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Research Article

НИРКИ KIDNEYS

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Psychological and Neurocognitive Dimensions of Kidney Disease: Mental Health Impacts of Chronic Hypertension and Systemic Illness

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Abstract

Background:

Hypertension and chronic kidney disease are now considered systemic disorders associated with vascular, metabolic, and inflammatory dysfunction, which may also cause depressive symptoms and cognitive impairment in the elderly. In this study, the researchers assessed how kidney disease indicators, hypertension status, depressive symptoms and neurocognitive performance were related in a nationally representative ageing population.

Methods:

Secondary analysis was performed based on the 2013-2014 National Health and Nutrition Examination Survey. The key inclusion criteria were participants aged 60 to 80 years and full data on blood pressure, estimated glomerular filtration rate, urine albumin-to-creatinine ratio, and depressive symptoms measured by the Patient Health Questionnaire-9 and standardized cognitive tests. Associations between kidney markers, hypertension status, depressive symptoms and cognitive outcomes were investigated using multivariable linear regression models after adjusting for age and sex.

Results:

The poorer cognitive performance was linked to higher albuminuria, especially in the processing speed and executive ability. Estimated glomerular filtration rate was not independently associated with cognitive outcomes after adjustment. Greater depressive symptom burden was consistently associated with lower cognitive scores across all domains. Both lower estimated glomerular filtration rate and higher albuminuria were associated with increased depressive symptoms. Hypertension status demonstrated domain-specific associations with cognitive performance.

Conclusions:

Albuminuria and depressive symptoms are independently associated with neurocognitive performance in older adults, highlighting the importance of integrated renal, mental health, and cognitive screening strategies in aging populations.

Keywords: Chronic kidney disease, albuminuria, cognition, depression, hypertension

Introduction

Chronic kidney disease (CKD) is becoming more and more appreciated as a multi-system disorder, not the condition of compromised renal activity. Impaired metabolic homeostasis, chronic inflammation, and rapid vascular injury are caused by progressive kidney dysfunction, resulting in the rapid involvement of other organs. There is experimental and clinical evidence that acute and chronic renal injury trigger molecular cascades of oxidative stress, mitochondrial impairment and systemically propagating inflammatory signaling pathways. Research on nephrotoxicity also demonstrates that kidney damage leads to cellular stress, including mitochondrial damage and apoptosis, which supports the idea of CKD being a multisystem disease with devastating health and survival outcomes [1].

Mitochondrial dysfunction is at the center stage of kidney disease pathogenesis at the cellular level.

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Mitochondrial injury is especially prone to renal tubular cells since they have high energy requirements. Mitochondrial bioenergetics disruption is a major cause of renal dysfunction and disease. Nephrotoxic injury experimental models have indicated that mitochondrial damage enhances oxidative stress, which subsequently triggers cell injury and fibrosis in the kidney. The recent data found on the basis of natural product therapeutic research indicates that mitochondrial pathways could be targeted in order to restore the integrity of kidneys, highlighting the relevance of mitochondrial homeostasis to renal functioning [2].

The close-knit mechanisms between kidney damage and systemic complications are oxidative stress and inflammation. Ongoing oxidative damages induces inflammatory response, endothelial malfunction, and pathological tissue remodelling, hence hastening the advancement of the disease. Experimental research has shown that small-molecule molecules with the potential to alter mitochondrial oxidative stress have the ability to reduce renal injury and maintain cellular viability. The results proved the hypothesis that the role of renal oxidative stress as a mechanistic mediator linking kidney disease and systemic/neurological phenotypes is feasible [3].The increasing knowledge about CKD pathophysiology has aroused interest in herbal and plants-based therapeutic methods. Different studies have explored the potential of herbal medicines to reverse mitochondrial dysfunction and oxidative damage in CKD. Phytochemicals were found to possess renoprotective properties through mitochondrial signaling, inflammatory prevention, and enhancing the generation of energy by the cells. The findings also emphasize the systemic purity of kidney disease and the relevance of metabolic and mitochondrial pathways in the pathogenesis of the disease [4].Mitochondrial DNA (mtDNA) damage is also a possible biomarker of CKD severity and progression. The damage to the mitDNA accrued is a marker of excessive oxidative stress and insufficiency of mitochondrial repair system; both markers are strongly associated with chronic renal dysfunction. There is evidence that the damage of the mitochondrial DNA would not only contribute to renal impairment, but also potentially facilitate systemic inflammatory responses, which is the route by which kidney disease could act on remote organs, such as the central nervous system [5].

