Walking while Talking in Older Adults with Chronic Kidney Disease

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Abstract

Background and objectives Walking while talking is a dual cognitive-motor task that predicts frailty, falls, and cognitive decline in the general elderly population. Adults with CKD have gait abnormalities during usual walking. It is unknown whether they have greater gait abnormalities and cognitive-motor interference during walking while talking.

Design, setting, participants, & measurements Community-dwelling, nondisabled adults ($n=330$) ≥65 years of age underwent quantitative gait analysis, including walking while talking. Differences in walking-while-talking performance by CKD status were evaluated, and relative changes between walking-while-talking and walking alone performance were computed to quantify cognitive-motor interference (dual-task cost). Associations were tested using multivariable linear spline regression models, and independent gait domains were derived using factor analysis. CKD was defined as an eGFR<60 ml/min per 1.73 m^2.

Results CKD was present in 134 (41%) participants. Participants with CKD had slower gait speed along with various gait cycle abnormalities during walking while talking: among those with CKD, every 10-ml/min per 1.73 m^2 lower eGFR was associated with 3.3-cm/s (95% confidence interval, 0.4 to 6.1) slower gait speed, 1.8-cm (95% confidence interval, 0.6 to 3.0) shorter step length, 1.1% (95% confidence interval, 0.6 to 1.7) less time in the swing phase, and 1.4% (95% confidence interval, 0.5 to 2.3) greater time in double support after multivariable adjustment. When comparing walking while talking with walking alone, every 10-ml/min per 1.73 m^2 lower eGFR was associated with 1.8% (95% confidence interval, 0.5 to 3.2) greater decrease in time in the swing phase and 0.9% (95% confidence interval, 0.2 to 1.5) greater increase in time in the stance phase. Factor analysis identified three walking-while-talking domains and three dual-task cost domains: eGFR was associated specifically with the rhythm domain for both walking-while-talking and dual-task cost. Every 10-ml/min per 1.73 m^2 lower eGFR was associated with a poorer performance of 0.2 SD (95% confidence interval, 0.1 to 0.3) for walking while talking and 0.2 SD (95% confidence interval, 0.03 to 0.3) for dual-task cost.

Conclusions During walking while talking, CKD is associated with gait abnormalities, possibly due to increased cognitive-motor interference.

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Introduction

CKD is one of the leading causes of death worldwide and affects approximately 8%–16% of the global population (1,2). Older adults are especially affected, with more than 20% of people ≥65 years of age having CKD (3,4). Elderly patients with CKD are highly susceptible to functional limitation, falls, and cognitive decline, which contribute to disability, hospitalization, and death (5–9). It is important both to identify markers of functional decline in patients with CKD and to understand underlying mechanisms; this would facilitate preventive measures to improve health outcomes. Gait disturbances are a promising area of investigation: slow gait speed is a useful marker because it is associated with functional limitation and higher mortality (10,11), and we recently identified additional gait abnormalities associated with increased fall risk (12).

Gait is a complex motor phenomenon with both physiologic and cognitive components (13). Deterioration in physiologic function, such as loss of sensation or motor control, may affect ambulation (14). Additionally, the role of cognitive function in walking impairment has become increasingly recognized (13). Cognitive decline is associated with both gait abnormalities and falls (15–17), and changes in brain structure have been identified that link cognitive impairment with gait abnormalities (18,19). The influence of cognition on gait is particularly relevant to patients with CKD, who have comorbid conditions that may be associated with gait abnormalities (20–22).

Specific gait markers have been identified for predicting adverse outcomes in clinical geriatrics (23). Dual-task paradigms, such as the walking-while-talking test, involve the simultaneous performance of cognitive

and motor tasks to study their interactions (24,25). They can assess cognitive-motor interference, a phenomenon in which concurrently performing these two tasks may lead to a decline in either or both tasks (26). The walking-while-talking test places high demands on the attention system, which may decrease gait performance because of interference and competition for the same brain resources (27). This decrease in gait performance due to cognitive-motor interference may help reveal early or subtle gait dysfunction (in contrast to normal pace walking-alone paradigms) and can be measured by the dual-task cost (27,28). Dual-task paradigms have clinically relevant implications: poorer performance on the walking-while-talking test is associated with an increased risk of falls, frailty, disability, and mortality in the general elderly population (27,29,30).

