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Impact of Chronic Kidney Disease on Activities of Daily Living in Community-Dwelling Older Adults

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Background. Although chronic kidney disease (CKD) is associated with poor physical function, less is known about the longitudinal association between CKD and the decline of instrumental activities of daily living (IADL) and basic activities of daily living (BADL) among community-dwelling older adults.

Methods. Participants were part of the prospective observational University of Alabama at Birmingham Study of Aging (n = 357). CKD was defined as an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2 using the Modification of Diet in Renal Disease equation. Primary outcomes were IADL and BADL decline defined as an increase in the number of activities for which participants reported difficulty after 2 years. Forward stepwise logistic regression was used to determine associations of baseline CKD and functional decline.

Results. Participants had a mean age of 77.4 (SD = 5.8) years, 41% were African American, and 52% women. IADL decline occurred in 35% of those with CKD and 17% of those without (unadjusted odds ratio, 2.62, 95% confidence intervals [95% CI], 1.59–4.30, $p < .001$). BADL decline occurred in 20% and 7% of those with and without CKD, respectively (unadjusted odds ratio, 3.37; 95% CI, 1.73–6.57; $p < .001$). Multivariable-adjusted odds ratio's (95% CI's) for CKD-associated IADL and BADL decline were 1.83 (1.06–3.17, p =.030) and 2.46 (1.19–5.12, p = .016), respectively. CKD Stage ≥3B (estimated glomerular filtration rate <45 mL/min/1.73 m^2) was associated with higher multivariable-adjusted odds of both IADL (3.12, 95% CI, 1.38–7.06, p = .006) and BADL (3.78, 95% CI, 1.36–9.77, p = .006) decline.

Conclusion. In community-dwelling older adults, CKD is associated with IADL and BADL decline.

Key Words: Activities of daily living—Chronic kidney disease—Functional decline.

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CHRONIC kidney disease (CKD) is common in older adults and associated with poor outcomes (1–3). Although kidney function has been shown to predict incident limitations in mobility and worsening physical functional (4,5), less is known about the relationship between CKD and difficulty with instrumental activities of daily living (IADL) or basic activities of daily living (BADL). In the spectrum of disability, IADL and BADL difficulty often precedes dependence and provides important prognostic information. Self-reported BADL difficulty has been shown to predict mortality and nursing home placement (6). The aim of this study was to examine the longitudinal association between CKD and the decline of IADLs and BADLs among community-dwelling older adults.

Methods

Participants

Participants were part of the University of Alabama at Birmingham Study of Aging, a prospective observational study of a racially balanced sample of 1,000 community-dwelling older African American and white Medicare beneficiaries from five central Alabama counties. Background, study design, and recruitment process for the University of Alabama at Birmingham Study of Aging have been previously reported (7,8). Of the 1,000 participants initially enrolled, 624 remained eligible for an in-home assessment 4 years after their baseline assessment. Of these, 400 (64%) agreed to a one-time blood draw scheduled within 1 month of the in-home assessment. The time of this assessment and lab draw serves as baseline for this

analysis. Participants who died (n = 30) or who were lost to follow-up (n = 13) within the 2-year follow-up period after the blood draw were excluded, leaving 357 participants for analysis of the associations of CKD with IADL and BADL decline. This protocol was approved by the University of Alabama at Birmingham Institutional Review Board.

Measures

During in-home assessments, trained interviewers obtained information on sociodemographic factors and medical diseases. Medical diseases were verified by use of a prescription drug for the condition or confirmation by medical doctor questionnaire or review of a hospital discharge summary. Participants showed the interviewer all medications currently used. A cognitive screening test was performed and ranged from 0 to 30 with higher scores representing better mental status (9). Depressive symptoms were obtained using the 15-item Geriatric Depression Scale (10). Participants were asked to report physical activity as not active, minimally active, moderately active, or active. Body mass index was calculated from measurements of height and weight (kilograms per square meter). Laboratory studies included serum creatinine, hemoglobin, C-reactive protein, and interleukin-6.

Chronic Kidney Disease

CKD was defined as an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2 body surface area, estimated using the Modification of Diet in Renal Disease (MDRD) equation (11). To determine the impact of CKD severity, we defined moderate CKD (Stage 3A) as eGFR 45–59 mL/min/1.73 m^2 and more advanced CKD (Stage ≥3B) as eGFR less than 45 mL/min/1.73 m^2. Although the risk of death, cardiovascular disease, and hospitalization have been shown to substantially increase as eGFR drops to less than 45 mL/min/1.73 m^2 (3), the association between CKD Stage ≥3B and functional impairment has not been previously evaluated.

