Journal of Physical Activity and Health, 2024, 21, 1064-1079
https://doi.org/10.1123/jpah.2023-0597

Human Kinetics
ORIGINAL RESEARCH

Dose–Response Relationships of Moderate to Vigorous Physical Activity and Sedentary Time With Renal Function Indices in Adolescents With Reduced Renal Function: A Cross-Sectional Study

Zisai Wang, Qiuwei Tian, Yujie Xu, Marady Hun, Lin Hu, Mingyi Zhao, and Qingnan He
Department of Pediatrics, Third Xiangya Hospital, Central South University, Changsha, China

Background: This study aimed to explore the associations between moderate to vigorous physical activity (MVPA) and sedentary time with renal function indices in adolescents with kidney disease. ***Methods:*** A cross-sectional study was conducted on 719 adolescents (median age 15 y, 40.6% female) with kidney disease from the National Health and Nutrition Examination Survey 2007–2016. The exposures were MVPA time and sedentary time. Renal metabolic parameters included serum uric acid (SUA), creatinine, blood urea nitrogen, the estimated glomerular filtration rate (eGFR), and the albumin creatinine ratio. Weighted multivariate regression analysis was used to estimate associations between exposures and outcomes. ***Results:*** After stratifying MVPA time, the regression effect values β (95% CI) for MVPA on SUA (Q2: −0.22 [−0.41 to −0.03]; Q3: −0.32 [−0.53 to −0.11]) and creatinine (Q2: −0.08 [−0.15 to −0.01]; Q3: −0.04 [−0.11 to 0.03]) gradually decreased with increasing MVPA time. In males (−0.76 [−1.19 to −0.32]), MVPA time was significantly associated with lower SUA levels compared with females (−0.14 [−0.38 to 0.10]). Notably, female adolescents who had an MVPA time exceeding 420 minutes exhibited lower albumin creatinine ratio (−75.37 [−146.63 to −4.11]). In addition, both recreational MVPA time (−0.26 [−0.45 to −0.06]) and sedentary time (−3.15 [−5.83 to −0.46]) were negatively associated with eGFR. ***Conclusions:*** Our study found an association between MVPA and lower levels of SUA in male adolescents with kidney disease and albuminuria in female adolescents with kidney disease. In addition, MVPA was also negatively associated with creatinine and eGFR, whereas sedentary time was only associated with eGFR. Further studies are needed to confirm these findings.

Keywords: sedentary behavior, kidney disease, NHANES, weighted multivariate regression analysis, sex stratification

Key Points

- In adolescents with kidney disease, participation in moderate to vigorous physical activity (MVPA) is negatively correlated with levels of creatinine and estimated glomerular filtration rate (eGFR).
- Sex stratification reveals that MVPA is associated with lower serum uric acid levels in males and lower albuminuria levels in females. However, sedentary time is only associated with eGFR.

Tian https://orcid.org/0009-0001-6155-3704
Xu https://orcid.org/0009-0000-2462-190X
Hun https://orcid.org/0000-0001-8339-3361
Hu https://orcid.org/0000-0002-2987-4209
Zhao https://orcid.org/0000-0002-2884-0736
He https://orcid.org/0000-0001-5229-9583
Wang https://orcid.org/0009-0005-3746-7741
Wang and Tian contributed equally to this work and are co-first authors. He (heqn2629@csu.edu.cn) and Zhao (zhao_mingyi@csu.edu.cn) are corresponding authors.

Reduced renal function is a hallmark of kidney disease and is usually defined as an estimated glomerular filtration rate (eGFR) of ≤60 mL/min/1.73 m^2.[1] The latest report indicates that the prevalence of a reduced eGFR among children aged 12–17 years in the United States is approximately 0.51%, and the prevalence of progression to end-stage renal disease has increased by approximately 1.8% over the past decade.[2] Although renal replacement therapy significantly extends the survival of adolescents with end-stage renal disease, it also entails a concomitant decline in health-related quality of life.[3] Furthermore, as adolescent chronic kidney disease (CKD) patients are also in a critical period of growth and development, rapid growth may exacerbate CKD-related complications, such as abnormalities in bone metabolism, anemia, endocrine disorders, and malnutrition, potentially impacting into adulthood.[4] CKD has emerged as a major threat to the quality of life of adolescents.[5]

Moderate to vigorous physical activity (MVPA) refers to PA performed at >3 METs.[6] Numerous observational studies have

found that appropriate PA is associated with improved kidney function and blood pressure in patients with kidney disease.[7] However, nearly all of these studies focus on adult CKD patients. Sedentary time typically refers to time spent in sitting, reclining, or lying positions, which can occur during various educational, cultural, social, and transportation activities.[8] In middle-aged adults, increased sedentary time has been independently associated with decreased eGFR, accelerated renal unit loss, and a higher risk of CKD.[9] However, similar research among adolescents is limited. Evidence suggests that long-term management of CKD can delay its progression to requiring dialysis or kidney replacement therapy.[10] Therefore, exploring preventive strategies beneficial to kidney function in pediatric and adolescent kidney disease patients is essential.

Many indicators are used to evaluate kidney function in kidney disease patients. For example, serum uric acid (SUA) is the end product of purine metabolism, with about 2/3 being excreted through urine.[11] Its elevation indirectly reflects a decline in kidney filtration function. Similarly, creatinine and blood urea nitrogen are end products of creatine and protein metabolism, respectively, both of which typically increase when kidney function loss exceeds 50%, indicating more severe kidney damage.[12] The eGFR is an imperfect estimate of true kidney filtration, usually based on measurement of endogenous or exogenous markers, but is susceptible to influences such as ethnicity.[13] Finally, the albumin creatinine ratio (ACR) is a recommended indicator comparable with 24-hour urine protein quantification, accurately identifying urinary protein excretion in the population.[14]

Previous research has identified a notable sex differences in the PA levels of adolescents.[15] Based on this finding, we hypothesize that MVPA is positively associated with renal function indices in adolescents with kidney disease and sedentary time is negatively associated, potentially with sex differences. Therefore, this study was conducted to investigate the dose–response relationship between MVPA and sedentary time with various renal function indices in adolescents with kidney disease, aiming to provide guidance for renal function protection strategies.

Methods

Study Population

The National Health and Nutrition Examination Survey (NHANES) is a large-scale cross-sectional survey that began in the early 1970s. This survey employs a methodology involving multistage and multiple probability sampling, surveying approximately 5000 individuals across 15 different counties in the United States. Ultimately, it represents a population of about 65,000 individuals nationwide with similar characteristics. The survey is periodically updated with new data on a 2-year cycle.[16] Individuals aged 18 years and older provided informed consent, and consent was obtained from guardians for those under 18 years.

All demographic, examination, laboratory, and questionnaire data from the NHANES for the 5 survey periods (2007–2016) were included. This study first excluded adolescents under 12 years old (n = 14,789) and over 19 years old (n = 29,201). Further exclusions were made for individuals with missing renal function indices (n = 1078), MVPA time (n = 139), and sedentary time (n = 2). Finally, nonkidney disease adolescents were excluded based on guidelines (n = 4660), resulting in a total of 719 adolescents with kidney disease included in the study. The analysis and processing of the included data were performed under the relevant guidelines published on the NHANES website. The NHANES protocol was reviewed by the National Center for Health Statistics Research Ethics Review Board. The data are publicly available and accessible at www.cdc.gov/nchs/nhanes/. The inclusion and exclusion criteria are shown in Figure A1 in the Appendix section.