Although a small 2013 study reported poorer performance during walking while talking among patients on hemodialysis compared with healthy age-matched controls, no study has evaluated dual-task function in patients with nondialysis-dependent CKD (31). Because cognitive impairment is associated with gait abnormalities and because both are common to CKD, we hypothesized that CKD is associated with gait abnormalities during walking while talking due to elevated cognitive-motor interference. Insight into dual-task function among patients with CKD may have major clinical implications in predicting adverse outcomes and developing novel therapeutic strategies.

Materials and Methods

Study Population

The Central Control of Mobility in Aging (CCMA) study examined mobility and problems related to mobility disability in older adults (32). From June 2011 to October 2017, residents 65 years old or older from a population list of lower Westchester County, New York were recruited. Exclusions included inability to speak English, dementia, severe vision or hearing loss that would interfere with cognitive testing, terminal neurologic (*e.g.*, amyotrophic lateral sclerosis) or active psychiatric conditions, recent or planned medical procedures affecting mobility, and hemodialysis. In-person visits occurred annually. The Institutional Review Board of the Albert Einstein College of Medicine approved the protocols for the CCMA study. Written informed consent was provided by all participants.

Our analyses use a subsample from the CCMA study of 330 participants who had study visits and laboratory data collected between July 2013 (when the CCMA protocol first included blood sample collection) and June 2017. The selection of this sample has been described previously (12). Overall, blood samples were collected from 350 of 586 participants. Serum creatinine values were available from all participants with laboratory data. For these analyses, acquisition of comorbidity and medication information and assessment of gait parameters occurred on the same visit as the laboratory sample collection. Participants who lacked gait assessment on the same visit as the laboratory collection ($n=1$) or were missing information for specific covariates of interest ($n=19$) were excluded. Among the 236 in whom blood samples were not collected, 125 had left the study prior to July 2013, and the remainder did not consent to blood collection. Importantly, there were no systematic differences in age, sex, race, comorbidity burden, or usual gait speed between participants with and without laboratory data (12).

Study Design

Medical questionnaires were used to collect information about the participants, including demographics, physician diagnoses, and medications. Study clinicians performed comprehensive neurologic examinations to evaluate the presence of neuropathy. The Chronic Kidney Disease Epidemiology Collaboration equation on the basis of creatinine levels was used to calculate the eGFR (33). A modified kinetic Jaffe reaction was used to measure the serum creatinine. An eGFR of <60 ml/min per 1.73 m^2 was used to define CKD (34). Metabolic acidosis was defined as serum bicarbonate <23 mEq/L.

Gait Assessment

The gait cycle refers to the time between subsequent contacts of the same foot with the ground. For each foot, there are two main phases of the gait cycle: the stance phase and the swing phase. The time during which the foot is in contact with the ground is called the stance phase. It has a subphase called double support in which both feet contact the ground. The time during which the foot is not in contact with the ground is called the swing phase. Among older adults, less time in swing phase and greater time in double support are associated with a higher risk of falls (23). A 20-foot instrumental computerized walkway with embedded pressure sensors (GAITRite; CIR Systems, Havertown, PA) acquired quantitative gait data regarding the gait cycle. The GAITRite system is a validated, reliable tool for quantitatively assessing gait (35,36). On the mat, participants walked at their usual pace without any attached devices or sensors, and the mean of two trials was calculated for the gait markers. This evaluation has demonstrated high reliability and validity for multiple outcomes in the general elderly population (37,38).

Walking while Talking and Dual-Task Cost

Following an established protocol, participants recited alternate letters of the alphabet while performing the GAITRite assessment (27). They were told to pay equal attention to walking and talking to avoid task prioritization. Subjects were randomly assigned to begin with letter "A" or "B" to decrease practice effects. The numbers of correctly and incorrectly recited alternate letters were noted. Evaluators did not advise or encourage the participants during the task, and they intervened only if their safety became a concern. Gait dual-task cost was calculated for the eight gait markers using the formula: (walking-while-talking dual-task gait variable – walking-only single-task gait variable)/(walking-only single-task gait variable) $\times 100\%$ (28). Dual-task values could not be calculated for step time SD and swing time SD in four participants who had values of zero during the walking-only condition.

