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Supervised Exercise Intervention and Overall Activity in CKD

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Introduction: Patients are often instructed to engage in multiple weekly sessions of exercise to increase physical activity. We aimed to determine whether assignment to a supervised exercise regimen increases overall weekly activity in individuals with chronic kidney disease (CKD).

Methods: We performed a secondary analysis of a pilot randomized 2 $\times$ 2 factorial design trial examining the effects of diet and exercise (10%–15% reduction in caloric intake, 3 supervised exercise sessions/wk, combined diet restriction/exercise, and control). Activity was measured as counts detected by accelerometer. Counts data were collected on all days for which an accelerometer was worn at baseline, month 2, and month 4 follow-up. The primary outcome was a relative change from baseline in log-transformed counts/min. Generalized estimating equations were used to compare the primary outcome in individuals in the exercise group and the nonexercise group.

Results: We examined 111 individuals randomized to aerobic exercise or usual activity (n = 48 in the exercise group and n = 44 controls). The mean age was 57 years, 42% were female, and 28% were black. Median overall adherence over all time was 73%. Median (25th, 75th percentile) counts/min over nonsupervised exercise days at months 2 and 4 were 237.5 (6.5, 444.4) for controls and 250.9 (7.7, 529.8) for the exercise group ($P = 0.74$). No difference was observed in the change in counts/min between the exercise and control groups over 3 time points (β [fold change], 0.96, 95% confidence interval [CI], 0.91, 1.02).

Conclusion: Engaging in a supervised exercise program does not increase overall weekly physical activity in individuals with stage 3 to 4 CKD.

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Physical activity confers a multitude of benefits that may counteract the adverse metabolic environment of kidney dysfunction. Among individuals with CKD, greater physical activity has been associated with better physical functioning, slower rates of kidney function decline, and lower risks of cardiovascular events and mortality.[1–6] Concurrently, these individuals are less likely than their counterparts with preserved kidney function to achieve recommended physical activity levels. As such, increasing regular physical activity is considered an important target to counteract the development of complications of CKD.

Although health care providers encourage increases in physical activity levels by recommending regular exercise sessions, adherence is often poor.[7,8] More intensive interventions involving supervised activity may improve adherence. However, these exercise interventions may account for only a small percentage of total physical activity and may have little impact on total physical activity levels, although this has not been investigated extensively.

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We recently reported the results of a pilot randomized clinical trial examining the efficacy, feasibility, and safety of supervised exercise and calorie restriction in patients with stage 3 to 4 CKD. In this secondary analysis, we aimed to determine whether assignment to a supervised exercise regimen would increase overall weekly physical activity in individuals with CKD.

METHODS

Study Design

We performed a secondary analysis of a pilot randomized 2 $\times$ 2 factorial design trial examining the effects of diet and exercise.[9] We used the Consolidated Standards of Reporting Trials (CONSORT) checklist when writing our report. Details of the parent randomized controlled trial have previously been described.[8] In brief, participants were randomized to 1 of 4 interventions, for a duration of 4 months: (i) dietary restriction (10%−15% daily caloric restriction); (ii) supervised exercise regimen (3 times/wk); (iii) combined dietary restriction and supervised exercise regimen; or (iv) control (usual exercise and diet) (NCT01150851). Participants in the supervised exercise group were scheduled to perform low-impact aerobic exercise for 30 to 45 minutes, 3 times per week for 4 months. To provide variety, participants alternated exercise with the use of a treadmill, elliptical cross-trainer, Nu-Step cross-trainer, and recumbent stationary bicycle.

Inclusion criteria consisted of estimated glomerular filtration rate (eGFR) 15 to 60 ml/min per 1.73 m^2, age 18 to 75 years, body mass index (BMI) $\geq$25 kg/m^2, life expectancy $\geq$1 year, and the ability to understand and to provide informed consent. Participants were excluded for any acute inflammatory condition, pregnancy, high-dose antioxidant use, chronic use of anti-inflammatory medication, significant cardiac or vascular disease, significant occlusive atherosclerotic disease or ischemic disease, significant physical immobility or disabilities, type 1 diabetes mellitus or type 2 diabetes mellitus requiring insulin therapy, and history of poor adherence to a medical regimen.[8]

The study was approved by the Institutional Review Boards at participating sites (Vanderbilt University Medical Center (VUMC), the Veterans Affairs Tennessee Valley Healthcare System Nashville (VATVHS), University of Washington (UW), Providence Medical Research Center (PMRC), and Springfield College (SC)). All participants provided written informed consent before study enrollment. The study began in October 2010 and was completed in February 2014. The safety profile of the initial study was overseen by a Data Safety Monitoring Board. A total of 122 participants consented, 111 were randomized, 104 started intervention, and 92 completed the original study (completed all baseline, 2-month, and 4-month visits) (Figure 1).