Measurement of MVPA Time and Sedentary Time

One of the exposure variables was weekly duration of MVPA. The NHANES PA questionnaire is based on the Global Physical Activity Questionnaire and includes questions related to daily activities, leisure-time activities, and sedentary activities.[17] MVPA was collected across 3 domains, including recreational, occupational, and transportation. Total MVPA time was defined in this study as the sum of the 3 measurements. Recreational MVPA time was used as the predominant MVPA time for adolescents. It includes moderate-intensity exercise, fitness, or recreational activities (such as brisk walking, bicycling, swimming, and volleyball) and vigorous-intensity exercise, fitness, or recreational activities (such as running and basketball), each lasting at least 10 minutes and causing a slight or significant increase in breathing or heart rate.[17] The definition of weekly transportation MVPA time includes the time spent walking or cycling for commuting purposes (such as going to school, going shopping, or going to work).[17] Weekly occupational MVPA time refers to the time spent each week on moderate- (such as brisk walking or carrying light loads) and vigorous-intensity activities (such as carrying heavy loads, digging, or construction work) during paid or unpaid work, study or training, housework, and yard work.[17,18] Similarly, each activity lasts at least 10 minutes and causes a slight or significant increase in breathing or heart rate. Another exposure variable included in this study was daily sedentary time, defined as the time spent sitting during activities such as schooling, commuting, and socializing, including time at a desk, in a vehicle, reading, playing cards, watching television, or using a computer, excluding time spent sleeping.[8,17]

Measurement of Indices of Kidney Function

The eGFR was calculated using the Schwartz equation: $eGFR = 0.413 \times [\text{height (cm)}/\text{creatinine (mg/dL)}]$.[19] Adolescent kidney disease was defined as an eGFR < 60 mL/min/1.73 m^2 or an ACR ≥ 30 mg/g.[20] The uric acid in the serum concentrations was measured using the timed endpoint method.[21] The Jaffe rate method was used to measure creatinine concentrations and blood urea nitrogen concentrations in serum.[22] Urinary albumin and urinary creatinine concentrations were measured using fluorometric and enzymatic assays, respectively.[23,24] The ACR was derived from the ratio of urinary albumin to creatinine.

Examination and Screening of Covariates

Based on previous studies, we included age, sex, race, income-to-poverty ratio, 6-month time period, and insurance type as fixed adjusted covariates in this study.[24,25] Regression coefficients (β values) and 95% CIs for associations between independent variables and indices of renal function were estimated one at a time using a linear risk regression model. The model included 1 covariate at a time, and if the covariate changed, the estimate of the independent variable on the dependent variable by >10%, it was included as a confounder in the final model.

Statistical Analysis

Data analysis was always performed under the guidance of the Centers for Disease Control and Prevention. Based on the complex sampling design, we integrated the sample weights of the included variables during the analysis of the data. All continuous variables are expressed as medians of the first and third quartiles; categorical variables are expressed as counts and percentages of 95% CIs. The recommended amount of MVPA (>420 min/wk) for adolescents was used to indicate meeting guidelines.[26] The median sedentary time (exceeding 480 min/d) was used as the cutoff for categorizing high or low sedentary time.

Two models were constructed for the analysis. Model 1 was the baseline model without adjusting for any covariates. Model 2 was the adjusted model incorporating the following covariates: age, sex, race, income-to-poverty ratio, 6-month time period, insurance coverage, and additional variables identified as potentially influencing the associations between the independent and dependent variables. To investigate sex differences in the results, data analysis was stratified by sex in various models. Recreational MVPA time and total MVPA time were included as continuous variables in the multiple regression model. Trend tests were used to evaluate the stability of regression analysis results obtained after stratifying the independent variables. As sedentary time was only significantly associated with eGFR, further stratified analysis and interaction tests were conducted to describe differences among adolescents with varying characteristics.

Smoothed curve fitting and weighted generalized additive models were used to describe the nonlinear correlations. The curvilinear relationship between time spent in MVPA and renal function indices was further fitted, stratified by sex. A 2-segment linear regression model was further applied to determine the inflection point values of time spent in MVPA on each renal function index. All analyses were performed with the R (http://www.Rproject.org) and EmpowerStats (http://www.empowerstats.com) packages, with a P value < .05 considered to indicate statistical significance.

Results

Description of the Baseline Characteristics of the Population

The demographic characteristics and covariate distributions are shown in Table 1. In the present study, we included 719 individuals with a median age of 15 years, 40.60% of whom were female and 59.40% of whom were male. The ethnic distribution demonstrated diversity, with 11.68% being non-Hispanic Black, 28.23% Mexican American, 29.07% other Hispanic, and 10.29% representing other races. After sex stratification, there were significant differences in examination indices, including weight, height, systolic blood pressure, and diastolic blood pressure (P < .05). Male adolescents had higher median values for weight (60.30 vs 54.90 kg), height (170.30 vs 160.60 cm), and systolic blood pressure (109 vs 106 mm Hg) compared with female adolescents, whereas female adolescents had a higher median value for diastolic blood pressure (61 vs 59 mm Hg) compared with male adolescents. In addition to ACR, renal function indices also differed significantly between males and females (P < .05). Compared to females, males had significantly higher median values for blood urea nitrogen (11.00 vs 10.00 mg/dL), creatinine (0.78 vs 0.64 mg/dL), and SUA (5.40 vs 4.20 mg/dL). However, the median eGFR in females was significantly higher compared with males (104.20 vs 91.00 mL/min/1.73 m^2). Finally, in addition to transportation MVPA time, there were significant sex differences in weekly MVPA time and sedentary time between male and female adolescents (P < .05). Male adolescents reported significantly longer durations of MVPA compared with females, but the median sedentary time was the same (480 vs 480 min).

The Association Between MVPA and Renal Function in Adolescents With Kidney Disease

The associations between MVPA and various renal function indices are shown in Table 2 and Table A2 in the Appendix section. As shown in Table 2, a negative correlation was observed between weekly recreational MVPA time and eGFR (β = −0.26, 95% CI: −0.45 to −0.06; Table 2 and Figure A2 in Appendix section). However, after summing the recreation, transportation, and occupational times, the association between total MVPA time and eGFR changed to − 0.07 mL/min/1.73 m^2 (β = −0.07, 95% CI: −0.17 to 0.02; Table 2 and Figure A3 in Appendix section). The MVPA time has been stratified to better observe the associations between different MVPA durations and various renal function indices. The results showed that adolescents who engaged in 0 to 420 minutes of recreational MVPA per week had lower creatinine levels (Q2: β = −0.08, 95% CI:−0.15 to −0.01) than did those who did not engage in any MVPA during the week. Similarly, the SUA levels (Q2: β = −0.22, 95% CI:−0.41 to −0.03; Q3: β = −0.32, 95% CI:−0.53 to −0.11) were lower in the group with a longer duration of MVPA each week. The result of the trend test for the association between MVPA duration and SUA was significant (P for trend < .05). In addition, there was a significant difference between adolescents who engaged in more than 420 minutes of MVPA per week and those with no weekly MVPA in model 2 (β = −0.31, 95% CI: −0.54 to −0.08). Sex stratification revealed that the decrease in SUA levels was greater in males (β = −0.76, 95% CI: −1.19 to −0.32) compared with females (β = −0.14, 95% CI: −0.38 to 0.10) (Table A2 in Appendix section and Figure 1). Notably, female adolescents who had a weekly MVPA duration exceeding 420 minutes exhibited lower ACR (β = −75.37, 95% CI: −146.23 to −4.11; Table A2 in Appendix section and Figure 1).

