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Short Communication

Free-living physical activity, executive function, and kidney disease

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ABSTRACT

Objective: We evaluated the specific association between physical activity and cognition among older adults with chronic kidney disease in the United States. **Methods:** Data from the 1999-2002 National Health and Nutrition Examination Survey were used to identify 66 older adults, between 60 and 85 years, with complete data on selected study variables. Diagnosis of chronic kidney disease was assessed through self-report. Participation in physical activity was determined from self-report data. The digit symbol substitution test (DSST) was used to assess participant executive cognitive functioning tasks of pairing and free recall. Individuals were excluded if they had missing data on the study variables assessed, or if they self-reported having coronary artery disease, congestive heart failure, stroke, or a heart attack. **Results:** Physical activity was associated with higher cognitive performance in this sample. After adjustments, those meeting moderate to vigorous physical activity (MVPA) guidelines (vs. not) had an 8.77 higher DSST score ($\beta = 8.77$; 95% CI: 1.65-15.89; $P = 0.02$). Furthermore, after adjustments, for every 1 metabolic equivalent of task-min-month increase in MVPA, participants had a 0.0007 DSST increase ($\beta = 0.0007$; 95% CI: −0.0001-0.001; $P = 0.08$), although this result was not statistically significant. **Conclusion:** In this sample of older adults with chronic kidney disease, there was a positive association between physical activity participation and higher levels of cognitive functioning.

KEY WORDS: Chronic disease, epidemiology, health promotion, mental health, physical activity

INTRODUCTION

Older adults with advanced kidney disease are highly susceptible to progressive cognitive impairment and eventually dementia [1]. Mental health decline also poses a significant risk for individuals diagnosed with milder stages of kidney disease [2]. The Cardiovascular Health Cognition Study examined the prevalence of vascular dementia over time, finding the diagnosis of moderate renal disease predicted increased metabolic biomarkers, known to contribute to poor mental health, and vascular dementia after 6 years [3]. Inflammation, excess adiposity, hypertension, Type 2 diabetes, oxidative stress, vascular plaque deposition, endothelial dysfunction, and uremic toxins are among the possible physiological mechanisms underlying cognitive decline linked to impaired renal function [4-6]. In addition to physiologic alterations, kidney disease may also precede severe, concomitant disturbances in affect, including depression, delirium, and sleep disorders [1,7]. Although kidney transplantation may mitigate the adverse effect of dialysis treatments [8] on certain cognitive domains, previous work suggests impairments in executive functioning, and verbal memory persist following surgical interventions [9,10]. Despite widespread clinical evidence supporting the link between chronic kidney disease and mental dysfunction, early clinical diagnosis, and lifestyle prevention remains inadequate thus far [1].

The presence of chronic comorbidities, such as diabetes and hypertension have been shown to corroborate worse health outcomes among those with kidney disease [11]. The biological mechanisms underlying renal disease are consistent with those evident in diabetes and hypertension, such as neuronal damage, oxidative stress, thrombosis, vascular lesions, and atherosclerosis [2,4,12,13]. Physical activity has been shown to elicit metabolic and affectual improvements on the aforementioned physiological and psychological determinants of chronic disease, as well as improving the functional and social quality of life [14-19]. Specifically, physical activity is effective in weight management through stimulation of lipolysis, improving glucose metabolism, modulation of low-density lipoprotein and high-density lipoprotein cholesterol, regulation of endothelial function, as well as the prevention of more severe signs of renal failure, including glomerulosclerosis and end-stage renal disease [20-24]. The role of exercise in combatting the deleterious effects of diabetes and hypertension are instrumental advancing efforts to prevent and treat chronic kidney disease, as mortality among renal patients is often attributable to cardiovascular pathologies, rather than complications which arise from kidney disease [23]. To the best of our knowledge, however, we are unaware of a study that has specifically evaluated the associations of physical activity on executive cognitive functioning among older adults with evidence of chronic kidney disease. Therefore, the specific aim of this brief report was to evaluate the potential association between frequency, duration, and intensity of physical activity, in addition to meeting physical activity guidelines, on cognitive performance among a sample of individuals with known chronic renal disease.