Data Collection

Demographic, anthropometric, lifestyle, medication, physical examination, and laboratory data were collected at baseline (2 weeks prior to initiation of intervention phase). Follow-up visits were conducted at 2 months and 4 months. Hypertension and diabetes were ascertained by self-report, and glomerular filtration rate (eGFR) was estimated by the 2012 cystatin C-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[10]

All participants were issued an ActiGraph GT3X accelerometer (Actigraph, Fort Walton Beach, FL), a pager-sized device powered by a small lithium battery. Participants wore the accelerometer for 1 week after the initial baseline visit and for 1 week either before or after both the month 2 and month 4 study visits. The accelerometer was attached to an elasticized belt and worn on the right hip. Participants were instructed to wear the accelerometer throughout the waking hours except for instances when this was not feasible (e.g., during showering and swimming). The exercise group participants were instructed to wear the accelerometers during prescribed exercise sessions. The triaxial accelerometer estimates the duration and intensity of physical activity by capturing the magnitude of acceleration (intensity) in 3 dimensions and then summing the magnitudes as counts per minute (higher counts per minute indicate more physical activity).[11] Validation for this instrument has been previously reported.[12] A nonwear period was defined as an interval of $\geq$60 minutes of zero activity counts that contained no more than 2 minutes of counts between 0 and 100. A nonwear period ended with either a third minute of activity counts >0 or a 1-minute activity count >100.[11] Accelerometer data were available for up to 7 days at baseline, month 2, and month 4 visits.

Statistical Analyses

A total of 111 participants who were randomized were included in the intent-to-treat analysis (Figure 1). For the purposes of this analysis, the “control” group was defined as either the dietary restriction intervention (n = 28) or usual diet and exercise (n = 26) participants. The intervention group was defined as either the exercise regimen (n = 27) or combined dietary restriction and exercise regimen (n = 30) participants.

We tabulated baseline participant characteristics according to intervention group. Counts/min were calculated for each participant at baseline, month 2, and month 4. For participants with missing baseline

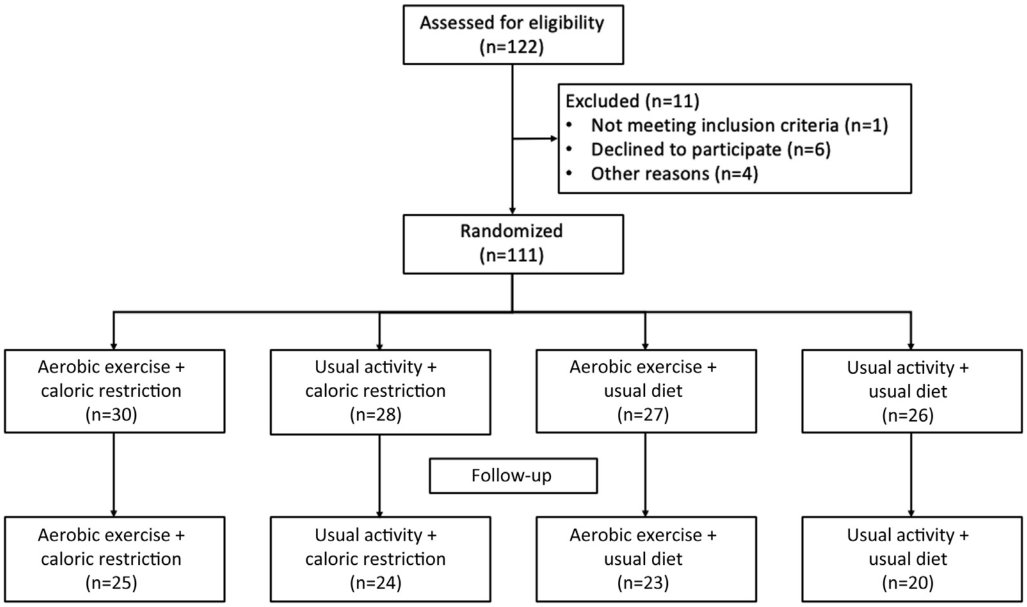

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram. Participants lost to follow-up were excluded in compliance analyses.

accelerometer data (n = 19), single imputation informed by age, race, gender, tobacco use, and comorbidities was performed. Log-transformed accelerometry counts per minute were modeled as the primary dependent variable.

Linear regression was used to evaluate differences in mean log-transformed counts/min at baseline, month 2, and month 4, and over all time points, between the exercise group and controls. Generalized estimating equations with exchangeable correlations were used to determine whether change per month of follow-up differed between exercise and control groups. Analyses were completed including all accelerometer days and, secondarily, excluding accelerometer days during which individuals in the exercise group participated in the supervised exercise intervention (i.e., restriction to "nonexercise" days).

