTAR asks individuals to read aloud a list of 50 irregular pronounced words. The WTAR is a valid estimate of premorbid intelligence [47].

2.2.7 Demographic and Medical Characteristics—The patient's medical history and currently prescribed medications were self-reported; data elements were reviewed and confirmed by a clinical cardiologist.

2.3 Statistical Analyses

All RBANS composite scores were converted to standard scores (i.e., a distribution with a mean of 100 and a standard deviation of 15) adjusted for age using normative values. A summary composite of volume for each brain region including frontal, temporal, parietal, and occipital was then calculated using the organization schema as described in Desikan et al. (2006) [48]. Whole brain volume consisted of the sum of frontal, temporal, parietal, and occipital lobe.

A multiple linear hierarchical regression analysis was performed for each RBANS composite including immediate memory, visuospatial/construction, language, attention, delayed memory, and the RBANS total index score. Demographic and medical characteristics were entered into block one of the model. Specifically, demographics included age, sex (−1 = male; 1 = female), years of education, and premorbid intelligence (as estimated by the WTAR). Medical characteristics included depressive symptomatology (as assessed by the BDI-II), LV ejection fraction, degree of mitral regurgitation (1 = mild, 2 = moderate, 3 = severe), end diastolic volume (EDV), diagnostic history of hypertension, diabetes, cardiac arrhythmia, thyroid disease, and heart failure (1 = positive history; 0 = negative history for all), and current cardiovascular medication status (1 = yes; 0 = no). These medical conditions were included as covariates to account for their well-established effects on both cognitive and cardiac function. LA diameter was then entered into the second block of each model to determine its incremental predictive validity on the RBANS composites beyond medical and demographic characteristics. Finally, hierarchical regression analysis adjusting for the same medical and demographic characteristics as above in addition to intracranial volume was then conducted to examine the relationship between LA diameter and whole brain volume.

3. Results

CVD Characteristics and Echocardiograph Findings

Overall, 10% of the sample exhibited a positive diagnostic history of coronary artery disease, 14.0% cardiac arrhythmia, 10.0% myocardial infarction, and 10.0% had a heart failure diagnosis. Comparatively, CVD risk factors were also prevalent with particularly high rates of hypertension in the current sample (e.g. 40%). Additionally, 64% of the sample were prescribed at least one CVD medication. Specifically, 15% of the sample was

prescribed angiotensin-converting enzyme inhibitor, 4.0% antiarrhythmics, 56.0% statins, and 77.0% antihypertensive agents. The sample demonstrated an average LV ejection fraction of 51.09 (SD = 9.38) and an average LA diameter of 3.21 cm (SD = .65). Of the sample, 30% exhibited an LVEF > 55 and 4.0% had an LA diameter > 4.0 cm. Similarly, 70% of the sample was characterized as having mild mitral regurgitation and end diastolic volume levels fell within the normal range ($M = 75.60$, $SD = 22.78$). Refer to Table 1 for remaining CVD and CVD risk factor characteristics in the current sample. Of note, LA diameter was not significantly associated with LV ejection fraction in the current sample ($r(48) = .17$, $p = .23$).

Neuropsychological Test Performance

When considered as a group, the current sample demonstrated average performance across all of the RBANS composite scores, with an RBANS total index composite average of 104.22 (SD = 14.78). However, when using clinical convention to define cognitive impairment (i.e., 1.5 SD below the mean), a number of participants exhibited impairments on RBANS composite scores (see Table 2).

LA Diameter is Independently Associated with Cognitive Function

See Table 3 for a summary of medical and demographic predictors of the RBANS composites. Notably, LV ejection fraction was not significantly associated with any of the RBANS composite scores ($p > .05$ for all). After accounting for medical and demographic characteristics, LA diameter demonstrated significant associations with the RBANS language composite ($\beta = -.45$, $p = .04$), delayed memory composite ($\beta = -.47$, $p = .02$), and the total index composite ($\beta = -.41$; $p = .04$). In each case, greater LA diameter was associated with reduced test performance. No such pattern emerged for the RBANS immediate memory, visual/construction or attention composite ($p > .10$ for both).

