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“Chronic Kidney Disease, Life-space Restriction, and Mortality in the UAB Study of Aging”

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Abstract

"Chronic Kidney Disease, Life-space Restriction, and Mortality in the UAB Study of Aging"

By Justin Kappel, Theodore M Johnson II, and C. Barrett Bowling

Background: Chronic kidney disease (CKD) prognosis relies on estimated glomerular filtration rate (eGFR). The life-space mobility assessment is a novel measure that quantifies the distance, frequency, and independence achieved as older adults move through their environment. Although life-space restriction (LSR) has been shown to be associated with mortality, its prognostic significance has yet to be examined in older adults with CKD.
Methods: Using a subset (n=400) of the University of Alabama-Birmingham Study of Aging, we investigated the joint effects of CKD, defined by eGFR<60 ml/min/1.73m^2, and LSR, defined as composite life-space score<60, on all-cause mortality using Cox proportional hazards regression adjusting for sociodemographics and medical comorbidities.
Results: Overall, 50% of participants had CKD and 45% had LSR. Mortality rates (per 1,000 person-years) were 31.3, 38.6, 87.4, and 80.0 among those with No CKD/No LSR, CKD/No LSR, No CKD/LSR, and CKD/LSR. Compared to participants with neither exposure (No CKD/No LSR), hazard ratios (HR; 95% confidence intervals) for mortality were 1.07 (0.52-2.19), 2.11 (1.06-4.17), and 1.94 (0.97-3.90) for the CKD/No LSR, No CKD/LSR, and CKD/LSR groups. Using a CKD cut-point of eGFR<45 ml/min/1.73m^2, multivariable adjusted HRs were 1.51 (0.63-3.60), 1.86 (1.03-3.35) and 3.26 (1.64-6.50) for the eGFR<45/No LSR, eGFR≥45/LSR, and eGFR<45/LSR groups, respectively. After stratification of the sample by CKD status, HRs for the association between LSR and mortality, adjusted as above, were 1.79 (0.89-3.64) in those with CKD and 2.48 (1.13-5.43) in those without CKD.
Conclusions: Restricted life-space is associated with increased mortality risk and may provide additional prognostic information to guide CKD management beyond that offered by eGFR.

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For Madeline,

And with gratitude to my many learned teachers

Table of Contents

Introduction

Chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73m^2, is a common disorder that increases in prevalence with older age (1). The risk of adverse outcomes associated with CKD, including functional decline, loss of independence, and death, is higher at lower levels of eGFR. However, there is significant heterogeneity of risk at any given level of kidney function, especially among older adults, who exhibit multimorbidity and competing risks for death (2-4). For many older adults, prognosis and treatment guidelines based solely on eGFR may thus be inappropriate.

A geriatric approach to patient care emphasizes measurements that are not part of routine care, including of functional status, mobility, and quality of life. Incorporation of geriatric assessments into the care of older CKD patients may improve prognostication and support individualized care (5). Some measurements of function and mobility, such as dependence for activities of daily living (ADLs) and slower gait speed, have been shown to be strong predictors of adverse outcomes, including mortality, in the older CKD population (6, 7). Life-space mobility, a novel geriatric assessment, quantifies the distance, frequency, and assistance needed as older adults move through geographic areas extending from their bedroom to beyond their town. Because older adults often report their mobility goals in terms of broader community engagement and participation in social activities (8), life-space mobility may be a more patient-centered measure than gait speed or other task-specific assessments.

Lower levels of eGFR have been associated with declines in life-space over time (8) and restrictions of life-space mobility have been shown to be predictive of mortality (9,

10), health care utilization (11, 12), and decreased quality of life (13) among older adults. However, the risks of life-space restriction have not been well studied in older adults with CKD. The purpose of this study was to assess the risk of mortality in a population with known life-space mobility and CKD status.

Methods

Study Population

During the period of November 1999 to February 2001, the UAB Study of Aging recruited 1,000 Medicare beneficiaries ≥65 years old from five counties in Alabama with oversampling of rural dwellers, men and African-Americans to achieve a sample balanced by race, gender, and urban/rural residence. Enrollment and initial evaluation of study participants is described elsewhere (14). Follow-up interviews were conducted by phone every 6 months, and after 4 years (8th follow-up point), 624 participants were actively enrolled in the study and provided consent for a second in-home visit, occurring between February 2004 and February 2005. Of those who agreed to the second in-home visit, which included a blood draw for laboratory analysis, 400 participants had recorded serum creatinine values and were included in this current analysis.

