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PHYSICAL ACTIVITY AND RAPID DECLINE IN KIDNEY FUNCTION AMONG OLDER ADULTS

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Abstract

BACKGROUND—Physical activity promotes diverse metabolic benefits that may moderate the long-term risk of progressive kidney dysfunction.

OBJECTIVE—To test the hypothesis that greater physical activity is associated with a lower risk of rapid kidney function decline among a general population of older adults.

DESIGN—Prospective cohort study of community-dwelling older men and women.

SETTING—Community-based sample in 4 U.S. sites recruited from Medicare eligibility files.

PARTICIPANTS—A total of 5888 men and women aged 65 years or older participating in the Cardiovascular Health Study. Participants who did not complete at least two measurements of kidney function, those who were unable to complete basic household chores, and those with missing physical activity data were excluded, leaving 4011 participants for analysis.

MAIN EXPOSURE MEASURE—Physical activity score calculated by summation of leisure-time activity (ordinal score of 1–5 for quintiles of 105, 480, 1012.5, and 2089 kilocalories per week) and walking pace (ordinal score of 1–3 for categories of less than 2, 2–3, and greater than 3 miles per hour).

MAIN OUTCOME MEASURE—Rapid kidney function decline, defined by the loss of >3.0 mL/min per 1.73 m² per year in the estimated glomerular filtration rate, calculated using longitudinal serum measurements of cystatin C.

RESULTS—There were 958 participants (23.9%) with a rapid decline in kidney function, (4.1 events per 100 person-years). The estimated risk of rapid kidney function decline was 16% in the highest physical activity group and 30% in the lowest physical activity group. After full adjustment for demographics, clinical, and subclinical disease characteristics, the two highest physical activity groups were associated with a 28% lower (95% CI: 21% to 41% lower) risk of rapid kidney function decline, compared to the two lowest physical activity groups. Greater kilocalories of leisure time physical activity, walking pace, and exercise intensity were each also associated with a lower incidence of rapid kidney function decline.

CONCLUSION—Greater physical activity is associated with a lower risk of rapid kidney function decline among older adults.

Keywords

physical activity; exercise; kilocalories; kidney disease; progression; cystatin C

INTRODUCTION

Chronic kidney disease (CKD) is one of the fastest growing health conditions in older people. Approximately 30% of individuals over 70 years old have CKD, defined by an estimated glomerular filtration rate (GFR) <60 ml/min/1.73m², which is less than half of normal for a young, healthy adult.(1) Kidney dysfunction is a major risk factor for cardiovascular events and mortality across multiple populations. In older individuals, a lower estimated GFR, as estimated by serum cystatin C levels, is linearly related to the risk of cardiovascular events, premature death, and a decline in functional status.(2–4) The age-associated decline in kidney function is highly variable;(5, 6) identifying modifiable factors that could preserve kidney function later in life could have a substantial public health impact.

In the general population, greater physical activity is associated with lower risks of coronary heart disease, stroke, and cardiovascular death.(7–9) Physical activity confers diverse metabolic benefits that may moderate the long-term risks of glomerulosclerosis and progressive kidney dysfunction. Exercise stimulates glucose uptake by skeletal muscle, thereby reducing insulin secretion and promoting lipolysis.(10) Exercise also contributes to a fall in systemic blood pressure and a reduction in body mass.(11–14) In contrast, a sedentary lifestyle predisposes to adiposity, which promotes inflammation, insulin resistance, and hypertension.(15, 16) These adverse processes may directly injure the kidney.(17, 18)

We hypothesized that greater physical activity would be associated with a lower incidence of kidney function decline among older adults. To test this hypothesis we evaluated physical activity level among 4011 participants in the Cardiovascular Health Study, a community-based study of ambulatory adults aged 65 years or older. Because exercise may influence serum creatinine levels via changes in muscle mass, we estimated longitudinal changes in kidney function using serial measurements of cystatin C, which is less dependent on muscle mass.(19)

