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MODIFIERS OF CARDIOVASCULAR RISK SCORE ON DISABILITY IN THE ELDERLY

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ABSTRACT

Cardiovascular disease (CVD) affects daily living functionality, cognitive ability, and mood. We evaluated the effects of a CVD risk score on disability and assessed the characteristics that may modify this relationship in 192 older adults (mean age: 65.6 years, 96 women). WHODAS 2.0 was used to measure global disability and mobility difficulty. Framingham Risk Score (FRS) was used to predict 10-year cardiovascular mortality risk. Sociodemographic characteristics, mental status, overall mood, and gait speed were evaluated for their potential modification of the effect of FRS on WHODAS. We used general linear models to estimate the main effect and interaction effects for the modifiers. A higher effect of FRS was significantly associated with worse WHODAS total score and mobility sub-score. We found female gender, younger age, higher IQ, more years of education, higher MMSE, faster gait speed, and higher GDS to be potential effect modifiers.

Key words: Cardiovascular disease, functionality, mobility, gait speed, depression, disability, WHODAS

1. INTRODUCTION

The global population of older adults is expected to outnumber children under 5 by 2020 (World Health Organization 2018). Functionality progressively declines with advancing age (Lopes et al. 2013). Over 15 million people in the United States report having at least one limitation performing tasks that are essential for independent living (Manini 2011). Health care spending for adults over the age of 65 has been rapidly increasing, consuming over 30% of the national health care budget (De Nardi et al. 2015, Rice and Fineman 2004). However, disease and disability are not an inevitable part of just aging (National Institutes of Health 2010). Disability and functionality results from interactions between an individual's health conditions and their environment (Weltgesundheitsorganisation 2001). The World Health Organization Disability Assessment Schedule 2.0 (WHODAS) was developed and tested within a wide variety of cultural settings and provides a common measure of the impact that health conditions have over an individual's functionality (Üstün 2010).

Cardiovascular disease risk (CVD risk) is a strong predictor of physical disability (Wong et al. 2015). Maintaining low CVD risk has been suggested as a logical strategy for achieving long-term wellbeing (Keil et al. 1989; Pinsky et al. 1987). However, it is not well known which individual characteristics influence the relationship between CVD risk and disability in older adults.

The aim of this study is to measure the effects of CVD risk factors on disability and to determine which physical and demographic characteristics modify this relationship. We examined cross sectional data from 192 older adults from our on-going MemAID study.

2. METHODS

We used data from the Memory Advancement by Intranasal Insulin in Type 2 Diabetes (MemAID) study. MemAID is a five year, randomized, double-blinded, placebo-controlled clinical trial (ClinicalTrials.gov NCT02415556, FDA IND 107690) conducted at the Syncope and Falls in the Elderly (SAFE) Laboratory at

the Beth Israel Deaconess Medical Center (BIDMC) and Brigham and Women's Hospital (BWH). Eligible participants that signed an informed consent approved by the BIDMC Committee on Clinical Investigations were enrolled and randomized. Eligible participants were between 50 and 85 years old, with or without type 2 diabetes, able to walk for six minutes, had a Mini Mental Status Examination (MMSE) >20, and had no major medical conditions or surgeries within the last six months. At baseline, participants underwent functionality, cognitive, and mobility testing which include the following:

- **WHODAS**: provides a global disability score that describes the degree of functional limitation by evaluating the difficulty functioning during the prior 30 days in six domains of life: cognition (understanding and communicating), mobility (getting around), self-care, getting along with people, life activities, and participation in society. Scores assigned to each item were summed (Üstün 2010). Maximum score is 128; higher scores indicate more disability. Adjusted mean for general population is 32 (Üstün et al. 2010).
- **MMSE**: test of cognitive functioning by assessing orientation, attention, memory, language, and visuo-spatial skills. Maximum best score is 30 and a score of less than 25 indicates cognitive impairment.
- **Geriatric Depression Scale (GDS):** assessment of self-reported overall mood in the elderly. Maximum score is 30, higher scores are worse, more than 20 is considered severe depression.
- **Wechsler Test of Adult Reading (WTAR™):** provides an estimate of premorbid intellectual functioning (Bright 2018). Participants read a list of 50 words and each correct pronunciation is given a score of 1, with 50 as the maximum raw score. The raw score is then standardized by age and reference group. Higher scores correspond with higher IQ.
- **Gait speed:** assessed by the Mobility Lab System (APDM, Inc., Portland, OR.) during 6 minutes of natural and regular pace walking (normal walk, NW) and during 6 minutes of walking while counting backwards in multiples of 7 (dual-task, DT). Gait speed is measured in centimeters per second (cm/sec). Speeds of more than 10 cm/sec are associated with longer survival than expected by age and sex alone (Studenski 2011).