The Association Between Sedentary Time and Renal Function in Adolescents With Kidney Disease

The associations between sedentary time and various renal function indices are shown in Table 2 and Table A3 in the Appendix section. As shown in Table 2, each 1-hour increase in sedentary time showed a lower level of SUA (β = −0.00, 95% CI:−0.03 to 0.02), creatinine (β = −0.01, 95% CI: −0.02 to 0.00), eGFR (β = −0.22, 95% CI: −0.70 to 0.25), and ACR (β = −4.35, 95% CI: −12.04 to 3.35), but none of the findings reached statistical significance. However, model 2 showed that individuals with >8 hours of daily sedentary time had a lower mean eGFR (β = −3.35, 95% CI: −5.83 to −0.46) compared with those who spent <8 hours per day. The trend test results were significant (P for trend < .05; Table 2 and Table A3 in Appendix section).

In addition, we further analyzed the variability in the association between sedentary behavior and the eGFR by subgroup analysis (Table A4 in Appendix section). The results showed that the association between sedentary behavior and the eGFR was significant among adolescents younger than 15 years old (β = −4.72, 95% CI: −9.04 to −0.40) and among adolescents from

Table 1 Description of 719 Participants Included in the Present Study

Characteristics	Overall (N = 719)	Males (n = 292)	Females (n = 427)	*P*
Age, median (Q1–Q3)	15.00 (13.00–17.00)	15.00 (13.00–17.00)	15.00 (13.00–17.00)	.605
Race, %				.222
Non-Hispanic Black	84 (11.68%)	31 (10.62%)	53 (12.41%)	
Mexican American	203 (28.23%)	93 (31.85%)	110 (25.76%)	
Other Hispanic	209 (29.07%)	89 (30.48%)	120 (28.10%)	
Non-Hispanic Black	74 (10.29%)	25 (8.56%)	49 (11.48%)	
Other race	149 (20.72%)	54 (18.49%)	95 (22.25%)	
Income-to-poverty ratio, %				.532
<1	191 (28.81%)	81 (30.11%)	110 (27.92%)	
≥1, <2	185 (27.90%)	68 (25.28%)	117 (29.70%)	
≥2, <3	107 (16.14%)	40 (14.87%)	67 (17.01%)	
≥3, <4	73 (11.01%)	31 (11.52%)	42 (10.66%)	
≥4	107 (16.14%)	49 (18.22%)	58 (14.72%)	
Missing	56 (7.78%)	23 (7.87%)	33 (7.73%)	
Insurance coverage, %				.596
No insurance	107 (14.88%)	41 (14.04%)	66 (15.46%)	
Private insurance	311 (43.25%)	133 (45.55%)	178 (41.69%)	
Medicaid insurance	183 (25.45%)	68 (23.29%)	115 (26.93%)	
Missing	118 (16.41%)	50 (17.12%)	68 (15.93%)	
Weight, kg	56.90 (49.45–68.85)	60.30 (52.08–72.83)	54.90 (48.75–65.20)	<.001
Height, cm	163.90 (158.35–170.20)	170.30 (163.80–177.22)	160.60 (156.05–165.50)	<.001
BMI, kg/m^2	21.00 (18.70–24.39)	20.70 (18.51–23.96)	21.10 (19.09–24.65)	.051
SBP, mm Hg	107.00 (101.00–114.00)	109.00 (102.25–115.00)	106.00 (100.00–112.00)	<.001
DBP, mm Hg	60.00 (53.00–67.00)	59.00 (51.00–67.00)	61.00 (55.00–68.00)	.004
BUN, mg/dL	10.00 (8.00–13.00)	11.00 (9.00–14.00)	10.00 (8.00–12.00)	<.001
Creatinine, mg/dL	0.68 (0.58–0.80)	0.78 (0.65–0.97)	0.64 (0.56–0.72)	<.001
SUA, mg/dL	4.60 (3.90–5.50)	5.40 (4.70–6.30)	4.20 (3.70–4.85)	<.001
Urinary albumin, mg/dL	81.40 (35.90–163.30)	79.50 (30.80–163.45)	83.20 (39.25–162.75)	.597
Urinary creatinine, mg/dL	139.00 (76.00–205.00)	159.00 (94.75–231.25)	127.00 (67.50–185.00)	<.001
ACR, mg/g	57.86 (38.07–112.55)	51.22 (34.17–97.68)	61.00 (41.16–116.60)	.151
eGFR, mL/min/1.73 m^2	99.90 (86.55–114.70)	91.00 (75.90–105.12)	104.20 (93.05–118.50)	<.001
Occupational MVPA time, min	0.00 (0.00–90.00)	0.00 (0.00–180.00)	0.00 (0.00–60.00)	.039
Transportation MVPA time, min	0.00 (0.00–90.00)	20.00 (0.00–125.25)	0.00 (0.00–90.00)	.121
Recreational MVPA time, min	180.00 (20.00–465.00)	312.50 (120.00–600.00)	120.00 (0.00–347.50)	<.001
Total MVPA time, min	360.00 (120.00–750.00)	535.00 (240.00–960.00)	240.00 (75.00–600.00)	<.001
Sedentary time, min	480.00 (360.00–600.00)	480.00 (360.00–600.00)	480.00 (360.00–600.00)	.018

Abbreviations: ACR, albumin creatinine ratio; BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity; SBP, systolic blood pressure; SUA, serum uric acid. Note: Median (Q1–Q3) for continuous variables: *P* value was calculated using a weighted linear regression model. n (%) for categorical variables: *P* value was calculated by weighted chi-square test. *P* value < .05 indicates significant differences in characteristics between males and females.

families with higher poverty ratios ($\beta = -14.28$, 95% CI: −24.08 to −4.49 and $\beta = -5.70$, 95% CI: −11.05 to −0.34). After ACR stratification of the study population, it was observed that adolescents with ACR < 30 mg/g had a lower eGFR ($\beta = -2.82$, 95% CI: −5.62 to −0.02).

Threshold Effect Analysis and Smoothing Curve Fitting Based on Sex

Smooth curve fitting was used to describe the potential relationships between MVPA duration and various renal function indices (Figures 1 and 2, Figures A2 and A3 in Appendix section). The relationships of recreational MVPA with SUA and eGFR stratified by sex are shown in Figure 1A and 1D. The 2-segment model revealed the curvilinear relationship between time spent in recreational MVPA and SUA (log likelihood ratio < 0.05; Table A1 in Appendix section). The regression analysis results indicated that with weekly MVPA time <12 hours, each additional hour was associated with a decrease of 0.04 mg/dL in SUA ($\beta = -0.04$, 95% CI: −0.08 to −0.01). However, when the duration of MVPA was between 12 and 24 hours, SUA increased by 0.07 mg/dL ($\beta = 0.07$, 95% CI: −0.00 to 0.14). Finally, MVPA time was negatively

Table 2 The Association of MVPA Time, Sedentary Time, and Various Renal Function Indices