METHODS

Study Design

Data from the 1999-2002 National Health and Nutrition Examination Survey (NHANES) were used. NHANES is an ongoing survey conducted by the National Center for Health Statistics, a major section of the Centers for Disease Control and Prevention. NHANES evaluates a representative sample of non-institutionalized U.S. civilians, selected by a complex, multistage probability design. All procedures for data collection were approved by the National Center for Health Statistics ethics review board, and all participants provided written informed consent before data collection.

Participants

Participants were considered to have chronic kidney disease if they answered "yes" to the following question, "Have you ever been told by a doctor or other health professional that you had weak or failing kidneys?" Participants were excluded if they had missing data on the study variables or if they self-reported having coronary artery disease, congestive heart failure, stroke, or a heart attack. The analyzed sample included 66 older adults between 60 and 85 years who had evidence of chronic kidney disease.

Physical Activity

As described elsewhere [25], participants were asked open-ended questions about participation in leisure-time physical activity over the past 30 days. Data were coded into 48 activities, including 16 sports-related activities, 14 exercise-related activities, and 18 recreational-related activities.

For each of the 48 activities where participants reported moderate or vigorous intensity for the respective activity, they were asked to report the number of times they engaged in that activity over the past 30 days and the average duration they engaged in that activity.

For each activity, metabolic equivalent of task (MET)-min-month was calculated by multiplying the number of days, by the mean duration, by the respective MET level (MET-min-month = days * duration * MET level). The MET levels for each activity are provided elsewhere. Participants engaging in 2000+ moderate to vigorous physical activity (MVPA) MET-min-month were defined as meeting physical activity guidelines. As described elsewhere [25], this self-reported physical activity measure has demonstrated evidence of convergent validity by associating with accelerometer-assessed physical activity.

Cognitive Function

The digit symbol substitution test (DSST) [26] was used to assess cognitive function among older adults 60 + years of age. The DSST, a component of the Wechsler Adult Intelligence Test and a test of visuospatial and motor speed-of-processing, has a considerable executive function component and is frequently used as a sensitive measure of frontal lobe executive functions [27,28]. The DSST was used to assess participant cognitive function tasks of pairing (each digit 1-9 has a symbol it is associated with) and free recall (allowing participants to draw more figures in the limited time due to remembering pairs). Participants were asked to draw as many symbols as possible that were paired with numbers within 2 min. Following the standard scoring method, one point is given for each correctly drawn and matched symbol, and one point is subtracted for each incorrectly drawn and matched symbol, with a maximum score of 133.

Measurement of Covariates

Covariates included: Age (continuous; years), gender, race-ethnicity (Mexican American, non-Hispanic white, non-Hispanic black, and other), measured body mass index (continuous; kg/m^2), C-reactive protein (continuous; mg/dL; marker of inflammation), self-reported smoking status (current, former, never), self-reported diabetes status (yes/no), and measured mean arterial pressure (continuous; mmHg; average of 4 blood pressure measurements).

Analysis

All statistical analyses were computed in Stata (version 12) and accounted for the complex survey design employed in NHANES. Multivariable linear regression analyses were computed that examined the association between physical activity and cognitive function (outcome variable). Statistical significance was set at an alpha of 0.05.