The systemic effect of renal dysfunction is also supported by the literature on acute kidney injury (AKI). Experimental studies of phytocompounds on AKI subjects show evidence of protective effects that occur via mitigating oxidative stress and inflammation. These results have some mechanistic parallels in CKD although they are concerned with acute injury, to show how renal insults might trigger systemic pathophysiological responses [6]. More studies on traditional medicine and food derived substances have drawn attention to their role in protecting the kidneys. Medicinal phytochemicals were proven to control inflammatory mediators and damage to renal tissue. This literature supports the idea that the mechanisms of kidney disease development are metabolic and inflammatory and occur beyond the renal system [7].

The gut gutrenal interface is an emerging focus as an important determinant of system and renal health. According to experimental research, the severity of renal injury can be affected by the modulation of the gut-derived metabolites and inflammatory pathways. Such results support the multifaceted nature of inter-organ communication during CKD and indicate the possible connection to the neurological and psychological outcomes [8].Bioactive compounds Clinical trials involving bioactive compounds have been initiated to translate theoretical research to practical uses. The clinical utility of focusing on the oxidative and inflammatory pathways and the timely response to the indicators of kidney damage have been emphasized by randomized studies of curcumin-based interventions with a slight positive effect on renal outcomes [9]. Albuminuria is considered to be a clinical sign of renal damage and general vascular dysfunction. Albuminuria-lowering therapeutic interventions have also shown protective effects, especially in diabetic nephropathy, indicating its suitability as a marker of systemic disease burden and not renal isolated pathology [10]. A growing amount of research confirms the renoprotective properties of certain phytochemicals including quercetin. They have antioxidant and anti-inflammatory effects that decrease the renal damage and increase cellular stability, which further supports oxidative stress management as a means to alleviate systemic complications of kidney disease [11].

The changes in lipid metabolism and mitochondrial energy control have also been suggested in the etiology of diabetic and chronic kidney disease. Experimental studies have proven that medications such as berberine can raise the fatty acid metabolism in the renal cells and prevent lipid accumulation in these cells that signal metabolic imbalance as a leading cause of kidney diseases [12]. The inflammatory signaling pathways play a role in the destruction and death of renal cells. It has been shown that inhibition of some transcription regulators suppress oxidative stress and inflammation, which, in its turn, suppress kidney injury and disease progression [13]. Clinical trials have demonstrated a clinical effect of natural compounds such as propolis on proteinuria and renal activity in CKD patients. These findings underscore the treatment opportunities of assaulting systemic inflammatory and oxidative pathways and support additional study of conciliatory treatment choices [14].This research sought to examine kidney disease markers and hypertension status in relation to psychological and neurocognitive outcomes in old age. Specifically, the study was to be able to compare estimated glomerular filtration rate and albuminuria with depressive symptom burden and performance in different cognitive domains such as processing speed, executive functioning, and memory.

2. Materials and Methods

2.1 Study Design and Data Source

It was a cross-sectional, secondary analysis of a study focusing on the National Health and Nutrition Examination Survey (NHANES) 2013-2014. NHANES is a non-institutionalized survey of the U.S. population that is conducted by Centers of Disease Control and

Prevention. The survey uses a multistage, complex probability sampling plan and involves standardized interviews, physical examinations, lab tests, and cognitive tests. The current analysis targeted older adults who have available data on blood pressure, kidney functioning, depressive symptoms, and neurocognitive performance [15].

2.2 Study Population

People aged 60-80 years whose data on blood pressure, kidney disease indicators, depressive symptoms, and cognitive tests had full data were taken. Kidney evaluations needed serum creatinine estimation of glomerular filtration rate (eGFR) and urinary albumin and creatinine to estimate the urine albumin-to-creatinine ratio (UACR). Cognitive measures were the Digit Symbol Substitution Test (DSST), Animal Fluency test and Consortium to Establish a Registry of Alzheimer Disease (CERAD) delayed recall test. Patient Health Questionnaire-9 (PHQ-9) was used to measure depressive symptoms. It used a complete-case analytic method and eliminated all participants without exposure or outcome data.