	Measurement of renal function, β (95% CI)				
Measure	**SUA, mg/dL**	**Creatinine, mg/dL**	**BUN, mg/dL**	**eGFR, mL/min/1.73 m^2**	**ACR, mg/g**
Total MVPA time, h	0.00 (–0.00 to 0.01)	0.00 (–0.00 to 0.00)	0.02 (–0.00 to 0.04)	–0.07 (–0.17 to 0.02)	–1.47 (–3.04 to 0.11)
Recreational MVPA time, h	–0.01 (–0.02 to 0.00)	0.00 (–0.00 to 0.01)	0.03 (–0.01 to 0.07)	**−0.26 (−0.45** to **−0.06)***	–2.62 (–5.87 to 0.62)
Q1, 0 min weekly	Reference	Reference	Reference	Reference	Reference
Q2, 0–420 min weekly	**−0.22 (−0.41** to **−0.03)***	**−0.08 (−0.15** to **−0.01)***	0.08 (–0.72 to 0.88)	1.68 (–1.76 to 5.12)	–29.94 (–85.87 to 25.99)
Q3, ≥420 min weekly	**−0.32 (−0.53** to **−0.11)***	–0.04 (–0.11 to 0.03)	0.18 (–0.70 to 1.06)	–2.10 (–5.87 to 1.66)	–45.97 (–106.88 to 14.95)
P for trend	**.004**	.450	.678	.136	.149
Sedentary time, h	–0.00 (–0.03 to 0.02)	–0.01 (–0.02 to 0.00)	0.00 (–0.10 to 0.10)	–0.22 (–0.70 to 0.25)	–4.35 (–12.04 to 3.35)
Q1, <480 min weekly	Reference	Reference	Reference	Reference	Reference
Q2, ≥480 min weekly	–0.04 (–0.19 to 0.12)	–0.01 (–0.06 to 0.05)	–0.43 (–1.07 to 0.20)	**−3.15 (−5.83** to **−0.46)***	–12.15 (–54.96 to 30.65)
P for trend	.638	.822	.181	**.022**	.578

Abbreviations: ACR, albumin creatinine ratio; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity; SUA, serum uric acid.
*Statistical significance ($P < .05$). Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates.

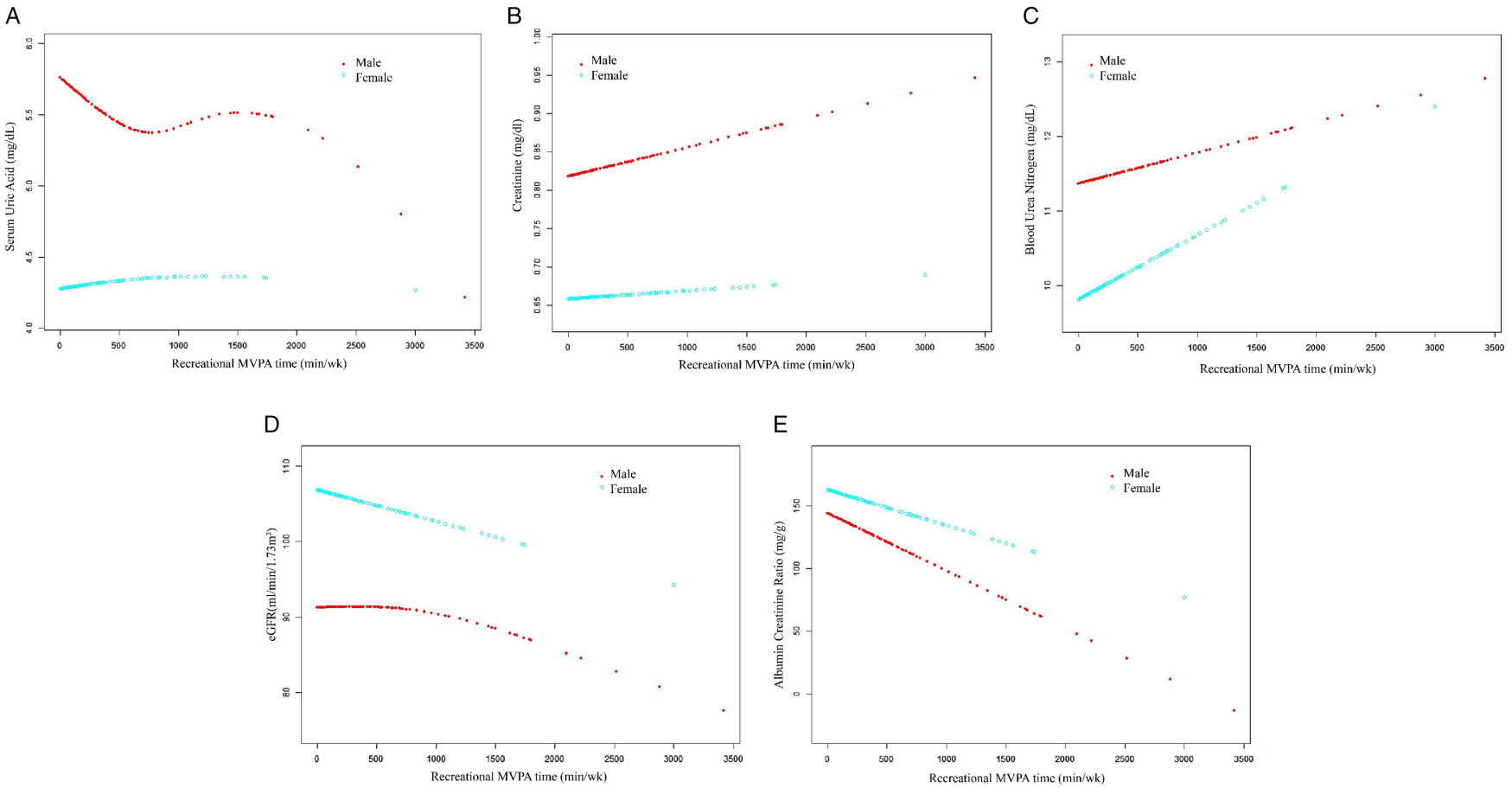

Figure 1 — The association of recreational MVPA time and renal function indices stratified by sex. The dark (red) solid line represents males, and the light (blue) band represents females. Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates. eGFR indicates estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity.

