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Association Between Cardiovascular Health and Cognitive Performance: A Twins Study

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Abstract

Background/Objective: The 2020 Strategic Impact Goal introduced by the American Heart Association (AHA) aims at improving cardiovascular health (CVH) of all Americans by 20%. AHA defined ideal CVH across seven established modifiable risk factors for cardiovascular diseases. Prior studies have indicated that ideal CVH also benefits brain health and cognitive aging, but it is possible that this association is explained by familial factors.

Methods: We examined 272 male monozygotic and dizygotic twin pairs (total 544 subjects) free of overt cardiovascular disease and dementia from the Vietnam Era Twin Registry. Memory and learning were measured by Trail Making tests and Wechsler Memory Scale (Immediate and Delayed Memory tests and Visual Reproductive Test). Each of the seven CVH components (smoking, body mass index, physical activity, diet, total cholesterol, blood pressure, and blood glucose) was scored per established criterion.

Results: The mean age of the twins was 55 years, 96% were whites, and 61% monozygotic. When considering twins as individuals, for every unit increase in CVH score (indicating better cardiovascular health), twins demonstrated faster cognitive processing speed (Trail B: –5.6 s,

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95%CI -10.3, -0.9; $p = 0.03$) and better story recall, both immediate (0.35, 95%CI 0.06, 0.62; $p = 0.02$) and delayed (0.39, 95%CI 0.08, 0.70; $p = 0.01$).

Conclusions: Better CVH is associated with better cognitive health in several domains. As suggested by within-pair analysis, this association is largely explained by familial factors, implying that early life exposures are shared determinants of both brain health and cardiovascular health.

Keywords

Epidemiology; prevention; risk factors

INTRODUCTION

Observational studies support a role of cardiovascular risk factors such as smoking and hypertension in the development of cognitive deficits in later life [1, 2]. In addition to risk factors, cardiovascular disease (CVD) and cognitive disorders including Alzheimer's disease and mild cognitive impairment share pathophysiological pathways such as inflammation and increased oxidative stress [3]. Studies have also reported associations of both clinical and subclinical cardiovascular disease with impaired cognitive function [4]. Some longitudinal studies exploring the association of cardiovascular risk factors and cognition have, however, produced conflicting findings for CVD risk factors such as diabetes and cholesterol levels [5–8]. The pathways involved in cognitive performance are quite complex and involve multiple biological processes that are subject to regulation. Studies that focus on underlying biological pathways and shared risks (common genetic variants, environmental risk factors) would help clarify any potential links between CVD and risk of cognitive impairment.

“Cardiovascular health” (CVH), as defined by the American Heart Association, emphasizes primary prevention and sets goals for modifiable health factors and behaviors to reduce mortality from cardiovascular disease by 20% by 2020 [9, 10]. CVH is a composite measure with seven components: blood sugar, serum cholesterol, blood pressure, body mass index (BMI), physical activity, diet, and cigarette smoking, and classifies each of them into ideal, intermediate and poor levels to yield a CVH score. Higher CVH scores are indicative of better cardiovascular health and have been associated with favorable outcomes for several diseases including dementia [11–13]. It is unclear, however, if the association between cardiovascular risk factors and cognition is confounded by genes and/or environment. Previous studies assessing the relationship of CVD risk factors and cognition have not accounted for heritable or other familial factors [14]. Several health behaviors in adult life are influenced by the familial environment experienced during childhood and adolescence, and by genetic factors [15, 16]. The relationship between cardiovascular risk factors and cognition may be explained by exposures or behaviors that are shared by members of the same family [17–19]. Given the high prevalence of cognitive disorders in older Americans, even modest improvements in cognitive reserve could have important public health implications to reduce disease burden from dementia [20, 21]. Several of the vascular risk factors in CVH are potentially modifiable and understanding their relationship with cognitive status could direct toward preventive approaches for dementia [22, 23].

Our objective in this study was to assess the relationship between CVH and cognitive status while accounting for the influence of unmeasured familial factors (including genetic and early environment factors) in a twin sample. We hypothesized that people with poorer CVH would have lower cognitive function (in domains such as executive function and memory) and that this relationship is continuous and graded across all levels of CVH and not explained by shared genetic and other familial factors. The co-twin study design is unique as it can control for within-twin pair similarities of genetic and early environmental influences. Comparing differences in cognitive performance within twin pairs who are discordant for CVH can provide support for an association of CVH with cognitive decline that is not confounded by these factors.