CVD risk was assessed by the Framingham risk score (FRS) using the FRS worksheet developed by the Canadian Cardiovascular Society (Canadian Cardiovascular Society 2019). FRS total points were calculated according to age, gender, history of type 2 diabetes mellitus, smoking status, systolic blood pressure, current use of antihypertensive treatment, HDL, and total cholesterol levels. All parameters were measured and assessed during the first in-person visit. Risk of developing CVD to 10 years was calculated based on total points and categorized as low if less than 10%, moderate if between 10% and 19% and high if 20% or higher.

2. 1. Data analysis

Our primary outcome was the WHODAS 2.0 total score. Mobility score was used in the sub-analysis. Linear regression models were performed assessing the effect of CVD risk (FRS total points) on WHODAS total score and on mobility sub-score when each modifiable (MMSE, years of education, gait speed and GDS) and non-modifiable (gender, age, IQ-WTAR) predictors, and their interaction with FRS were included in the model. Type-I error was set at 0.05. We used STATA version 12 for all statistical analysis.

3. RESULTS

Demographic characteristics, medical history, and current medications of 192 participants were analyzed (Table 1). The sample was equally distributed between women and men (N=96) and the majority of them had high CVD risk (N=79) and a broad range of disability (mean ± SD of 14.9 ± 15.6).

Table 1: Cohort Characteristics

Characteristic	N=192
Gender: men,women	50(96), 50(96)
Race: white, AA, asian, other	77(149), 16(30), 3(6), 4(7)
Age (years)	65.6 ± 9 (50 – 84)
Diabetes: yes, no	42(80), 58(112)
Hypertension: yes, no	47(90), 53(102)
Dyslipidemia: yes, no	51(98), 49(94)
Years of education	16.2 ± 3.3 (8 – 28)
MMSE score	28.3 ± 1.8 (21 – 30)
FRS category: low, moderate, high	29(56), 30(57), 41(79)
FRS total points	14.6 ± 4.8 (3 – 25)
WHODAS total score	14.9 ± 15.6 (0 – 72)
WHODAS mobility sub-score	2.5 ± 3.4 (0 – 13)
GDS Total Score	5.5 ± 5.4 (0 – 26)
WTAR score	113 ± 13.7 (71 – 131)
NW gait speed (cm/s)	115.8 ± 21.4 (36.8 – 189.2)

Continuous variables are expressed as mean ± SD (min – max) and categorical variables are expressed as percentages, % (N). MMSE: Mini Mental Status Examination; FRS: Framingham Risk Score WHODAS: World Health Organization Disability Assessment Schedule 2.0; GDS: Geriatric Depression Scale; WTAR™: Wechsler Test of Adult Reading; NW: Normal Walk

3.1 Linear regression of the effect of CVD risk on disability

FRS Total Points showed a significant linear relationship with both WHODAS total score (p=0.0025, Figure 1a) and WHODAS mobility sub-score (p=0.0002, Figure 1b). Diabetic participants had more disability in both WHODAS total score and WHODAS mobility sub-score.

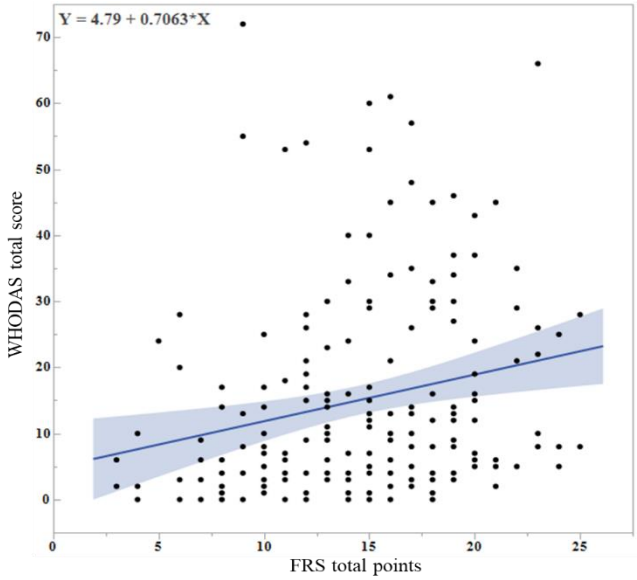

Figure 1a: Linear relation of WHODAS total score and FRS total points.