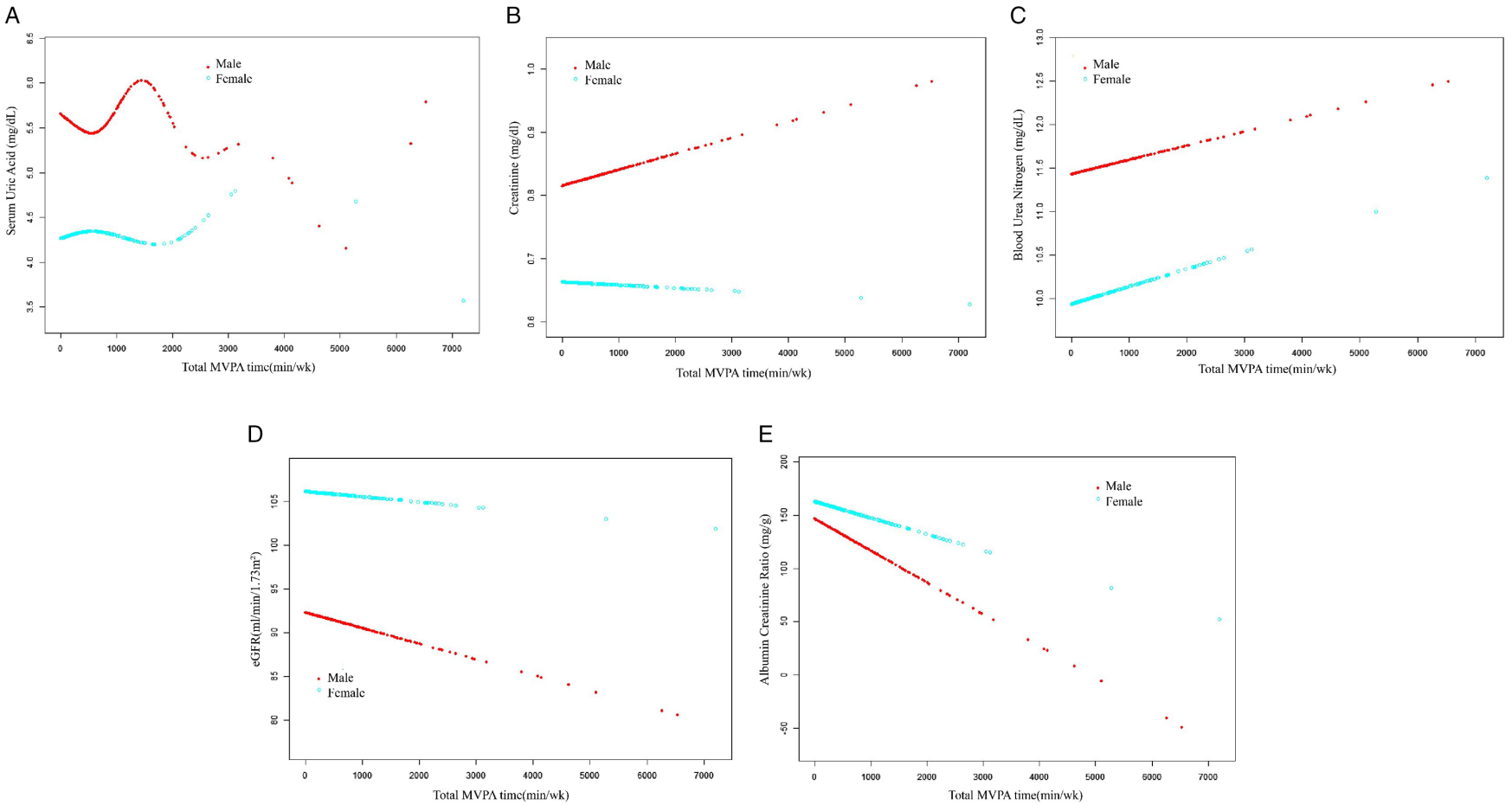

Figure 2 — The association of total MVPA time and renal function indices stratified by sex. The dark (red) line represents males, and the light (blue) band represents females. Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates. eGFR indicates estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity.

associated with eGFR ($\beta = -0.30$, 95% CI: −0.55 to −0.05), which was similar to the results of the regression analysis in Table 2.

Discussion

The present study aimed to investigate the dose-dependent relationship between MVPA time and sedentary time and their respective renal function indices in adolescents with kidney disease aged 12–19 years, with an emphasis on exploring sex differences. The results showed that after stratifying for MVPA time, adolescents with kidney disease showed a gradual decrease in mean SUA and creatinine levels with increasing weekly MVPA time. In males, weekly MVPA time was significantly associated with lower SUA levels compared with females. Notably, female adolescents who had a weekly MVPA time exceeding 420 minutes exhibited lower ACR. In addition, both recreational MVPA time and sedentary time (>480 min/d) were negatively associated with eGFR. However, sedentary time showed no significant association with other renal function indices.

The prevailing view is that patients with CKD should undergo continuous long-term management of uric acid levels.[27] In this study, we observed a negative association between PA and SUA levels, consistent with previous correlational research findings.[28] Some cohort studies also indicate a reduced incidence of hyperuricemia associated with vigorous PA.[29,30] However, the specific mechanisms involved are still unclear and are possibly associated with the improvement of insulin resistance through PA and its indirect role in weight reduction.[28,29]

Further research has shown that the impact of PA on SUA levels varies by sex.[30] For example, Park et al[28] found in their study of nearly 367,000 healthy Korean adults that health-enhancing PA was associated with hyperuricemia in men (odds ratio [OR] = 0.90, 95% CI: 0.86–0.93) but not in women (OR = 1.04, 95% CI: 0.77–1.41). Similarly, our study found that male adolescents with kidney disease engaging in over 420 minutes of MVPA per week had lower average SUA levels. This suggests that MVPA may serve as an effective strategy for reducing SUA levels in male adolescents with kidney disease, although longitudinal studies are needed to confirm this finding.

Serum creatinine is a widely utilized clinical biomarker for evaluating kidney function. In this study, we identified a negative association between creatinine and MVPA time of <420 minutes per week. However, in previous studies, researchers found that PA appears to be associated with both increases and decreases in creatinine levels.[31,32] It is worth noting that these studies were conducted on different populations with various diseases. Furthermore, differences in the intensity and duration of PA, as well as the baseline kidney function of the study subjects, may account for some of the observed discrepancies in the results.

The presence of albuminuria indicates endothelial cell dysfunction and predicts poor prognosis in CKD.[33] Previous studies on the association between PA and ACR have been contentious. Finkelstein et al[34] conducted a survey of 13,753 participants aged 18 years and older and found no significant association between PA and ACR. However, Robinson et al[35] found a significant association between the 2 in a cross-sectional study involving 3587 nondiabetic women. Our study only found this association among female adolescents with kidney disease. The underlying mechanisms by which PA reduces albuminuria remain unclear. One possible reason is that PA affects the regulation of endothelial cell function.[36]

Studies on the association between MVPA and eGFR have shown inconsistent results. A cross-sectional study conducted among Japanese adults aged 35–79 years revealed that, after adjusting for potential covariates, an increase of 10 minutes per day in MVPA was significantly associated with an increase in the eGFR in both men ($\beta = 0.91$; 95% CI: 0.14–1.69) and women ($\beta = 0.70$; 95% CI: 0.055–1.34).[37] Another similar study used metabolic equivalents as a measure of PA time. The results showed that participants engaging in <20 MET-h of MVPA per day had a 0.79 mL/min/1.73 m^2 lower eGFR than those engaging in >20 MET-h per day ($\beta = 0.79$; 95% CI: 0.69–0.87).[38] However, another longitudinal cohort study involving 3935 individuals aged between 26 and 65 years revealed no association between PA and the eGFR.[39] This study revealed an opposite result, showing a negative association between PA and eGFR. The specific mechanism is not clear yet, but it may be influenced by thyroid hormones. Thyroid dysfunction is a common complication in patients with CKD.[40] Study has found that thyroid dysfunction can directly lead to a decrease in renal plasma flow and glomerular filtration rate.[41] In addition, research indicates that thyroid hormone secretion transiently fluctuates during vigorous PA.[42] The decrease in eGFR may be mediated by MVPA affecting the thyroid hormone levels in adolescents with kidney disease. However, further research is needed to investigate the mediating role of thyroid hormones.

Finally, this study revealed a negative correlation between sedentary time and eGFR among adolescents with kidney disease, with no association observed with other renal function indices. Many studies have identified the adverse effects of sedentary behavior on kidney function. Using 2-sample Mendelian randomization analysis, a large observational cohort study revealed both a negative correlation between sedentary behavior and the eGFR and a preliminary validation of genetic susceptibility-mediated causality.[43] Moreover, a study by Hawkins et al[44] revealed that an increase in sedentary time, represented by time spent watching television, was followed by a significant decrease in the eGFR. Although researchers have revealed a significant negative correlation between sedentary behavior and the eGFR,[38,45] the inflection point for the risk is inconclusive. In this study, compared with adolescents with renal disease who were sedentary for <8 hours per day, those who were sedentary for >8 hours per day had a mean decrease in the eGFR of 3.15 mL/min/1.73 m^2. Based on this finding, adolescents with kidney disease should reduce their sedentary time to delay the decline in kidney function, but this conclusion needs causal validation.