METHODS

Study population

The Emory Twins Study is an ongoing study of twins at Emory University with the overall objective to elucidate the role of psychological, behavioral, and biologic risk factors for subclinical cardiovascular disease. The study included 562 middle-aged male monozygotic (MZ) and dizygotic (DZ) twins (281 pairs), both of whom served in the US military during the time of the Vietnam War, who were part of the Vietnam Era Twin (VET) Registry as previously described [24–26]. For the current cross-sectional study, we excluded participants with a history of cardiovascular disease and dementia and twins missing information on cognitive performance. Each twin in a recruited pair was examined at the same time from 2002–2010 at the Emory University General Clinical Research Center, and all data collection, including medical history, physical examination, cognitive battery, and blood tests, occurred during a 24-h admission under controlled conditions. Information on sociodemographic, lifestyle factors, and mood questionnaires (anxiety, depression) was collected using standardized questionnaires [27, 28]. The Structured Clinical Interview for DSM IV was used for the assessment of psychiatric diagnoses such as depression and anxiety. Information on current use of medications was also collected. All twins gave informed consent and the study was approved by the Emory Institutional Review Board. Zygosity information by means of DNA typing was available for all twin pairs.

Cardiovascular health (CVH)

Components of the CVH metric include blood pressure, fasting glucose, total cholesterol, BMI, physical activity, diet, and smoking. Each CVH component was given a point score of 0, 1 or 2 to represent poor, intermediate, or ideal health, respectively, according to pre-defined categories[29]. Based on the sum of all seven CVH components, an overall CVH score, ranging from 0 to 14, was categorized as inadequate (0–4), average (5–9) or optimum (10–14) cardiovascular health (Supplementary Table 1). Systolic blood pressure and diastolic blood pressure were measured by mercury sphygmomanometer on the right arm with the subject in sitting position after 10 min of rest. The average of two measurements 5 min apart was used in the statistical analyses. Venous blood samples were drawn for the measurement of glucose and lipid profile after an overnight fast. The Emory Lipid Research Laboratory, a participant in the Centers for Disease Control/National Heart, Lung and Blood Institute Lipid Standardization Program, performed all analyses from freshly isolated

ethylenediaminetetraacetic acid (EDTA) plasma. Glucose levels were measured on the Beckman CX7 chemistry autoanalyzer. BMI was calculated from height and weight measurement of participants. Physical activity was determined by means of a modified version of the Baecke Questionnaire of habitual physical activity [30]. We used tertiles of the cumulative Baecke score to classify individuals into poor, intermediate, and ideal levels of physical activity. To measure diet quality, we used the DASH (Dietary Approaches to Stop Hypertension) diet score which is endorsed by the AHA and has been linked to diminished risk of coronary heart disease and stroke [31, 32]. We constructed the DASH score according to the method proposed by Fung et al., used in several epidemiological studies [33]. It is calculated based on eight food items (fruits, vegetables, nuts and legumes, low fat dairy products, whole grains, sodium, sweetened beverages, red and processed meats) and on the following principles: 1) high intake of fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains are beneficial for human health and receive high scores; 2) high intake of sodium, sweetened beverages, and red and processed meats are harmful and receive lower scores. For each of the above eight food groups, we categorized study subjects into quintiles (assigned 1–5 points) according to their individual food intake component scores. Scoring by quintile helped to reduce the potential for misclassification. The scores for each food group were then summed to yield an overall score ranging from 8 to 40, where higher scores represent greater adherence to the DASH diet. The cumulative score was grouped into tertiles to classify individuals with ideal, intermediate, and poor diets [29, 34]. Cigarette smoking was classified into current smoker (poor); quit in the past year (intermediate), and never smoker or quit more than one year ago (ideal) (see Supplementary Table 1).