2.3 Measures

2.3.1 Kidney Disease Markers

Serum and urinary biomarkers were used to evaluate kidney function with serum creatinine used to compute eGFR using a creatinine-based estimating equation. UACR was computed from urinary albumin and creatinine and analyzed as a continuous variable, with clinical categorization as A1 (<30 mg/g), A2 (30–299 mg/g), and A3 (≥300 mg/g). Chronic kidney disease status was additionally defined in sensitivity analyses as eGFR <60 mL/min/1.73 m² and/or UACR ≥30 mg/g.

2.3.2 Hypertension

The blood pressure was measured by standardized procedures of NHANES up to three measurements per individual. The average systolic and diastolic blood pressure were determined. Hypertension was considered as systolic blood pressure 130mmHg or higher and diastolic blood pressure 80mmHg or higher. Sensitivity analyses were done on both continuous and categorical variables based on blood pressure.

2.3.3 Depressive Symptoms

The PHQ-9, a self-validated measure, was used to assess depressive symptom burden. A total score was obtained by adding all item scores with a higher score representing a stronger level of depressive symptom. PHQ-9 scores are continuous variables.

2.3.4 Neurocognitive Outcomes

The NHANES cognitive battery was used to measure neurocognitive performance. The DSST was used in processing speed, executive functioning, the Animal Fluency Test in semantic fluency, and the CERAD delayed recall test in episodic memory. Cognitive scores were all continuous outcomes.

2.3.5 Covariates

The covariates were age and sex since they have been known to be associated with kidney functioning, hypertension, depression, and cognitive functioning among Elderly adults.

2.4 Statistical Analysis

NHANES data was combined based on participant identifiers and limited to eligible persons. All variables were given descriptive statistics. Welch t-tests compared groups and Spearman coefficient of correlation was used to examine relationships between continuous variables. Multivariate linear regression analyses were used to determine relationships between kidney disease indicators, blood pressure, depressive symptoms, and cognitive outcomes and they adjusted by age and sex. Categorical definitions of chronic kidney disease and hypertension were applied in sensitivity analysis. It was analyzed with Python, and data processed in pandas and NumPy and statistical analysis in SciPy and statsmodels. $p < 0.05$ was considered the statistical significance.

5. Results

5.1 Sample Characteristics

A total of 1,319 older adults (60-80 years) were included in the final analytic sample. Participants had a mean age of 69.64 ± 6.74 years, and the sex distribution was balanced (50.4% female). Blood pressure levels were consistent with a high vascular risk profile, with mean SBP/DBP of 132.39 ± 19.27 / 66.89 ± 14.54 mmHg, and more than half (53.9%) meeting the hypertension phenotype definition (SBP ≥130 and/or DBP ≥80). Kidney disease burden was substantial: median UACR was 9.52 mg/g (IQR 5.94–20.44), 17.4% had albuminuria (UACR ≥30), and 25.1% had eGFR <60 mL/min/1.73m². Under the composite definition (eGFR <60 and/or UACR ≥30), 35.9% met criteria for CKD. Depressive symptoms were generally low at the population level (PHQ-9 3.45 ± 4.44), though 10.5% exhibited moderate-to-severe depression (PHQ-9 ≥10). Neurocognitive outcomes showed wide variability across domains, including processing speed/executive function (DSST), verbal fluency, and delayed recall. Full baseline characteristics are presented in Table 1.

Table 1. Participant Characteristics (NHANES 2013–2014; Age 60–80; n = 1319)

Variable	Value
Age (years), mean ± SD	69.64 ± 6.74
Sex = Female, n (%)	665 (50.4%)
Mean SBP (mmHg), mean ± SD	132.39 ± 19.27
Mean DBP (mmHg), mean ± SD	66.89 ± 14.54
Hypertension phenotype (SBP ≥130 or DBP ≥80), n (%)	711 (53.9%)
UACR (mg/g), median (IQR)	9.52 (5.94–20.44)
Albuminuria (UACR ≥30), n (%)	230 (17.4%)

eGFR (mL/min/1.73m²), mean ± SD	71.42 ± 17.94
Reduced eGFR (<60), n (%)	331 (25.1%)
CKD definition (eGFR <60 or UACR ≥30), n (%)	474 (35.9%)
PHQ-9 total, mean ± SD	3.45 ± 4.44
Moderate-to-severe depression (PHQ-9 ≥10), n (%)	139 (10.5%)
DSST score, mean ± SD	46.80 ± 16.90
Animal Fluency score, mean ± SD	16.84 ± 5.50
CERAD Delayed Recall score, mean ± SD	6.28 ± 2.27