This study has several limitations. First, this was a cross-sectional study that could not reveal causality. Second, the eGFR is a proxy for the true glomerular filtration rate based on creatinine, and there may be an error between it and the true value. Third, both MVPA time and sedentary time were obtained from questionnaires and may require more precise instrumental measurements for simultaneous correction. Finally, considering that adolescents with impaired kidney function may avoid engaging in MVPA, the observed negative association between MVPA and eGFR may reflect a reverse causality. Therefore, the generalizability of the findings needs to be verified in a more thorough longitudinal follow-up study.

Conclusions

For adolescents with kidney disease, there is a negative association between MVPA time and SUA, creatinine, eGFR, and ACR. MVPA may benefit males by reducing SUA levels and females by lowering albuminuria. However, due to the negative association between MVPA time and eGFR, caution is necessary for

adolescents with kidney disease engaging in MVPA as it may be necessary to consider the potential overall impact of MVPA on their renal function. Sedentary time is only negatively associated with eGFR. Therefore, we suggest reducing sedentary time in this population. Further longitudinal studies are needed to validate causal relationships.

Acknowledgments

The authors appreciate the time and effort given by participants during the data collection phase of the NHANES project. **Author Contributions:** Wang and Tian contributed equally to this work and are co-first authors. *Participated in the conceptualization, methodology, software, data curation, formal analysis, visualization, and writing original draft:* Wang, Tian. *Participated in the investigation and data curation:* Xu. *Participated in the visualization and data curation:* Hun, Hun. *Participated in the writing—review and editing, supervision, and project administration:* Zhao. *Participated in the writing—review and editing, supervision, project administration, and funding acquisition:* He. **Funding**: This research was funded by Hunan innovative province construction project (Grant No. 2019SK2211), Key Research and Development Project of Hunan Province (Grant No. 2020SK2089), the Natural Science Foundation of Hunan Province (Grant Nos 2020JJ4833, 2019SK2211, and XY040019), Hunan Province Key Field R&D Program (Grant No. 2020SK2097), and Hunan Province Horizontal Project (Grant Nos. KY080269, KY080262, XY080323, and XY080324).

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Appendix

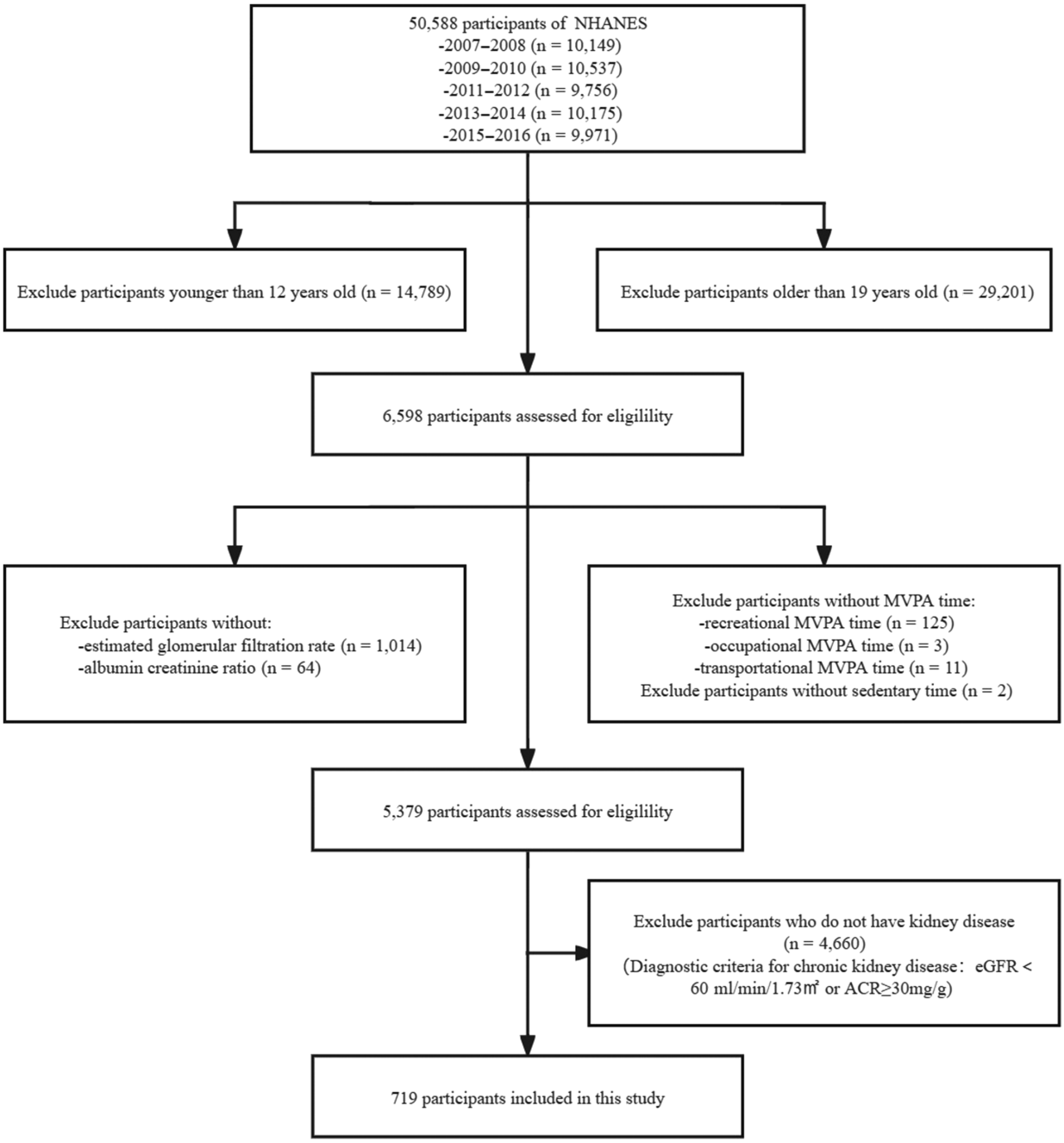

Figure A1 — The inclusion process of study participants. ACR indicates albumin creatinine ratio; eGFR, estimated glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey; MVPA, moderate to vigorous physical activity.