Analyses were repeated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The CKD-EPI equation has been shown to be more accurate than the MDRD Study equation especially in the GFR less than 60 mL/min/1.73 m^2 range, however, has not yet been validated in older adults (12).

Functional Outcomes

Functional outcomes included self-reported difficulty with six IADLs (using the telephone, light housework, heavy housework, preparing meals, shopping, and managing money) and five BADLs (bathing, transferring out of a bed or chair, eating, toileting, and dressing). Self-reported difficulty was obtained during the in-home assessment and by subsequent telephone interviews. Participants were asked every 6 months if they had difficulty with each IADL and BADL, respectively, and were given 1 point for each positive response. A sum score of difficulty was calculated separately for IADLs (range 0–6) and BADLs (range 0–5) with higher scores representing more difficulty.

Our primary outcomes were IADL and BADL decline defined as an increase in the number of activities for which participants reported difficulty after 2 years of follow-up. Considering that functional impairment may be a dynamic process and may achieve a more stable status during longer term follow-up, we used 2-year outcomes data for our primary analysis. To measure IADL or BADL decline, we subtracted each participant's baseline score from their 2-year follow-up score separately for each outcome, a positive score indicating a decline.

Statistical Analysis

Baseline characteristics for participants with and without CKD were examined using chi-square tests for categorical variables and Student's t tests for continuous variables. Student's t tests were used to compare the mean changes in IADL and BADL scores from baseline with 2 years between those with and without CKD. Paired t tests were then used to evaluate the change in mean in IADL and BADL scores from baseline to 2 years, separately for participants with and without CKD.

Logistic regression was used to determine the association of CKD with IADL and BADL decline after 2 years, adjusting for comorbidities, cognitive impairment, depression, body mass index, poor physical activity, hemoglobin, and markers of inflammation (13–19). These covariates were entered into the model in a forward stepwise manner and the final model included age, baseline IADL score, osteoarthritis, hemoglobin, and physical activity. The model for BADL also included cognitive function score but hemoglobin was not retained in that model. We then repeated the above analyses separately in participants with Stages 3A and ≥3B CKD. To determine if time to functional decline varied by CKD, we used Cox regression models in which CKD was used as the predictor variable, first decline in IADL and BADL were used as outcomes variables, and time to first decline (as 6, 12, 18, and 24 months) as a time to event variable. Models for both outcomes were adjusted for covariates used in their respective logistic regression models. Finally, a sensitivity analysis was done to examine the association of CKD with IADL and BADL decline in subsets of participants without baseline IADL or BADL difficulties. All statistical tests were evaluated using two-tailed 95% confidence levels and tests with p value <.05 were considered significant. SPSS for Windows, Version 15 (2006, Chicago: SPSS Inc.) was used for all data analysis.

Results

Characteristics of Participants

The mean (±*SD*) age of the 357 participants was 77.4 (±5.8), 41% were African American, and 52% women. Of

Table 1. Characteristics of Participants With and Without Chronic Kidney Disease (CKD) at Baseline

	No CKD (N = 217)	CKD (N = 140)	p Value
Demographics			
Age, M (SD)	77 ± 5.4	78 ± 6.2	.028
Female, n (%)	96 (44)	89 (64)	<.001
African American, n (%)	92 (42)	55 (39)	.560
Married, n (%)	130 (60)	61 (44)	.026
Functional status			
IADL score (0–6), M (SD)	0.94 ± 1.55	1.14 ±1.60	.224
No IADL difficulties, n (%)	143 (66)	78 (56)	.114
BADL score (0–5), M (SD)	0.41 ± 1.01	0.50 ± 1.10	.428
No BADL difficulties, n (%)	179 (83)	110 (79)	.615
Health-related factors and medical conditions			
Hypertension, n (%)	150 (69)	119 (85)	.001
Heart failure, n (%)	26 (12)	18 (13)	.806
Diabetes, n (%)	57 (26)	43 (31)	.361
Osteoarthritis, n (%)	60 (28)	58 (41)	.007
Cognitive score (0–30), M (SD)	26.1 ± 4.1	25.9 ± 3.4	.559
Geriatric Depression Scale (0–15), M (SD)	1.8 ± 2.1	2.0 ± 1.9	.393
BMI (kg/m^2), M(SD)	27.8 ± 6.6	28.5 ± 5.3	.314
Physical activity (not or minimally active), n (%)	42 (20)	40 (29)	.043
Hemoglobin (g/dL), M (SD)	13.8 ± 1.5	13.2 ± 2.0	.002
CRP >2.65 mg/L, n (%)	4 (2)	8 (6)	.048
IL-6 >3.8 pg/mL, n (%)	95 (45)	79 (60)	.008

