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The Association of Daily Activity Levels and Estimated Kidney Function in Men and Women With Predialysis Chronic Kidney Disease

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Introduction: Chronic kidney disease (CKD) is often accompanied by complications including poor physical activity level. However, only a few studies have objectively characterized physical activity levels in predialysis CKD. Our study sought to measure daily activity levels by accelerometry in individuals with CKD (stages III–V) and to determine the association between daily activity and kidney function.

Methods: We determined kidney function by means of the estimated glomerular filtration rate (eGFR) using the Modification of Diet and Renal Disease (MDRD) equation. Participants wore an accelerometer for 7 consecutive days, and we measured multiple physical activity outcomes including total daily activity, sedentary, light, and moderate–vigorous activity. Average durations and intensity of activity were determined according to stage of CKD. The association between kidney function and activity level was determined by regression analysis.

Results: We analyzed data from 110 individuals (60% men and 40% women) with stages III to V CKD. The mean age of our participants was 64 years, mean body mass index was 27.5 kg/m^2, and mean eGFR was 23.7 $\pm$ 1.2 ml/min/1.73 m^2. Our participants were primarily sedentary (mean duration of inactivity = 1152 $\pm$ 100 minutes per day; 79% of day). Light activity was performed 280 $\pm$ 99 minutes per day, and individuals participated in only 6 $\pm$ 9 minutes per day of moderate–vigorous activity. The eGFR did not predict physical activity level ($P > 0.05$ for all).

Discussion: Individuals with stages III to V CKD are sedentary, and do not meet the national recommendations of 150 minutes of moderate–vigorous activity per week. Further study is required to determine whether interventions to increase activity levels in patients with CKD are associated with improved health outcomes.

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Chronic kidney disease (CKD) is an increasingly prevalent condition[1,2] that is associated with significant morbidity and mortality.[3–5] One important complication of CKD is impaired musculoskeletal health. CKD is associated with fatigue, muscle cramps, weakness, and low energy.[6,7] These symptoms begin early in predialysis CKD and progress over time as kidney function decreases to end-stage kidney failure,[8,9] and may contribute to decreased participation in physical activity. Poor participation in moderate–vigorous physical activity is associated with multiple health risks including obesity, cardiovascular disease, metablic syndrome, and type 2 diabetes.

The first step in determining whether improving physical activity levels in individuals with CKD is necessary is to objectively measure how active or inactive they may be. If reduced kidney function is associated with poor physical activity levels in men and women with predialysis CKD, it may be important to target CKD stage–appropriate exercise interventions before the initiation of dialysis therapy to preserve or enhance outcomes such as musculoskeletal and cardiovascular health. To date, only a few studies have characterized physical activity in individuals with

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predialysis CKD using accelerometry (an objective measure of physical activity),[10–12] and only 1 of these studies evaluated the association between kidney function and physical activity.[10] Hawkins *et al*. reported that the total amount of physical activity performed was positively associated with better kidney function[10]; however, only individuals with an estimated glomerular filtration rate (eGFR) of > 30 ml/min (CKD stages I−III) were included, and those with more advanced predialysis CKD stages IV−V (eGFR ≤ 30 ml/min) were excluded.

Therefore, the purposes of our study were (i) to characterize daily activity levels by accelerometry in individuals with stages III to V predialysis CKD, and (ii) to determine the association between total daily activity, sedentary, light, and moderate−vigorous activity and kidney function in individuals with stages III to V CKD. We hypothesized that those with stage III to V CKD would be inactive, and that better kidney function would be associated with greater physical activity levels.

MATERIALS AND METHODS

Study Participants

We enrolled 122 participants aged 18 years and older from predialysis CKD clinics in Toronto, Ontario, Canada. The majority of participants (88%) were recruited from the Renal Management Clinic at the University Health Network, a multidisciplinary tertiary care clinic for men and women with CKD. All participants were diagnosed with having CKD by a nephrologist, and provided written informed consent to participate. All appropriate institutional review boards approved the study.

