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Relationship between global cognition and cardiovascular risk factors

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Abstract

Alzheimer's disease (AD) is currently affecting the lives of 5.8 million Americans and is expected to double within the next 30 years. With an aging populace of baby boomers, this will place great economic strain on the U.S. creating a burden of almost $1 trillion in healthcare costs. Currently, there is no cure for AD. However, studies report that many individuals with AD experience changes in the brain up to 10-15 years before the disease's onset. It is imperative to detect future risk of developing AD or mild cognitive impairment (MCI) before significant cognitive changes arise. Many of the risk factors for AD are similar to those of cardiovascular disease (CVD). Thus, CVD risk factors will be targeted to identify if they show any correlation with diminished cognitive status. Participants in this study were women over the age of 40 who are at risk of developing MCI. Each subject reported to the Exercise Science Research Center to collect demographic information, perform a body composition, complete cognitive activities, and undergo an assessment determining their cardiovascular health status. In each of the cognitive assessments, a different aspect of cognition was evaluated, including working memory, episodic memory, language, attention, recognition, coordination, and visuospatial skills to give a measure of global cognition. Cardiovascular health status was assessed through self-reported questionnaires including CVD risk factors such as smoking, dyslipidemia, and hypertension, as well as with a procedure called Flow Mediated Dilation (FMD). FMD measures the change in the brachial artery diameter before and after a period of occlusion. The degree of arterial compliance is known to serve as an indicator of cardiovascular health. Pearson and Spearman's correlation matrices were performed to examine any relationships between CVD risk and cognitive status. A one-way ANOVA was also completed to analyze if a difference in cognition existed between groups of increasing number of CVD risk factors. The results of these analyses showed no statistically significant relationships and only a few weak correlations, specifically

between attention and increased CVD risk factors (*r* = -0.32). Cerebral hypoperfusion, common in heart failure and post-myocardial infarction patients, has resulted in lower attention scores, which could serve as a possible mechanism behind this correlation. The reduced strength in such correlations could be attributed to a homogenous study population, issues in software and technology, and poor data collection methods. Nonetheless, the results of this study still support the hypothesis that a relationship between CVD risk and cognitive decline exists in some capacity.

Introduction

Alzheimer's disease (AD) has become one of the most prevalent and detrimental health concerns in the United States today. In fact, every 65 seconds, an American is diagnosed with AD. It is the sixth leading cause of death nationally, resulting in the deaths of 1 in 3 seniors. Currently, 5.8 million Americans have AD, and this number is expected to exceed 14 million by 2050. Not only does this deadly disease cause the loss of many loved ones, but it also places a substantial financial burden on the country. AD is the most expensive disease in the United States costing over $290 billion in 2019. This number is predicted to quadruple in the next 30 years, totaling over $1 trillion. Furthermore, the cost for Medicare and Medicaid to cover an older adult with AD is over 20-times more expensive than for the average older adult (Alzheimer's Association, 2019). Clearly, these statistics illustrate the threat this disease poses to the nation's public health and economic stability. The emotional trauma, increasing prevalence, and economic shock resulting from AD's impact has recently shed light onto the urgency of this situation.

Unfortunately, there is no cure for Alzheimer's at this time. However, the use of various measures to delay its onset has been a recent topic of interest in Alzheimer's research. Modifiable risk factor measurement scales are a valuable tool in identifying the at-risk population who have the capacity to reduce their chances of developing early signs of dementia or alter the negative trajectory of their illness. These risk factors typically include hypertension, dyslipidemia, diabetes, obesity, smoking, and physical inactivity, among others. Interestingly, many of these risk factors are similar to those of cardiovascular disease (CVD). In fact, one-third of AD cases worldwide are attributable to these risk factors (Kivipelto et al., 2018). As a result, the identification of CVD risk factors is an ideal target to measure one's risk of developing AD.

Literature Review

Clinical Symptoms of Alzheimer's Disease

AD is known to affect specific types of memory and function. Unspecified dementia is characterized by global symptoms such as loss of functionality with daily activities and changes in personality or behavior. Additionally, a reduced ability to acquire new information, as well as impairment of reasoning, visuospatial abilities, and language are common. Hallmark symptoms of AD include these abnormal functions plus deficits in executive function and visuospatial cognition. Executive function is primarily important for problem solving. Visuospatial skills aid in object and facial recognition, as well as reading (McKhann et al., 2011). Early on in the disease onset, working and declarative memory both become impaired. More specifically, deficits in semantic and episodic memory are seen (Jahn, 2013). Each of these symptoms may serve as target variables in cognitive assessments.

Importance of Detection of Preclinical Changes in Cognition

It is known that many of the neurophysiological changes that cause AD can occur up to 10 years prior to the onset of the disease. As previously mentioned, one of the most noticeable clinical indicators is a decline in episodic memory (Sperling et al., 2011). If these changes can be identified in the preclinical stage, intervention can occur and thereby have the potential to improve a patient's prognosis. As a result, an assessment that is sensitive enough to measure preclinical changes is needed. To-date, cognitive assessments are valid when differentiating between cognitively intact adults and adults with cognitive impairment; however, there are no known assessments that can accurately determine these preclinical changes.

Target Population & The Effect of Gender and Sex

Currently, more than two-thirds of individuals diagnosed with AD are women. Cerebral volume and blood flow, brain circuitry, relative ratio of white matter compared to grey matter, and hormonal influence are sex-related explanations that have been explored. Additionally, some gender-related differences such as education, occupation, and lifestyle have also been researched for a possible cause for the increased incidence of AD in women. More specifically, higher educational attainment lowers risk for developing AD. An individual's occupation can cause specific stressors that may have a negative impact on cognition. Lifestyle factors that may differ between genders and may be linked to AD include exercise, diet, and alcohol and drug habits (Mielke et al., 2014). Ultimately, the precise mechanism behind this trend is still poorly understood but it is likely that a biological explanation for this sex difference exists. Therefore, it is important to stratify or isolate sexes when studying AD.