Statistical Analyses

Comparisons between participants with and without CKD at baseline were made using two-tailed t tests (or Mann–Whitney U tests as appropriate) for continuous

variables and chi-squared tests (or Fisher exact test as appropriate) for categorical variables. Associations between eGFR and quantitative gait markers were investigated using linear regression models in which unstandardized coefficients and 95% confidence intervals (95% CIs) were calculated. Covariates selected *a priori* as possible confounders included age, sex, race, education, body mass index, neuropathy, number of comorbidities, and number of medications. Linear splines with a knot at eGFR=60 ml/min per 1.73 m^2 were constructed because a threshold relationship was suggested by graphical analysis. Because quantitative gait markers are strongly correlated, independent effects may be difficult to analyze (27). Therefore, factor analysis of eight quantitative gait markers using the principal component method with varimax rotation was performed to derive independent gait domains following the protocol of a prior study (27). Factor analysis was also performed for the dual-task cost gait markers; the four participants with missing values for step time SD and swing time SD dual-task cost were excluded from this analysis. $P<0.05$ was considered statistically significant. All analyses were conducted using Stata/MP version 13.0 (StataCorp, College Station, TX).

Sensitivity Analyses

To account for other possible confounders, we repeated the gait variable analyses after including diuretic use, acidosis status (acidosis has been linked with impairment of both cognition and physical function) (39,40), hemoglobin, mean arterial pressure, and exercise in the past 30 days as additional covariates. To determine whether the gait domain findings were influenced by the statistical methodology chosen, we repeated these analyses using principal component analysis with varimax rotation. Because the severity of diabetes and neuropathy may differ between people with and without CKD, we repeated the gait domain analyses in subgroups without diabetes and without neuropathy.

Results

Participant Characteristics

One hundred thirty-four (41%) of the 330 participants included in our analysis had CKD. Participants with CKD were older than those without CKD (81±7 versus 76±6 years old), but they were not more likely to have diabetes, neuropathy, or other comorbidities. Additionally, medication burden did not differ by CKD status (Table 1) (12).

Table 1. Baseline characteristics by CKD status

Characteristic	No CKD, n=196	CKD, n=134
Age, yr	76±6	81±7
Women, *n* (%)	109 (56)	68 (51)
Race, *n* (%)		
Black	41 (21)	23 (17)
White	148 (76)	109 (81)
Other	7 (4)	2 (2)
Education, *n* (%)		
High school or less	61 (31)	44 (33)
College	82 (42)	63 (47)
Postgraduate	53 (27)	27 (20)
Body mass index, kg/m^2	29±7	29±5
Diabetes, *n* (%)	36 (18)	29 (22)
Neuropathy, *n* (%)	22 (11)	15 (11)
Peripheral arterial disease, n=327, *n* (%)	7 (4)	1 (1)
Hypertension, n=329, *n* (%)	114 (59)	85 (63)
Stroke, n=329, *n* (%)	4 (2)	3 (2)
Cardiovascular disease, *n* (%)	7 (4)	16 (12)
Comorbidities (global health score), *n* (%)		
0	40 (20)	15 (11)
1	57 (29)	41 (31)
2	65 (33)	45 (34)
3+	34 (17)	33 (25)
Medication count	4 (2–6)	5 (3–7)
Diuretic use, *n* (%)	23 (12)	30 (22)
eGFR, ml/min per 1.73 m^2	76±10	45±11
Serum bicarbonate, mEq/L	26±2	25±3
Acidosis, *n* (%)[a]	26 (13)	20 (15)
Hemoglobin, g/dl (n=318)	13.6±1.2	13.1±1.7
Mean arterial pressure, n=323, mm Hg	97±10	94±11
Exercise (in past 30 d), n=320, *n* (%)	152 (79)	93 (73)
Walking while talking variables		
Speed, cm/s	75±23	65±24
Cadence, steps per 1 min	84±19	79±19
Step length, cm	53±11	48±12
Swing, %	33±5	31±5
Stance, %	67±5	69±5
Double support, %	34±8	37±9
Step time SD, s	0.04 (0.02–0.07)	0.05 (0.03–0.1)
Swing time SD, s	0.03 (0.02–0.06)	0.04 (0.03–0.08)
Alphabet recited correctly, no. of letters	7±3	7±3