METHODS

Study population

The Cardiovascular Health Study is a community-based prospective cohort study of cardiovascular disease among people 65 years of age or older. The design and recruitment criteria have been previously described.(20, 21) Briefly, 5,201 men and women ages 65 and older who were ambulatory and non-institutionalized were randomly selected and enrolled from Medicare eligibility lists in 4 U.S. communities in 1989–90; an additional 687 African American participants were recruited and enrolled in 1992–93. Subjects were excluded from CHS if they required a wheelchair in the home, were institutionalized, required a proxy to give consent, were receiving hospice care, were planning to move out of the area within 3 years, or were undergoing radiation or chemotherapy for cancer. Each center's institutional review committee approved the study and all participants gave informed consent. The baseline evaluation included a standardized physical examination, diagnostic testing, laboratory evaluation, and questionnaires regarding health status, medical history, and cardiovascular and lifestyle risk factors.

Beginning with the 5,888 CHS participants from the baseline exam (1989–1990 for the main CHS cohort and 1992–1993 for the African American cohort), we excluded 1452 participants who did not complete at least two cystatin C measurements that were necessary to calculate a slope. To focus on adults who had the capacity to exercise, we further excluded 280 participants who were unable to complete one or more basic household chores

(walking around at home, getting out of bed, dressing, bathing, or using the toilet) and 9 participants who were unable to complete the timed 15-foot walk. Finally, we excluded 63 participants who were missing key physical activity variables or diabetes status and 73 participants with a baseline estimated GFR >120 ml/min/1.73m². We chose to exclude participants with a very high estimated GFR because serologic markers poorly correlate with kidney function within this GFR range(22) and because we detected considerable regression to the mean for these outlying GFR values (49/73 showed rapid progression of kidney disease). Following these exclusions, 4011 participants were included in the analyses.

Assessment of physical activity and other lifestyle risk factors

Questionnaires were administered at baseline to estimate each participants' self-reported walking pace, exercise intensity, number of blocks walked weekly and leisure-time activity levels. During the baseline examination, participants were asked whether they had engaged in any of the following 15 leisure time activities in the prior 2 weeks: swimming, hiking, aerobics, tennis, jogging, racquetball, walking, gardening, mowing, raking, golfing, bicycling, dancing, calisthenics, and riding an exercise cycle. The intensity of each activity has been established and validated by the Minnesota Heart Survey.(23) Participant responses regarding each type of activity, frequency, and duration were used to calculate leisure time physical activity, expressed in kilocalories per week.

We summed leisure-time activity (ordinal score of 1–5 for quintiles) and pace of walking (ordinal score of 1–3 for pace <2 mph, 2–3 mph, >3 mph) into a single physical activity score variable according to a previous CHS analysis of lifestyle factors and diabetes.(24) We also examined leisure time activity and walking pace individually and further evaluated exercise intensity and the number of blocks walked per week.

Ascertainment of the outcome

The study outcome was a rapid decline in kidney function, defined previously in CHS by the loss of more than 3.0 mL/min per 1.73 m² per year in estimated GFR.(25, 26) An annual eGFR loss of 3.0 mL/min per 1.73 m² corresponds to the 25% of the CHS cohort with the most rapid decline in eGFR, represents a magnitude of change that is more than 3 times greater than the rate previously described in studies of aging, and is beyond the range of noise in measurement.(6)

We used serum cystatin C levels to estimate GFR because serum creatinine levels, the traditional serologic marker of kidney function, depend on muscle mass, which declines with older age and may be influenced by exercise.(19) Cystatin C levels were measured from frozen serum samples stored at -70°C using a particle-enhanced immunonephelometric assay (N Latex Cystatin C; Dade Behring, now Siemens Healthcare Diagnostics Inc, Deerfield, Illinois) with a nephelometer (BNII, Siemens Healthcare Diagnostics Inc). The assay is stable through several freeze-thaw cycles.(27) We calculated estimated GFR at the CHS baseline (1989–1990), year 3 (1992), and year 7 (1996–1997) exam using the equation:

$$\text{Estimated GFR}_{\text{cystatin C}} = 76.7 * (\text{cystatin C})^{-1.18}$$

Derived in a recent pooling study of 3418 adults who underwent simultaneous cystatin C measurements and gold-standard radionuclide measurements of GFR, this equation explains approximately 82% of the variation in directly measured GFR.(28)