Chronic Kidney Disease

eGFR was calculated at baseline using the CKD-Epi equation from the study variables serum creatinine, race, and age (15). Standard diagnostic criteria for CKD are met at an eGFR < 60 ml/min/1.73m^2, and study participants were stratified at this level of eGFR into those with and without CKD.

Life space mobility

Life-space mobility was measured using the UAB Study of Aging Life Space Assessment (LSA), a short questionnaire conducted by study investigators over the phone or in-person at each 6 month follow-up interview. Life-space mobility is conceptualized as five concentrically expanding levels centered on the room in which someone sleeps, starting with other rooms within the home (Level 1), progressing to common areas such

as a porch or lawn (Level 2), locations within the neighborhood (Level 3) and within one's town (Level 4), then finally areas outside of one's town defined as greater than 10 miles from the home (Level 5). Participants are asked which levels of life-space they have visited within the last four weeks, as well as the frequency with which they visited that space and the level of assistance they required. Within each level of life space, scores are calculated by multiplying the level of life-space (range: 1-5) by the frequency (range: 1=less than once/week to 4=daily) and the level of assistance required (1 = personal assistance, 1.5 = medical equipment, 2 = no assistance required). The composite life-space score (LS-C) is then calculated by summing each level-specific score. The LS-C ranges from 0-120, with larger numbers indicating greater life-space mobility. For a theoretical participant who, in the last four weeks, was able to ambulate independently in an apartment and to the common areas of a senior living facility on a daily basis, walk to nearby neighborhood locations with a cane for balance on most days, take public transit to church once a week and travelled roughly 20 miles (out of town) one time for a specialist medical appointment, the LS-C score would be 57 (see **Appendix 1** for example assessment form) (16).

In the UAB Study of Aging, LS-C is normally distributed with a mean of 60, remains stable at two weeks follow-up, and is sensitive to changes in health status (14). The risk of adverse outcomes increases at lower levels of LS-C and previous work has used a LS-C <60 to define life-space restriction (LSR) (10, 17, 18). Participants in this study were stratified at this level into those with and without LSR.

All-cause mortality

The dates for the final follow-up interviews in this dataset ranged from October 2008 to May 2009. Mortality prior to this time was ascertained by study investigators during follow-up and the date of death was verified through vital statistic registries. Due to ongoing data collection in a second phase of the UAB Study of Aging, three study participants had verified dates of death occurring after this period and were recoded as alive and censored at the end of the study.

Other study variables

Demographics: Participants' age, White vs. African-American race, urban vs. rural residence, and number of years of education completed were recorded during the second in-home interview. For the purpose of our analysis, those who completed 12 or more years of education were considered to have completed high-school.

Health Conditions: Participants' health conditions were verified by questionnaires submitted by their primary care providers and/or by a review of hospital discharge records. Data on diabetes, angina, myocardial infarction (MI), peripheral vascular disease (PVD), stroke, chronic obstructive pulmonary disease (COPD), heart failure (HF), chronic liver disease, non-skin cancers, and Alzheimer's disease was considered in our analysis. Diabetes was considered individually. Participants were considered to have cardiovascular disease if they were verified as having one of the following conditions: angina, MI, PVD, or stroke. The number of other health conditions from the list of COPD, HF, chronic liver disease, and non-skin cancer was considered as an index measure of comorbidity (possible range 0-4).

Cognitive impairment: Data from the in-person interview included the Mini-mental status exam (MMSE). Participants were considered to have evidence of cognitive

impairment if they had a score on the MMSE less than 24 and/or a physician-verified diagnosis of Alzheimer's disease.

ADL Difficulty: Participants were asked whether they had any difficulty with transferring, bathing, dressing, feeding, and toileting. Participants who answered "yes" to any of these questions indicating difficulty with these specific tasks were considered to exhibit ADL difficulty.

Gait speed: The Short Physical Performance Battery (SPPB) was also performed during the in-home evaluation, including two trials of a timed 2.7 meter walk. The faster of these two times was used to calculate a gait speed, reported as a continuous variable with units in meters per second.