Accelerometry

We assessed daily activity by accelerometry using a triaxial activity monitor (i.e., measures movement on 3 axes [X, Y, Z]; StayHealthy, RT3) worn on the participant's left hip for 7 consecutive days. Participants were instructed to wear the monitor during all waking hours, and to remove the monitor only to sleep, shower, or partake in water-based activities. Participants kept a log of when they wore or removed the monitor, and when purposeful physical activity (i.e., exercise) was performed. It should be noted that we did not exclude sleep time (i.e., when the monitor was removed for recorded sleep) in our analysis because of the possibility that our participants were sleeping more due to fatigue associated with CKD. We wanted to evaluate overall activity level in a 24-hour period, and not only activity level during awake time.

RT3 minute-by-minute data were evaluated and compared to those in the monitor logs when necessary for each participant. RT3 data were divided into 24-hour periods from the time that the participant began wearing the monitor. When a block of time ≥ 60 minutes of consecutive zeros was identified within a 24-hour period of RT3 wear, this data point was examined more carefully. Within a 24-hour period, "no wear time" > 4 hours that was unaccounted for would void the 24-hour collection period. Participants with a minimum of 4 days of valid data were included in the analyses[10] because, in adults, 3 to 5 days of wear time are required to reliably estimate daily physical activity.[13]

To determine average total kilocalories (kcals) expended per day, the activity in kcal per minute for each minute of a valid 24-hour collection period was summed and divided by the number of valid days of wear time to estimate average total daily activity kcal expenditure for each participant. Intensity of daily activity was determined using previously validated cut points for the RT3.[14] Each minute of accelerometry data for all participants was coded by intensity level. A minute of accelerometer data was coded as sedentary behavior if the vector magnitude (unit-less activity count produced by the RT3) was between 0 and 100 counts[10]; as light intensity if the vector magnitude was between 100 and 1772[14] (equivalent to up to 3.9 metabolic equivalents [METs], which include activities such as washing dishes and cooking [3.3 METs], vacuuming [3.3 METs], mopping [3.5 METs], and walking for pleasure [3.5 METs][15]); and as moderate−vigorous intensity (≥ 4 METs, which include activities such as leisurely bicycling [6.0 METs], shoveling snow [6.0 METs], and carrying groceries upstairs [7.5 METs][15]) if the vector magnitude was ≥ 1772 counts.[14] Each minute of sedentary, light, and moderate−vigorous activity was summed separately and divided by the number of valid days of wear time to estimate daily activity intensity averages (minutes) for each participant.

Calculation of Kidney Function

We estimated kidney function (based on eGFR) using the Modification of Diet and Renal Disease (MDRD) equation.[16,17] Kidney function was calculated for each participant using the National Kidney Foundation online GFR calculator.[18] Following eGFR calculation, we categorized participants by stage of CKD (stages III−V) per the National Kidney Foundation, Kidney Disease Outcomes Quality Initiative (KDOQI).[6]

Statistical Analyses

Participants' demographic data was summarized using t tests and χ^2 tests as appropriate. Accelerometry variables were analyzed as continuous variables. One-way analysis of variance was used to examine accelerometry by stage of CKD (stages III−V). Bonferroni *post hoc* analyses were conducted to determine between-group differences. We conducted regression analyses to explore associations and to examine whether kidney function (eGFR by MDRD) predicted participants' levels of physical activity. We evaluated 2 regression models, 1 model with eGFR alone, and 1 model adjusted for body mass index (BMI). Analyses were performed with STATA (version 11.1, StataCorp, College Station, TX). Statistical tests were considered significant at a level of 0.05 and were not adjusted for multiple comparisons.