Note: BADL = basic activities of daily living; BMI = body mass index; CRP, C-reactive protein; IADL = instrumental activities of daily living; IL-6 = interleukin 6.

the 357 participants, 140 (39%) had CKD defined as eGFR less than 60 mL/min/1.73 m^2, of which 110 (28%) had Stage 3A (eGFR 45–59 mL/min/1.73 m^2) and 40 (11%) had Stage ≥3B (eGFR <45 mL/min/1.73 m^2). At baseline, participants with CKD were more likely to be older, female, and have hypertension, osteoarthritis, lower self-reported physical activity, lower hemoglobin, and elevated C-reactive protein and interleukin-6 (Table 1).

CKD and Functional Decline

Mean changes in IADL and BADL scores from baseline to 2-year follow-up are displayed in Table 2. Although among those with CKD, there was a significant increase in mean IADL score from baseline to Year 2 by 0.58, 95% confidence intervals (95% CI) (0.29–0.87); $p < .001$, among those without CKD it changed by only 0.12 (95% CI, −0.05 to +0.28); $p = .162$ (Table 2). These differences in IADL score from baseline to Year 2 between those with and without CKD were statistically significant (Student's t test, $p < .001$). Changes in mean BADL score from baseline to Year 2 are displayed in Table 2.

IADL decline occurred in 35% and 17% of participants with and without CKD, respectively, after 2 years of follow-up (unadjusted odds ratio [OR], 2.62; 95% CI, 1.59–4.30; $p < .001$). Multivariable-adjusted odds for CKD-associated IADL decline was 1.83 (95% CI, 1.06–3.17; $p = .030$; Table 3). Similar results were found after excluding participants with baseline IADL difficulty (unadjusted OR, 3.21; 95% CI, 1.49–6.85; $p = .003$). Unadjusted and multivariable-adjusted hazard ratios for IADL decline associated with CKD were 1.61 (95% CI, 1.16–2.24; $p = .005$) and 1.32 (95% CI, 0.94–1.86; $p = .114$), respectively. Associations of CKD Stages 3A and ≥3B with IADL decline at 2 years are displayed in Table 3.

BADL decline occurred in 20% and 7% of participants with and without CKD, respectively, after 2 years of follow-up (unadjusted OR, 3.37; 95% CI, 1.73–6.57; $p < .001$). Multivariable-adjusted odds for CKD-associated BADL decline was 2.46 (95% CI, 1.19–5.12; $p = .016$; Table 3). Similar results were found in the subset of participants without baseline IADL and BADL difficulties (unadjusted OR, 4.74; 95% CI, 1.19–18.90; $p = .028$). Unadjusted and multivariable-adjusted hazard ratios for IADL decline associated with CKD were 2.18 (95% CI, 1.37–3.47; $p = .001$) and 1.79 (95% CI, 1.10–2.90; $p = .019$), respectively. Associations of CKD Stages 3A and ≥3B with BADL decline at 2 years are displayed in Table 3.

Analyses were repeated using the CKD-EPI equation to define CKD. In these analyses, 179 (50%) of participants had an eGFR less than 60 mL/min/1.73 m^2 compared with 140 (39%) using the MDRD equation. IADL decline occurred in 35% of those with CKD and 14% of those without (unadjusted OR, 3.40, 95% CI, 2.00–5.77; $p < .001$). BADL decline occurred in 17% and 7% of those with and without CKD, respectively (unadjusted OR, 2.56; 95% CI, 1.29–5.08; $p = .007$). These associations were similar after multivariable adjustment.