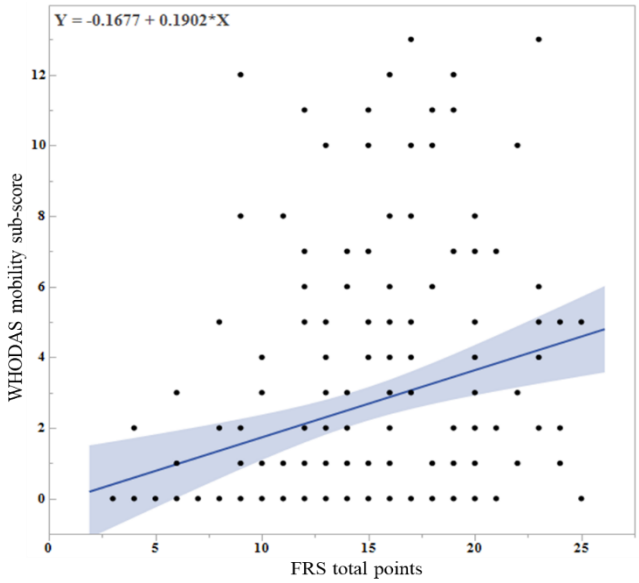

Figure 1b: Linear relation of WHODAS mobility sub-score and FRS total points.

3.2 Modifiers of the effect of CVD risk on global disability

The regression model showed that all covariates except for gender were significant predictors of WHODAS total score, when controlling for FRS Total Points (Table 2a).

Age, male gender, years of education, IQ, NW gait speed, DT gait speed, and MMSE were negatively associated with WHODAS total score. Advanced age and male gender increased the effect of FRS Total Points on WHODAS total score by 28% and 11%, respectively. The effect of FRS total points on WHODAS total score was decreased by 29% with higher IQ, by 11% with higher MMSE, and by 10% with more years of education. Faster gait-speed decreased the impact of CVD risk on WHODAS total score by 35% on normal walk and 18% on dual-task walking.

Table 2a: Regression model: Association between CVD risk and Disability (CVD risk in terms of FRS total points as predictor of WHODAS total score)

Covariate in a linear model	% Change in β FRS Total Points	Change in R^2	β covariate	Uncorrected p-value covariate
Age	**28.18**	0.019	-0.26	**0.046**
Gender	11.05	0.009	-3.15	0.165
Years of Education	-10.25	0.023	-0.73	**0.032**
IQ - WTAR	**-29.17**	0.058	-0.28	**0.001**
GDS	**-41.00**	**0.398**	1.84	**<0.001**
NW Gait Speed	**-35.00**	0.046	-0.16	**0.002**
DT Gait Speed	-18.22	0.025	-0.11	**0.024**
MMSE	-11.44	0.046	-1.89	**0.002**

Highlighted values correspond to change in β more than 20%, change in R^2 more than 0.1, and uncorrected p-value less than 0.05, respectively.

GDS was the only covariate with a positive relationship with WHODAS total score. A higher depression score was related to greater disability when controlling for CVD risk. However, when GDS was added to the model, the effect of FRS total points on WHODAS total score was decreased by 41%. Depression accounted for the largest change in variance for WHODAS total score (change in R^2=0.39) and WHODAS mobility sub-score (change in R^2=0.14).

3.3 Modifiers of the effect of CVD risk on mobility

Further, a subsequent regression analysis showed that all covariates except for age were significant predictors of WHODAS mobility sub-score, when controlling for FRS Total Points (Table 2b).

Age, male gender, years of education, IQ, NW gait speed, DT gait speed, and MMSE were negatively associated with WHODAS mobility sub-score.