5.2 Depression and Kidney Marker Profiles

On the whole, the sample had a largely low distribution of depressive symptoms, as the minimal symptoms were found in 73.24% and weak symptoms in 16.22% of the respondents, whereas moderate-to-severe depressive symptoms were observed in 10.54%. Clinically relevant heterogeneity in kidney disease markers was also observed: most of the participants had A1 albuminuria (<30 mg/g; 82.64%), with smaller and yet significant proportions of A2 (14.25%) and A3 (3.11) markers. The staging based on kidney function was also a mixed-risk distribution with the most significant count in G2 (6089; 5823.06%), but also with a good representation of G3a(4559; 1668) and more severe impairment (G3bG5). The summary of the distributions of the severity of depression and kidney categories is presented in Table 2, and the distributions of the symptoms of depression are presented in Figure 1.

Table 2. Depression Severity and Kidney Category Distributions (n = 1319)

A) PHQ-9 Depression Severity		
Category	**n**	**%**
Minimal (0–4)	966	73.24
Mild (5–9)	214	16.22
Moderate (10–14)	90	6.82
Moderately severe (15–19)	38	2.88
Severe (20–27)	11	0.83
B) UACR Categories		
Category	**n**	**%**
A1 (<30 mg/g)	1090	82.64
A2 (30–300 mg/g)	188	14.25
A3 (>300 mg/g)	41	3.11
C) eGFR Categories		
Category	**n**	**%**
G1 (≥90)	220	16.68
G2 (60–89)	768	58.23
G3a (45–59)	220	16.68
G3b (30–44)	91	6.90
G4 (15–29)	15	1.14
G5 (<15)	5	0.38

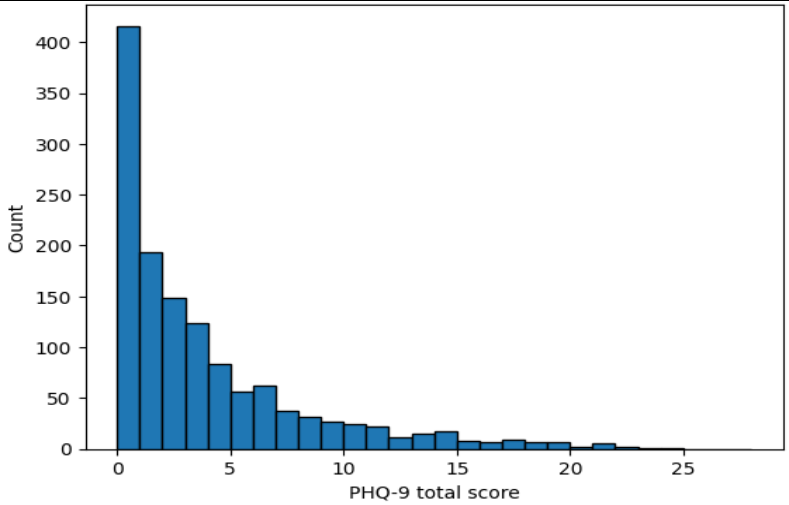

Figure 1. Distribution of depressive symptom severity (PHQ-9 total score) in the analytic sample (n = 1319).

5.3 Bivariate Associations

Bivariate analyses revealed a consistent pattern of poorer neurocognitive performance among participants with kidney disease burden, particularly for processing speed/executive function and verbal fluency. Participants meeting the CKD definition showed significantly lower cognitive scores across all domains, with the largest difference observed for DSST. CKD status was also associated with a modest but significant increase in PHQ-9 score. Albuminuria demonstrated a similar robust association: participants with UACR ≥30 mg/g exhibited lower DSST, lower Animal Fluency, and reduced delayed recall performance, alongside higher depressive symptom burden. Reduced eGFR (<60) showed clear associations with lower cognition, especially DSST and Animal Fluency, while the PHQ-9 difference by eGFR category did not reach statistical significance. Hypertension phenotype was associated with lower DSST and lower verbal fluency but showed no significant difference for delayed recall or PHQ-9, suggesting a stronger relationship with executive/processing domains than memory-related outcomes. Detailed bivariate comparisons across CKD definition, albuminuria, reduced eGFR, and hypertension phenotype are reported in Table 3, with DSST differences across albuminuria categories illustrated in Figure 2.