RESULTS

Participant Demographic and Clinical Characteristics

Out of the 122 participants enrolled, 9 participants did not wear the accelerometer (i.e., the accelerometer data read 0 for the entire collection period) and were excluded from analysis. Three individuals were excluded because their calculated eGFR CKD staging equaled stage I or II CKD. Therefore we present data from 110 individuals (66 men and 44 women) with stages III−V CKD (Table 1). The majority of individuals were of white ethnicity, with a mean age of 64 years, and the men were slightly older than the women ($P = 0.03$). Mean BMI (27.5 kg/m^2) was similar between men and women. More than 40% of our participants had a diagnosis of diabetes (34 of 81 participants with diabetes data), and 55% of our population was retired (33 of 60 participants with employment data). The mean eGFR as calculated by the MDRD equation was 23.7 ± 1.2 ml/min/1.73 m^2, and we had a relatively equal distribution of participants with stages III, IV and V CKD.

Table 1. Demographic characteristics of the study participants

Variable	All participants (N = 110)	Men (n = 66)	Women (n = 44)	*P* value
Age, yr	64.3 ± 1.6	67.0 ± 1.7	60.2 ± 2.9	0.03
Weight, kg	75.6 ± 1.7	78.8 ± 2.1	70.7 ± 2.8	0.02
Height, cm	165.7 ± 1.0	170.5 ± 1.1	158.5 ± 1.3	0.00
BMI (kg/m^2)	27.5 ± 0.6	27.0 ± 0.6	28.2 ± 1.2	0.30
Ethnicity				
White	59 (53.6%)	40 (60.6%)	19 (43.1%)	0.20
Asian	22 (20%)	12 (18.2%)	9 (20.5%)	
African American	7 (6.4%)	2 (3.0%)	5 (11.4%)	
Other/unable to determine	23 (20.9%)	12 (18.2%)	11 (25%)	
Current diabetes	34/81 (42%)	26/53 (49%)	8/28 (29%)	0.08
Employment status				
Full-time	14/60 (23%)			
Part-time	4/60 (6.7%)			
Disability	4/60 (6.7%)			
Retired	33/60 (55%)			
Self-employed/homemaker	3/60 (5%)			
Unemployed	1/60 (1.7%)			
Student	1/60 (1.7%)			
Serum creatinine (μmol/L)	275.4 ± 13.0	286.1 ± 16.5	259.4 ± 21.3	0.32
eGFR by MDRD (ml/min/1.73 m^2)	23.7 ± 1.2	24.1 ± 1.4	23.1 ± 2.0	0.66
Stage of CKD, by MDRD				
Stage III	30 (26.6%)	18 (27.3%)	12 (27.3%)	0.76
Stage IV	49 (43.4%)	31 (47%)	18 (40.9%)	
Stage V	31 (27.4%)	17 (25.8%)	14 (31.8%)	

Data are mean ± standard error mean unless otherwise indicated. BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet and Renal Disease [equation].

Activity Data

Accelerometry data are presented in Table 2. All participants (N = 110) completed at least 4 days of valid accelerometer wear time; on average, participants completed 6 days of valid accelerometer wear time. The majority of the participants (n = 81, 74%) had 6 or 7 days of valid accelerometry data included in the analysis. Participants expended an average of 373.9 ± 211.5 kcal per day completing daily activity (i.e., calories expended above resting energy expenditure). For all participants, the majority of daily minutes (1152 ± 100 min/d) were spent performing sedentary activity. This is equal to approximately 19 hours per 24-hour day (or 79% of the day) of sedentary activity. Light activity was performed an average of about 280 minutes per day, with moderate−vigorous activity performed only an average of 6 minutes per day. Men participated in more total daily activity when compared with women (407 vs. 325 kcal/d expenditure; $t_{108} = 2.02$, $P = 0.05$). However, when activity level was compared by intensity (min/d) there was no difference between the men and women ($P > 0.05$).

Kidney Function and Accelerometry

Physical activity levels by stage of CKD is presented in Table 3. Participants with stage III, IV, and V CKD expended a similar number of kcals per day ($F_{2,107} = 2.37$, $P = 0.10$) and participated in similar durations (min/d) of sedentary ($F_{2,107} = 2.77$, $P = 0.07$), light ($F_{2,107} = 1.78$, $P = 0.17$), and moderate−vigorous ($F_{2,107} = 2.83$, $P = 0.06$) physical activity.