Statistical Analysis

After determination of CKD and LSR status as above, participants were grouped into four dual-exposure categories: No CKD/No LSR, No CKD/LSR, CKD/No LSR, and CKD/LSR. Descriptive statistics were then generated for all other study variables within these groups. Follow-up time was calculated for participants starting from the recorded date of the second in-home visit when consent for blood work was obtained. For those who died, the verified date of death was used as the end-point. For all others, time was calculated to the date of the final completed 6-month follow-up assessment. Mortality rates were then calculated and Kaplan-Meier cumulative mortality plots generated by dual-exposure group.

Multivariable Cox proportional hazard models were generated to estimate the association between LSR, CKD, and mortality. The association between life-space mobility and mortality was assayed by comparing the risk of mortality in those with LSR

to those without LSR using the full study sample as well as sub-populations stratified by CKD status. Initial models adjusted for the sociodemographic variables age, sex, race, and high school completion. Diabetes status, cardiovascular disease, and the comorbidity index were then added in iterative fashion to construct a fully adjusted model controlling for sociodemographics and health comorbidity. The effect of possible mediating variables, including ADL difficulty, cognitive impairment, and gait speed were then assessed by individual addition to the fully adjusted model. The joint effects of CKD and LSR on mortality were assessed using the fully adjusted model from above and comparing the risk of mortality in the four dual-exposure groupings using No CKD/No LSR as the referent group.

Previous work had identified that a potentially important higher-risk subgroup of CKD patients was those with an eGFR < 45 ml/min/1.73m^2 (4, 8, 19). An a priori determined secondary analysis for our study was thus conducted by stratifying the sample by eGFR < or ≥ 45 ml/min/1.73m^2 and creating four dual-exposure groups of eGFR≥45/No LSR, eGFR≥45/LSR, eGFR<45/No LSR, and eGFR<45/LSR. Descriptive statistics, mortality rates, cumulative mortality curves, and cox proportional hazard models were then conducted as above using these four secondary exposure groups.

Variable creation, cleaning, and modeling were all conducted using SAS v9.4. Kaplan-Meier mortality curves were generated using StataSE v 14.2.

Results

Baseline characteristics

In our study sample, baseline mean ± standard deviation for eGFR and composite life-space were 61.1±18 ml/min/1.73m^2 and 63.5±23 respectively. Of the 400 participants, 199 (50%) had an eGFR less than 60 ml/min/1.73m^2 and 178 (45%) had LSR. Baseline characteristics of the study sample, stratified by the four dual-exposure categories of No CKD/No LSR, No CKD/LSR, CKD/No LSR, and CKD/LSR are shown in **Table 1**.

Compared to those with No CKD/No LSR, participants with both exposures were more likely to be older (80.6 vs. 75.4 years), female (68% vs. 41%), and diabetic (40% vs. 24%), and were less likely to have completed high school (40% vs. 74%). The CKD/LSR group also had a high prevalence of HF (26%) compared to the other groups. Those with LSR, regardless of CKD status, were also more likely to be African-American race and report ADL difficulty, cognitive impairment, and reduced gait speed.

LSR and Mortality

Median follow-up time in the study was 4.4 years (IQR: 3.9-4.5) with a total time under observation of 1,550.6 person-years. During this period, there were 85 verified deaths. Counts and mortality rates are shown in **Table 2**, stratified by category of CKD/LSR exposure. Mortality rates per 1,000 person-years were higher in those with LSR (80.0 and 87.4 in those with and without CKD respectively) compared to those without LSR (38.6 and 31.3 in those with and without CKD). Mortality curves for the four exposure groups are shown in **Figure 1**.

Results from hazard models for the risk of mortality due to restricted life-space are shown in **Table 3**. Among all participants, the hazard ratio (95% confidence interval) comparing all-cause mortality in those with LSR to those without was 1.95 (1.17-3.25) after adjusting for age, race, sex, high school completion, diabetes, cardiovascular disease and other comorbid conditions. Individual addition of ADL difficulty, presence of cognitive impairment, and gait speed resulted in a reduction in the point estimate of the LSR-mortality association, resulting in point estimates for the HR of 1.60, 1.67, and 1.62 in each of these models respectively. After stratification of the sample by CKD status, the association between LSR and risk of mortality was stronger in those without CKD (HR=2.48, 95% CI: 1.13-5.43) than in those with CKD (HR=1.79, 95% CI: 0.89-3.64) using our fully adjusted model. There were differences in the pattern of attenuation after addition of ADL difficulty, cognitive impairment, and gait speed to the fully adjusted model in those with and without CKD.