Discussion

The findings from the current study suggest that in community-dwelling older adults, CKD predicts future decline in both IADLs and BADLs. Furthermore, we demonstrate

Table 2. Change in Instrumental and Basic Activities of Daily Living (IADL and BADL) From Baseline to 2 Years in Participants With and Without Chronic Kidney Disease (CKD)

	IADL				BADL			
	Decline*, *n* (%)	No Change, *n* (%)	Increase, *n* (%)	Mean Change† (95% CI); Paired *t* Test *p* Value	Decline‡, *n* (%)	No Change, *n* (%)	Increase, *n* (%)	Mean Change§ (95% CI); Paired *t* Test *p* Value
No CKD (*N* = 217)	37 (17)	154 (71)	26 (12)	0.12 (−0.05 to 0.28); .162	15 (7)	176 (81)	26 (12)	−0.11 (−0.22 to +0.01); .085
CKD (*N* = 140)	49 (35)	70 (50)	21 (15)	0.58 (0.29–0.87); <.001	28 (20)	101 (72)	11 (8)	0.38 (0.15–0.61); .001
3A (*N* = 100)	27 (27)	58 (58)	15 (15)	0.39 (0.08–0.70); .015	15 (15)	75 (75)	10 (10)	0.27 (−0.05 to 0.47); .107
≥3B (*N* = 40)	22 (55)	12 (30)	6 (15)	1.1 (0.41–1.69); .002	13 (33)	26 (65)	1 (3)	0.80 (0.34–1.26); .001

Notes: BADL = basic activities of daily living; CI = confidence interval; IADL = instrumental activities of daily living. CKD 3A = estimated glomerular filtration rate 45–59 mL/min/1.73 m^2CKD ≥3B, estimated glomerular filtration rate <45 mL/min/1.73 m2. Positive values indicate an increase in self-reported difficulty and a decline in function at 2-year follow-up compared with baseline.

*Chi square $p < .001$.

†Differences in IADL score from baseline to Year 2 between those with and without CKD were statistically significant (Student's *t* test, $p < .001$).

‡Chi square $p = .001$.

§Differences in BADL score from baseline to Year 2 between those with and without CKD were statistically significant (Student's *t* test, $p < .001$).

Table 3. Unadjusted and Multivariable-Adjusted Association Between Baseline Chronic Kidney Disease (CKD) and Functional Decline at 2 Years

	IADL			BADL		
	Decline, *n* (%)	Unadjusted OR (95% CI); *p* Value	Adjusted OR* (95% CI); *p* Value	Decline, *n* (%)	Unadjusted OR (95% CI); *p* Value	Adjusted OR† (95% CI); *p* Value
No CKD (*N* = 217)	37 (17)	1.0	1.0	15 (7)	1.0	1.0
CKD (*N* = 140)	49 (35)	2.62 (1.59–4.30); <.001	1.83 (1.06–3.17); .030	28 (20)	3.37 (1.73–6.57); <.001	2.46 (1.19–5.12); .016
3A (*N* = 100)	27 (27)	1.80 (1.02–3.17); .042	1.47 (0.80–2.71); .215	15 (15)	2.38 (1.11–5.08); .025	1.96 (0.86–4.47); .109
≥3B (*N* = 40)	22 (55)	5.95 (2.91–12.17); <.001	3.12 (1.38–7.06); .006	13 (33)	6.48 (2.79–15.08); <.001	3.78 (1.46–9.77); .006

Notes: BADL = basic activities of daily living; CI = confidence interval; IADL = instrumental activities of daily living; OR = odds ratio. CKD 3A, estimated glomerular filtration rate 45–59 mL/min/1.73 m^2. CKD ≥3B, estimated glomerular filtration rate <45 mL/min/1.73 m^2.

* Variables in the adjusted model: age, baseline IADL score, osteoarthritis, hemoglobin, and physical activity.

†Variables in the adjusted model: age, baseline ADL score, osteoarthritis, cognitive screen score, and physical activity.

the importance of severity of CKD stage for predicting functional decline. For participants with eGFR less than 45 mL/min/1.73 m^2, the odds of IADL or BADL decline were more than threefold greater compared with participants without CKD. Determining the association between CKD severity and functional impairment is important because of the high prevalence of eGFR less than 60 mL/min/1.73 m^2 in older adults. With the aging of the U.S. population and routine reporting of eGFR, CKD may be useful as a tool for identifying incident functional decline in community-dwelling older adults.

There are several potential mechanisms to explain the association between CKD and functional decline. First, CKD has multiple known complications including anemia, electrolyte and acid–base disturbances, hyperphosphatemia, bone and mineral disorders, and neuropathy. Recent evidence has also shown an association between CKD and depression and cognitive impairment (20,21). These complications alone, or more likely as part of the complex multimorbidity associated with CKD, might explain the risk for functional decline. Although hemoglobin was also significantly associated with IADL decline, CKD itself remained a significant predictor even after adjusting for hemoglobin. A second explanation is that a decline in GFR might reflect disease severity of cardiovascular disease and/or diabetes mellitus. A lower eGFR and thus a diagnosis of CKD might be a marker for cumulative disease burden rather than a direct cause of functional decline. Lastly, CKD has been shown to be a risk factor for cardiovascular disease, incident heart failure, and stroke, thus the association between CKD and functional decline may be through subsequent development of these disabling conditions or hospitalizations associated with cardiovascular events. Although there are potential explanations for the association between CKD and functional decline, more research is required to further understand CKD-associated functional decline and to evaluate underlying biological mechanisms.