Cognitive battery

Executive functioning and cognitive flexibility was measured using the Trail Making test (TMT) which was administered in two parts [35]. Part A is a visual-scanning, timed task where participants were asked to connect with lines 25 circles numbered from 1 to 25 as quickly as possible. The test is terminated after 5 min even if not completed. In Part B, participants are asked to connect circles containing numbers (from 1 to 13) or letters (from A to L) in an alternate numeric/alphabetical order (i.e., 1-A, 2-B, 3-C, etc.) Errors must be corrected immediately and the sequence re-established. The time (in seconds) to complete both Trail A and Trail B was recorded. TMT-A was discontinued at 150 s and TMT-B was discontinued at 300 s, per standard procedures. Time to complete the task in seconds was used as the primary outcome measure in data analyses. Both Trail A and B measure attention, sequential control, visual scanning, and visuomotor processing speed. In addition, Trail B also measures cognitive flexibility, which is an executive function related to the ability to switch between thinking different concepts simultaneously. These complex processing abilities are likely to be affected early in Alzheimer's disease [36].

Memory function was evaluated using the Wechsler Memory Scale-Revised (WMS-R) [37, 38]. This test has logical memory indices (Verbal and Visual subtests). The Verbal sub-test consists of two short stories that are read aloud to the participant. The participant is subsequently asked to retell each of the stories as closely as possible to the original immediately after hearing the story (Wechsler -Immediate recall) and after an interval of 30

min (Wechsler Delayed recall). Between the two tests, subjects completed unrelated tasks. Well-experienced examiners who were blinded to the participant's clinical and study status performed all the psychological tests. A maximum score of 50 is attainable for both the immediate and the delayed recall task based on pre-defined criteria. Immediate recall measures attention and memory while delayed recall are measures of memory consolidation. A higher score is indicative of better performance on the story recall tests. Finally, the Wechsler-Visual Memory subtest assesses the subject's immediate recall of a series of visually presented abstract symbols each shown to the subject for 10 s and it is scored by independent raters using established scoring criteria [39].

Statistical analyses

Continuous variables were described as mean $\pm$ standard deviation (SD) and categorical variables as frequencies (percent). We examined baseline sociodemographic characteristics, CVH factors and medications across CVH categories, treating the twins as individuals. We also compared individual CVH components across cognitive function tests while accounting for correlated data using mixed models or generalized estimating equation (GEE) models.

Next, we analyzed the relationship between cognitive function test scores (each as a separate dependent variable) and CVH scores using mixed model regression analysis adapted for twin studies [40]. Cognition tests, other than Trail A and B tests, were normally distributed. Trail A and B tests had a skewed distribution. We used different analytical approaches to analyze the Trail tests including log-transformation and also dichotomizing the scores per established cut-offs [41]. Regression models were used to examine the association between cognitive performance and CVH. All models were adjusted for age, education, income, anxiety, and depression.

In the last step of our analysis, we fitted mixed models for twins, which allowed for partitioning within and between pair differences in the dependent variable as a function of the independent variables. In these models, the within-pair term was defined as a difference of at least 1 point in the CVH score between the two brothers. This within-pair analysis by design takes into account shared genetic and many early environmental factors. The within-pair analysis was further stratified by zygosity to determine whether the relationship between CVH and cognitive function was different between MZ and DZ twins. Monozygotic twins share 100% of their genetic material, and therefore differences between MZ twins are controlled for genetic factors. Dizygotic twins share on average 50% of genes and differences between the twins are only partially controlled for shared genetic factors. Shared genetic factors would be implicated if the within-pair difference in cognitive function in CVH-discordant pairs were smaller in MZ than in DZ pairs. Potential multicollinearity was investigated using condition indices and variance decomposition proportions. The fully adjusted models were adjusted for age, income, education, anxiety, and depression.

All statistical analyses were conducted using SAS software, version 9.4 (SAS Institute Inc, NC). Significance level was set at 0.05, two- sided.

RESULTS

After excluding twins with history of coronary artery disease and pre-existing dementia from the initial sample of 562 twins, the analytical sample included 544 twins or 272 twin pairs. The mean age of participants was 55.4 years and 96% were white; 61% were MZ, a distribution that reflects that of the entire Vietnam Era Twin Registry. The mean CVH score was 7.7 (SD, 0.5). Overall, 18% of participants had optimum, 77% had average, and 5% had inadequate cardiovascular health. The age-adjusted prevalence of ideal CVH components ranged from 15% for BMI to 75% for smoking (Fig. 1). Among socio-economic factors, lower education, and being unemployed were associated with inadequate cardiovascular health (Table 1).