Data are expressed as mean ± SD, median (interquartile range), or count (percentage). CKD is defined as eGFR<60 ml/min per 1.73 m^2.
[a]Acidosis defined as serum bicarbonate <23 mEq/L.

Individual Gait Marker Analysis of Walking while Talking and Dual-Task Cost

When performing the walking-while-talking task, participants with CKD had slower gait speed and cadence, shorter step length, less time in the swing phase of the gait cycle, and more time in the stance and double-support phases (Table 1). They also exhibited greater variability in step time and swing time. The number of letters recited correctly did not differ by CKD status.

Among participants with CKD, there was a linear association between lower eGFR and poorer performance on a number of gait parameters during walking while talking (Table 2, walking while talking). After multivariable adjustment, every 10-ml/min per 1.73 m^2 lower eGFR was associated with 3.3-cm/s (95% CI, 0.4 to 6.1) slower gait speed, 1.8-cm (95% CI, 0.6 to 3.0) shorter step length, 1.1% (95% CI, 0.6 to 1.7) less time in the swing phase, and 1.4% (95% CI, 0.5 to 2.3) greater time in double support. For eGFR≥60 ml/min per 1.73 m^2, every 10-ml/min per 1.73 m^2 lower eGFR was associated with 0.5% (95%

Table 2. Associations of continuous eGFR with individual gait variables

Gait Variable	eGFR≥60, per 10-ml/min per 1.73 m^2 Lower eGFR, n=196		eGFR<60, per 10-ml/min per 1.73 m^2 Lower eGFR, n=134		Age, per 5-yr Older Age, n=330	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
Walking while talking						
Speed, cm/s	0.01 (−2.7 to 2.7)	0.99	−3.3 (−6.1 to −0.4)	0.03	−6.1 (−8.2 to −4.0)	<0.001
Cadence, steps per 1 min	−0.7 (−3.0 to 1.7)	0.57	−1.0 (−3.5 to 1.5)	0.43	−1.7 (−3.5 to 0.2)	0.07
Step length, cm	0.6 (−0.6 to 1.7)	0.35	−1.8 (−3.0 to −0.6)	0.005	−3.5 (−4.4 to −2.6)	<0.001
Swing, %	0.5 (0.01 to 1.1)	0.05	−1.1 (−1.7 to −0.6)	<0.001	−0.9 (−1.3 to −0.5)	<0.001
Stance, %	−0.5 (−1.1 to −0.01)	0.05	1.1 (0.6 to 1.7)	<0.001	0.9 (0.5 to 1.3)	<0.001
Double support, %	−0.4 (−1.2 to 0.5)	0.38	1.4 (0.5 to 2.3)	0.003	1.8 (1.2 to 2.5)	<0.001
Step time SD, s	0.02 (−0.01 to 0.05)	0.20	−0.01 (−0.04 to 0.03)	0.77	0.01 (−0.01 to 0.03)	0.39
Swing time SD, s	0.01 (−0.01 to 0.02)	0.36	−0.01 (−0.02 to 0.01)	0.50	0.01 (−0.00 to 0.02)	0.29
DTC						
Speed DTC, %	0.4 (−2.0 to 2.7)	0.76	−1.3 (−3.8 to 1.2)	0.30	−1.2 (−3.0 to 0.6)	0.18
Cadence DTC, %	−0.2 (−2.3 to 1.9)	0.87	−0.9 (−3.1 to 1.3)	0.41	−0.5 (−2.1 to 1.1)	0.53
Step length DTC, %	0.5 (−0.9 to 1.9)	0.46	−0.6 (−2.0 to 0.9)	0.42	−1.3 (−2.3 to −0.2)	0.02
Swing DTC, %	1.3 (0.03 to 2.6)	0.04	−1.8 (−3.2 to −0.5)	0.01	−0.9 (−1.9 to 0.1)	0.09
Stance DTC, %	−0.6 (−1.2 to 0.01)	0.05	0.9 (0.2 to 1.5)	0.01	0.3 (−0.2 to 0.7)	0.29
Double-support DTC, %	−0.9 (−2.5 to 0.7)	0.26	1.5 (−0.2 to 3.2)	0.09	1.1 (−0.2 to 2.3)	0.10
Step time SD DTC, % (n=327)	144.4 (−69.8 to 358.6)	0.19	−62.0 (−288.5 to 164.4)	0.59	17.9 (−145.9 to 181.7)	0.83
Swing time SD DTC, % (n=329)	58.2 (−16.0 to 132.5)	0.12	−34.3 (−113.2 to 44.6)	0.39	−7.9 (−65.0 to 49.2)	0.79