Sensitivity analyses were conducted to examine the robustness of our findings. First, to examine the impact among more physically active individuals, we stratified by median baseline counts per minute and by baseline percentage of sedentary time. Second, to examine the impact of adherence to the exercise regimen (attendance of supervised exercise sessions), we stratified participants in the exercise group by median adherence (73% adherence). Only participants who completed the study (n = 92) were included in the adherence analyses. Third, to examine differences in sedentary, light, moderate, and vigorous activity, linear regression was used to evaluate differences in mean log-transformed minutes/day at baseline, month 2, and month 4, and over all time points. Fourth, we stratified by gender. Fifth, we examined the influence of caloric restriction on activity by comparing the counts/min between the usual diet and caloric restriction groups among participants randomized to aerobic exercise.

Statistical analyses were conducted with Stata version 14.2 (StataCorp, College Station, TX) and R Studio (RStudio, PBC, Boston, MA).[13] The nominal level of significance was defined as $P < 0.05$ (2-sided).

RESULTS

A total of 111 individuals were randomized in the original randomized controlled trial and were included in this analysis (57 exercise group and 54 controls) (Table 1). Most participants were male (58%), white (67%), and hypertensive (90%). Participants with diabetes comprised 25% of participants. Median (25th, 75th percentile) age was 59.5 years (49.0, 65.0 years) for controls and 55.0 years (49.0, 61.0 years) for participants in the exercise group. Median (25th, 75th percentile) baseline eGFR was 36.7 ml/min per 1.73 m^2 (28.9, 50.4 ml/min per 1.73 m^2) and 40.1 ml/min per 1.73 m^2 (26.5, 51.3 ml/min per 1.73 m^2) for control and exercise groups, respectively.

At baseline, the mean number of days in which an accelerometer was worn was 5.4 days for both the exercise and controls groups. At month 2, the mean number of days in which an accelerometer was worn was 6.3 days and 6.5 days for the exercise and control groups, respectively. At month 4, the mean number of days with an accelerometer was 4.3 days for controls and 3.6 days for the exercise group (Figure 2).

Median (25th, 75th percentile) counts/min for all accelerometer days at months 2 and 4 were 237.5 (6.5,

Table 1. Participant baseline characteristics, according to randomization to exercise intervention

Characteristic	Overall (n = 111)	Control (n = 54)	Treatment (n = 57)
Age, yr	57.0 (49.0, 63.0)	59.5 (49.0, 65.0)	55.0 (49.0, 61.0)
Gender			
Female	47 (42.3)	22 (40.7)	25 (43.9)
Male	64 (57.7)	32 (59.3)	32 (56.1)
Race			
Black	31 (27.9)	17 (31.5)	14 (24.6)
White	74 (66.7)	35 (64.8)	39 (68.4)
Other	6 (5.4)	2 (3.7)	4 (7.0)
Caloric restriction	58 (52.3)	28 (51.9)	30 (52.6)
Current tobacco use	10 (9.0)	4 (7.4)	6 (10.5)
Body mass index, kg/m^2	33.0 (28.8, 37.3)	33.7 (29.6, 38.8)	32.3 (28.5, 36.2)
Prevalent disease			
Hypertension	100 (90.1)	48 (88.9)	52 (91.2)
Diabetes	28 (25.2)	14 (25.9)	14 (24.6)
Congestive heart failure	5 (4.5)	2 (3.7)	3 (5.3)
Myocardial infarction	2 (1.8)	0 (0.0)	2 (3.5)
Coronary artery disease	6 (5.4)	2 (3.7)	4 (7.0)
eGFR, ml/min per 1.73 m^2	38.0 (28.1, 50.4)	36.7 (28.9, 50.4)	40.1 (26.5, 51.3)
Systolic BP, mm Hg	131 (115, 142)	132 (117, 142)	129 (114, 141)
Diastolic BP, mm Hg	78 (72, 84)	78 (72, 84)	78 (70, 85)
Light activity, min/d	155.9 (74.3, 225.9)	149.1 (63.9, 216.9)	163.9 (75.6, 228.0)
Moderate activity, min/d	10.7 (1.9, 25.6)	8.3 (1.0, 20.9)	12.4 (4.0, 25.7)
Vigorous activity, min/d	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)
Sedentary time, min/d	498.3 (286.3, 618.4)	560.7 (309.4, 652.3)	446.4 (286.3, 586.6)
Baseline accelerometer days	7 (5, 7)	7 (5, 7)	7 (5, 7)
Month 2 accelerometer days	7 (6.5, 7)	7 (7, 7)	7 (6, 7)
Month 4 accelerometer days	5 (0, 7)	5 (0, 7)	5 (0, 7)

Data are n (%) or median (25th, 75th percentile). BP, blood pressure.