The association of individual CVD factors and behaviors with cognitive function tests is presented in Table 2. Compared to intermediate and poor CVH, optimum CVH was significantly associated with better cognitive performance in the immediate and delayed story recall. The average times to complete the Trail A and Trail B tests were respectively 93 (SD, 9) and 158 (SD, 19) s. When CVH was treated as a continuous score, with higher score indicative of better cardiovascular health, the score was correlated with better performance on both Trail A (Spearman $r = -0.09$, $p = 0.05$) and Trail B (Spearman $r = -0.11$, $p = 0.008$). Similarly, a higher CVH score was correlated with better performance on the Wechsler immediate story recall (Spearman $r = 0.10$, $p = 0.02$), and the Wechsler delayed story recall (Spearman $r = 0.12$, $p = 0.007$) (Fig. 2a). With a higher number of ideal factors, performance on the Wechsler immediate and delayed story recall was better in a gradient manner (p -trend = 0.04) (Fig. 2b). The Wechsler visual reproductive score was similarly correlated with better CVH score (Spearman $r = 0.14$, $p < 0.01$) with a significant gradient trend with the number of ideal factors (Fig. 3).

Our modeling strategy first considered twins as individuals and then analyzed twins within pairs who were discordant for CVH, that is, where one member of the twin pair had a higher CVH score (a difference of at least 1 point) than the other. The CVH score was treated as a continuous variable for this analysis and the results were stratified by zygosity. There were a total of 197 discordant twin pairs: 76 were DZ and 121 were MZ. Using mixed model regression adapted for twin studies and treating twins as individuals, in the unadjusted analysis, Wechsler Immediate Recall, Wechsler Delayed Recall, and Wechsler Visual Memory were all significantly associated with CVH score (Table 3). After adjusting for demographics, income, education, anxiety, and depression, all previous associations remained significant with minimal change in effect estimates. For example, participants with one unit higher CVH score (indicating better cardiovascular health) were able to finish the Trail- B test 5.6 s faster (coefficient -5.6 , 95% CI, -10.3 , 1.0 ; data not shown in tables), and had approximately 11% higher odds of completing Trail B faster (OR = 0.89, 95% CI, 0.81, 0.98). For the Wechsler tests, participants with one unit higher CVH score had better immediate and delayed recall scores (on average, a 0.4 units higher score, 95% CI, 0.08, 0.70). The visual memory recall score was also better with increasing values of the CVH score (0.24 units higher, 95% CI, 0.03, 0.47). Similarly, the Trail B test was better with higher values of CVH score (OR = 0.89, 95% CI, 0.81, 0.98). Trail A test was also better with higher values of CVH score but the association was not significant (OR = 0.99, 95%

CI, 0.88, 1.11). In within pair analysis, the associations weakened and were no longer significant except for the Trail B test (Table 3). The coefficients tended to be smaller in the MZ than the DZ pairs, but the p value for the interaction with zygosity was not significant (p interaction = 0.83) (Supplementary Table 2). None of the individual CVH score components were significant predictors in the within pair analysis.

DISCUSSION

A favorable CVH profile including a healthy lifestyle have been recognized to provide protection against neurocognitive decline and dementia [20, 42]. Improving population-level cardiovascular health thus has the potential to reduce the burden of dementia [43]. It is well known that both genetic and environmental factors play a role in cognitive aging. Our study in a twin sample of cognitively normal middle-aged men showed that CVH is associated with better cognitive health in several domains. The associations between cognitive performance tests and CVH weakened in within-pair analysis, suggesting that familial factors are likely explaining a large part of the association. As the within-pair association is similar in MZ and DZ twins, we can exclude that genetic factors are confounding the association. Therefore, familial factors (but not genetics), such as early family environment, early socioeconomic status and education, and parental factors, may be important precursors of both cardiovascular and brain health, and thus may explain some of the association between CVH and cognition.