Ascertainment of covariates

Participants completed standardized interviews by trained interviewers and an extensive examination. Medical records were reviewed and standardized criteria applied, when needed, to verify the presence of self-reported cardiovascular diseases.(29) Medications were ascertained using the inventory method in which participants brought all prescription and non-prescription medication bottles to each study examination.(20) Diabetes was defined by fasting glucose level greater than 7.8mmol/L or taking insulin or oral hypoglycemic agents. Systolic and diastolic blood pressures were calculated from the mean of two consecutive readings in the seated position. Carotid ultrasound was performed to measure the maximal stenosis of the internal and common carotid arteries.(30) A water-sealed, Collins Survey II spirometer (WE Collins, Braintree, MA) was used to measure forced expiratory volume in one second, according to American Thoracic Society (ATS) criteria.(31) Phlebotomy was performed under fasting conditions and the blood was analyzed at the 4 field centers for levels of hemoglobin, high-density lipoprotein cholesterol, triglyceride levels, serum albumin, creatinine and fibrinogen.(32) C-reactive protein (CRP) was measured in the entire cohort using stored plasma and a validated in-house high-sensitivity enzyme-linked immunoabsorbent assay (ELISA).(33) Fasting plasma lipid analyses were performed, and low-density lipoprotein cholesterol was calculated using the Friedewald equation.

Statistical analysis

We tabulated baseline participant characteristics according to physical activity category. We calculated at-risk time for each participant as the time from the baseline examination until the final cystatin C measurement, and we calculated the slope of kidney function change for each individual using linear regression. We created the binary outcome variable of rapid kidney function decline based on an *a priori* defined slope cut point of $-3.0 \text{ ml/min/1.73m}^2$ per year. We used Poisson regression with robust variance estimation to estimate the association of physical activity covariates with rapid kidney function decline after adjusting for potential confounding variables. We chose covariates as potential confounding factors based on plausibility that they could confound the association of physical activity level with kidney function decline, and we investigated groups of potential confounding factors by constructing nested multivariate models.

We conducted sensitivity analyses to evaluate whether associations of physical activity with change in kidney function change were robust after excluding participants who had prevalent cardiovascular disease, poor or fair self-reporter health status, and those who had two or more components of the frailty phenotype (components were: (1) shrinking, 10 pounds or greater unintentional weight loss in the previous year (or $>5\%$ loss in body weight); (2) poor endurance and energy, based on 2 questions from the Center for Epidemiologic Studies Depression (CES-D) scale; (3) weakness, grip strength in the lowest 20% (adjusted for sex and body mass index); (4) slow walking speed, the slowest 20% in a 15-foot walk (adjusted for sex and height)). We used the likelihood ratio test to evaluate whether associations of physical activity and rapid kidney function decline differed according to baseline kidney function, sex, race, diabetes, and body mass index. We evaluated the continuous slope of eGFR in a secondary analysis. All p values were two-tailed ($\alpha=0.05$). All analyses were performed using STATA release 10.1 (College Station, TX).

RESULTS

Compared to participants who were included in the study, the 1452 participants who were excluded due to the lack of follow-up kidney function measurements were older (75.3 years

vs. 72.0 years, respectively), had a lower combined physical activity score (4.4 vs. 5.3), a lower proportions of Caucasians (76.2% vs. 88.5%), and females (51% vs. 59%), and a lower baseline estimated GFR (69 mL/min per 1.73 m² vs. 78 mL/min per 1.73 m²) than those who completed follow-up measurements. Of the 1452 participants excluded, 1212 (83.5%) died prior the scheduled follow-up kidney measurements. The remainder of analyses pertains to the 4011 included study participants.

Demographics, co-morbid diseases, and laboratory characteristics differed between participants in the highest versus lowest physical activity groups (Table 1). The highest physical activity group was characterized by a greater proportion of men and Caucasians, a higher education level, a lower prevalence of cardiovascular diseases, better lung function, and leaner body mass. Baseline estimated GFR was modestly higher among participants in the highest physical activity group.