The average age of onset for AD is 65 years (Alzheimer's Association, 2011). As previously noted, physiological changes in the brain may occur at least 10 years prior to the onset of AD symptoms Sperling et al., 2011). Therefore, it is important to study participants who are significantly younger than the typical age of onset in order to detect preclinical changes in cognition. An earlier target age for participants is also essential for identifying individuals who may benefit the most from intervention. This modification would not be effective if subjects are already experiencing significant symptoms, which would be more likely in older participants.

Review of Current Diagnostic Tools Techniques

There are a wide variety of cognitive assessments that have been used to assess a multitude of neuropsychological conditions. Many of these tests are known to effectively identify a deficit or abnormal finding for a cognitive function. The strengths and weaknesses of some common assessments will be reviewed.

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) has been validated for use in identifying the neuropsychological state of individuals with various diseases associated with cognitive ability, such as Alzheimer's, schizophrenia, or Huntington's, due to its multifaceted examination of the global cognition. However, this test may not be able to consistently distinguish between generalized dementia and AD (Randolph, et al., 1998). RBANS can successfully determine the subject's cognition in the areas of language, immediate memory, delayed memory, attention, and visuospatial and constructional skills.

The Dual-Task test is a physical assessment which evaluates coordination and working memory. The assessment itself has both a cognitive and a motor component. This allows for a unique analysis of an individual's interaction between cognition and mobility. This test is limited by not being sensitive enough to produce results that significantly vary between individuals with healthy aging and individuals with MCI (Foley et al., 2011). The results of this assessment are useful in determining one's ability to function in daily life.

Hand-grip strength is an important indicator of overall functionality in older individuals. This assessment can help to predict physical fitness, social health, and cognition. The predictive strength of this measure decreases when testing very old and frail individuals (Taekema, et al., 2010). The correlations that hand-grip strength provides may aid in detecting early declines in cognition and functionality.

Dual-energy X-ray absorptiometry (DXA) measures fat mass, lean fat mass, and bone density. Each of these variables have predictive value on the cognitive function of older individuals. In middle aged individuals, higher fat mass has shown to be correlated with lower cognition, especially in women (Pedditizi et al., 2016). However, a decreased incidence of AD has been shown in those over 65 years with higher body mass index (BMI). These findings may be explained by the inability of BMI to account for the increased fat mass and decreased lean mass (Noh et al., 2017). This explanation illustrates the importance of using DXA to evaluate body composition, as it may provide more accurate, raw data points for these factors.

The Visual Paired Comparison (VPC) test has been shown to effectively measure declarative memory as a function of global cognition. Individuals with AD tend to show impairment with recognition memory while healthy adults retain this ability through aging, thereby demonstrating the assessment's capacity to isolate individuals who are experiencing abnormal declines in cognition (Gills et al., 2019). Currently, it has not been tested as a measure of detecting preclinical changes in cognition, but its sensitivity shows promise.

Ultimately, each of these assessments measure important variables and aspects of AD. Although there is not one superior measure available that can assess all of these factors, a combined use of RBANS, Dual Task, body composition, hand-grip strength, and VPC can help to produce a more comprehensive picture of one's cognitive state.

Analysis of the Role of Cardiovascular Health on Cognition

As previously mentioned, several significant CVD risk factors have been isolated and appear to be consistent across many different populations. The variables of interest include hypertension, dyslipidemia, diabetes, obesity, smoking, and physical inactivity. These will be evaluated regarding their relationship to cognitive impairment.

Individuals with hypertension or dyslipidemia have shown a much higher risk of developing AD, especially if the conditions are comorbid (Kivipelto et al., 2001). AD has also been associated with the presence of atherosclerosis, with the frequency of all dementia, including AD, being directly proportional to the severity of atherosclerosis (Hofman et al., 1997). When collectively evaluating the effects of diabetes, hypertension, heart disease, and smoking, the risk of developing AD significantly increased. More specifically, a diagnosis of cardiovascular disease increases the possibility of having probable AD by 10%, while the possibility of having probable AD as a current smoker was increased by more than 8%, both of which compared to that condition being absent (Luchsinger et al., 2005). At the population level, diabetes and hypertension significantly increase the risk for developing AD, especially if left untreated (Viswanathan et al., 2009). The specific mechanism of damage caused by uncontrolled high blood pressure is an increased number of white matter lesions, which are also linked to cognitive impairment (Verhaaren et al., 2013). Beyond the increased incidence of AD in individuals who experience CVD risk factors, these variables have also shown to accelerate the rate of cognitive decline. This acceleration was specifically observable with the presence of atrial fibrillation, hypertension, and angina (Mielke et al., 2007). Clearly, there are many relationships that have been established between CVD risk factors and the risk of developing AD. However, much of the current determinations were based off self-reported conditions and physical examinations that measure blood pressure, heart rate, and blood sugar to construct a basic picture of one's cardiovascular health. In order to establish stronger relationships between the presence of these risk factors and AD risk, more global and tangible evidence is needed.

An increasingly useful technique to measure one's general cardiovascular health is Flow Mediated Dilation (FMD). This procedure assesses vascular endothelial function by measuring arterial compliance, which can be used as a clinical indicator of hypertension, CVD, and other vascular related conditions (Harris et al., 2010). This measure not only provides quantifiable and experimental evidence of vascular health, but also parallels the relationship of risk factors to the disease. FMD results have shown a strong correlation with CVD risk factors such as age, blood pressure, blood sugar, smoking status, and a chronic disease diagnosis (Maruhashi et al., 2013). This relationship is important in establishing the effectiveness of utilizing FMD to provide data for one's cardiovascular health. By applying this technique, a stronger argument may be made for the correlation between cognitive decline and vascular disease states. From that point, an opportunity to intervene and reduce these modifiable risks arises.