444.4) for controls and 354.5 (8.1, 531.0) for participants in the exercise group ($P = 0.38$) (Table 2, Figure 3). When including only nonexercise days in the exercise group, no difference in counts/min was observed between the control and exercise groups (237.5 [interquartile range, 6.5, 444.4] vs. 250.9 [interquartile range, 7.7, 529.8], respectively, $P = 0.74$). No statistically significant differences were observed in counts/min for all accelerometer days between the control and exercise groups at baseline, month 2, or month 4 (Table 2, Figure 4). Similarly, no statistically significant differences were observed when only nonexercise days were included. The change per month in counts/min for all accelerometer days and nonexercise

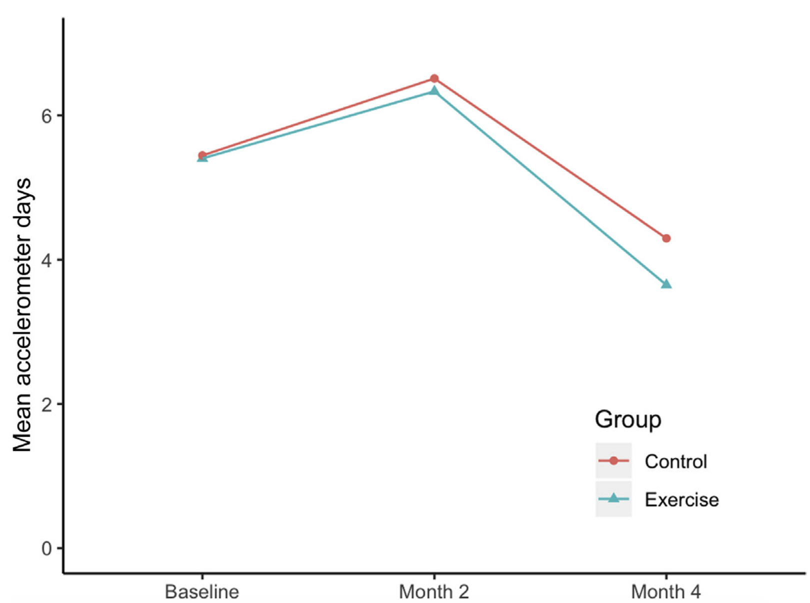

Figure 2. Mean days that accelerometer was worn at baseline, month 2, and month 4 for controls and exercise groups.

Table 2. Counts per minute for controls and treatment group

	Nonexercise days			All accelerometer days		
Time point	Control (n = 44)	Treatment (n = 48)	*P* value	Control (n = 44)	Treatment (n = 48)	*P* value
Baseline	250.0 (7.2, 460.6)	344.3 (12.4, 507.2)	0.281	250.0 (7.2, 460.6)	344.3 (12.4, 507.2)	0.281
Mo 2	247.2 (8.9, 447.3)	378.8 (9.0, 562.5)	0.880	247.2 (8.9, 447.3)	378.8 (7.4, 645.9)	0.639
Mo 4	257.5 (6.2, 467.3)	201.0 (6.2, 527.2)	0.985	257.5 (6.2, 467.3)	319.4 (8.7, 566.2)	0.718
Mo 2 and 4	237.5 (6.5, 444.4)	250.9 (7.7, 529.8)	0.740	237.5 (6.5, 444.4)	354.5 (8.1, 531.0)	0.381
Baseline to mo 2	−1.5 (−53.5, 26.7)	1.9 (−29.4, 39.2)	0.863	−1.5 (−53.5, 26.7)	0.9 (−11.1, 83.6)	0.611
Baseline to mo 4	−1.3 (−74.0, 5.6)	−2.1 (−59.8, 2.5)	0.319	−1.3 (−74.0, 5.6)	2.3 (−19.1, 41.2)	0.868
Change/mo	Ref	0.96 (0.91, 1.02)	0.208	Ref	0.96 (0.91, 1.02)	0.197

Ref, Reference.
Data are median (25th, 75th percentile) or β (95% confidence interval). "All accelerometer days" includes all days on which an accelerometer was worn. "Nonexercise days" includes only accelerometer days on which individuals in the exercise group did not participate in the exercise intervention.

days was 4% lower in the exercise group relative to that in the controls (95% CI = 9% lower – 2% higher) (Table 2).

No differences were found for baseline, month 2, month 4, counts/min over months 2 and 4, or change in counts/min between control and exercise groups