Multivariable linear regression adjusting for age, sex, race, education, body mass index, neuropathy, number of comorbidities, and number of medications was performed. Linear splines for eGFR were constructed with knot placed at 60 ml/min per 1.73 m^2. DTC = (walking while talking dual-task gait variable – walking-only single-task gait variable)/(walking-only single-task gait variable) ×100%. 95% CI, 95% confidence interval; DTC, dual-task cost.

CI, 0.01 to 1.1) more time in the swing phase and 0.5% (95% CI, 0.01 to 1.1) less time in the stance phase. For comparison, every 5-years older age was associated with 6.1-cm/s (95% CI, 4.0 to 8.2) slower gait speed, 3.5-cm (95% CI, 2.6 to 4.4) shorter step length, 0.9% (95% CI, 0.5 to 1.3) less time in the swing phase, and 1.8% (95% CI, 1.2 to 2.5) greater time in double support.

Next, we examined changes during the walking-while-talking dual task compared with the walking alone single task (*i.e.*, dual-task cost); this provides additional information regarding the magnitude of change induced by the cognitive task. Among participants with eGFR<60 ml/min per 1.73 m^2, lower eGFR was associated with greater worsening of certain gait parameters during walking while talking: every 10-ml/min per 1.73 m^2 lower eGFR was independently associated with a 1.8% (95% CI, 0.5 to 3.2) greater reduction in the time spent in the swing phase during walking while talking and with a 0.9% (95% CI, 0.2 to 1.5) larger increase in time spent in the stance phase (Table 2, dual-task cost). Related to these phases of the gait cycle, there was a nonsignificant 1.5% (95% CI, −0.2 to 3.2) greater increase in time spent in double support. For eGFR≥60 ml/min per 1.73 m^2, lower eGFR was associated with less reduction in time spent in swing phase. Every 5-year older age was associated with 1.3-cm (95% CI, 0.2 to 2.3) greater decrease in step length during walking while talking compared with walking alone.

Factor Analysis of Walking while Talking and Dual-Task Cost Gait Markers

Factor analysis of eight walking-while-talking variables led to three different gait domains that explained 88% of the variance (Table 3, walking while talking). The rhythm domain (factor 1), which accounted for 46% of the variance, loaded heavily in percentage of the gait cycle in the swing phase, stance phase, and double support along with step length. The pace domain (factor 2), which accounted for 24% of the variance, loaded mainly in cadence, speed, and swing time SD. The variability domain (factor 3), which accounted for 17% of the variance, loaded mostly in step time SD. Among participants with CKD, every 10-ml/min per 1.73 m^2 lower eGFR was associated with 0.2-SD (95% CI, 0.1 to 0.3) poorer performance in the rhythm domain (Table 4). There was no association between eGFR and the pace or variability domains. For comparison, every 5-year older age was associated with 0.2-SD (95% CI, 0.2 to 0.3) poorer performance in rhythm.