RESULTS

The analyzed sample included 66 older adults (60-85 years) with evidence of chronic kidney disease. Table 1 displays the weighted

Table 1: Weighted characteristics of the analyzed sample (*N*=66)

Variable	Point estimate	SE
DSST, mean	43.5	1.92
MVPA MET min/month	1104.5	453.3
% meeting MVPA guidelines	16.2	0.06
Age, mean years	71.2	0.86
% male	59.1	0.08
% white	81.1	0.04
BMI, mean kg/m^2	29.9	0.97
CRP, mean mg/dL	0.52	0.06
MAP, mean mmHg	92.5	2.97
% diabetes	25.0	0.08
% smoker	23.6	0.08

DSST: Digit symbol substitution test, MVPA: Moderate to vigorous physical activity, MET: Metabolic equivalent of task, BMI: Body mass index, CRP: C-reactive protein, MAP: Mean arterial pressure, SE: Standard error characteristics of the study variables. Participants, on average, were 71 years; the majorities were male (52%) and non-Hispanic white (81%). MVPA was 1104.5 MET minutes per month and 16.2% of the sample met MVPA guidelines. Classification of participants as meeting, or not meeting, MVPA guidelines was determined through self-report on 48 coded activities included for analysis. Participants self-reported the number of times they engaged in moderate or vigorous sports, exercise, or recreational activities over the past 30 days and the average duration they engaged in that activity.

Regarding the main findings, time spent engaging in MVPA as well as meeting MVPA guidelines was independently associated with DSST performance performance ($\beta = 8.77$; 95% CI: 1.65-15.89; P=0.02) among this sample of kidney disease patients. After adjustments, for every 1 MET-min-month increase in MVPA, participants had a 0.0007 DSST increase ($\beta = 0.0007$; 95% CI: −0.0001-0.001; $P = 0.08$).

DISCUSSION

The main finding of this brief report was that among older individuals with evidence of chronic kidney disease, engaging in higher levels of MVPA, and/or meeting physical activity guidelines, resulted in increased cognitive performance on the DSST. Inactive participants achieved lower scores on the DSST. To date, no research has confirmed exercise prescriptions are beneficial in reducing the prevalence and consequences of chronic kidney disease [29]. However, no studies have found exercise to be associated with worse physical or mental health among patients with renal pathology. Therefore, the purpose of our study was to add to the literature by examining the association between physical activity participation and cognitive function among those with chronic kidney disease. Our main finding was that among those with chronic kidney disease, those with higher physical activity engagement had better cognitive function.

Older individuals may be mentally or physically limited by complications linked with chronic kidney disease or pre-existing comorbidities. However, these limitations may become more pronounced with increased inactivity and weight gain. Maximal exercise capacity may be impaired in those with chronic kidney disease; however, recent work has shown light-intensity physical activities may be associated with improved health within this population [30-32]. Movement-based behaviors such as moderate-intensity exercise, vigorous-intensity exercise, muscular strength activities, and active transport are potential modalities which health professionals should consider when tailoring education and programs to meet the needs of patients with preventable lifestyle diseases [33]. Resistance training may also be a viable exercise choice for patients with chronic kidney disease, as this modality is believed to reduce inflammation, induce mitochondrial proliferation, and improve weight status [34,35]. However, severe contraindications may present in chronic kidney disease and should be closely monitored by clinicians. These may include uremic toxins, hyperparathyroidism, vitamin D deficiency, anemia, and metabolic acidosis, which could derail physical activity engagement and maintenance [29].

In conclusion, the present study identifies an association between MVPA participation and higher cognitive functioning among aging individuals with a diagnosis of chronic kidney disease. Obesity, inflammation, hypertension, diabetes, oxidative stress, atherosclerosis, endothelial dysfunction, and uremic toxins have been associated with cognitive impairment among those with chronic kidney disease [4-6]. To date, research has yet to examine the relationship between physical activity and cognitive performance within this special population. Therefore, our findings are not only novel but also underscore important conclusions drawn from a growing body of literature commending the preventative, attenuating, and sometimes reversing effects of exercise on the mechanisms of cognitive dysfunction and physiological deterioration [15-17,29,36]. Future experimental and longitudinal research should aim to strengthen early diagnosis and effective treatment strategies, and should also overcome a limitation of our study, which was the use of a cross-sectional research design, self-reported assessment of physical activity, and small sample size.

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