Lifestyle Modification

The finding that a potential link may exist between CVD risk factors and dementia has allowed for the execution of smaller intervention studies that exploit this correlation by attempting to improve these vascular risks. This is an important area of development for the field of aging and dementia (Kivipelto et al., 2018). Within the last 10 years, there have been a few large-scale studies that also examine and apply this relationship. A prime example was the groundbreaking Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). This study involved implementing an intervention that included diet, physical activity, and mental fitness exercises for adults who demonstrated risk of developing AD in order to reduce the negative impact of the identified CVD risk factors. These actions ultimately led to a 25% increase in cognitive abilities, validating the effectiveness of lifestyle modification for delaying the onset of symptoms of dementia in Finland (Ngandu et al., 2015). The study itself utilized the Cardiovascular Risk Factors, Aging, and Incidence of Dementia (CAIDE) Risk Score as a screening tool to find the at-risk population. The CAIDE score specifically evaluated blood pressure, blood cholesterol levels, obesity, exercise level, and educational attainment, all of which represent variables that can be altered through lifestyle modification (Sindi et al., 2015). This scale also exemplifies the effect of vascular-related conditions on dementia. Several other studies have been done that also target modifiable vascular risk factors to impact future cognitive status. Similarly, the Systolic Blood Pressure Intervention Trial (SPRINT) utilized early intervention to manage hypertensive conditions. The goal was to diminish the degree of cognitive debilitation experienced by an individual by decreasing the number of white matter lesions inflicted by chronically elevated blood pressure. The result of this management of hypertension through prescription drugs was shown to significantly decrease the risk for MCI and dementia. However, this study did not thoroughly evaluate baseline cognition, which could weaken the correlations found (Williamson et al., 2019). An additional study with similar interests includes the Multidomain Alzheimer Preventive Trial (MAPT). This investigation applied a program of intervention including nutritional counseling, physical activity education, and cognitive stimulation activities to show a decreased decline in cognitive function. However, this study targeted participants age 70 or older with notable deficits in activities of daily living. This population may already be experiencing the early stages of AD and may be past the point of effective intervention (Vellas et al., 2014). Ultimately, each of these trials have the same goal of attempting to reduce likelihood of developing symptoms of AD or reducing the severity of these symptoms through CVD risk factor modification. However, the finding of more experimental and comprehensive data to measure pre- and post-modification cardiovascular health could strengthen the hypothesis that vascular dysfunction is a key factor related to AD progression. Furthermore, the MAPT and FINGER studies were performed in Europe. There is still a need to show generalizability of these trends in the United States, where environmental conditions may differ.

Ultimately, current research exploring the co-morbidity of AD and CVD risk factors is still lacking necessary tangible data, specifically regarding cardiovascular health. Furthermore, there is still progress to be made in isolating a target population in the United States to apply lifestyle modification once the strength of such a relationship is demonstrated. Thus, the primary purpose of this study is to cross-examine global cognition among older adults experiencing self-reported memory issues with the co-occurrence of CVD risk factors. In identifying individuals who have experienced preclinical changes in cognition, an opportunity arises to potentially identify adults with future risk of mild cognitive impairment (MCI) or AD. As a result, lifestyle modification that specifically targets vascular factors could be implemented with this affected population in the future.

Methods

Screening

Women over the age of 40 were recruited to participate in this study. Additionally, a battery of questionnaires that assessed physical and psychological well-being was sent to subjects who were enrolled in the study in order to identify any possible confounding factors. These self-reported surveys included questions about mental health, sleep quality, physical activity, blood pressure, blood cholesterol, the presence of any organ system diseases, smoking, and alcohol consumption. Consequently, risk factors for CVD were captured by these surveys.

Research Design for Cognitive Assessment

During the study visit, demographic data including height, weight, age, and body composition were collected. Body composition was assessed using a DXA machine. Hand-grip strength was also measured using a Takei Hand Grip Dynamometer. During this procedure, the participant holds the dynamometer at their side and squeezes for 3 seconds. This process is performed a total of 3 times for each hand. Next, the cognitive assessments were administered. The measures used in this study included the VPC, RBANS, and Dual-Task assessments.

The Visual Paired Comparison (VPC) test assesses recognition memory of an individual by showing a series of two images at a time on a computer screen, with one of these images being previously shown during a familiarization phase, and one being novel. The subject is to identify and focus their eyes on the new image. Adults who spend more time gazing at that previously viewed image have a lower cognition status. VPC use has been deemed both valid and reliable for showing cognitive dysfunction compared to other cognitive assessments (Gills et al., 2019). This assessment will aid in evaluating the subject's recognition memory as a factor of their global cognition.

RBANS is administered using 2 tablets and a packet for the written portions of the examination. The investigator utilizes the QIActive application on one of the tablets to read off prompts and instructions to the participant for each section. The sections that comprise the assessment are List Learning, Story Memory, Figure Copy, Line Orientation, Picture Naming, Semantic Fluency, Digit Span, Coding, List Recall, List Recognition, Story Recall, and Figure Recall. For Figure Copy, Coding, and Figure Recall, the written packet is required. The second tablet is used to show the subject various images through the QIActive application which are required for that specific activity in the sections Figure Copy, Line Orientation, Picture Naming, and Figure Recall. The validity and reliability of RBANS in its ability to identify individuals with AD has been demonstrated (Randolph et al., 1998). This assessment will aid in providing measures for attention, language, visuospatial/constructional abilities, and both immediate and delayed memory.

The format of the Dual-Task assessment used for this study consisted of a series of four trials in which the participant is asked to walk 20-meters. The first trial was at normal speed without an additional task. The second trial was at a faster walking pace with no additional task.