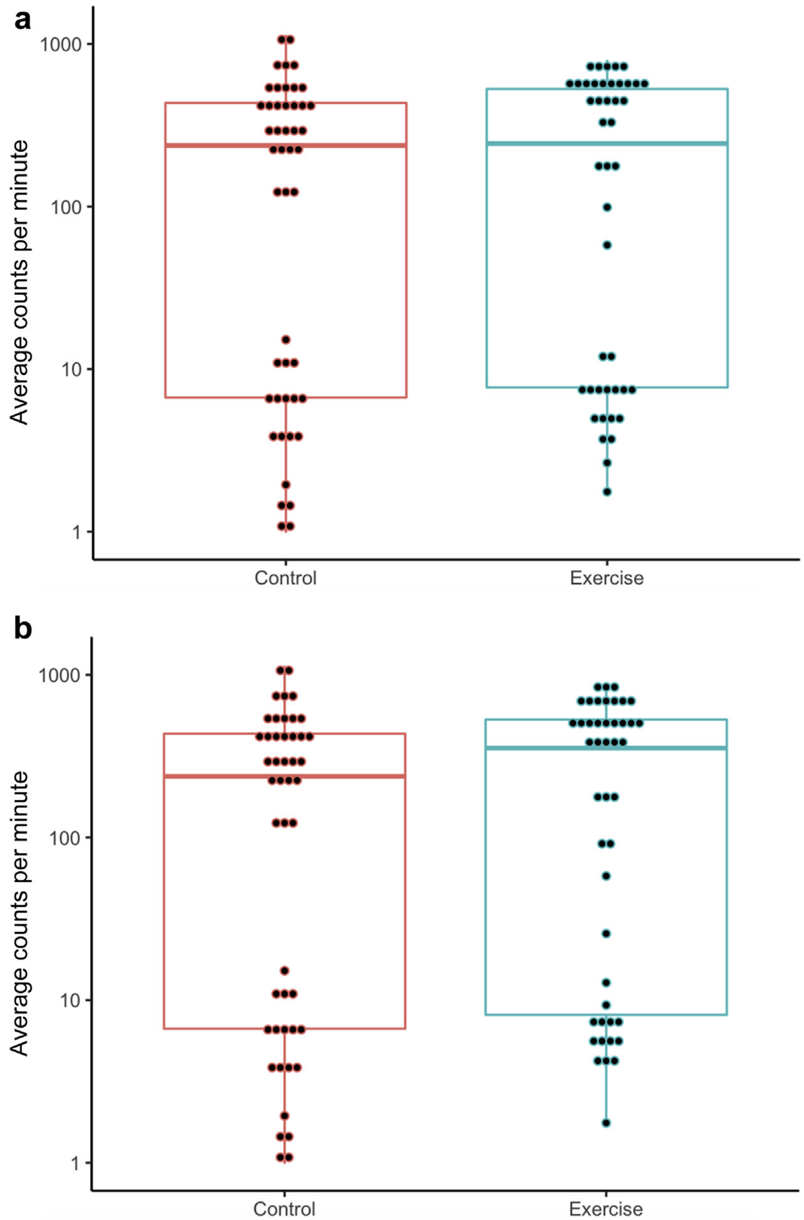

Figure 3. Boxplot of counts/min over month 2 and month 4 for controls and exercise groups for (a) nonexercise days and (b) all accelerometer days.