Quintiles of leisure-time physical activity for the entire CHS cohort were defined by cut-points of 105, 480, 1012.5, and 2089 kilocalories per week. Interpretations of these values in terms of activity types and durations are presented in Table 2.

There were 1663 participants who completed one follow-up cystatin C measurement and 2348 participants who completed two measurements, with a median follow-up time of 7 years. The mean and median annual declines in estimated GFR_{cystatin C} were 1.73 and 1.55 mL/min per 1.73 m², respectively (interquartile range 0.33, 2.96 mL/min per 1.73 m² per year). There were 958 participants (23.9%) with a rapid decline in kidney function, defined by >3.0 mL/min per 1.73 m² per year loss in estimated GFR_{cystatinC} (4.1 events per 100 person-years).

The age, race, and sex adjusted rate of rapid kidney function decline decreased in graded fashion with greater physical activity scores (Figure 1), ranging from 15.8 rapid decline events per 100 person-years among participants in the highest physical activity group (physical activity score of 8) to 30.2 rapid decline events per 100 person-years among participants in the lowest physical activity group (physical activity score of 2).

After adjustment for demographics, prevalent cardiovascular disease, medication use, smoking, alcohol use, body mass, blood pressure, and laboratory measurements, greater physical activity scores were associated with statistically lower risks of rapid kidney function decline (Table 3). Further adjustment for subclinical disease measurements (ankle arm index, lung function, common carotid intima-media thickness), plus impaired fasting glucose, and self-reported health status did not materially alter these estimates. After full adjustment, the two highest physical activity scores combined (7–8) were associated with an estimated 28% lower (95% CI 21% to 41% lower) adjusted risk of rapid kidney function decline compared to the two lowest physical activity scores combined (2–3). Other physical function measures, including total kilocalories of leisure time physical activity, walking pace, and exercise intensity, but not the number of blocks walked per week, were also associated with a statistically lower risk of rapid kidney function decline.

To evaluate whether observed associations of physical activity with kidney function decline might reflect poor health status among individuals with the lowest physical activity scores, we repeated our analyses after removing subjects with prevalent cardiovascular disease and those with fair or poor self reported health status. The size of the association between physical activity and rapid kidney function decline was similar in the restricted subgroup of 2904 participants with no prevalent cardiovascular disease (risk for the two highest physical activity scores (7–8) compared to two lowest physical activity scores (2–3): 0.7, 95% CI: 0.56–0.83). Similarly, in the subgroup of 3111 participants with self-reported health status of “good”, “very good” or “excellent”, the relative risk for the two highest physical activity

scores (7–8) compared to the two lowest physical activity scores (2–3) was 0.67 (95% CI: 0.55–0.82). The association between physical activity and rapid kidney function decline were similar in the subgroup of 3845 participants with no more than one component of the frailty phenotype (risk for the two highest physical activity scores (7–8) compared to two lowest physical activity scores (2–3): 0.74, 95% CI: 0.58–0.95). Associations of physical activity score with of rapid kidney function decline were also similar comparing subsets of the participants with a baseline estimated GFR of <60, 60–90, and 90–119 mL/min per 1.73 m² (Table 4; p-for-interaction=0.46). No statistical interaction of physical activity and rapid kidney function decline was observed for sex (p=0.87), race (p=0.48), body mass index (p=0.22), diabetes (p=0.97) or prevalent cardiovascular disease (p=0.71).

Comparing participants in the two lowest (scores of 2–3) versus two highest (scores of 7–8) physical activity groups, the mean difference in estimated annual GFR decline was –0.31 mL/min per 1.73 m² per year (95% CI –0.55, –0.06) after full adjustment. For leisure time physical activity groups (quintiles of kilocalories per week), comparing participants in the lowest quintile versus those in the highest quintile) the difference was –0.39 mL/min per 1.73 m² per year (95% CI –0.65, –0.13 mL/min per 1.73 m² per year).