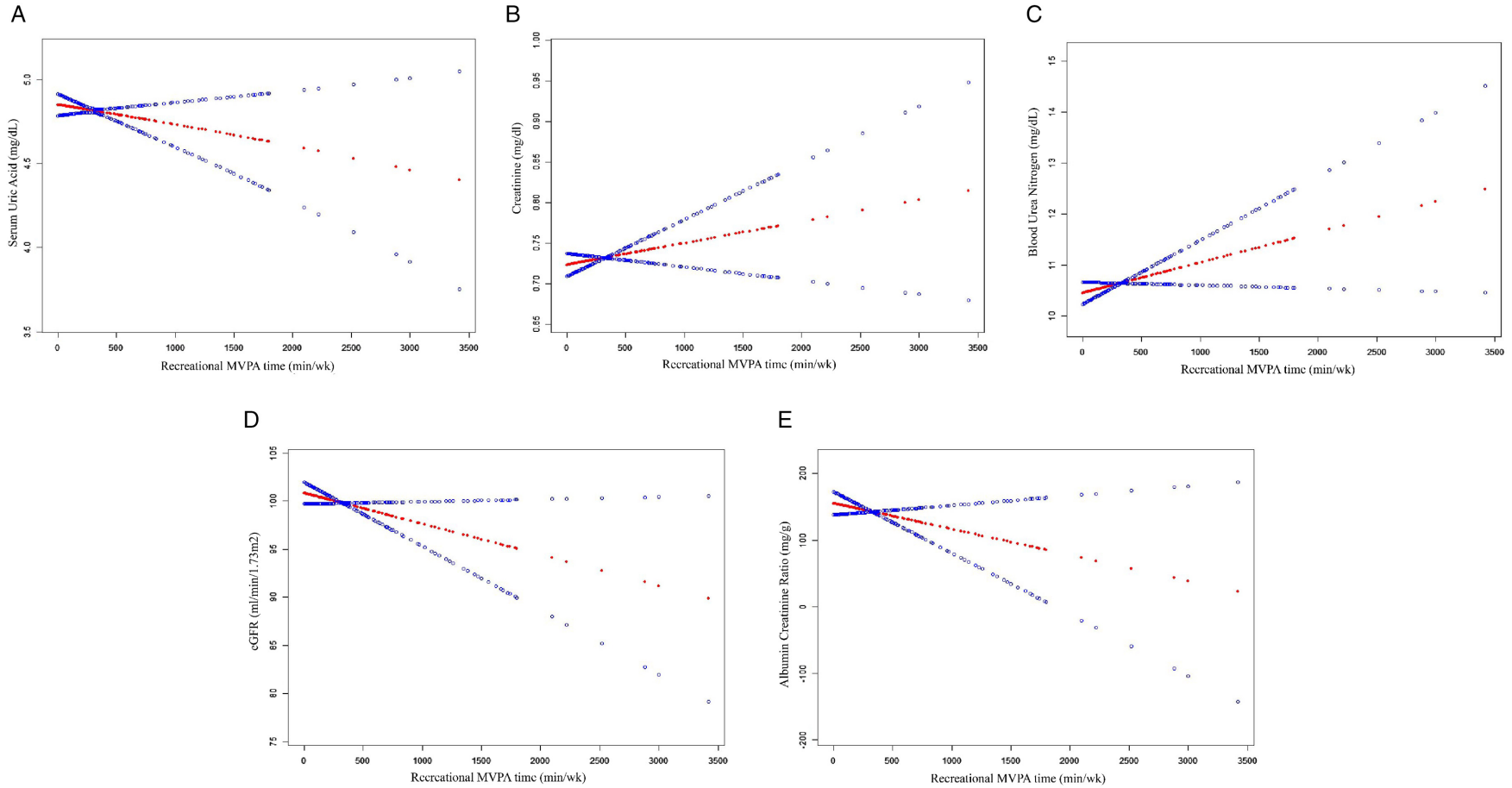

Figure A2 — The association of recreational MVPA time and renal function indices. Each point represents 1 sample. The solid dark (red) line represents the smooth curve fit between variables. The light (blue) bands represent the 95% CIs from the fits. Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates. eGFR, estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity.

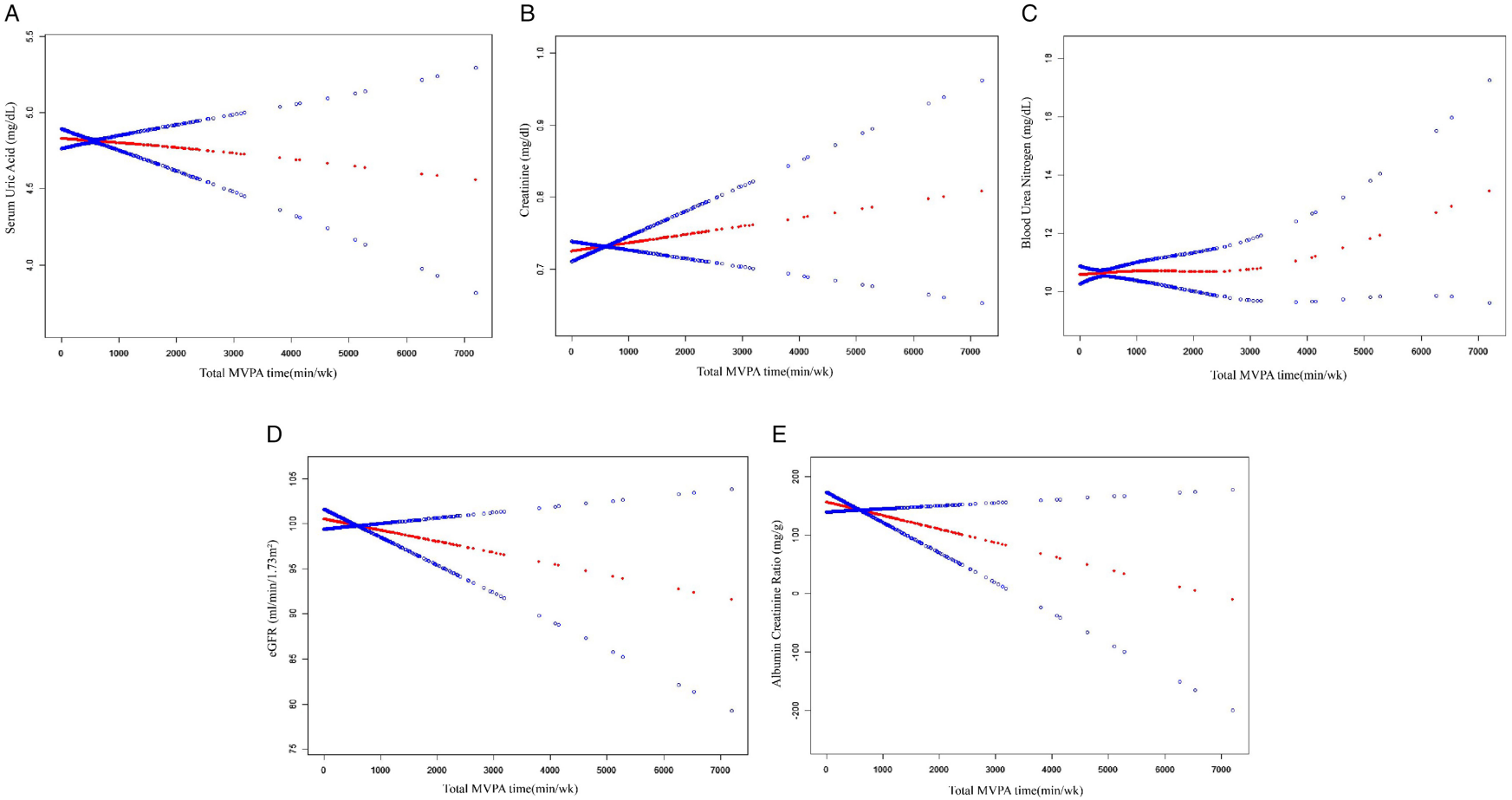

Figure A3 — The association of total MVPA time and renal function indices. Each point represents 1 sample. The solid dark (red) line represents the smooth curve fit between variables. The light (blue) bands represent the 95% CIs from the fits. Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates. eGFR indicates estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity.

Table A1 Thresholds for Analyzing the Association Between Recreational MVPA Time and SUA, eGFR

	Measurement of renal function β (95% CI)		
Measure	**SUA, mg/dL**		**eGFR, mL/min/1.73 m^2**
Recreational MVPA time, h			
Fitting by the standard linear model	**−0.02 (−0.04 to −0.01)***		**−0.30 (−0.55 to −0.05)***
Fitting by the two-piecewise linear model			
Inflection point (K1, K2)	(12,24)		2
Recreational MVPA time < 12 h	**−0.04 (−0.08 to −0.01)***	Recreational MVPA time < 2 h	0.95 (–2.05 to 3.95)
12 ≤ Recreational MVPA time ≤ 24 h	0.07 (–0.00 to 0.14)	Recreational MVPA time ≥ 2 h	–0.35 (–0.64 to –0.07)*
Recreational MVPA time > 24 h	–0.06 (–0.12 to 0.01)		
Log likelihood ratio	**0.004**		0.392

Abbreviations: eGFR, estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity; SUA, serum uric acid.
*Statistical significance ($P < .05$). Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates.