In the third and fourth trials, the participant was asked to count backwards by 3's from a given 3-digit number while walking the 20-meter distance. The third trial was performed at a normal pace and the fourth trial was at a faster speed. Dual-Task assessments have shown to be a valid and reliable distinguishing factor between individuals with MCI and individuals with AD (Foley et al., 2011). Each of these assessments will help to generate a comprehensive evaluation of a participant's cognition.

Research Design for Cardiovascular Disease Risk Assessment

Flow mediated dilation (FMD) was performed on participants following the cognitive assessments. Participants were asked not to consume caffeine or engage in any physical activity prior to the study. For this procedure, the subject was asked to be seated with their right arm resting elevated in the supine position to best expose the brachial artery. An inflatable cuff, connected to a Hokanson compressor cart, was fastened to the participant's forearm, about 2 to 4 centimeters below the antecubital fold. Using the ultrasound probe, the participant's brachial artery was identified by searching 2 to 4 inches above the antecubital fold of their arm. After isolating the artery, a probe holder was used to secure the probe in place and maintain a steady image throughout the process. At this point, the ultrasound was switched to Duplex Doppler Mode and the procedure was ready to begin.

Using a computer with screen capturing software that was attached to the ultrasound device, the recording began. For the first 2 minutes of the process, the ultrasound was held steady over the participant's brachial artery to obtain baseline data. After this, the subject's artery was occluded by instantaneously inflating the blood pressure cuff to 250 mmHg. This inflated position was held for the next 5 minutes, while continuing to hold the ultrasound probe over the brachial artery. At the 7-minute mark, the cuff was deflated, and the brachial artery was visualized for 3 minutes during a post-occlusion period. Once the three phases, totaling 10 minutes, were complete, the screen recording was stopped and the procedure was finished. To analyze this data, the screen capture recording was uploaded onto Edge Detection Software on Cardiovascular Suite. This program measured the peak post-occlusion diameter of the artery and percent change from baseline to maximum. As a result, the degree of vascular compliance can be extrapolated as a measure of the participant's cardiovascular health.

Statistical Analysis

To determine the association between CVD risk and cognition, both a Pearson and a Spearman bivariate correlation were conducted. Additionally, CVD risk groups were determined by the number of CVD risk factors from 1 to 5. A one-way ANOVA was conducted to determine possible differences between CVD risk groups for cognition. Data are reported as means $\pm$ standard deviation. Statistical significance is set at $\alpha = .05$.

Results

Table 1 describes the demographic data of the study population. This includes average age, average CAIDE score, average biometric features, education level, and frequency of CVD risk factors. The group can be described overall as slightly overweight, with an average BMI of 26.5, highly educated, with 80% over the population being college educated and beyond, and somewhat healthy, with one-third of the group having no CVD risk factors.

Table 1. Demographic Information

Demographic	*n* = 24
Age (years)	61.27 ± 5.20
CAIDE Score	4.78 ± 1.18
Biometric	
Height (cm)	163.51 ± 5.39
Weight (kg)	70.90 ± 13.07
BMI (kg/m^2)	26.54 ± 4.88
Education	
High School Graduate	0.0%
Some college	20.0%
College Graduate or higher	80.0%
CVD Risk Factors	
Hypertension	33.3%
Dyslipidemia	20.8%
Diabetes	4.17%
Smoker	12.5%
Sedentary	45.8%
No CVD Risk Factors	33.3%

Note. Age and biometric measures are reported as mean ± standard deviation. Education and CVD Risk Factors are reported as a percentage of the study population.

Table 2 displays the mean and standard deviation of each variable tested, as well as the significance level when a One-Way ANOVA between groups of increasing number of CVD risk factors (1-5) was performed. A statistically significant difference was noted in attention between cardiovascular disease risk factor groups.

Table 2. One-Way ANOVA

Variable	Mean ± SD	Significance Level
FMD (%)	32.90 ± 20.49	0.41
RBANS Immediate Memory Percentile	64.09 ± 21.95	0.34
RBANS Visuospatial/Constructional Percentile	70.97 ± 27.75	0.69
RBANS Language Percentile	63.85 ± 21.65	0.43
RBANS Attention Percentile	68.35 ± 23.87	0.03**
RBANS Delayed Memory Percentile	64.44 ± 22.25	0.92
RBANS Total Percentile	72.34 ± 18.37	0.35
VPC	0.74 ± 0.23	0.17

Note. A double asterisk (**) denotes statistical significance at a significance level of $\alpha = 0.05$.

Figure 1 is a graph showing differences in the average RBANS Attention Percentile for each CVD Risk Factor group. The results of the One-Way ANOVA indicated a statistically significant relationship between the variables analyzed in this graph. This graph shows the highest average RBANS Attention Percentile in individuals who had zero CVD risk factors. It also shows the lowest average RBANS Attention Percentile in individuals with 5 CVD risk factors.