Similar to the walking-while-talking analyses, factor analysis produced three dual-task cost domains that explained 84% of the variance (Table 3, dual-task cost). Loadings for each were very similar to those seen with walking while talking. Among participants with eGFR<60 ml/min per 1.73 m^2, every 10-ml/min per 1.73 m^2 lower eGFR was associated specifically with 0.2-SD (95% CI, 0.03 to 0.3) worse performance in the rhythm dual-task cost domain (Table 5).

Sensitivity Analyses

Additional adjustment for diuretic use, acidosis, hemoglobin, mean arterial pressure, and performance of exercise in the past 30 days did not meaningfully alter our results for eGFR<60 ml/min per 1.73 m^2; eGFR was no longer

Table 3. Rotated factor loadings of eight gait variables using factor analysis

Gait Variable	Gait Domain		
	Rhythm	Pace	Variability
Walking while talking, *n*=330			
Swing, %	0.95[a]	0.06	0.14
Step length, cm	0.80[a]	0.13	−0.33
Double support, %	−0.90[a]	−0.23	0.11
Stance, %	−0.95[a]	−0.06	−0.14
Cadence, steps per 1 min	0.19	0.94[a]	−0.03
Speed, cm/s	0.60	0.73[a]	−0.22
Swing time SD, s	0.20	−0.65[a]	0.59
Step time SD, s	−0.08	−0.10	0.91[a]
Variance explained, %	46	24	17
DTC, *n*=326			
Swing DTC, %	0.95[a]	−0.02	0.09
Step length DTC, %	0.63[a]	0.26	−0.45
Double-support DTC, %	−0.79[a]	−0.27	0.10
Stance DTC, %	−0.94[a]	0.05	−0.10
Cadence DTC, %	0.16	0.93[a]	0.08
Speed DTC, %	0.39	0.89[a]	−0.09
Swing time SD DTC, %	0.38	−0.74[a]	0.27
Step time SD DTC, %	0.03	−0.03	0.93[a]
Variance explained, %	39	30	15

Factor analysis was performed using the principal component method with varimax rotation. Step time SD DTC, $n=327$; swing time SD DTC, $n=329$. DTC, dual-task cost.
[a]The highest loading variables.

significantly associated with any gait markers for eGFR≥60 ml/min per 1.73 m² (Supplemental Tables 1 and 2). Principal component analysis results were similar to the factor analysis results (Supplemental Tables 3 and 4). Exclusion of participants with diabetes or neuropathy did not affect the walking-while-talking and dual-task cost results (Supplemental Table 5).

Discussion

Our results indicate that CKD severity is associated with worse walking performance when paired with a cognitive task. In a group of 330 community-residing older adults, lower eGFR was associated with marked differences in spatiotemporal gait parameters during walking while talking. To examine whether these gait abnormalities were due to elevated cognitive-motor interference, the dual-task cost between walking while talking and walking alone was calculated for the same individual gait markers. Poorer kidney function among participants with CKD was independently associated with greater worsening in the time spent in the swing and stance phases of the gait cycle during walking while talking compared with walking alone. Next, because individual gait markers may not fully capture the multidimensional features of gait, factor analysis was performed to identify underlying domains that may influence gait. Kidney dysfunction was associated with worse performance in the rhythm domain but not the pace or variability domains. Overall, our findings suggest that CKD is associated with gait abnormalities during walking while talking, and these are partly attributable to greater cognitive-motor interference.

This study is the first to link nondialysis-dependent CKD with gait abnormalities and increased cognitive-motor interference during walking while talking. A recent systematic review noted the lack of data on dual-task function in predialysis patients with CKD and the dearth of studies on gait quality (41). Our study had a relatively large sample size, used a validated and standardized dual-task assessment, measured a variety of spatiotemporal gait parameters, included multiple confounders in linear regression models, and used factor analysis to find latent, independent domains in the individual gait variables.