Table 3. Bivariate Differences in Cognition and Depression by Kidney and Hypertension Groups (Unadjusted)

Grouping Variable	Outcome	Group 0 Mean	Group 1 Mean	Mean Difference (1–0)	p-value
CKD_def (0 vs 1)	DSST	48.90	43.06	−5.84	1.59×10^{-9}
	Animal Fluency	17.41	15.82	−1.58	3.67×10^{-7}
	CERAD Recall	6.46	5.96	−0.50	1.46×10^{-4}
	PHQ-9	3.22	3.84	+0.62	0.016
Albuminuria (UACR <30 vs ≥30)	DSST	47.81	42.01	−5.80	0.000002
	Animal Fluency	17.07	15.77	−1.30	0.000785
	CERAD Recall	6.34	5.98	−0.37	0.0256
	PHQ-9	3.28	4.24	+0.96	0.00759
eGFR (≥60 vs <60)	DSST	48.23	42.52	−5.71	1.01×10^{-7}
	Animal Fluency	17.26	15.57	−1.69	5.85×10^{-7}
	CERAD Recall	6.40	5.92	−0.49	0.000985
	PHQ-9	3.32	3.81	+0.48	0.0939
Hypertension phenotype (0 vs 1)	DSST	48.47	45.37	−3.09	0.000899
	Animal Fluency	17.22	16.52	−0.70	0.0222
	CERAD Recall	6.36	6.21	−0.15	0.2207
	PHQ-9	3.54	3.36	−0.18	0.4709

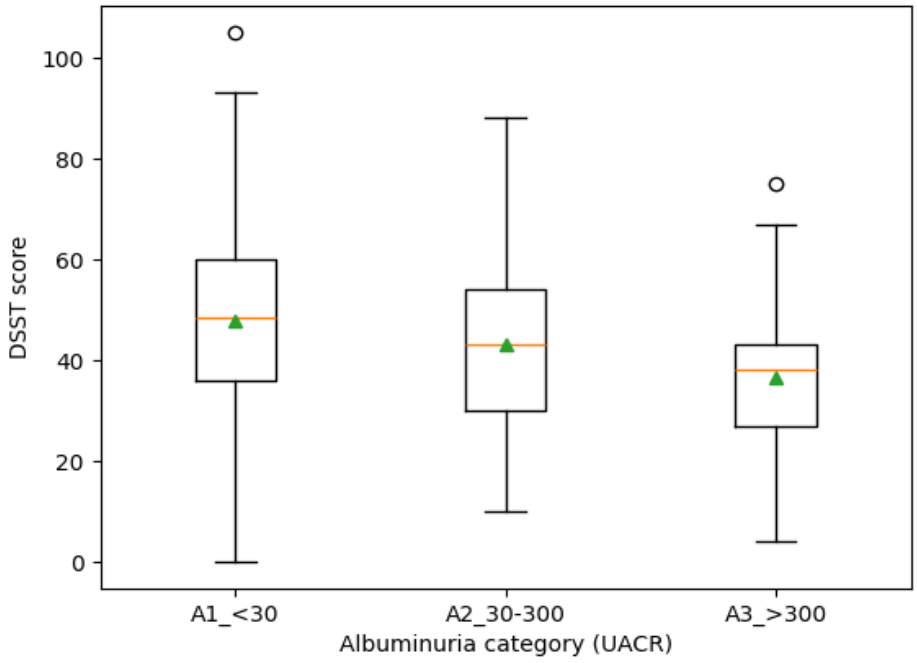

Figure 2. Processing speed and executive function (DSST score) across albuminuria categories (A1–A3).

5.4 Correlation Analysis

An integrated kidney-vascular-psychological profile that is associated with neurocognitive performance was also supported by Spearman correlation analysis. An increase in albuminuria was linked to an increase in the systolic blood pressure and a decrease in cognitive performance especially the DSST and Animal Fluency. The depressive symptoms had a uniform negative correlation with the cognition with the most significant correlation with DSST. Higher eGFR on the other hand had weak positive relationships with all cognitive outcomes. Table 4 shows the correlation estimates of all the key variables.