Our findings are consistent with previous studies of CKD in older adults but also add to the understanding of CKD in this population. Novel findings from our study include the association between CKD and IADL decline, the importance of CKD Stage ≥3B (eGFR <45 mL/min/1.73 m2) in functional decline, and the association of CKD defined by the new CKD-EPI equation with functional outcomes. In cross-sectional studies, serum creatinine has been shown to be associated with self-reported physical performance, and lower eGFR is associated with being dependent in two or more ADLs (22,23). In one prospective study, CKD defined by the highest quartile of cystatin C, a biomarker for kidney function, was associated with the development of persistent inability to walk one-quarter mile or climb 10 steps (4). However, to our knowledge, the longitudinal association between CKD and self-reported difficulty with IADLs has not been previously reported in community-dwelling older adults. This functional measure is part of a comprehensive geriatric assessment and is important in assessing a patient's ability to live independently. We have also shown a significant increase in the odds of functional decline as eGFR falls less than 45 mL/min/1.73 m^2 which parallels the substantial increases in mortality, cardiovascular disease, and hospitalizations that occur with this eGFR category. Finally, we have shown that the association between CKD and functional decline is similar whether eGFR is calculated by CKD-EPI or the MDRD Study equations.

Recent attention has focused on the significant functional decline in nursing home patients with end-stage renal disease. In these patients, initiation of dialysis was associated with a significant and permanent decline in function (24). Despite the concern over these findings, the prevalence of moderate CKD is much greater than advanced kidney disease requiring dialysis in older adults, and the risk of death has been shown to outweigh the risk of end-stage renal disease for many in this population (25). Because of the low prevalence and poor functional prognosis of advanced kidney disease in older adults, evaluating and intervening earlier in the disease course may be an effective strategy in these patients. We have shown that CKD-associated functional decline in a community-dwelling cohort occurs earlier in the spectrum of kidney disease and in the spectrum of disability. Future studies can determine if recognizing functional impairment and intervening can change this functional trajectory.

There are a few limitations of our study. CKD diagnosis was based on a one-time blood draw; however, CKD diagnosis requires kidney damage or an eGFR <60 mL/min/1.73 m^2 for at least 3 months. Although it is possible that a low eGFR may represent an episode of acute kidney injury rather than CKD, this is less likely in a community-dwelling cohort. There are limitations to estimating GFR in older adults regardless of method. The MDRD formula has been shown to underestimate GFR in patients with GFR greater than 60 mL/min/1.73 m^2, and the study population for the CKD-EPI equation included few elderly participants (11,12). Both formulas are used clinically, and understanding the association between reported eGFR and functional outcomes remains important. Also, urine protein or albumin measurements were not available and could have provided important information about CKD severity and prognosis. Despite these limitations, it is reassuring that we found a similar dose–response relationship between CKD and odds of functional decline regardless of method used to define CKD.

As with disability, functional difficulty is likely a dynamic process with transitions between episodes of difficulty and recovery (26). For our primary analysis, baseline and 2-year follow-up functional scores were used. Because of the dynamic nature of functional impairment, there is both a risk of underestimating the prevalence of difficulty with IADLs and BADLS and of overemphasizing the importance of these changes. Long assessment intervals

have been shown to underestimate the prevalence of disability (27). Despite the possible underestimation of functional difficulty, we were able to detect a significant association between baseline CKD and functional decline. Although it is also possible that we may have detected participants with transient IADL or BADL difficulty who later improved, one would expect such improvement to be similar for persons with and without CKD. We have used multiple statistical methods, showing consistent associations of CKD with increased incidence of functional decline, differences in mean IADL and BADL scores at 2 years, increased odds of functional decline, and a significant difference in a time-to-decline analysis.

In conclusion, among community-dwelling older adults, baseline CKD is associated with decline in IADLs and BADLs at 2-year follow-up, and these associations seem to become stronger with more advanced CKD. Baseline CKD may be used to risk-stratify community-dwelling older adults for targeted interventions to prevent decline in physical and social functioning.

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