Figure 1. Number of CVD Risk Factors vs Average RBANS Attention Percentile

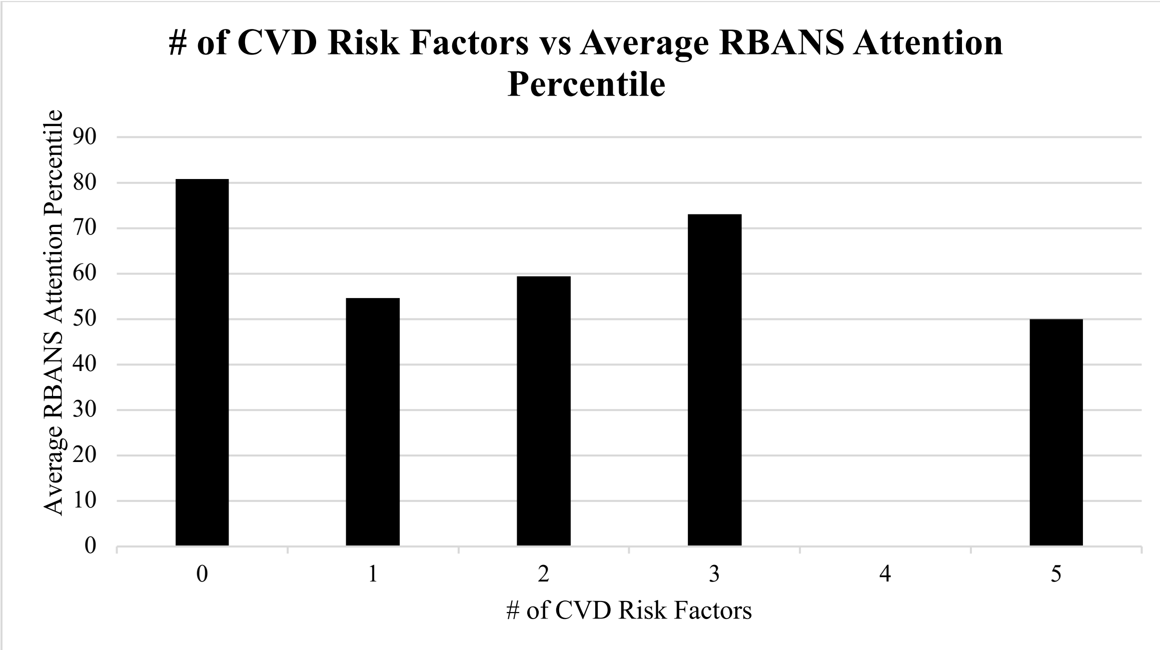


Table 3 shows Pearson correlation coefficients. Variables on the horizontal axis are related to CVD risk while variables on the vertical axis are related to cognitive status. Statistically significant correlations are seen between both CAIDE score and BMI, and CAIDE score and weight ($r = 0.64$, $p = 0.001$; $r = 0.64$, $p = 0.002$). Some meaningful weak correlations can also be found. There is a weak correlation between FMD and weight ($r = -0.30$, $p = 0.33$). A weak correlation can also be found from FMD and BMI ($r = -0.29$, $p = 0.34$). Another weak correlation can be identified between FMD and RBANS Visuospatial/Constructional Percentile ($r = 0.30$, $p = 0.32$).

Table 3. Pearson correlation matrix between continuous variables.

	CAIDE	FMD (%)	BMI	Weight
BMI	0.64**	-0.29*		
Weight	0.64**	-0.30*	0.94**	
RBANS Immediate Memory Percentile	0.10	-0.14	0.24	0.23
RBANS Visuospatial/Constructional Percentile	0.26	0.30*	-0.03	0.04
RBANS Language Percentile	0.41**	0.16	0.20	0.15
RBANS Attention Percentile	-0.25	0.06	-0.15	-0.13
RBANS Delayed Memory Percentile	0.19	0.01	0.09	0.08
RBANS Total Percentile	0.25	0.26	0.13	0.12
VPC	0.42*	-0.23	0.30*	0.29*
Hand Grip – Right Average	-0.15	0.26	-0.17	0.02
Hand Grip – Left Average	-0.20	0.26	-0.19	-0.02
10-meter Habitual	0.32	0.04	0.03	-0.01
10-meter Fast	0.26	0.33*	0.06	0.06
Dual Task Habitual	0.29*	0.17	0.06	0.05
Dual Task Fast	0.28*	0.26	0.01	0.05

Note. A double asterisk (**) denotes statistical significance at a significance level of $\alpha = 0.05$. A single asterisk (*) denotes a weak correlation.

Figure 2 is a graph that relates BMI (in kg/m^2) and FMD (in percent change in brachial artery diameter from baseline to maximum). As previously mentioned, a very weak correlation exists ($r = -0.29$).

Figure 2. FMD vs BMI

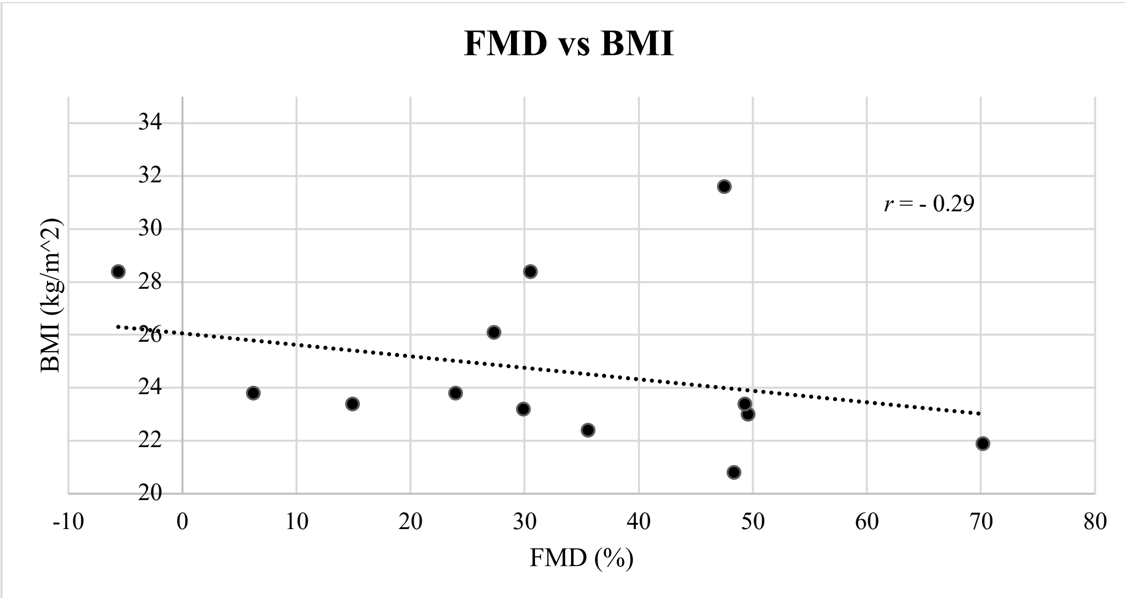


Figure 3 is a graph that shows raw data relating CAIDE scores and BMI (in kg/m^2). A moderate correlation exists (r = 0.64).