LA Diameter and MRI Findings

Hierarchical regression analysis adjusting for medical variables, demographic characteristics, and intracranial volume revealed LA diameter was not associated with WBV ($\beta = .09$, $p = .43$). In light of the effects of LA size on memory, we conducted post-hoc analyses examining the association between LA diameter and temporal lobe structures (i.e., parahippocampal gyrus, transverse temporal, temporal pole, superior, middle, and inferior temporal gyrus, and insula cortex). Partial correlations adjusting for medical variables, demographic characteristics, and intracranial volume showed no significant association between LA diameter and any of these structures for either hemisphere ($p > .05$ for all).

4. Discussion

Past work has shown indices of cardiac function commonly obtained from echocardiography are independent predictors of CVD risk and associated with cognitive function [12–16,49–52]. Assessment of LA diameter is part of standard echocardiography and has been identified as a predictor of hospitalization and mortality among patients with CVD [29]. The current study extends these findings and suggests that LA diameter is also independently

associated with cognitive function. Several aspects of these findings warrant brief discussion.

The current results suggest that larger LA diameter is associated with reduced cognitive function independent of medical and demographic characteristics in a sample of older adults, despite largely intact performance on cognitive testing. A likely explanation for these findings is the sensitivity of LA size to underlying CVD severity, as it is reflective of abnormalities in diastolic filling [25,27] and closely related to LV diastolic pressure [25]. Interestingly, the enlargement of the LA causes secretion of atrial natriuretic peptide (ANP) [51], which is involved in the regulation of many physiological processes, including natriuresis, diuresis, and vasodilation—factors commonly linked with cognitive function [54–57]. Recent work also has shown proatrial natriuretic peptide—a stored inactive molecule synthesized from ANP—to be elevated in Alzheimer’s disease patients and to predict conversion from mild cognitive impairment to Alzheimer’s disease [58–60]. These findings suggest that LA diameter may be useful in the detection of cognitive impairment and prospective studies are needed to determine the mechanisms for this association.

The current study found no association between LA size and whole brain volume. Although Oh and colleagues [31] found a significant association between LA size and neuroimaging abnormalities in a sample of geriatric patients with dementia, this relationship may have been confounded by neuropathology secondary to dementia or other confounding medical conditions (i.e., hypertension). It has been proposed that cardiac dysfunction alters cerebral blood flow to produce subsequent cerebral damage [8,9,16,61] and there is extant evidence linking measures of cardiac morphology (i.e., aortic root diameter, LV hypertrophy, carotid intima media thickness) and cardiac dysfunction with neuroimaging indices [15–18]. The current findings suggest that LA size may predict cognitive decline before structural damage is revealed on traditional neuroimaging indices. Future studies are needed to determine whether LA diameter is associated with vascular-related changes on neuroimaging (e.g. perfusion) or the degree to which medical intervention for LA dilation [62] may improve cognitive function.

LV ejection fraction was not related with cognitive function in the current study. LV ejection fraction is commonly used to assess cardiac function among patients with CVD, though the association (i.e., linear vs. non-linear) between LV ejection fraction and cognitive function varies across studies [7,63,64]. Similarly, much of past work demonstrating a relationship between reduced LV ejection fraction and cognitive impairment are among samples of patients with advanced CVD (i.e., mean LV ejection fraction < 30) [28,64,65]. It is possible that no relationship emerged in the current study as the sample exhibited largely preserved levels of cardiac function. Additionally, previous work suggests that CVD and CVD risk factors may influence the relationship between echocardiographic findings and cognition and this phenomenon may be occurring with LV ejection fraction in the present study [66]. Finally, the current study also found no association between LA size and LVEF. This finding is in contrast to previous work that shows LA enlargement is a sensitive predictor to abnormal LV ejection fraction [67]. Past work has suggested that LA dilation is indicative of structural cardiac damage and may be a more sensitive indicator of disease severity relative to a patient’s current rates of cardiac

function (e.g., LV ejection fraction) [68]. Our findings support this notion and given that LVEF fell within the normal range, LA size may still predict neurocognitive outcomes. Future studies are needed to clarify the role and sensitivity of LA diameter and LV ejection fraction in identifying patients at risk for cognitive decline.