The CVH metric used in our study has been defined by the American Heart Association as part of a national effort to improve cardiovascular health of all Americans by 20% by 2020 [10]. Previous studies have found a strong relationship between the number of ideal CVH factors and incidence of stroke and myocardial infarction [44, 45]. Increasing favorable levels of cardiovascular health in the population is likely to have health benefits beyond heart disease and stroke. The prevalence of ideal cardiovascular health is extremely low in the United States as measured in several studies [44–48]. The distribution of CVH factors in our sample of middle-aged male Vietnam era veterans was comparable to what was reported in the National Health and Nutrition Examination Survey, but few factors such as BMI and physical activity were less favorable in the Emory Twins Study than the United States general population. Other studies have suggested that even though veterans are more likely to have health insurance as compared to nonveterans, they tend to have a more negative risk factor profile [46, 49–52].

The relationship between CVH and cognition suggests a role of metabolic and vascular damage in the etiology of dementia. Previous studies have suggested that there are several mechanistic pathways involved in how vascular risk factors can affect cerebral vascular and cognition [53]. Studies that have examined composite measures of risk such as the Framingham risk score have found higher risk scores to be associated with worse cognitive function [54–56]. In the REasons for Geographic and Racial Differences in Stroke (REGARDS), ideal levels of CVH were associated with lower incident neurocognitive impairment [11]. The Hispanic Community Health Study (HCHS/SOL) extended this work to community dwelling Hispanic/Latino adults, and also showed that the benefits appear to be consistent across multiple domains of neurocognitive health, including episodic learning

and memory, verbal fluency, and psychomotor speed [43]. In the Coronary Artery Risk Development in Young Adults (CARDIA) study, a favorable cardiovascular health profile was similarly associated with better neurocognitive function in midlife [12]. Finally, in the Northern Manhattan Study, the number of ideal CVH factors was associated with less decline in the domains of processing speed, but had a weaker association with executive function and episodic memory [57]. In the Duke Twins Study of Memory in Aging, elderly individuals with diabetes demonstrated greater cognitive decline over a 12-year time span than their nondiabetic co-twins [58]. Our study results are in agreement with above studies but also highlight that familial confounding may be present in the association between CVH and cognitive indices.

Genetic factors and other familial factors influence health behaviors and other cardiovascular risk factors from an early age [15]. Previous studies have indicated that for cognitive decline, environmental factors seem to have a more substantial influence than genetic factors. Studies have highlighted small differences in the concordance of dementia between MZ and DZ twins to support this finding. For example, the Swedish Twin Registry study showed that genetic background had a limited role in determining cognitive decline and pointed towards a more prominent role of environmental factors [59, 60]. Our study builds on these previous data by showing that the association of CVH and cognitive performance is likely confounded by familial factors other than genes, i.e., environmental exposures of people growing up in the same family. This implies that cognitive decline and cardiovascular risk factors share similar precursors beginning early in life, and that both health dimensions can be potentially improved using a life course approach focusing on primordial prevention. More favorable socioeconomic resources early in life, better school education and a more cognitively stimulating environment in childhood may play a major role on levels of cognitive function as well as CVH status later in life [61, 62]. Prior studies have shown that mid-life uncontrolled CV risk factors are associated with risk of cognitive impairment in later life [63]. Our results also suggest that preventive measures for improving CVH need to be instituted even earlier at the family level (for example, in youth) to be more effective for preventing late-life dementia.

Our study has many strengths. The co-twin study design helps strengthening causal inference in observational studies [64]. Twins provide naturally matched pairs where the confounding effects of a large number of potentially causal factors such as genetics, parental factors and early environment can be removed by comparisons between twins who share them. Thus any differences in cognitive performance between co-twins discordant for CVH is more likely attributable to differences in CVH scores between the twins than to other unaccounted factors. Our study also has the advantage of using standardized cognitive tests and objectively measured cardiovascular risk factors, which were used for ascertainment of the CVH score. Important limitations, however, need to be acknowledged. Our study is cross-sectional, and thus the temporal relation between CVH factors and cognitive performance cannot be ascertained. While reverse causation is possible, i.e., that declining cognitive status affect CVH (especially health behaviors), our matched-pair analysis suggests that in large part the association may not be causal, but rather driven by early life influences. However, if these influences affect CVH starting in early in life a causal relationship still cannot be excluded. Moreover, since our sample included middle-aged male

Vietnam era veterans, these results may not be generalizable to women or younger subjects. Finally, we acknowledge that the sample sizes for within-pair twin analyses stratified by zygosity are small and the power is limited to detect differences and make inferences regarding the true influence of genetic factors.