Table 4. Spearman Correlations Among Kidney Markers, Blood Pressure, Depression, and Cognition

	eGFR	UACR	SBP	DBP	PHQ-9	DSST	Fluency	CERAD
eGFR	1.000	−0.075	−0.055	0.176	−0.055	0.132	0.135	0.113
UACR	−0.075	1.000	0.233	0.005	0.079	−0.156	−0.135	−0.079
SBP	−0.055	0.233	1.000	0.296	−0.020	−0.146	−0.099	−0.065
DBP	0.176	0.005	0.296	1.000	−0.077	0.072	0.077	0.097
PHQ-9	−0.055	0.079	−0.020	−0.077	1.000	−0.113	−0.084	−0.071
DSST	0.132	−0.156	−0.146	0.072	−0.113	1.000	0.510	0.446
Animal Fluency	0.135	−0.135	−0.099	0.077	−0.084	0.510	1.000	0.371
CERAD Recall	0.113	−0.079	−0.065	0.097	−0.071	0.446	0.371	1.000

5.5 Multivariable Regression Analysis

Multivariate regression analyses were conducted to determine whether the relationships between kidney disease markers, blood pressure, depressive symptoms, and cognition remained significant after the control over the following significant demographic and clinical variables. Poor performance in the DSST model was also independently related with older age, male sex, high systolic blood pressure, high PHQ-9 and albuminuria burden (logUACR), but not eGFR. In the case of Animal Fluency, depressive symptom burden and age were still predictors of importance and albuminuria was still predicted negatively independently. In CERAD delayed recall, the independent predictors were age, sex and PHQ-9 score and kidney markers (eGFR and log UACR) did not show significant differences in the fully adjusted model, indicating that renal-related cognitive vulnerability might be stronger in the executive/processing and weaker in memory-based delayed recall in this cohort.

Kidney markers were independent predictors of depressive symptoms in the depression outcome model with lower eGFR and increased albuminuria having higher PHQ-9 scores and no significant impact on systolic blood pressure after correction. The summary of the regression coefficients, confidence intervals, and p-values are presented in Table 5, and continuous relationships between depressive symptom burden and DSST, albuminuria burden and DSST are plotted in Figures 3 and 4, respectively.

Table 5. Multivariable Regression Models for Cognition and Depression (Adjusted)

Adjusted for: Age, Sex, SBP_mean, PHQ-9 total, eGFR, log(UACR)

A) Cognitive Outcomes			
Predictor	**DSST β (p)**	**Animal Fluency β (p)**	**CERAD Recall β (p)**
Age	−0.63 (1.15×10^{-18})	−0.14 (3.34×10^{-9})	−0.08 (1.72×10^{-15})
Male sex	−5.90 (1.20×10^{-11})	0.21 (0.470)	−0.78 (1.42×10^{-10})
SBP_mean	−0.09 (0.000200)	−0.01 (0.093)	−0.003 (0.300)
PHQ-9 total	−0.74 (9.40×10^{-14})	−0.14 (3.31×10^{-5})	−0.06 (1.09×10^{-5})
eGFR	0.01 (0.685)	0.02 (0.0888)	0.002 (0.614)
log(UACR)	−1.21 (0.00115)	−0.33 (0.00955)	−0.04 (0.409)
B) Depression Outcome (PHQ-9 total)			
Predictor	**β (p-value)**	**Predictor**	**β (p-value)**
Age	−0.07 (0.000823)	Age	−0.07 (0.000823)
Male sex	−0.94 (0.000112)	Male sex	−0.94 (0.000112)
SBP_mean	−0.001 (0.864)	SBP_mean	−0.001 (0.864)
eGFR	−0.02 (0.0153)	eGFR	−0.02 (0.0153)
log(UACR)	+0.33 (0.00165)	log(UACR)	+0.33 (0.00165)