Finally, the current association between LA size and memory and language deficits is in contrast to the more typical findings of frontal-mediated impairments in persons with CVD, including attention, executive dysfunction and psychomotor slowing [69–72]. The exact reason for this pattern of findings is unclear. One possibility is that diastolic dysfunction and subsequent LA dilation produce a different pattern of impairments than the more commonly examined systolic dysfunction. For instance, higher diastolic pressure has been shown to accelerate damage to subcortical regions, including atrophy of the hippocampus [73,74]. Methodological limitations may have also accounted for the non-significant association between LA size and frontal-mediated impairments, including the use of the relatively brief RBANS. Indeed, the RBANS does not contain any measures designed to assess executive functions. Future work is needed to examine whether the above findings regarding diastolic pressure also extend to LA diameter and to also differentiate the underpinnings of neurocognitive consequences associated with LA size compared to other measures of cardiac function.

Several limitations of the current study deserve brief mention. First, the current study consisted of cross-sectional data, and prospective studies are needed to validate our findings and clarify whether cognition declines as a function of LA size. Additionally, future work should also examine the validity of LA diameter as an indicator of CVD severity relative to other indices of cardiac function, including its predictive validity of psychosocial outcomes (i.e., adherence behaviors, quality of life). Consistent with this notion, future studies should examine whether healthy lifestyle habits (e.g., physical activity, diet) produce cognitive benefits through their impact on improved cardiac function, including LA size.

Several other areas are also in need of further research. Future work should also elucidate whether LA dilation increases risk for post-operative cardiac surgery neurocognitive impairment, as LA size has been identified as a predictor of atrial fibrillation following cardiac surgery [75]. Similarly, the association between LA size and neurocognition should also be investigated using additional neuropsychological measures that complement brief cognitive screening batteries as well as more detailed estimates of LA volume [23]. In addition, prospective studies that examine the association between LA size and brain volume would help clarify the differential effects of LA dilation on regions associated with memory and language. Finally, larger and more diverse samples, including across various CVD populations (i.e., heart failure, coronary heart disease), are also needed to confirm and increase the external validity of the current findings.

Conclusions

In brief summary, the current study found that LA diameter is associated with cognitive function above and beyond medical and demographic characteristics and measures of cardiac function. LA diameter is easily attainable from echocardiograph and may provide unique insight into cognitive function not otherwise provided by other commonly used

indices of cardiac function (e.g., LV ejection fraction). Prospective studies are needed to validate our findings and elucidate underlying mechanisms between LA diameter and cognitive function.

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Table 1Demographic and Medical Characteristics (*N* = 50)

Demographic Characteristics	
Age, mean (SD)	64.50 (9.41)
Sex (% Women)	58.0
Race (% Caucasian)	92.0
Education, mean (SD)	15.94 (2.49)
WTAR, mean (SD)	111.66 (7.24)
Echocardiograph Findings	
LV Ejection Fraction, mean (SD)	51.09 (9.38)
LA Diameter, mean (SD)	3.21 (.65)
Severity of Mitral Regurgitation (% mild, moderate, severe)	70.0, 28.0, 2.0
End Diastolic Volume, mean (SD)	75.76 (22.78)
Neuroimaging Findings	
Whole Brain Volume, mean (SD)	443618.94 (50529.51) mm ³
Medical and Clinical Characteristics (% yes)	
BDI-II, mean (SD)	5.20 (5.89)
Body Mass Index, mean (SD)	26.49 (4.67)
Smoker	44.0
RAPA, mean (SD)	1.52 (1.18)
Coronary Artery Disease	14.0
Cardiac Arrhythmia	14.0
Myocardial Infarction	10.0
Heart Failure	10.0
Hypertension	40.0
Diabetes	10.0
Thyroid Disease	16.0
CVD Medication Status	64.0
ACE Inhibitor	30.0
Antidysrhythmics	4.0
Antihyperlipidemics	56.0
Antihypertensive Agents	77.0
Heart Valve Replacement Surgery	8.0
Stent Insertion	2.0
Coronary Artery Bypass Graft Surgery	14.0