Regression analyses were used to test whether kidney function significantly predicted participants' levels of physical activity (Tables 4–7). Kidney function (i.e., eGFR) was not associated with total daily activity level or duration of sedentary, light, or moderate−vigorous physical activity. The model that included both eGFR and BMI explained only 1% of the variance in daily activity expenditure (adjusted $R^2 = 0.01$, $F_{2,107} = 1.64$, $P = 0.199$), 1% of the variance in sedentary activity performed (adjusted $R^2 = 0.01$, $F_{2,107} = 1.56$, $P = 0.214$), and less than 1% of the variance in light activity performed (adjusted $R^2 = 0.009$, $F_{2,107} = 1.50$, $P = 0.228$). eGFR and BMI explained 5% of the

Table 2. Average accelerometry data in men and women with stage III to V chronic kidney disease

Accelerometry measure	All participants (N = 110)	Men (n = 66)	Women (n = 44)	Test statistics
Daily activity expenditure (kcal)	373.9 ± 211.5	406.8 ± 234.5	324.7 ± 161.5	$t_{108} = 2.02$, $P = 0.05$
Sedentary activity (min/d)	1151.9 ± 100.5	1151.7 ± 101.9	1152.3 ± 100.5	$t_{108} = -0.03$, $P = 0.98$
Light activity (min/d)	279.5 ± 99.4	277.6 ± 101.8	282.4 ± 96.9	$t_{108} = -0.25$, $P = 0.81$
Moderate−vigorous activity (min/d)	6.3 ± 9.2	7.0 ± 9.0	5.3 ± 9.5	$t_{108} = 0.97$, $P = 0.34$

Data are mean ± standard deviation.

variance in moderate−vigorous activity (adjusted $R^2 = 0.05$, $F_{2,107} = 4.00$, $P = 0.02$); however, it was BMI that predicted moderate−vigorous activity level ($\beta = -0.36$, $P = 0.01$). Kidney function was not associated with physical activity level in our cohort of men and women with stages III to V CKD.

DISCUSSION

In our study, we objectively measured daily physical activity levels by accelerometry in men and women with a range of predialysis CKD (stages III−V). Our key finding is that men and women with stage III to V CKD are extremely inactive, spending almost 80% of their day participating in sedentary activity. Indeed, we found that individuals with predialysis CKD accumulated an average of more than 19 hours per day of sedentary activity. Furthermore, when time was spent participating in activity, it was primarily light-intensity activity. Participants engaged in moderate−vigorous intensity activity an average of only 6 minutes per day, which equals approximately 40 minutes per week. This is well below the Canadian Society for Exercise Physiology Physical Activity Recommendations of at least 150 minutes per week[19] and below physical activity levels reported in aged-matched men and women without CKD.[20,21]

Surprisingly, physical activity participation was similar among each of stages III, IV, and V CKD, and we did not find that kidney function predicted physical activity level. One possible explanation for this observation is a selection bias, such that patients seen in our multidisciplinary CKD clinic are those who are more chronically ill and need multidisciplinary care. Having such a complex chronic disease state may predispose patients to be extremely inactive, independent of their CKD stage. In addition, we can speculate that once individuals reach stage III CKD, clinical symptoms that contribute to poor physical activity (such as fatigue, muscle cramps, muscle atrophy, and weakness) may start to appear.[8] Due to the complexity of CKD (various etiologies and multiple comorbidities), there may not be a stepwise decline in physical activity level by stage of CKD or kidney function but, rather, a "cut-off" point of overall cumulative CKD severity that may be associated with poor participation in physical activity. However, we did not measure phyiscal acitivty in the earlier stages of CKD (I and II), and therefore cannot examine whether there is a difference between physical activity participation in individuals with CKD stages I and II versus CKD stages III to V. One future direction would be to compare physical activity participation in predialysis CKD patients with those who are currently on dialysis therapy (i.e., in end-stage kidney failure) and examine the entire spectrum of how CKD severity affects physical activity level. Futhermore, it might be valuable to examine the slope of eGFR decline and how this may affect physical activity level in CKD, as this may be more predictive of physical activity participation than the stages of CKD itself. CKD staging may differ according to the GRF estimating equation used, and whether or not urine albuminuria is incorporated.[6] It may also vary by patient characteristics such as age and ethnicity. Future research that aims to identify a kidney function "cut-off" point at which an exercise intervention should be targeted for preservation and improvement of outcomes is an important and interesting issue to address.