Joint exposure and mortality

The joint effect of CKD and LSR exposure on mortality is shown in **Table 4**. LSR, with and without CKD, was associated with increased mortality compared to those with No CKD/No LSR after adjustment for sociodemographics and health conditions as described above. The CKD/No LSR group did not show an increase in mortality (HR=1.07, 95% CI: 0.52-2.19).

Data from our secondary analysis using an eGFR cut-point of 45 ml/min/1.73m^2 is shown in **Table 5**. Mortality rates were 30.7, 71.9, 58.7, and 112.3 for the eGFR≥45/No LSR, eGFR≥45/LSR, eGFR<45/No LSR, and eGFR<45/LSR groups respectively. Compared to the eGFR≥45/No LSR group, the HR (95% CI) for mortality

in the dual exposed (eGFR<45/LSR) group was 3.26 (1.64-6.50). Kaplan-Meier cumulative mortality curves for these four secondary exposure groupings is shown in **Figure 2**.

Discussion

Life-space restriction was associated with a statistically significant increase in mortality in the full study sample and a smaller increase in mortality in those with CKD, after adjustment for a range of demographic variables and comorbid health conditions. While this association between LSR and mortality in those with CKD was not statistically significant in the fully adjusted model, it is likely still clinically meaningful and may also reflect that CKD (eGFR < 60 ml/min/1.73m^2) was not a significant risk factor for mortality in this sample. An eGFR< 45 ml/min/1.73m^2, however, captured CKD patients with a higher risk of mortality such that eGFR <45 ml/min/1.73m^2 and LSR together conferred a statistically significant 3-fold increase in mortality risk compared to participants with neither exposure. There remains a debate about the clinical significance of mild-to-moderate reductions in eGFR (i.e. 45-59 ml/min/1.73 m^2) in older populations based on findings of minimally increased mortality risk at this level of kidney function. Our study supports findings elsewhere that show, among older adults, a more marked increase in mortality risk at eGFR< 45 ml/min/1.73m^2 rather than the standard diagnostic value of 60 ml/min/1.73m^2 (19). The life-space score has been studied as a longitudinal marker of mobility in CKD previously, and as a risk factor for adverse outcomes in heart failure and orthopedic patients (8, 11, 12). However, this is the first account of LSR's effect on mortality in older adults with CKD, and provides further evidence of the prognostic significance of this measure of community mobility in older adults across multiple disease processes.

Life-space mobility has significant overlap with other measures of physical function and performance, but appears to capture additional components of mobility

compared to more commonly used measurements (16). In our hazard model analysis, the association between LSR and mortality attenuates but does not disappear after adjustment for ADL difficulty, gait speed, and cognitive impairment—common components of current geriatric assessments—supporting this interpretation. Moreover, the differential patterns of attenuation in those with and without CKD suggests that the mobility impairments in LSR with impacts on mortality may vary across populations and disease contexts. Previous work has also hypothesized that impairments in function could vary by level of life-space mobility with, for instance, gait disturbance being limiting within the home while cognitive function and social support become more limiting at the level of the town or outside of town (18). This variability makes elucidation of an exact causal mechanism of the LSR-mortality association difficult. However, given an understanding of functional decline as a final common pathway or mediator for mortality, this variability may increase the utility of life-space as a clinical tool due to its ability to capture a broad range of possible barriers to mobility in older adults.

Prognosis and decision making in older adults with CKD has suffered from a lack of accurate estimations of survival as well as inadequate consideration of function and quality of life as goals of care. Incorporation of geriatric assessments in the care of older adults with CKD has been shown to change management of CKD in this population by supporting the use of social work consults, physical therapy, and appropriate consideration of conservative management of end-stage renal disease (5). Given that older adults frequently frame their goals for mobility and medical care in terms of social interactions, which are complex actions poorly captured by traditional measures of function such as gait speed, our results suggest that the use of life-space mobility as part

of the clinical evaluation of older adults with CKD may offer a framework for more accurate survival estimation and more robust assessment of mobility and function. This combination could lead to more patient-centered decision making in CKD, with important implications for patient satisfaction as well as cost-savings in this high-utilization population.