In summary, our study provides further evidence and confirms that there is an association between CVH and cognitive performance, thus supporting the use of CVH metric as a correlate for brain health in addition to cardiovascular health. Our study also provides new evidence that the relationship between CVH and cognition in a middle-aged sample of cognitively normal people is in large part explained by early environmental factors. Our data support the notion that primordial prevention of cardiovascular risk factors and promotion of a healthy lifestyle beginning early in life should achieve the best results for promoting not only cardiovascular health, but also cognitive health. With rapidly aging populations, cardiovascular diseases and dementias will remain major challenges in public health. CVH has several components and each of these factors may have complex pathophysiological mechanisms in how they may be related to cognitive performance [53]. Further investigation into factors that are potentially reversible and are common in risk pathways between vascular and cognitive health is needed to design better interventions. Longitudinal studies are especially needed to evaluate whether CVH at young or middle age has an impact on later cognitive decline. Our results suggest that early stage targeting of shared modifiable risk factors can be most effective in curbing both heart disease and dementia epidemics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Cardiovascular health profile of emory twins study participants ($n = 544$).

Fig. 2a.

Spearman correlation between cardiovascular health and cognitive performance (Wechsler – Immediate and Delayed Story Recall).

b **Fig. 2b.**

Bar plot of mean cognitive performance (Wechsler: Immediate and Delayed Story Recall) according to number of ideal CVH factors.

Fig. 3.

Correlation and bar plot for the association between cardiovascular health and visual reproductive score.

Table 1
Distribution of covariates of Emory Twins Study participants ($n = 544$) by cardiovascular health categories

	Cardiovascular Health Category			<i>p</i>
	Optimum (CVH = 10–14) N=96	Average (CVH = 5–9) N=417	Inadequate (CVH = 0–4) N=31	
Age (y)	54.3	55.1	55.1	0.09
Systolic Blood Pressure (mmHg)	121.4	131.7	140.6	<0.001
Total Cholesterol (mg/dL)	178.4	185.5	207.4	0.001
Low Density Lipoprotein –Cholesterol (mg/dL)	116.1	121.6	128.6	0.17
Body Mass Index (Kg/m ²)	26.7	30.1	32.3	<0.001
Plasma glucose (mg/dl)	93.4	103.4	120.5	<0.001
Currently Employed (%)	95.8	80.3	58.1	<0.001
No. of alcoholic drinks/week	6.4	8.4	4.3	0.34
College education (%)	83.3	67.4	54.8	0.002
Current Smoking (%)	2.1	40	72	<0.001
Depression (%)	20.8	27.8	27.5	0.37
Anxiety (%)	7.7	4.8	2.0	0.32
Medication use, %				
Thiazide	1.0	7.2	6.5	0.07
Beta blocker	4.2	15.6	12.9	0.01
Aspirin	15.6	27.3	3.2	0.04
Angiotensin-converting enzyme inhibitors	6.3	16.3	25.8	0.01
Statin	9.4	27.8	3.5	0.003
Anti-depressant	8.3	8.9	1.3	0.72
Diabetes	1.0	8.4	3.5	<0.001

CVH, Cardiovascular Health.

Table 2Association of cardiovascular health factors and cognition tests ($n = 544$)