Figure 3. CAIDE Score vs BMI

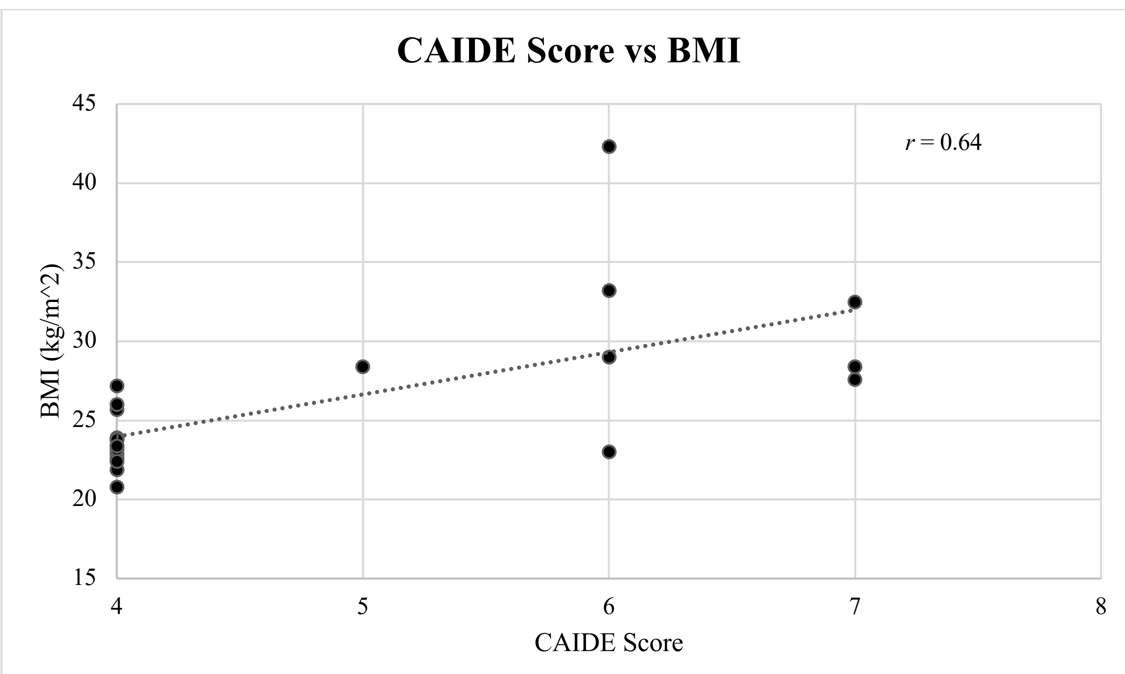


Figure 4 is a graph that shows raw data relating RBANS Visuospatial/Constructional percentile and FMD (in percent change in brachial artery diameter from baseline to maximum). As previously mentioned, a very weak correlation exists (*r* = 0.30).

Figure 4. FMD vs RBANS Visuospatial/Constructional Percentile

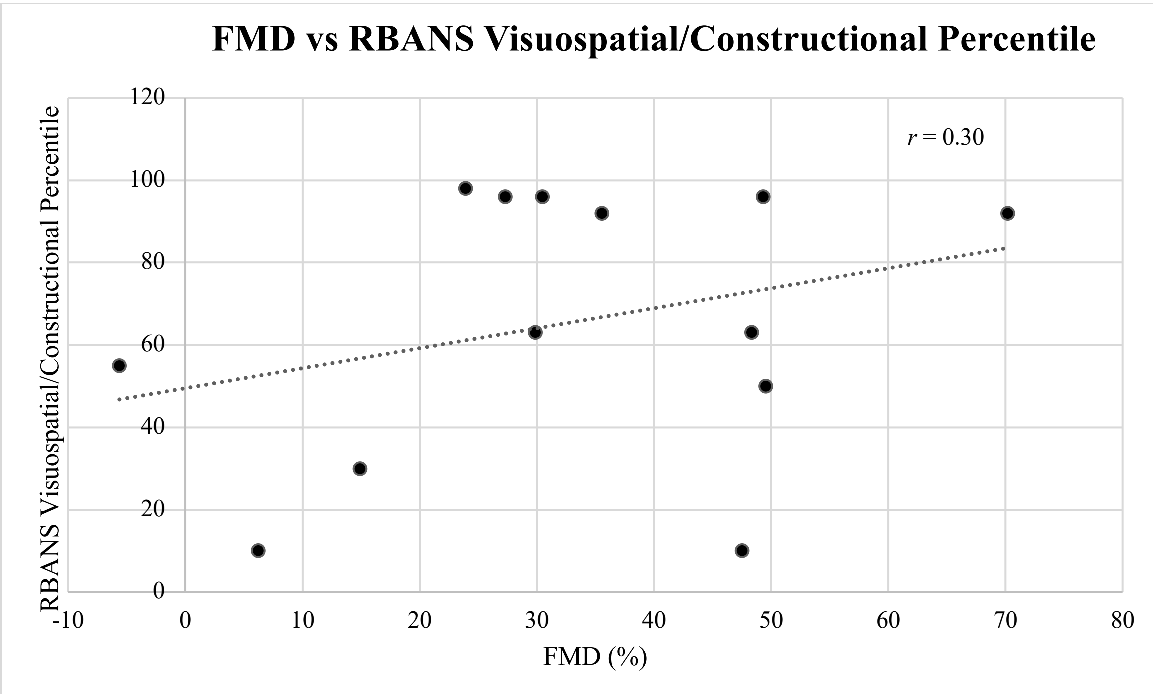


Table 4 displays Spearman's correlation coefficients. Variables on the horizontal axis are related to CVD risk while variables on the vertical axis are related to cognitive status. A weak correlation exists between RBANS Attention Percentile and number of CVD risk factors (*r = -0.32*). CAIDE score and RBANS Attention Percentile also show a weak correlation (*r* = -0.29)

Table 4. Spearman's correlation matrix between discrete/ordinal variables.