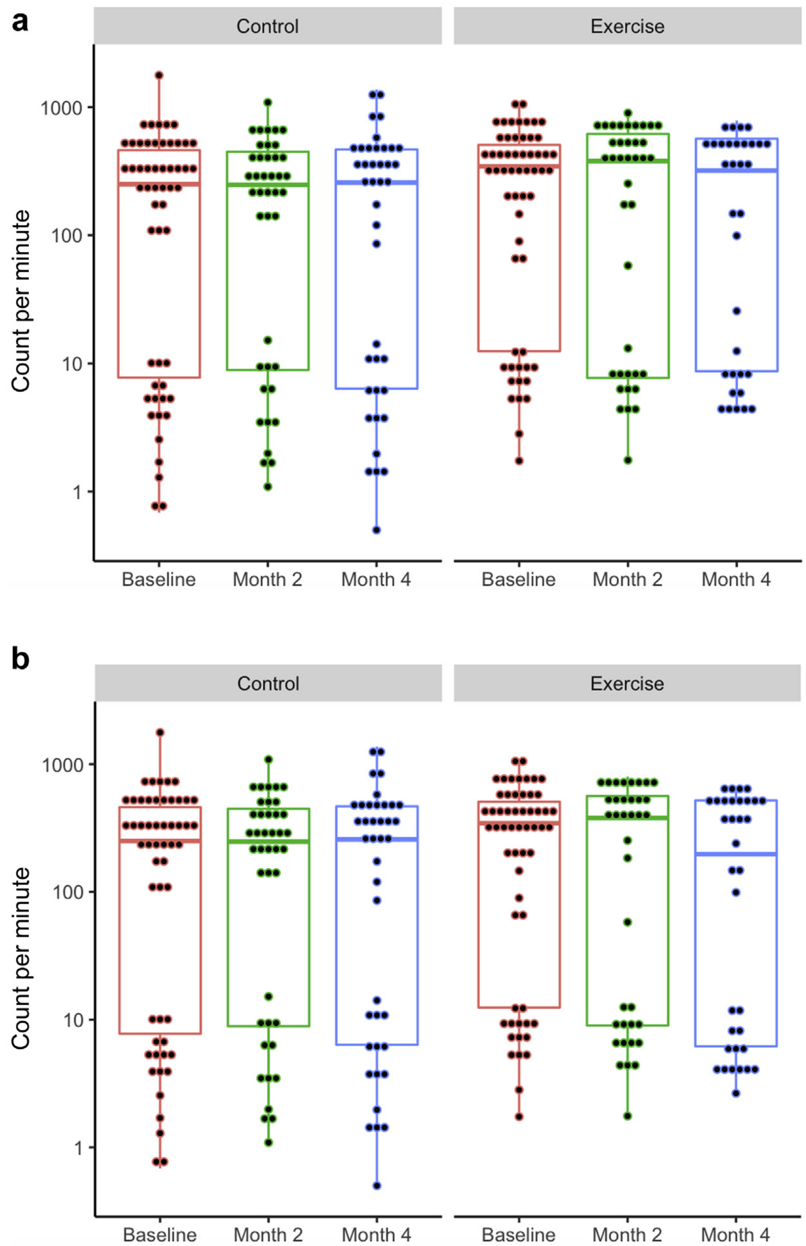

Figure 4. Boxplot of counts/min at baseline, month 2, and month 4 for controls and exercise groups for (a) nonexercise days and (b) all accelerometer days.

among participants below the median activity level (counts/min ≤345) (Table 3). In the group with baseline counts/min above median, counts/min did not differ between control and exercise groups for all accelerometer days (434.3 [interquartile range, 383.0, 557.7] vs. 531.0 [interquartile range, 450.5, 707.0], respectively, P=0.58). Similarly, no statistically significant differences were observed when only nonexercise days were included for those with baseline counts/min above the median. The change per month in counts/min for all accelerometer days in participants with above-median counts/min was 4% lower in the exercise group relative to the controls (95% CI, 15% lower – 9% higher). In participants with below-median counts/min, for all accelerometer days, the change per month was 13% lower in the exercise group relative to controls (95% CI, 33% lower – 14% higher; Table 3).

Participants with less than 73% adherence to the exercise intervention were younger and more likely to be black and to have hypertension (Supplemental Table S1). The median eGFR was higher in participants with more than 73% adherence. Counts/min at baseline, month 2, and month 4 for controls and each adherence group are shown in Table 4. Minutes/d in sedentary, light, moderate, and vigorous activity at baseline, month 2, and month 4 are shown in Supplemental Table S2. Counts/min at baseline, month 2, and month 4 stratified by baseline percentage of sedentary time are shown in

Table 3. Counts per minute for controls and treatment group stratified by baseline median counts/min

	Median ≤345			Median >345		
Time point	Control (n = 25)	Treatment (n = 19)	*P* value	Control (n = 26)	Treatment (n = 22)	*P* value
Nonexercise days						
Baseline	53.0 (4.7, 242.1)	38.5 (8.3, 211.0)	0.648	531.6 (458.8, 668.0)	528.0 (441.9, 713.9)	0.993
Mo 2	12.9 (3.7, 237.9)	9.3 (5.9, 183.9)	0.660	451.1 (326.9, 624.9)	576.5 (471.4, 739.3)	0.918
Mo 4	10.3 (3.3, 173.2)	8.2 (4.7, 133.1)	0.819	466.8 (370.2, 530.5)	535.9 (427.5, 598.3)	0.229
mo 2 and 4	10.4 (3.6, 200.9)	8.3 (5.2, 163.0)	0.980	434.3 (383.0, 557.7)	532.4 (502.2, 637.7)	0.444
Baseline–mo 2	–0.9 (–22.3, 3.9)	1.9 (–4.2, 5.6)	0.764	–19.6 (–182.5, 95.4)	–2.1 (–75.3, 68.0)	0.994
Baseline–mo 4	–0.2 (–38.6, 1.9)	–0.7 (–2.0, 5.0)	0.941	–53.3 (–105.8, 42.5)	–57.6 (–118.3, –2.7)	0.195
Change/mo	Ref	0.87 (0.67, 1.13)	0.312	Ref	0.96 (0.85, 1.10)	0.567
All accelerometer days						
Baseline	53.0 (4.7, 242.1)	38.5 (8.3, 211.0)	0.648	531.6 (458.8, 668.0)	528.0 (441.9, 713.9)	0.993
Mo 2	12.9 (3.7, 237.9)	7.4 (5.5, 183.9)	0.776	451.1 (326.9, 624.9)	618.2 (461.4, 747.1)	0.766
Mo 4	10.3 (3.3, 173.2)	8.9 (6.2, 133.1)	0.539	466.8 (370.2, 530.5)	566.3 (464.3, 600.6)	0.292
Mo 2 and 4	10.4 (3.6, 200.9)	11.1 (6.2, 163.0)	0.727	434.3 (383.0, 557.7)	531.0 (450.5, 707.0)	0.583
Baseline–mo 2	–0.9 (–22.3, 3.9)	0.3 (–4.2, 39.2)	0.584	–19.6 (–182.5, 95.4)	16.2 (–53.9, 122.4)	0.836
Baseline–mo 4	–0.2 (–38.6, 1.9)	2.3 (–0.8, 16.9)	0.258	–53.3 (–105.8, 42.5)	–7.9 (–125.8, 80.6)	0.249
Change/mo	Ref	0.87 (0.67, 1.14)	0.314	Ref	0.96 (0.85, 1.09)	0.559