CVH components	CVH categories	TMT-A N (%)	TMT-B n (%)	Immediate recall score Mean (SD)	Delayed recall score Mean (SD)	Figure total score Mean (SD)
CVH components		<150 s	<300 s			
Blood pressure	Poor	126 (32)	94 (31)	24 (7)	19 (7)	12 (5)
	Intermediate	201 (51)	161 (52)	24 (6)	19 (7)	12 (5)
	Ideal	67 (17)	53 (17)	25 (6)	21 (7)	14 (5)
	<i>p</i> -value	0.44	0.66	0.11	0.06	0.03
Fasting glucose	Poor	27 (7)	23 (7)	24 (7)	20 (7)	13 (5)
	Intermediate	166 (42)	115 (37)	24 (6)	19 (7)	12 (5)
	Ideal	201 (51)	170 (55)	24 (7)	20 (7)	12 (5)
	<i>p</i> -value	0.62	0.08	0.88	0.64	0.96
Cholesterol	Poor	35 (9)	26 (8)	22 (7)	19 (7)	13 (5)
	Intermediate	175 (44)	140 (45)	24 (7)	20 (7)	12 (5)
	Ideal	184 (47)	142 (46)	24 (6)	19 (7)	12 (5)
	<i>p</i> -value	0.14	0.76	0.20	0.70	0.48
BMI	Poor	162 (41)	120 (39)	24 (4)	20 (7)	13 (5)
	Intermediate	172 (44)	140 (46)	24 (6)	20 (7)	12 (5)
	Ideal	60 (15)	47 (15)	24 (7)	19 (8)	13 (5)
	<i>p</i> -value	0.75	0.75	0.47	0.57	0.99
Physical activity	Poor	53 (16)	40 (15)	24 (7)	20 (7)	13 (4)
	Intermediate	191 (57)	149 (57)	24 (6)	19 (7)	12 (5)
	Ideal	90 (27)	71 (27)	25 (7)	21 (8)	13 (5)
	<i>p</i> -value	0.21	0.52	0.36	0.64	0.47
Healthy diet	Poor	100 (27)	76 (26)	23 (7)	18 (7)	12 (5)
	Intermediate	199 (53)	150 (52)	24 (7)	20 (7)	13 (5)
	Ideal	73 (20)	65 (22)	25 (6)	21 (7)	13 (5)
	<i>p</i> -value	0.98	0.18	0.13	<0.01	0.07
Smoking	Poor	95 (24)	68 (22)	23 (7)	18 (7)	11 (5)
	Intermediate	6 (2)	7 (2)	24 (8)	19 (9)	9 (4)
	Ideal	293 (74)	233 (76)	24 (6)	20 (7)	13 (5)

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CVH categories	TMT-A N (%)	TMT-B n (%)	Immediate recall score Mean (SD)	Delayed recall score Mean (SD)	Figure total score Mean (SD)
Total CVH	<i>p</i> -value	0.11	0.07	0.01	<0.01
	Inadequate	21 (5)	22 (6)	19 (6)	13 (5)
	Average	299 (76)	24 (7)	19 (7)	12 (5)
	Optimum	74 (19)	25 (6)	21 (8)	14 (5)
	<i>p</i> -value	0.84	0.04	0.02	0.06

TMT, Trail Making Tests; CVH, Cardiovascular Health; BML, body mass index.

Table 3

Unadjusted and adjusted^{*} association between cognition tests (estimate and 95% CI) and overall cardiovascular health score ($n = 544$)

Cognition Instruments	Overall CVH Score			
	Individuals		Within-Pairs	
	Odds Ratio (95% CI) ^{**}	P	Odds Ratio (95% CI) ^{**}	P
Trail Making Test- A				
Unadjusted	0.99 (0.89, 1.10)	0.84	0.93 (0.75, 1.15)	0.52
Adjusted	0.99 (0.88, 1.11)	0.88	0.93 (0.75, 1.17)	0.75
Trail Making Test- B				
Unadjusted	0.92 (0.84, 1.01)	0.08	0.81 (0.67, 0.99)	0.04
Adjusted	0.89 (0.81, 0.98)	0.02	0.79 (0.64, 0.97)	0.03
	Estimate (95% CI)	P	Estimate (95% CI)	P
W. Immediate Recall				
Unadjusted	0.39 (0.12, 0.66)	<0.01	0.25 (-0.18, 0.69)	0.26
Adjusted	0.35 (0.06, 0.62)	0.02	0.26 (-0.19, 0.71)	0.26
W. Delayed Recall				
Unadjusted	0.45 (0.15, 0.75)	<0.01	0.26 (-0.24, 0.75)	0.31
Adjusted	0.39 (0.08, 0.70)	0.01	0.26 (-0.25, 0.78)	0.33
Wechsler Visual Memory				
Unadjusted	0.27 (0.06, 0.47)	0.01	0.09 (-0.23, 0.41)	0.60
Adjusted	0.24 (0.03, 0.47)	0.03	0.08 (-0.25, 0.42)	0.63

^{*} Model adjusted for age, education, income, anxiety, and depression.

^{**} Per 1 unit increment in CVH.