	Number of CVD Risk Factors	CAIDE	FMD (%)
RBANS Immediate Memory Percentile	0.04	-0.04	-0.18
RBANS Visuospatial/Constructional Percentile	-0.04	0.18	0.16
RBANS Language Percentile	0.28	0.34*	0.21
RBANS Attention Percentile	-0.32*	-0.29*	0.06
RBANS Delayed Memory Percentile	0.07	0.17	-0.06
RBANS Total Percentile	-0.04	0.15	0.21
VPC	-0.05	0.38	-0.06

Note. A double asterisk (**) denotes statistical significance at a significance level of $\alpha = 0.05$ A single asterisk (*) denotes a weak correlation.

Figure 5 is a graph showing raw data for RBANS Attention Percentile for CVD Risk Factor groups based on number (1-5). As previously mentioned, a very weak correlation exists ($r = -0.32$).

Figure 5. Number of CVD Risk Factors vs RBANS Attention Percentile

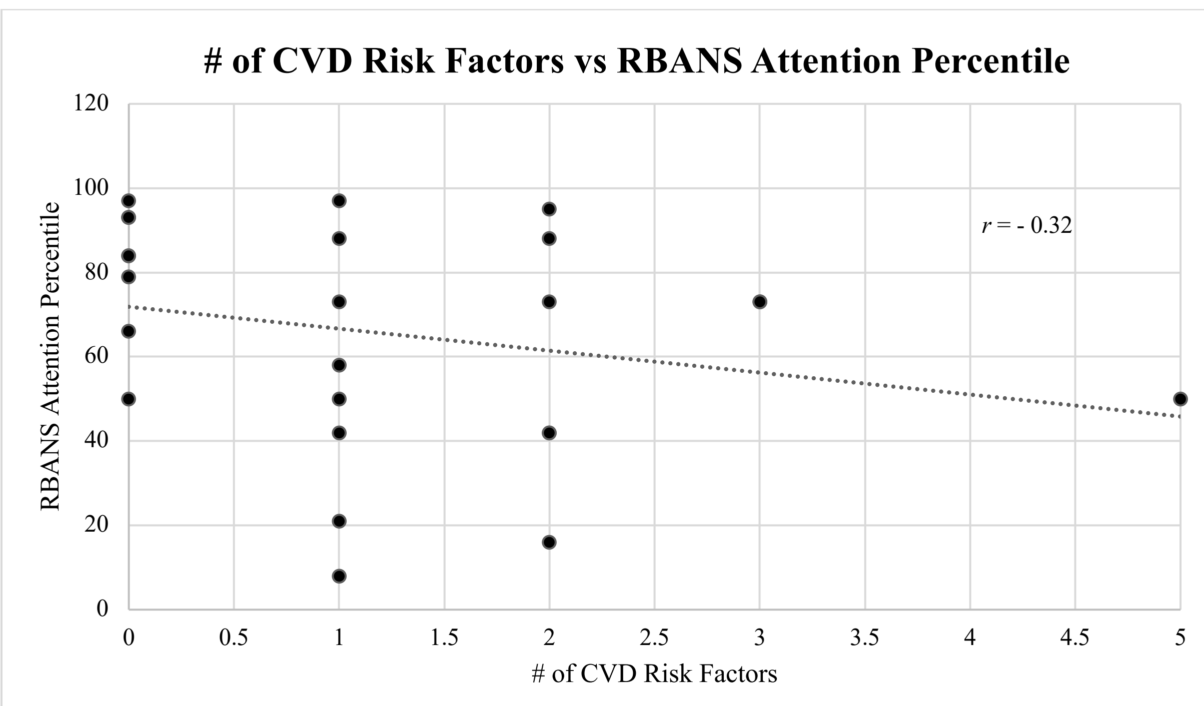
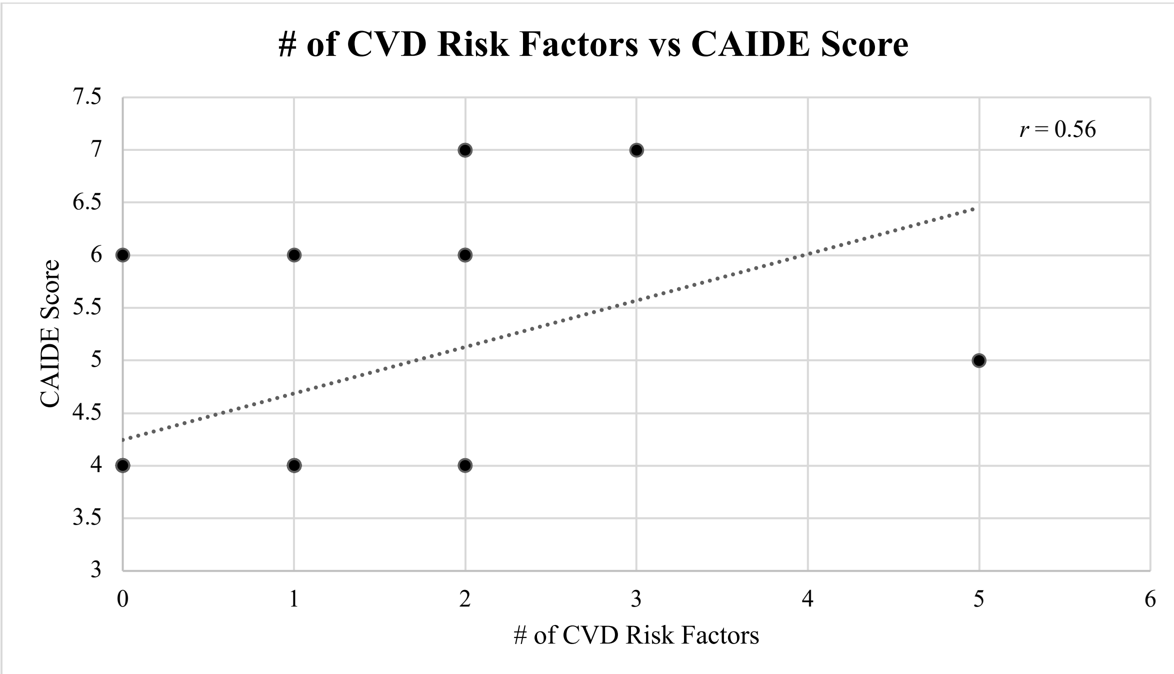