The UAB Study of Aging is a unique dataset for the study of mobility and health, with a robust sample size, data on many possible confounders, and repeated assessments over a long follow-up period. Our study incorporated information that would be readily available to a clinical provider from patient history and the medical record, and our results thus represent the clinical utility of the life-space assessment. However, our analysis was limited by the number of participants who received blood work, as well as the number of events in our study period. One benefit of life-space mobility as a measure of function and mobility, versus measures of functional impairment such as ADL difficulty or dependency, is that it can measure finer gradations in function than can be discerned with "yes" or "no" responses to task specific questions. This benefit is likely more pronounced at higher levels of life-space, before mobility limitations reach the point of a functional impairment or dependency (18). Due to the limitations mentioned above, we were unable to consider the full range of life-space mobility rather than the dichotomous exposure variable LSR. Further work in a larger population with known life-space and kidney function should attempt to examine the effects of life-space and eGFR on mortality across the full spectrums of these measures. Additionally, eGFR has been shown previously to be a limited predictor of mortality in older adults with CKD. Albumin-creatinine ratio and measures of albuminuria are more accurate predictors of

mortality in this population, and should be incorporated into further research in this field where possible (4, 19).

In conclusion, life-space is an easily administered community mobility instrument that captures aspects of function in geriatric patients beyond what is offered by traditional measures of physical function and performance. In our analysis of a population with known kidney function, LSR was associated with increased mortality, was a stronger risk factor than either of the two eGFR cut points we investigated, and had important joint effects on mortality in combination with eGFR. Further work should focus on applying the life-space assessment in clinical practice to assist in prognosis and decision-making with CKD patients, as well as measuring the impact of interventions to improve life-space on patient outcomes in this population.

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Tables

Table 1. Baseline participant characteristics (n=400) from the UAB Study of Aging by categories of chronic kidney disease[1] and life-space restriction[2] exposure

	No CKD[1]				CKD[1]			
Participant Characteristics	**No LSR[2] (n=127)**		**LSR[2] (n=74)**		**No LSR[2] (n=95)**		**LSR[2] (n=104)**	
Age[*], mean (SD)	75.4	(4.7)	78.9	(6.1)	76.5	(4.4)	80.6	(6.7)
Female[*], n (%)	52	(41%)	34	(46%)	42	(44%)	72	(69%)
African-American[*], n (%)	45	(35%)	39	(53%)	25	(26%)	59	(57%)
Rural Residence, n (%)	43	(34%)	34	(46%)	49	(52%)	57	(55%)
> High School Edu[3,*]., n (%)	94	(74%)	30	(41%)	69	(73%)	42	(40%)
Diabetes[4,*], n (%)	31	(24%)	20	(27%)	25	(26%)	42	(40%)
Cardiovasc. Disorders (CVD)								
Angina[4], n (%)	21	(17%)	12	(16%)	10	(11%)	13	(13%)
Myocardial Infarction[4], n (%)	15	(12%)	9	(12%)	15	(16%)	15	(14%)
Peripheral Vasc. Disease[4], n (%)	15	(12%)	18	(24%)	10	(11%)	13	(13%)
Stroke[4], n (%)	11	(9%)	12	(16%)	5	(5%)	18	(17%)
Any CVD[*], n (%)	40	(32%)	33	(45%)	25	(26%)	37	(36%)
Other Comorbidity								
Chronic liver disease[4], n (%)	1	(1%)	1	(1%)	0	(0%)	1	(1%)
Heart failure[4], n (%)	8	(6%)	12	(16%)	10	(11%)	27	(26%)
Chronic Obs. Pulm. Dis.[4], n (%)	15	(12%)	13	(18%)	15	(16%)	19	(18%)
Non-skin cancer[4], n (%)	32	(25%)	16	(22%)	28	(29%)	13	(13%)
Comorbidity count[*], mean (SD)	0.44	(0.6)	0.57	(0.7)	0.56	(0.7)	0.58	(0.8)
ADL Difficulty[5]								
Transferring, n (%)	6	(5%)	28	(38%)	7	(7%)	26	(25%)
Bathing, n (%)	2	(2%)	33	(45%)	2	(2%)	31	(30%)
Dressing, n (%)	1	(1%)	18	(24%)	0	(0%)	20	(19%)
Feeding, n (%)	1	(1%)	0	(0%)	0	(0%)	2	(2%)
Toileting, n (%)	1	(1%)	15	(20%)	1	(1%)	12	(12%)
Any ADL Difficulty[*], n (%)	8	(6%)	33	(45%)	7	(7%)	36	(35%)
Cognitive Impairment[6,*], n (%)	14	(11%)	37	(50%)	13	(14%)	46	(44%)
Gait Speed[7,*,&], mean (SD)	0.72	(0.2)	0.53	(0.2)	0.77	(0.3)	0.48	(0.2)

[1]Chronic kidney disease defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2

[2]Life-space restriction defined as a score on the composite life-space assessment (LS-C) < 60

*Variables included in Cox proportional hazard models

[3]Participants who reported completing 12 or more years of education were assumed to have completed high school

[4]Health conditions were verified by the participants' primary care physician or review of hospital discharge paperwork

[5]ADL Difficulty was determined by asking participants "Do you have any difficulty with ____?"