ACE = Angiotensin-converting enzyme; BDI-II = Beck Depression Inventory-II; RAPA = Rapid Assessment of Physical Activity Assessment; CVD = Cardiovascular disease; LA = Left Atrial; LV = Left Ventricular; WTAR = Wechsler Test of Adult Reading

Table 2Descriptive statistics of cognitive test performance ($N = 50$)

<u>RBANS COMPOSITES</u>	<u>Mean, (SD)</u>	<u>% 1.5 SD Below Average</u>
Immediate Memory	103.96 (15.19)	6.0
Visuospatial/Construction	100.54 (18.04)	16.0
Language	103.30 (11.16)	2.0
Attention	105.82 (12.51)	4.0
Delayed Memory	100.90 (13.78)	8.0
Total Index	104.22 (14.78)	8.0

Table 3

Hierarchical Multiple Linear Regression Models Examining the Predictive Validity of Left Atrial Diameter on Cognitive Function ($N = 50$)

	RBANS composites				
	Immed. Mem. <i>b</i> (<i>SE b</i>)	Visuo <i>b</i> (<i>SE b</i>)	Lang <i>b</i> (<i>SE b</i>)	Atten. <i>b</i> (<i>SE b</i>)	Delay Memory <i>b</i> (<i>SE b</i>)
<i>Block 1</i>					
Age	-.41(.33)	.09(.41)	-.26(.27)	.35(.25)	.09(.30)
Sex	2.86(3.20)	-.51(3.89)	2.11(2.57)	4.02(2.34)	.50(2.87)
Education	1.26(1.12)	2.91(1.37)*	.89(.90)	-.32(.84)	1.71(1.01)
WTAR	.52(.35)	.53(.43)	.13(.28)	.98(.26)**	.66(.32)*
LVEF	.11(.25)	-.33(.29)	.11(.20)	.09(.18)	-.24(.22)
MR	7.45(4.88)	4.16(5.93)	5.60(3.92)	-6.75(3.62)	.16(4.38)
EDV	-.08(.14)	-.12(.17)	.01(.11)	.16(.10)	-.05(.13)
HTN	-4.66(5.41)	.55(6.58)	4.75(4.35)	-.53(4.02)	-8.93(4.86)
Arrythmia	-5.19(6.72)	-2.73(8.18)	2.58(5.41)	4.33(4.99)	-.87(6.04)
Thyroid	1.47(6.12)	4.94(7.45)	-2.15(4.93)	2.78(4.55)	-.65(5.50)
HF	.95(8.18)	-1.37(9.95)	4.09(6.58)	-2.03(6.08)	14.89(7.35)*
Diabetes	6.30(8.70)	-.11(10.56)	3.58(7.00)	-9.33(6.46)	.24(7.81)
CVD Med.	-.99(6.24)	3.74(7.59)	-8.93(5.02)	3.15(4.64)	.37(5.61)
BDI-II	.08(.43)	.43(.55)	.30(.36)	.37(.34)	.27(.41)
R^2	.35	.32	.22	.47	.36
F	1.34	1.15	.70	2.20*	1.41
<i>Block 2</i>					
LA Diam.	-7.14(4.57)	-4.71(5.70)	-7.74(3.57)*	-3.40(3.47)	-9.95(3.89)*
R^2	.39	.33	.31	.48	.41
F for R^2	2.44	.68	4.71*	.96	6.55*
					4.39*

Note.

* denotes $p < .05$

** denotes $p < .01$

Abbreviations: Atten = Attention; BDI-II = Beck Depression Inventory-II; CVD Med = Cardiovascular disease medication status; EDV = End Diastolic Volume; HF = Heart Failure; HTN = Hypertension; Immed. Memory = Immediate Memory; Lang = Language; LA Diam = Left Atrial Diameter; LVEF = Left Ventricular Ejection Fraction; MR = Mitral Regurgitation; Total = Total Index; Visuo = Visuospatial/construction; WTAR = Wechsler Test of Adult Reading