Several lines of evidence suggest that these findings are clinically meaningful. Falls are a major cause of morbidity, and impaired walking due to addition of a cognitive task has been associated with an increased risk of falling in older adults. We recently reported similar gait abnormalities in nondialysis-dependent CKD in the walking-only state and found that these were associated with an elevated risk of falls, including injurious falls (12). Also, the magnitude of the associations with eGFR are meaningful: associations during walking while talking were similar to those of 5-years older age, and the swing time dual-task cost of 1.8% per 10 ml/min per 1.73 m² is larger than the difference between community-living older adults (65–85 years old) and healthy young adults (18–35 years old), despite the use in the latter study of a cognitive task—serial subtractions of 7 starting from 500—that is more cognitively demanding than alphabet recitation (42). On the basis of data from a separate aging cohort, the difference in gait speed per 20 ml/min per 1.73 m² during walking while talking would be associated with an 8% increased risk of frailty, disability, or death in the ensuing 3 years (30). It is worth noting that

Table 4. Associations of continuous eGFR with walking-while-talking gait domains derived using factor analysis

Gait Domain	eGFR≥60, per 10-ml/min per 1.73 m² Lower eGFR, *n*=196		eGFR<60, per 10-ml/min per 1.73 m² Lower eGFR, *n*=134		Age, per 5-yr Older Age, *n*=330	
	Coefficient (95% CI)	*P* Value	Coefficient (95% CI)	*P* Value	Coefficient (95% CI)	*P* Value
Rhythm	0.1 (−0.01 to 0.2)	0.08	−0.2 (−0.3 to −0.1)	<0.001	−0.2 (−0.3 to −0.2)	<0.001
Pace	−0.04 (−0.2 to 0.1)	0.50	−0.01 (−0.1 to 0.1)	0.84	−0.1 (−0.2 to 0.02)	0.12
Variability	0.1 (−0.05 to 0.2)	0.23	−0.04 (−0.2 to 0.1)	0.52	0.1 (−0.02 to 0.2)	0.13

Multivariable linear regression adjusting for age, sex, race, education, body mass index, neuropathy, number of comorbidities, and number of medications was performed. Linear splines for eGFR were constructed with knot placed at 60 ml/min per 1.73 m². 95% CI, 95% confidence interval.

Table 5. Associations of continuous eGFR with dual-talk cost gait domains derived using factor analysis

Gait Domain	eGFR≥60, per 10-ml/min per 1.73 m^2 Lower eGFR, n=193		eGFR<60, per 10-ml/min per 1.73 m^2 Lower eGFR, n=133		Age, per 5-yr Older Age, n=326	
	Coefficient (95% CI)	*P* Value	Coefficient (95% CI)	*P* Value	Coefficient (95% CI)	*P* Value
Rhythm DTC	0.1 (0.00 to 0.2)	0.04	−0.2 (−0.3 to −0.03)	0.02	−0.1 (−0.2 to 0.01)	0.07
Pace DTC	−0.04 (−0.2 to 0.1)	0.58	−0.01 (−0.1 to 0.1)	0.83	−0.03 (−0.1 to 0.1)	0.60
Variability DTC	0.1 (−0.04 to 0.2)	0.20	−0.1 (−0.2 to 0.1)	0.43	0.03 (−0.1 to 0.1)	0.49

Multivariable linear regression adjusting for age, sex, race, education, body mass index, neuropathy, number of comorbidities, and number of medications was performed. Linear splines for eGFR were constructed with knot placed at 60 ml/min per 1.73 m^2. 95% CI, 95% confidence interval; DTC, dual-task cost.

the gait assessments used in our study are distinct from frailty assessment, which incorporates only usual gait speed and not other aspects of gait, such as gait stability or variability, or the effect of a cognitive task on any aspect of gait; as noted, difficulty with cognitive-motor interference may in fact precede the development of frailty (30).