Ref, Reference.
Data are median (25th, 75th percentile) or β (95% confidence interval). “All accelerometer days” includes all days on which an accelerometer was worn. “Nonexercise days” includes only accelerometer days on which individuals in the exercise group did not participate in the exercise intervention.

Supplemental Table S3. Counts/min stratified by gender are shown in Supplemental Table S4. No differences were found for baseline, month 2, month 4, counts/min over months 2 and 4, or change in counts/min between control and exercise groups stratified by percentage of sedentary time or gender. When stratified by dietary restriction, no differences in counts/min were found between the usual diet and caloric restriction groups among those in the exercise group.

DISCUSSION

In this study, we determined whether total weekly physical activity over a 4-month period increased with a supervised exercise intervention in patients with moderate-to-severe CKD. Engaging in this exercise intervention did not appreciably increase overall weekly physical activity in the study participants. No differences in counts per minute or change per month were found at any time point between the control and exercise groups.

Patients with chronic diseases benefit from engaging in healthy lifestyle behaviors. Recent studies have shown that higher physical activity levels are associated with lower risk of CKD and slower decline in eGFR.[14–20] The American Heart Association (AHA) gives practical guidance for exercise and physical activity, recommending moderate-intensity exercise for

Table 4. Counts per minute for controls and treatment group stratified by adherence

Time point	Control	Adherence <73%	*P* value	Control	Adherence ≥73%	*P* value
Nonexercise days						
Baseline	276.0 (6.1, 501.7)	312.2 (66.7, 441.9)	0.247	276.0 (6.1, 501.7)	353.5 (6.4, 533.9)	0.806
Mo 2	266.3 (12.0, 449.2)	365.1 (96.6, 630.3)	0.540	266.3 (12.0, 449.2)	415.1 (8.1, 590.6)	0.710
Mo 4	283.2 (6.5, 467.8)	163.0 (11.2, 527.2)	0.718	283.2 (6.5, 467.8)	394.7 (6.7, 550.1)	0.899
Mo 2 and 4	259.4 (6.9, 444.4)	250.9 (55.1, 536.6)	0.374	259.4 (6.9, 444.4)	399.0 (8.0, 532.4)	0.871
Baseline–mo 2	–1.2 (–42.6, 28.2)	14.8 (–8.3, 66.0)	0.106	–1.2 (–42.6, 28.2)	2.4 (–9.3, 56.6)	0.429
Baseline–mo 4	–0.6 (–61.0, 7.4)	–1.3 (–47.0, 38.4)	0.655	–0.6 (–61.0, 7.4)	–1.9 (–57.6, 2.4)	0.918
Change/mo	Ref	0.98 (0.93, 1.02)	0.311	Ref	0.99 (0.90, 1.08)	0.742
All accelerometer days						
Baseline	276.0 (6.1, 501.7)	312.2 (66.7, 441.9)	0.247	276.0 (6.1, 501.7)	353.5 (6.4, 533.9)	0.806
mo 2	266.3 (12.0, 449.2)	378.8 (183.9, 737.4)	0.260	266.3 (12.0, 449.2)	431.9 (7.3, 590.6)	0.652
mo 4	283.2 (6.5, 467.8)	163.0 (25.6, 566.4)	0.603	283.2 (6.5, 467.8)	427.3 (8.8, 570.7)	0.783
mo 2 and 4	259.4 (6.9, 444.4)	349.1 (99.0, 566.4)	0.188	259.4 (6.9, 444.4)	423.6 (6.6, 523.1)	0.845
Baseline–mo 2	–1.2 (–42.6, 28.2)	37.4 (–5.6, 156.0)	0.018	–1.2 (–42.6, 28.2)	0.7 (–4.2, 56.6)	0.674
Baseline–mo 4	–0.6 (–61.0, 7.4)	16.9 (–0.8, 54.3)	0.797	–0.6 (–61.0, 7.4)	1.0 (–11.0, 48.5)	0.429
Change/mo	Ref	1.01 (0.93, 1.09)	0.869	Ref	1.01 (0.92, 1.10)	0.844

Ref, Reference.
Data are median (25th, 75th percentile). “All accelerometer days” includes all days in which an accelerometer was worn. “Nonexercise days” include only accelerometer days on which individuals in the exercise group did not participate in the exercise intervention.