Table A2 Estimated Mean Values of Changes in Renal Function Indices Due to Recreational MVPA Time

	Recreational MVPA time (420 vs 0 weekly min)	
Measure	**Model 1**	**Model 2**
Male		
SUA, mg/dL	–0.71 (–1.19 to –0.24)*	–0.76 (–1.19 to –0.32)*
Creatinine, mg/dL	–0.00 (–0.10 to 0.09)	0.04 (–0.03 to 0.12)
BUN, mg/dL	1.23 (–0.05 to 2.51)	0.89 (–0.22 to 2.00)
eGFR, mL/min/1.73 m^2	2.59 (–5.66 to 10.84)	–1.25 (–7.64 to 5.14)
ACR, mg/g	–26.98 (–144.03 to 90.06)	41.41 (–70.06 to 152.88)
Female		
SUA, mg/dL	–0.01 (–0.26 to 0.25)	–0.14 (–0.38 to 0.10)
Creatinine, mg/dL	–0.11 (–0.25 to 0.02)	–0.13 (–0.28 to 0.02)
BUN, mg/dL	0.21 (–1.04 to 1.45)	0.87 (–0.05 to 1.79)
eGFR, mL/min/1.73 m^2	1.39 (–3.93 to 6.71)	–4.19 (–9.16 to 0.77)
ACR, mg/g	–57.07 (–121.59 to 7.45)	–75.37 (–146.63 to –4.11)*
Total		
SUA, mg/dL	–0.26 (–0.50 to –0.02)*	–0.31 (–0.54 to –0.08)*
Creatinine, mg/dL	–0.07 (–0.17 to 0.02)	–0.03 (–0.12 to 0.06)
BUN, mg/dL	0.57 (–0.34 to 1.48)	0.98 (0.29 to 1.66)*
eGFR, mL/min/1.73 m^2	1.82 (–2.73 to 6.36)	–2.94 (–6.71 to 0.83)
ACR, mg/g	–46.40 (–106.24 to 13.44)	–33.57 (–97.25 to 30.11)

Abbreviations: ACR, albumin creatinine ratio; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; Recreational MVPA time, recreational moderate to vigorous physical activity time; SUA, serum uric acid.
*Statistical significance ($P < .05$). Model 1, the baseline model without adjusting for any covariates. Model 2, the adjusted model incorporating the following covariates: age, sex, race, income-to-poverty ratio, 6-month time period, insurance coverage, and additional variables identified as potentially influencing the associations between the independent and dependent variables.

Table A3 Estimated Mean Values of Changes in Renal Function Indices Due to Sedentary Time

Measure	Sedentary time (high vs low sedentary time)	
	Model 1	Model 2
Male		
SUA, mg/dL	–0.12 (–0.41 to 0.16)	–0.12 (–0.38 to 0.14)
Creatinine, mg/dL	–0.03 (–0.09 to 0.03)	0.02 (–0.03 to 0.07)
BUN, mg/dL	–0.68 (–1.46 to 0.11)	–0.71 (–1.50 to 0.08)
eGFR, mL/min/1.73 m^2	1.66 (–3.49 to 6.81)	–3.10 (–6.98 to 0.77)
ACR, mg/g	3.92 (–65.82 to 73.66)	–27.95 (–99.39 to 43.50)
Female		
SUA, mg/dL	0.02 (–0.17 to 0.21)	0.02 (–0.16 to 0.20)
Creatinine, mg/dL	–0.07 (–0.15 to 0.00)	–0.04 (–0.12 to 0.04)
BUN, mg/dL	0.05 (–0.91 to 1.00)	0.33 (–0.45 to 1.12)
eGFR, mL/min/1.73 m^2	1.09 (–3.02 to 5.20)	–2.50 (–6.09 to 1.08)
ACR, mg/g	–17.84 (–68.33 to 32.65)	–6.04 (–56.98 to 44.89)
Total		
SUA, mg/dL	–0.04 (–0.20 to 0.12)	–0.04 (–0.19 to 0.12)
Creatinine, mg/dL	–0.06 (–0.11 to –0.00)*	–0.01 (–0.06 to 0.05)
BUN, mg/dL	–0.26 (–0.91 to 0.38)	–0.16 (–0.72 to 0.40)
eGFR, mL/min/1.73 m^2	1.34 (–1.88 to 4.55)	–3.15 (–5.83 to –0.46)*
ACR, mg/g	–8.43 (–49.80 to 32.93)	–12.15 (–54.96 to 30.65)

Abbreviations: ACR, albumin creatinine ratio; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; SUA, serum uric acid.
*Statistical significance ($P < .05$). Model 1, the baseline model without adjusting for any covariates. Model 2, the adjusted model incorporating the following covariates: age, sex, race, income-to-poverty ratio, 6-month time period, insurance coverage, and additional variables identified as potentially influencing the associations between the independent and dependent variables.

Table A4 The Association of Sedentary Time and eGFR, a Population-Based Stratified Analysis

Subgroups	N	Mean (SD)	β (95% CI)	*P* for interaction
Sex				
Male	292	91.72 (22.23)	–3.10 (–6.98 to 0.77)	.819
Female	427	103.18 (20.86)	–2.50 (–6.09 to 1.08)	
Age				
12–14	329	108.68 (20.59)	**–4.72 (–9.04 to –0.40)***	**.047**
15–19	390	90.69 (20.11)	–0.22 (–3.66 to 3.21)	
Race				
Non-Hispanic Black	149	104.93 (24.37)	–2.66 (–10.76 to 5.45)	.816
Mexican American	184	105.85 (21.23)	–7.54 (–22.15 to 7.07)	
Other Hispanic	203	96.55 (21.07)	–3.06 (–7.50 to 1.38)	
Non-Hispanic Black	209	95.36 (23.61)	–1.30 (–6.73 to 4.13)	
Other race	74	101.90 (19.98)	2.65 (–4.53 to 9.82)	
Income-to-poverty ratio				
<1	191	99.35 (23.10)	–3.78 (–9.57 to 2.01)	.017
≥1, <2	185	100.47 (25.66)	1.84 (–4.79 to 8.46)	
≥2, <3	107	100.39 (22.00)	2.48 (–4.81 to 9.78)	
≥3, <4	73	94.00 (22.46)	–14.28 (–24.08 to –4.49)*	
≥4	107	95.87 (17.89)	–5.70 (–11.05 to –0.34)*	
Missing	56	—	—	
Yes	193	86.53 (23.45)	–6.27 (–11.60 to –0.94)*	
ACR, mg/g				
<30	650	98.34 (21.70)	–2.82 (–5.62 to –0.02)*	.937
≥30	69	98.86 (26.61)	–2.23 (–17.17 to 12.72)	

(continued)

Table A4 ***(continued)***

Subgroups	N	Mean (SD)	β (95% CI)	*P* for interaction
Recreational MVPA time, min				
0 min weekly	176	96.13 (22.87)	−4.47 (−10.48 to 1.55)	.569
0–420 min weekly	332	102.64 (22.20)	−1.10 (−5.54 to 3.35)	
≥420 min weekly	211	94.02 (20.65)	−3.66 (−8.05 to 0.74)	

Abbreviations: ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate; MVPA, moderate to vigorous physical activity.
*Statistical significance ($P < .05$). Adjusted by age, sex, race, insurance coverage, 6-month time period, income-to-poverty ratio, and other covariates.