Gait is a complex motor phenomenon with physiologic and cognitive bases (14). Intricate neural pathways and cognitive processes control gait (24,27,43). The walking-while-talking test studies cognitive-motor interactions by assessing gait performance while placing heavy demands on the attention system through a concurrent cognitive task (27). Similar cortical regions of the brain are involved in gait and recitation of alternate letters of the alphabet while walking (44,45). Both activities involve the attention, executive function, and memory regions of the prefrontal cortex (45). This may be especially relevant to CKD: the cognitive demand in dual-task walking is greater than that of normal walking (46); cognitive impairment and brain structure abnormalities have been associated with poorer performance in divided attention tasks (47,48), and in all stages of CKD, cognitive impairment is common, especially in attention, executive function, and processing speed (20–22). Taken together, gait abnormalities and higher dual-task cost in people with CKD may be due to impaired cognitive function and changes in brain structure. These gait abnormalities may become especially prominent during a demanding cognitive task that takes attention away from walking. Indeed, with increasing task complexity, dual-task cost increases: when requiring participants to memorize a word list while navigating a narrow walking track, dual-task cost for walking speed was approximately 8% higher for 60- to 70-year-old adults compared with 20- to 30-year-old adults (49). Therefore, future studies examining the relationship of CKD severity with gait dual-task cost under more challenging conditions that are representative of real-world circumstances could be highly informative for understanding the effects of various cognitive demands on control of gait in CKD.

Consistent with our findings on gait abnormalities are the results of a study by Shin *et al.* (31) on dual-task function among patients on hemodialysis. Similar to our results in nondialysis CKD, they determined that velocity, step length, and percentage of gait cycle in the swing phase were reduced and that percentage of gait cycle in double support was elevated. There were also several differences in dual-task cost results, which partly may be due to the different cognitive tasks used, as well as disparities in the clinical characteristics of our cohorts. It is possible that the choice of cognitive task affects which aspects of gait are most affected in CKD.

Comparing gait markers and domains associated with CKD in the single- and dual-task conditions may elucidate overlapping or unique gait characteristics. A previous study by our group on the same cohort investigated gait abnormalities in single-task walking (12). Lower eGFR was associated with slower gait speed, smaller percentage of the gait cycle in the swing phase, and larger percentage of the gait cycle in double support. Many other studies on walking alone have demonstrated slower gait speed among patients with CKD relative to controls (41). These individual gait marker differences in CKD observed in single-task conditions are similar to those in the dual-task condition of this study. However, we further demonstrated a relative difference between single- and dual-task performance in the rhythm domain within the same group of participants. In a recent study of kidney function and different walking-only conditions, Sedaghat *et al.* (50) derived seven gait domains and found that lower eGFR was associated with greater variability but was not associated with rhythm or pace. Because we only found an association with rhythm during walking while talking, this discrepancy suggests a difference in single- and dual-task gait abnormalities associated with kidney dysfunction. Indeed, differences in gait domains between single- and dual-task conditions have been previously reported in the context of predicting falls (27).

There were several limitations of this study. CKD was defined on the basis of a single measure of serum creatinine, such as has been done in prior studies (3). Information on albuminuria and cystatin C was not collected; given the relationship between serum creatinine and muscle mass, estimation of GFR using cystatin C would have been useful. Residual confounding is possible because comorbidities were self-reported, and we cannot exclude the possibility of reverse causality. The prevalence of comorbidities is low, which is consistent with the relatively low number of medications and may be due to the recruitment of a relatively healthy group of participants with mild decrease in GFR. This may decrease the generalizability of our results.

In sum, CKD is associated with abnormalities in quantitative spatiotemporal gait parameters and elevated cognitive-motor interference while performing walking

while talking tasks. These findings are present at various stages of CKD severity, and they are worse in those with more advanced CKD. Future studies should investigate whether the walking-while-talking test and dual-task cost can predict adverse outcomes, such as fall risk and cognitive dysfunction, and whether dual-task performance training may improve outcomes in CKD.

Disclosures

Dr. Abramowitz has received consulting fees from Tricida, Inc. Dr. Ho and Dr. Verghese have nothing to disclose.

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Supplemental Material

This article contains the following supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.12401019/-/DCSupplemental.

Supplemental Table 1. Associations of continuous eGFR with individual gait variables (additional covariates included).

Supplemental Table 2. Associations of continuous eGFR with factor analysis gait domains (additional covariates included).

Supplemental Table 3. Rotated component loadings of eight gait variables using principal component analysis.

Supplemental Table 4. Associations of continuous eGFR with principal component analysis gait domains.

Supplemental Table 5. Associations of continuous eGFR with factor analysis gait domains after exclusion of diabetes or neuropathy.

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