[6]Cognitive impairment defined as a primary care physician-verified diagnosis of Alzheimer's Disease and/or a score <24 on the mini-mental status exam

[7]Gait speed calculated from time to walk 2.7 m, conducted as part of the SPPB, presented in meters/second

[&]Data on gait speed was missing from 15 participants with LSR, giving the categories n = 127, 64, 95, 99

Table 2. Deaths and mortality rate in the UAB Study of Aging by chronic kidney disease (CKD)[1] and life-space restriction (LSR)[2] (n=400)

	No CKD[1]		CKD[1]	
	No LSR[3]	**LSR[3]**	**No LSR[3]**	**LSR[3]**
All-cause Mortality, n (%)	16 (13%)	23 (31%)	15 (16%)	31 (30%)
Mortality Rate (per 1,000 person-years)	31.3	87.4	38.6	80.0

[1]CKD defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2

[2]Life-space restriction defined as a score on the composite life-space assessment (LS-C) < 60

Table 3. Multi-variable hazard regression models presenting hazard ratios (HR) for the risk of all-cause mortality for those with life-space restriction* in all study participants, in those with chronic kidney disease (CKD) and in those without CKD from the UAB Study of Aging (n=400)**

	All Participants		No CKD**		CKD**	
Model adjusting for:	HR¥	(95% CI)	HR¥	(95% CI)	HR¥	(95% CI)
1. Sociodemographics[1]	2.24	(1.36-3.71)	2.52	(1.20-5.29)	1.97	(0.97-4.00)
2. Soc.demo. + Diabetes[2]	2.15	(1.29-3.57)	2.58	(1.22-5.44)	1.88	(0.92-3.84)
3. Soc.demo. + Diabetes + Other Health Conditions[3]	1.95	(1.17-3.25)	2.48	(1.13-5.43)	1.79	(0.89-3.64)
4. Functional measures:						
4a. +ADL Difficulty[4]	1.60	(0.93-2.77)	1.91	(0.79-4.62)	1.55	(0.74-3.25)
4b. +Gait Speed[5,&]	1.67	(0.96-2.91)	2.32	(0.99-5.43)	1.54	(0.71-3.35)
4c. +Cog. Impairment[6]	1.62	(0.96-2.74)	1.77	(0.79-3.94)	1.62	(0.80-3.31)

**Chronic kidney disease defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2

*Life-space restriction defined as a score on the composite life-space assessment (LS-C) < 60

¥Reference group is those without restricted life-space (LS-C ≥60)

[1]Adjusted for sociodemographic variables: age, sex, race, and educational attainment (≥high school completion)

[2]Adjusted for the sociodemographic variables in Model 1 plus diabetes status

[3]Adjusted for the sociodemographic variables and diabetes from Model 2 as well as presence of cardiovascular disease and score on the comorbidity index

[4]Adjusted for the sociodemographic and health variables from Model 3 and presence of ADL difficulty

[5]Adjusted for the sociodemographic and health variables from Model 3 and participants' measured gait speed

[6]Adjusted for the sociodemographic and health variables from Model 3 and presence of cognitive impairment

[&] Data on gait speed was missing for 15 participants

Table 4. Adjusted hazard ratios[1] for risk of all-cause mortality from the joint exposure of chronic kidney disease (CKD)[2] and life-space restriction (LSR)[3] in the UAB Study of Aging

	No CKD[2]	CKD[2]
No LSR[3]	1.00 (Ref)	1.07 (0.52-2.19)
LSR[3]	2.11 (1.06-4.17))	1.94 (0.97-3.90)

[1]Multivariable Cox regression model adjusted for age, sex, race, high-school completion, diabetes status, cardiovascular disease, and comorbidity index
[2]CKD defined as eGFR < 60 ml/min/m^2
[3]LSR defined as a composite life-space score < 60