COMMENT

We observed an association of greater physical activity levels with a lower risk of rapid decline in kidney function among a general population of older adults. Associations were consistent across different types of self-reported physical activity, increased in magnitude with the intensity and amount of physical activity, and persisted after adjustment for well-measured clinical and subclinical disease characteristics. Kilocalories of leisure-time physical activity and exercise intensity were the two physical activity characteristics that were most strongly associated with rapid kidney function decline, whereas the number of blocks walked per week and walking pace were less strongly associated. Physical activity was associated with a statistically significant but materially small difference in the mean decline in estimated GFR, assessed continuously. If these observed associations are causal, then exercise could represent a viable means to prevent progressive kidney disease in this vulnerable population.

To our knowledge, these are the first data to directly demonstrate an association of physical activity with the long-term change in kidney function among older adults. Kronborg et al. recently evaluated sex-specific risk factors for the change in kidney function in a non-diabetic Norwegian population. In age-adjusted analyses, lesser physical activity was associated with a greater increase in the serum creatinine level over time among women.(35) However, these associations did not persist after adjustment in either sex. One possibility is that previous studies of physical activity are hampered by the use of serum creatinine levels to estimate kidney function. Since exercise may increase muscle mass, or limit the decline in muscle mass that occurs with inactivity, potential benefits of exercise on kidney function may be obscured by a concomitant rise in the serum creatinine level.

A small non-randomized study of the effect of regular aquatic exercise in moderate chronic renal failure (CRF) patients assigned 17 adults with CRF to low-intensity aerobic exercise in the pool during a period of 12 weeks, twice a week, with sessions lasting for 30 min and matched them to 9 control participants who remained sedentary.(36) The participants in the exercise group had cystatin-C levels (in mg/l) that diminished significantly (from 1.7 ± 0.2 at baseline to 1.4 ± 0.1 at 12 weeks) whereas no such change was noted in the control group (from 1.7 ± 0.3 at baseline to 2.0 ± 0.5 at 12 weeks). Also, the estimated creatinine clearance (measured in ml/min) was enhanced in the exercise group (from 62.9 ± 5.9 at baseline to

67.1 ± 7.0 at 12 weeks) while remaining relatively constant in the control group (from 69.8 ± 12.3 at baseline to 66.3 ± 13.2 at 12 weeks).

Exercise has both short-term and long-term beneficial effects on metabolism in non-diabetic subjects. In controlled trials, moderate physical activity improves fasting and postprandial glucose-insulin homeostasis, induces and maintains weight loss, raises HDL cholesterol, lowers LDL cholesterol and triglycerides, lowers blood pressure, and probably lowers inflammation and improves endothelial function.(13, 37–43) These metabolic benefits may impact the risk of kidney disease incidence and progression. Among more than 10,000 non-diabetic participants in the Atherosclerosis Risk in Communities Study, components of the metabolic syndrome, specifically insulin resistance, were associated with a greater incidence of CKD.(44) In the non-diabetic Norwegian population cited above, the non-fasting insulin to glucose ratio was associated with a greater decline in kidney function among both men and women.

Oxidative stress is another potential mediator in the association between physical activity and kidney function decline, and could help explain our finding of a persistent association after adjustment for markers of hypertension and inflammation. Oxidative stress is both a cause and a consequence of hypertension(45) and is present in patients with mild to moderate renal insufficiency, as well as those with end-stage renal disease (ESRD) receiving dialytic therapies.(46) Hypertension and oxidative stress improve within 3 weeks of moderate physical activity and the consumption of a diet low in fat and sugar and rich in natural antioxidants.(47)

The most important limitation of this observational study is the potential for confounding, because many healthy characteristics are linked with a greater desire and capacity to exercise. Indeed, in this study population, lesser physical activity was associated with a number of health factors, including smoking, greater body mass index, and a higher proportion of clinical and subclinical cardiovascular disease. CHS provides a unique opportunity to evaluate physical activity and kidney function decline in older adults because both exposure and outcome were assessed using validated methods and because cardiovascular risk factors and health status characteristics were carefully measured, increasing the ability to adjust for confounding. It is important to note that some of the adjustment covariates, namely systolic blood pressure, body mass index, cholesterol and C-reactive protein, could also be mediators of the effect of physical activity on kidney function decline, thereby potentially attenuating the size of the observed associations. Survivorship bias represents a second potential limitation. Analyses were limited to participants who survived for at least 3 years in order to undergo a second measurement of kidney function. Participants who did not return for a second study visit had lower baseline physical activity levels compared to those who were included in the study. If excluded individuals also had greater declines in kidney function, then associations of physical activity with rapid kidney function decline could be underestimated.