150 min/wk or 75 min/wk of vigorous activity, and routine counseling in health care visits about exercise and activity. For adults unable to meet the minimum recommendations, the AHA mentions that engaging in some moderate or vigorous physical activity, even if under the recommended amount, is beneficial.[21] Health care providers often recommend exercise to patients in the hope that physical activity levels will increase. Our findings indicate that when patients with CKD participated in a supervised exercise program for 4 months, no differences in overall weekly physical activity existed between those in the exercise and control groups. In addition, participants in this study were not encouraged to increase activity outside of the exercise sessions. The implications of these findings are that activity levels may not change outside of a supervised exercise intervention in patients with CKD, and that, when recommending exercise, patients should additionally be counseled on increasing their habitual level of activity.

Data from the 2016 National Health Interview Survey from the Centers for Disease Control and Prevention suggest that only 21.7% of adults in the United States meet physical activity guidelines for both aerobic and strengthening activity.[22] Individuals with chronic disease are less likely to adhere to healthy lifestyle guidelines. In a review on the effect of prescribed exercise on nonexercise activity, Washburn *et al*. found that compliance in exercise programs ranged from 83% to 100%.[23] Adherence to exercise interventions differs for older individuals and those with chronic diseases. For older individuals in randomized trials of exercise, adherence ranged from 25% to 76%.[24–27] In a review of exercise training in adults with CKD, the reported range of adherence to exercise was 58% to 100%.[28] The median adherence to the exercise intervention in our study was 73%. Compared to trials with healthier individuals, adherence in our study was lower, but it was comparable to that in populations of older individuals with chronic conditions. Our findings suggest that even when controls were compared to only those participants with greater than 73% adherence, no differences were seen in overall physical activity levels over 4 months of monitoring.

Why the exercise intervention did not produce increased overall weekly physical activity in our study is not fully clear. In a review of the effect of exercise on physical activity in adults, Melanson suggests that regular exercise leads to compensatory changes, such as an increase in sedentary time, which may attenuate an increase in physical activity.[29] Previous studies have reported mixed results when examining whether compensatory sedentary behaviors might negate some of the increases in physical activity levels of individuals on exercise regimens.[30–36] The results from the present analysis were consistent, and no differences were observed even when all accelerometer days were included in the analysis. Participants might have viewed the exercise intervention as meeting their "requirement" for healthy behaviors, and thus were less active at other times. A review by Hannan and Bronas suggests that in patients with CKD, fatigue or lack of energy is a primary reason for avoidance of exercise.[7] Additional recovery time may have been necessary to recuperate from the exercise intervention, which could lower activity on non-exercise days. Participants randomized to usual activity also might have increased their activity because of the presence of an accelerometer. A meta-analysis of the effect of wearing accelerometers on physical activity and weight found that accelerometer use only had small positive effects on activity levels, but that these small levels were not clinically relevant.[37] In our study, the small positive effects of accelerometers on activity would be present in both the usual activity and exercise groups.

The current study has several strengths. First, multiple days of accelerometer data were collected for each participant, and data were adjusted for wear time to standardize the measurement. Counts per minute in this study are representative of physical activity that actually occured over a given week. Second, the exercise program was supervised by clinical exercise physiologists and was personalized to the participants' physiological capabilities. Limitations of the study also exist. First, following an exercise regimen is often difficult for individuals to do long term. Second, participants in both the usual activity and exercise groups were asked to wear accelerometers to measure activity, which may have affected behavior. Participants in the control group may have increased their weekly activity because of the wearing of an accelerometer. In addition, our study group may not fully represent the CKD community at large. Finally, we did not collect details of daily activities to provide data for mechanistic insights.

In conclusion, a supervised exercise program did not noticeably increase overall weekly physical activity in patients with moderate-to-severe CKD. Although exercise regimens are often recommended, participation in enjoyable activities such as sports, hobbies, and recreational activities may prove more effective long term to increase physical activity.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

TAI, JH, AA, SAEH, KT, EEE, CMM, KAM, and MG researched the idea, designed the study, and acquired the data; MMP, TGS, LL, and CR-C analyzed and interpreted the data; MMP, TGS, and CR-C analyzed the statistics; and TAI, JH, CR-C, LL, and TGS supervised and mentored. Each author contributed important intellectual content during manuscript drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy and integrity of any portion of the work are appropriately investigated and resolved.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Participant baseline characteristics, according to adherence.

Table S2. Difference between sedentary time and light, moderate, and vigorous activity in the control and treatment group (median min/d [25th, 75th percentile]).

Table S3. Counts per minute for controls and treatment group stratified by baseline percentage sedentary time (median [25th, 75th percentile] or β [95% CI]).

Table S4. Counts per minute for controls and treatment group stratified by gender (median [25th, 75th percentile]).

CONSORT Checklist.

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