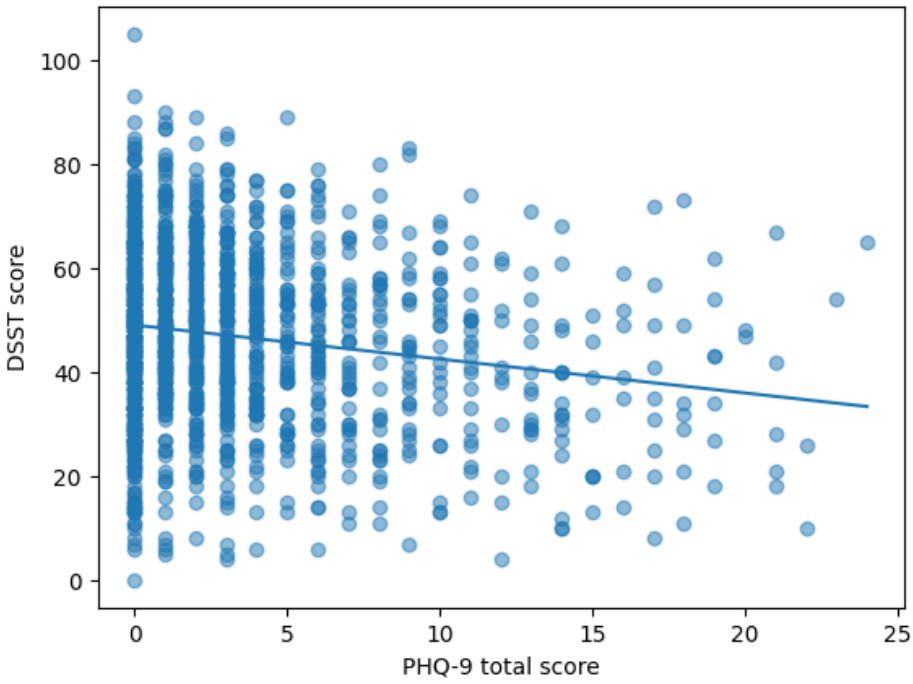

Figure 3. Association between depressive symptom burden (PHQ-9 total score) and DSST performance

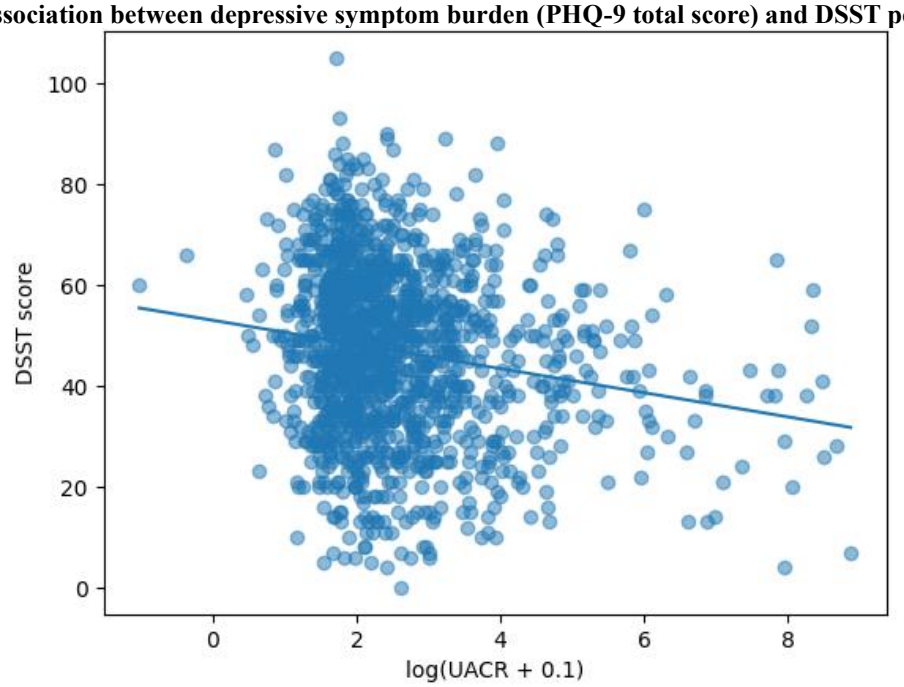

Figure 4. Association between albuminuria burden (log-transformed UACR) and DSST performance

Discussion

The results of the current study are added to the accumulating evidence that chronic kidney disease is a systemic condition and, not merely, a disorder merely limited to the inability to perform renal filtration. The noted correlations between the markers of kidney disease and vascular, metabolic, and psychological results indicate that kidney disease reflects a wider physiological susceptibility. The biological plausibility of systemic manifestations involved in kidney disease, especially in diabetic nephropathy, has consistently been supported experimentally and translational studies showing that antioxidant and anti-inflammatory events are central to the onset and progression of kidney disease [16].

The appreciation to the systemic kidney disease has led to more interest in bioactive compounds of plant-based foods and medicinal sources. Systematic reviews show that these compounds have positive effects on the renal and metabolic pathways through oxidative stress, inflammatory signaling, and endothelial activity modulation. These effects display a connection of renal injury with metabolic and vascular systems. The observed associations in the current paper are in line with the idea that kidney disease markers could reflect a larger inflammatory and metabolically unregulated setting instead of a specific organ dysfunction [17].