Similar to the findings of the current study, extreme sedentary behavior in predialysis CKD has previously

Table 3. Physical activity by stage of chronic kidney disease as calculated by MDRD equation

Stage	Daily activity expenditure (kcal)	Sedentary activity (min/d)	Light activity (min/d)	Moderate−vigorous activity (min/d)
Stage III	406.9 ± 233.2	1139.8 ± 103.3	291.6 ± 97.9	8.6 ± 12.1
Stage IV	325.8 ± 167.6	1176 ± 95.9	259.9 ± 94	4.1 ± 4.2
Stage V	418.2 ± 240.9	1125.6 ± 99.5	298.8 ±106.5	7.6 ± 11

Mean ± standard deviation. MDRD, Modification of Diet and Renal Disease.

Table 4. Regression analyses, daily activity expenditure (kcal/d)

Variables	β	SE β	t	P	R^2	Adj R^2
Model 1					0.01	
eGFR by MDRD	2.10	1.65	1.27	0.206		
Model 2					0.03	0.01
eGFR by MDRD	1.79	1.66	1.08	0.281		
BMI	4.30	3.34	1.29	0.201		

Adj, adjusted; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet and Renal Disease [equation].

Table 5. Regression analyses, sedentary activity (min/d)

Variables	β	SE β	*t*	*P*	R^2	Adj R^2
Model 1					0.007	
eGFR by MDRD	−0.70	0.79	−0.89	0.378		
Model 2					0.03	0.01
eGFR by MDRD	−0.87	0.79	−1.10	0.276		
BMI	2.43	1.60	1.53	0.129		

Adj, adjusted; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet and Renal Disease [equation].

Table 7. Regression analyses, moderate−vigorous activity (min/d)

Variables	β	SE β	*t*	*P*	R^2	Adj R^2
Model 1					0.01	
eGFR by MDRD	0.09	0.07	1.21	0.229		
Model 2					0.07	0.05
eGFR by MDRD	0.11	0.07	1.58	0.117		
BMI	−0.36	0.14	−2.54	0.012		

Adj, adjusted; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet and Renal Disease [equation].

been reported. Robinson-Cohen *et al*. found that their cohort of 46 predialysis CKD participants spent 95% of their time engaging in sedentary or light activity (in the current study, our participants spent 99% of their time participating in sedentary or light activity).[11] The mean eGFR (by MDRD) in the study by Robinson-Cohen *et al*. was 42 ± 15 ml/min/1.73 m^2, and the investigators did not categorize the participants into stages of CKD. The mean (± SEM) MDRD-calculated eGFR in the current study was 23.7 ± 1.2 ml/min/1.73 m^2; therefore, our participants had more advanced CKD, which may explain the even greater degree of sedentary/light activity observed.

Contrary to the findings of the current study, Hawkins *et al*. reported that light intensity activity and total physical activity was positively associated with kidney function, with a higher eGFR observed in more active men and women.[10] However, it is important to note that the study population used by Hawkins *et al*. was derived from the National Health and Nutrition Examination Survey (NHANES) database (i.e., men and women who are representative of the general US population), from which their kidney function was categorized into stages of CKD using laboratory values (serum creatinine and MDRD eGFR estimation) collected on a protocol basis. Unlike the current study, which exclusively involved patients diagnosed with CKD and managed by a nephrologist in a multidisciplinary setting, the population in the Hawkins *et al*. study was not clinically diagnosed with CKD. As well, the majority of individuals in the Hawkins *et al*. study had only slightly reduced eGFR (equivalent to CKD stages I−III)[10]; therefore, their results may not be generalizable to complex patients with more advanced stages of CKD who need multidisciplinary predialysis care, such as the individuals enrolled in the current study.