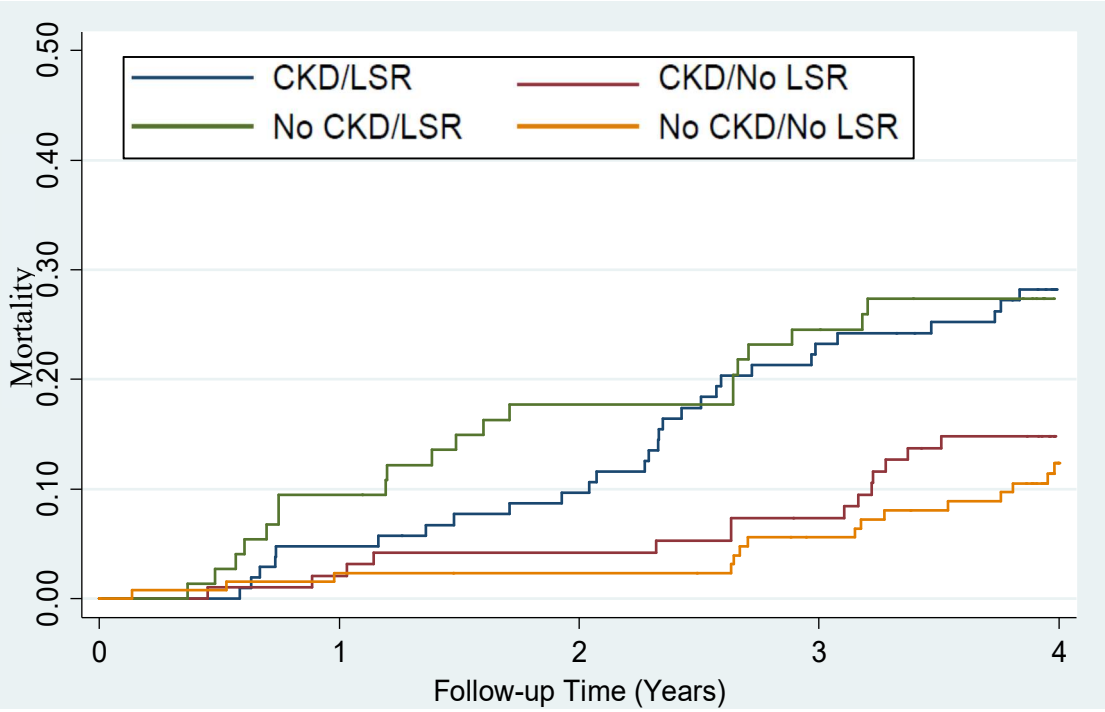
Table 5. Deaths, mortality rates, and adjusted hazard ratios (HR) for risk of mortality under the secondary eGFR analysis conditions in the UAB Study of Aging by eGFR and life-space restriction (LSR)[2] (n=400)

	eGFR≥45		eGFR<45	
	No LSR[2] (n= 192)	**LSR[2] (n= 127)**	**No LSR[2] (n= 30)**	**LSR[2] (n= 51)**
All-cause Mortality, n (%)	24 (13%)	34 (27%)	7 (23%)	20 (39%)
Mortality Rate (per 1,000 person-years)	30.7	71.9	58.7	112.3
Adjusted[3] HR for risk of all-cause mortality	1.00 (Ref)	1.86 (1.03-3.35)	1.51 (0.63-3.60)	3.26 (1.64-6.50)

[1]Chronic kidney disease defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2
[2]Life-space restriction defined as a score on the composite life-space assessment (LS-C) < 60
[3]Adjusted for age, sex, race, high-school education, diabetes, cardiovasc. disease, and comorbidity index