Chronic inflammation and oxidative stress are the significant biological pathways, which connect kidney disease to multisystem impairment. Randomized

controlled studies prove that dietary polyphenols may alter inflammatory biomarkers and oxidative stress levels in diabetic nephropathy patients significantly. The evidence supports the notion that kidney disease has a broader inflammatory background that can affect several organ systems. Aging population reviews also corroborate the kidney markers-systemic inflammation-adverse outcomes relationships, also found in this study [18].

Animal models give mechanistic understanding of the systemic spread of renal injury. Clinical trials of diabetic kidney disease prove that drugs like berberine can help to decrease renal damage by lowering oxidative stress levels, mitochondrial depression, and tissue damage. These results indicate the role of mitochondrial and metabolic pathways in the pathophysiology of kidney diseases. Though the current study is observational, associations observed might be due to biological processes as observed in experimental studies [19]. Lipotoxicity is currently becoming a significant cause of kidney disease. Strong lipid deposition in renal tissue enhances oxidative stress, inflammation, and dysfunction of cells, which hastens the progression of the disease. Lipotoxicity is also another systemic metabolic load that leads to vascular injury and chronic inflammation. The correlations between markers of kidney disease and poor outcomes in this study can be explained by the lipid-mediated processes that may not be limited to renal tissue only [20].

Systemic explanation of kidney disease is also supported by conceptual progress in nephrology. Tubulocentric models concentrate on key role of renal tubular cell in metabolism regulation, inflammatory signaling and mitochondrial homeostasis. Damage of these cells interferes with the system metabolism and regulation of inflammation. The current results confirm this point of view and support the idea that kidney disease is a symptom of the global cellular and metabolic failure, and not glomerular disease in isolation [21]. The mitochondrial dysfunction is a pathway that connects chronic kidney disease to other systemic effects. There is experimental evidence that restoration of mitochondrial energy homeostasis can lessen metabolic injury to the kidney and enhance metabolic performance. Transcriptional regulation of mitochondrial biogenesis and energy pathways seems critical in restricting the development of the disease. Such insights give a mechanistic explanation as to why kidney disease signs are linked to functional loss in population-based investigations [22].

Recurrent stimulation of oxidative and inflammatory signaling exercises define kidney illness and associated metabolic diseases. Blocking of the pathways experimentally alleviates damages to the kidney and improves the working capacity of the cells. Such mechanisms are systemic thus they offer a valid connection between kidney defect and the general health of the aged groups [23]. Endocrine signaling pathways also cause kidney disease. As in experimental studies, adiponectin receptor signaling can be targeted to ameliorate renal outcome in diabetic nephropathy. These findings highlight complex hormone and metabolic interaction in kidney disease pathogenesis and help to comprehend renal indicators as the expression of a systemic physiological stress but not local organ failure [24]. Pharmacological research is ongoing to establish the impacts of bioactive compounds on oxidative stress, inflammation and mitochondrial dysfunction. Although the present study is not an intervention, its results emphasize the necessity to identify indicators of kidney disease as a precursor of overall vulnerability. Longitudinal and interventional research in the future is needed to illuminate causal mechanisms and whether renal and metabolic risk factors can be exploited to enhance overall health outcomes of ageing populations [25].

Conclusion

The relevance of kidney disease markers in the broader system of older patients is accentuated, with particular attention to the links it has with the functional vulnerability of the older patients beyond renal failure as such. Results show that low kidney clearance and high albuminuria are associated with increased burden of depressive symptoms and low neurocognitive functioning, which is especially poor in processing speed and executive functioning domains. These correlations remain even after controlling for the most significant demographic and clinical variables, highlighting the significance of kidney disease variables as overall physiological stress indicators and not specific renal pathology. The relationships between depressive symptoms and cognitive performance observed also contribute to the idea that kidney, vascular and mental health are interrelated in the aging populations. Combined, these results support the idea of a kidney-brain-psychological axis, where metabolic, inflammatory and vascular processes can have a role in cognitive and emotional consequences. Clinically, albuminuria seems to be one of the most instructive indicators that can indicate initial systemic susceptibility when glomerular filtration deteriorates further. This research shows a need to incorporate mental health and cognitive screening into older adult kidney disease or hypertension evaluation. More longitudinal studies are required in the future to clarify the causes and effects and to see whether the neurocognitive deterioration and depressive load of later life can be alleviated by early detection and treatment of risk factors of kidney diseases.

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