The effect that FRS total points had over WHODAS mobility sub-score increased by 20% with older age and by 18% with male gender. The following factors decreased the impact of CVD risk on mobility: a higher IQ (by 20%), higher MMSE (by 7%), and more years of education (by 9%). Faster gait-speed decreased the relationship of CVD risk and WHODAS mobility sub-

score by 43% on normal walk and 27% on dual-task walking.

Table 2b: Regression model: Association between CVD risk and Mobility (CVD risk in terms of FRS total points as predictor of WHODAS mobility sub-score)

Covariate in a linear model	% Change in β FRS Total Points	Change in R^2	β covariate	Uncorrected p-value covariate
Age	**20.15**	0.016	-0.05	0.069
Gender	17.77	0.039	-1.38	**0.004**
Years of Education	-9.33	0.029	-0.18	**0.013**
IQ - WTAR	**-20.38**	0.043	-0.05	**0.003**
GDS	-19.58	**0.140**	0.24	**0.001**
NW Gait Speed	**-43.46**	**0.109**	-0.05	**<0.001**
DT Gait Speed	**-27.98**	0.083	-0.04	**<0.001**
MMSE	-7.49	0.032	-0.33	**0.01**

Highlighted values correspond to change in β more than 20%, change in R^2 more than 0.1, and uncorrected p-value less than 0.05, respectively.

GDS was the only covariate with a positive relationship with WHODAS mobility sub-score; with a higher depression score related to greater difficulty getting around when controlling for CVD risk. When GDS was added to the model, the effect of FRS total points on WHODAS mobility sub-score decreased by 20%.

4. DISCUSSION

The ability to maintain daily functionality with advancing age determines quality of life and survival. Daily functionality is a continuum of health states and depends on the interaction between an individual's health condition and their socio-demographic context across different domains (Weltgesundheitsorganisation 2001). The effect of these interactions on the different domains of functionality is not fully understood.

We examined the effect of CVD risk on disability, and measured the influence of gait speed upon this relationship. We saw CVD risk had a greater effect on the WHODAS total score than on the WHODAS mobility sub-score and found gait speed is a strong indicator of daily living difficulties. People with higher CVD risk scores had worse subjective (higher WHODAS mobility sub-scores) and objective (slower gait speeds) mobility measures.

Analysis of the impact of depression on daily functionality showed that higher levels of depression reduced the effect that CVD risk had on WHODAS total score and WHODAS mobility sub-score. These findings suggest that depression might have a direct independent effect on disability. Loss of primary motivation is a common symptom of depression in the elderly and has been shown to affect functionality and cognition (Sözeri-Varma et al.2019), therefore greater depressive symptoms may partially mediate the relationship between CVD risk and WHODAS score.

In people with higher IQ, more years of education, and higher MMSE score, CVD risk had a lesser impact on overall disability. This is consistent with prior studies which have suggested that higher educational levels promote better coping mechanisms, life satisfaction, subjective well-being, and overall functionality (Algilani et al. 2014). Furthermore, lifestyle modifications such as exercise and the Mediterranean diet that have been linked to reducing CVD risk (Martínez-González et al. 2019, Myers 2003) also have shown to decrease cognitive decline related to aging (Dumas 2017).

This study ratifies prior findings that cardiovascular risk factors such as diabetes, hypertension, hyperlipidemia, and tobacco use have significant deleterious effects on daily living functionality. Further, our results show that protective factors including higher IQ, higher MMSE, greater years of education, and faster gait speed may mitigate the relationship between CVD risk factors and functional impairment, suggesting possible future targets for improving functional outcomes in older adults.

Overall, our results suggest that providing better medical care for vulnerable older patients, such as people with slow gait speed, fewer years of education, and lower IQ might help prevent loss of functionality in the presence of strong CVD risk factors.

One of the biggest challenges for the health care system is to educate and train a workforce that can meet the complex health care needs of the elderly (Rice and Fineman 2004). Public health interventions aimed at influencing modifiable and non-modifiable characteristics might decrease disability and improve functionality amongst the unhealthy elderly population. Prevention of health problems by promoting lifestyle changes is one of the few known ways to reduce rising health care costs (Kojima et al. 2019, Rice and Fineman 2004). Accurate disability measurement tools may help monitor the impact of health care policy decisions (Üstün 2010) and may contribute to predict the most efficient measures to improve quality of life of vulnerable elderly populations.

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