Figure 6 is a graph showing raw data for CAIDE scores for CVD Risk Factor groups based on number (1-5). A moderate correlation exists ($r = 0.56$).

Figure 6. Number of CVD Risk Factors vs CAIDE Score



Discussion

The strongest correlations that were found among the data analysis between cardiovascular disease risk and cognition specifically involved attention. Patients with heart failure, a complication of cardiovascular disease, have shown reduced global cognition and specifically diminished attention when compared to healthy individuals (Leto & Feola, 2014). Cerebral hypoperfusion, commonly associated with heart failure, could be an underlying mechanism for the correlation seen between increased cardiovascular disease risk and poorer attention as a function of cognition. A higher proportion of individuals with diminished attention has also been observed among individuals who have suffered from a myocardial infarction (Chokron et al., 2013). Myocardial infarctions can result in temporary reduced perfusion to the brain or cause necrosis in such tissues if left untreated. Ultimately, a possible underlying explanation for poorer attention in individuals at risk of developing CVD is insufficient cerebral perfusion. The reduced strength of the observed relationship could be explained by a vascular disease process being in its early stages in the affected participants.

In general, this study produced only weak correlations for a variety of reasons. The explanation for these results includes the composition and size of the study sample, data collection methods, and technology issues. Additionally, the COVID-19 pandemic had a significant impact on data collection for this project.

In reference to the general characteristics of the population in this study, the average age is roughly 61 years. This is fairly low, especially when compared to the average age of participants in similar studies concerning cognition and memory. There may not have been enough cognitive decline occurring in this younger age bracket to observe strong correlations. Additionally, this group was very highly educated, with the vast majority of participants having completed a college degree or even more education. Higher educational attainment has shown to generally lead to higher cognitive function and a slower decline in cognition (Zahodne et al., 2015). Furthermore, this group can be considered as fairly healthy, with one-third of the population having none of the conditions listed, while 45% of all Americans suffer from at least one chronic disease (Raghupathi & Raghupathi, 2018). However, the average sample BMI is considered to be overweight, which is indicative of slightly poorer health. Another aspect to evaluate when providing context to these results is that voluntary response bias may have played a role. In general, it can be concluded that healthier individuals are more likely to elect to participate in studies concerning their health. Ultimately, the participants in this study can be considered a homogenous group. Each of these factors may have contributed to the lack of correlations seen in the analysis and weakened the generalizability of this study.

Suboptimal data collection methods may also be responsible for the weak conclusions produced by these results. The FMD procedure was recorded using a screen capturing technology. This produced lower quality videos that made it very difficult to analyze the data. The edge detection software used in analysis is very sensitive, however the grainy quality in videos made it difficult for the software to differentiate between brachial muscle tissue and vascular tissue in order to isolate the arterial walls. Furthermore, the video quality also suffered due to a lack of steadiness and consistency when holding the ultrasound probe over the brachial artery for visualization. This issue may have been resolved by monitoring the video quality throughout the data collection period to make adjustments along the way. However, the Cardiovascular Suite program in which the FMD data was analyzed was not functioning and being serviced throughout the entire data collection period. Therefore, once the software was functioning, all data had already been collected and no improvements could be made at that point. These issues led to decreased validity and reliability in the FMD procedure and results. Similarly, data collection involving VPC was impacted by a brief software issue in which some data points were not saved or capable of being analyzed. Data collection from the Dual-Task assessment was also impacted by construction being done at the Exercise Science Research Center. This was responsible for the absence of several data points. A lack of compliance in the completion of general health and demographic questionnaires that were administered over email prior to each study occurred in several cases, as well. Each of these issues could have contributed to several weak correlations observed that do not follow the expected trend. This includes a positive correlation RBANS Language Percentile and number of CVD risk factors. It would be more logical to assume that a negative correlation would exist in this scenario.

Lastly, data collection in general suffered due to the ongoing COVID-19 pandemic. As expected, many participants were hesitant to enter the lab and interact in close proximity with other people. This is especially understandable given that the target population of this study is older individuals. The number of recruited subjects for the additional FMD study was also significantly impacted by these reasons. Because this procedure requires the examiner to hold an ultrasound probe up to the participant's arm for 10 minutes, social distancing is not feasible. Furthermore, data collection in general was delayed due to the closure of lab facilities for at least six months, significantly shortening the data collection period.

Conclusions

The results of this study indicate a significant difference in attention as a function of cognition between groups of increasing CVD risk. No other statistically significant differences were found among these groups. Nonetheless, some weak correlations were found that may also support a proposed relationship between attention and number of CVD risk factors. In general, stronger conclusions could have been made with a larger sample size, as well as with improved technique when administering the FMD procedure to allow for enhanced reliability and validity.

While this study produced insufficient evidence to support any firm link between increased cardiovascular disease risk and poorer cognitive function, the trends found show promise. Future studies should focus on recruiting a more diverse population with regard to age, educational attainment, and health status. Overall, the results of this study continue to strengthen the hypothesis that cardiovascular and cognitive functions are interrelated in some capacity.

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