Table 6. Regression analyses, light activity (min/d)

Variables	β	SE β	*t*	*P*	R^2	Adj R^2
Model 1					0.01	
eGFR by MDRD	0.82	0.78	1.05	0.296		
Model 2					0.03	0.009
eGFR by MDRD	0.97	0.78	1.24	0.219		
BMI	−2.16	1.57	−1.37	0.172		

Adj, adjusted; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet and Renal Disease [equation].

The clinical implications of the current study are that the activity levels of individuals with stages III to V CKD are far below recommended physical activity guidelines—a concerning fact, as physical inactivity is associated with many high-risk conditions and comorbidities, such as frailty, musculoskeletal abnormalities (e.g., bone fractures), obesity, and cardiovascular disease, which are all common conditions in CKD.[22,23] Such conditions, in turn, are associated with further inactivity. A recent observational study examined whether replacing sedentary behavior with low- or light-intensity activities would result in survival benefits in both the general and CKD populations.[12] The authors reported that trading sedentary activity for light activity was associated with a lower hazard of death in both the general population and CKD population group.[12] This finding underscores the importance of addressing physical inactivity in CKD, to potentially improve health outcomes in this cohort.

Thus, the therapeutic implications of our study are apparent but may be challenging to effectively address. For example, as we observed that individuals with CKD stages III to V were extremely inactive, educational and exercise programs might be strategically targeted to such patients. Yet this is confounded by the fact that as patients' CKD progresses, they may also accumulate multiple comorbidities that limit the ability to be active, and that uremia itself is strongly associated with increasing fatigue, impaired muscle function, and reduced exercise tolerance.[24,25] The emphasis may also be to encourage greater physical activity in the early stages of CKD, to improve or maintain cardiac function, which may help to prevent associated kidney decline (e.g., cardiorenal syndrome). The threshold for when an exercise intervention is needed, and the type of intervention required to improve physical activity level and kidney health, requires further investigation.[26]

The current study has limitations. For example, light activity was defined as up to 3.9 METs and moderate−vigorous activity as ≥ 4 METs. Categorizing the intensity of activity by METs has limitations because every individual may perceive a certain MET level as a different intensity.[27] Furthermore, we used RT3 accelerometry cut-off points that were determined in healthy individuals,[14] therefore the ability of these cut-offs to transfer to adults with CKD may be limited. Choosing accelerometry cut-offs for activity intensity determination is not standard across studies in CKD,[10–12] which may make it difficult to properly compare study results. Another limitation with the use of accelerometry is that validation studies suggest that regardless of the brand of accelerometer used (including the RT3), accelerometry tends to underestimate the absolute amount of daily activity performed.[28] Although the validity of accelerometry monitors, including the RT3, has been confirmed in older adults with documented chronic disease,[27] we cannot be certain that accelerometry did not underestimate the amount of daily activity in our cohort. Finally, a limitation of the current study is that we did not describe or explore other factors that might contribute to poor physical acivity in predialysis CKD (e.g., the presence of cardiovascular disease, obesity, metabolic syndrome, anemia, and underlying fatigue, etc.). Yet these factors commonly coexist in patients living with CKD. The potential degree and relative contribution of these factors to the inactivity observed in patients with CKD may be an important future direction to be considered and explored.

In conclusion, individuals with predialysis stages III to V CKD are primarily sedentary and do not meet the current national activity guidelines. Further study is required to first explore the details of specific physical activity interventions (e.g., type, duration, timing) and then to determine whether interventions to increase activity levels in patients with CKD are associated with improved health outcomes.

DISCLOSURE

All the authors declared no competing interests.

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