Figures

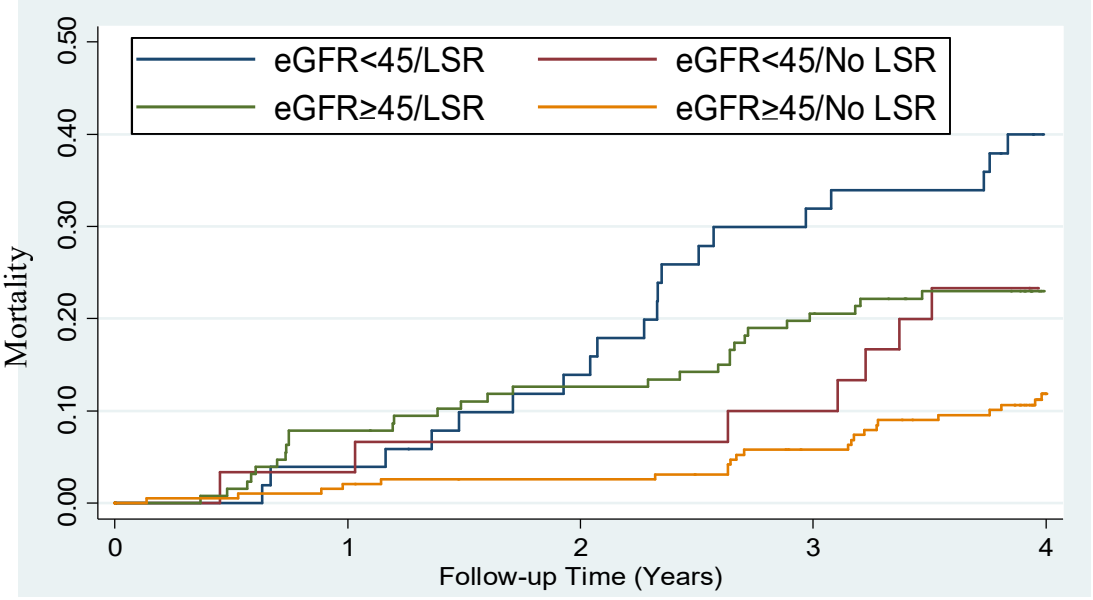
Figure 1. Cumulative mortality curves for dual exposure categories of chronic kidney disease (CKD) and life-space restriction (LSR) in the UAB Study of Aging



[1]CKD defined as eGFR < 60 ml/min/m[2]

[2]LSR defined as composite life-space score < 60

Figure 2. Cumulative mortality curves for dual exposure categories of reduced eGFR[1] and life-space restriction (LSR) in the UAB Study of Aging



[1]eGFR< 45 ml/min/m[2] considered as high-risk subgroup of CKD patients

[2]LSR defined as composite life-space score < 60

Appendix

Appendix 1. Sample Life-Space Assessment for a theoretical participant near the cut-point for life-space restriction (16)

Name:							Date:	
These questions refer to your activities just within the past month.								
LIFE-SPACE LEVEL			**FREQUENCY**				**INDEPENDENCE**	**SCORE**
During the past four weeks, have you been to . . .			**How often did you get there?**				**Did you use aids or equipment? Did you need help from another person?**	Level X Frequency X Independence
Life-Space Level 1. . . **Other rooms of your home besides the room where you sleep?**	Yes (1)	No 0	Less than 1 /week 1	1-3 times /week 2	4-6 times /week 3	Daily (4)	1 = personal assistance 1.5 = equipment only (2) = no equipment or personal assistance	8
Score	1	X		4	X		2 =	*Level 1 Score*
Life-Space Level 2. . . **An area outside your home such as your porch, deck or patio, hallway (of an apartment building) or garage, in your own yard or driveway?**	Yes (2)	No 0	Less than 1 /week 1	1-3 times /week 2	4-6 times /week 3	Daily (4)	1 = Personal assistance 1.5 = Equipment only (2) = No equipment or personal assistance	16
Score	2	X		4	X		2 =	*Level 2 Score*
Life-Space Level 3. . . **Places in your neighborhood, other than your own yard or apartment building?**	Yes (3)	No 0	Less than 1 /week 1	1-3 times /week 2	4-6 times /week (3)	Daily 4	1 = Personal assistance (1.5) Equipment only 2 = No equipment or personal assistance	13.5
Score	3	X		3	X		1.5 =	*Level 3 Score*
Life-Space Level 4. . . **Places outside your neighborhood, but within your town?**	Yes (4)	No 0	Less than 1 /week 1	1-3 times /week (2)	4-6 times /week 3	Daily 4	1 = Personal assistance (1.5) Equipment only 2 = No equipment or personal assistance	12
Score	4	X		2	X		1.5 =	*Level 4 Score*
Life-Space Level 5. . . **Places outside your town?**	Yes (5)	No 0	Less than 1 /week (1)	1-3 times /week 2	4-6 times /week 3	Daily 4	1 = Personal assistance (1.5) Equipment only 2 = No equipment or personal assistance	7.5
Score	5	X		1	X		1.5 =	*Level 5 Score*
							TOTAL SCORE (ADD)	57 *Sum of Levels*