Participant questionnaires were used to define physical activity variables. Although physical activity has been associated with several clinical outcomes in CHS(48, 49), some measurement error related to the ascertainment of physical activity characteristics is expected. Given the prospective nature of the data collection, it is probable that such error was random with respect to the decline in kidney function; such measurement error would be expected to dilute the study findings.

In conclusion, we present prospective data demonstrating an association of greater physical activity with a lower risk of rapid kidney function decline in a general population of older adults. Associations were independent of measured co-morbidity, were consistent across

different types of physical activity characteristics, strengthened with greater physical activity levels, and are supported by biologic evidence demonstrating effects of exercise on metabolic pathways that directly impact kidney function. These findings suggest a causal relationship of exercise with a lower risk of kidney disease progression in older people; however, this observational study cannot prove a cause-effect relationship. These findings motivate further studies to evaluate whether exercise represents a viable method for protecting against the age-related decline in kidney function.

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Figure 1.

Incidence proportion of rapid kidney function decline, by physical activity score among 3444 older adults.

Table 1Baseline characteristics according to physical activity score.[†]

Characteristic	Physical activity score		
	2 – 3 (N=896)	4 – 6 (N=2137)	7 – 8 (N=978)
Age, years	72.8 ± 5.4	72.0 ± 5.1	71.2 ± 4.4
Caucasian	725 (80.9)	1885 (88.2)	915 (93.6)
African American	171 (19.1)	252 (11.8)	63 (6.4)
Female	621 (69.3)	1276 (59.7)	423 (43.3)
Education			
< High school graduate	254 (28.3)	448 (21.0)	127 (13.0)
High school graduate	196 (21.9)	536 (25.1)	232 (23.7)
Some college or more	446 (49.8)	1153 (54.0)	619 (63.3)
Income, \$			
< 25,000	457 (51.0)	992 (46.4)	364 (37.2)
25,000–49,999	156 (17.4)	490 (22.9)	266 (27.2)
>50,000	283 (31.6)	655 (30.7)	348 (35.6)
Alcohol use	396 (44.2)	1121 (52.5)	613 (62.9)
Smoking status			
Never smoked	409 (45.8)	1029 (48.1)	416 (42.5)
Former smoker	360 (40.2)	882 (41.3)	483 (49.4)
Current smoker	125 (14.0)	224 (10.5)	77 (7.9)
Body mass index, kg/m ²	27.5 ± 5.3	26.4 ± 4.2	25.7 ± 3.6
Self-reported health status			
Fair-Poor	282 (31.5)	360 (16.8)	100 (10.2)
Good-Excellent	614 (68.5)	1777 (83.2)	878 (89.8)
Medication use			
ACE inhibitor	67 (7.5)	140 (6.6)	59 (6.0)
Non-steroidal anti-inflammatory	110 (12.3)	221 (10.3)	107 (10.9)
Diabetes status			
Impaired fasting glucose	127 (14.2)	291 (13.6)	103 (10.5)
Diabetes	164 (18.3)	259 (12.1)	112 (11.5)
Prevalent cardiovascular disease	254 (28.3)	493 (23.1)	211 (21.6)
Stroke	27 (3.0)	45 (2.1)	20 (2.0)
Coronary heart disease	171 (19.1)	348 (16.3)	164 (16.8)
Transient ischemic attack	27 (3.0)	47 (2.2)	17 (1.7)
Atrial fibrillation	18 (2.0)	29 (1.4)	17 (1.7)
Claudication	25 (2.8)	35 (1.6)	14 (1.4)
Left ventricular hypertrophy	38 (4.2)	63 (2.9)	16 (1.6)
Heart failure	41 (4.6)	52 (2.4)	14 (1.4)
Hypertension	449 (60.7)	982 (52.9)	397 (47.1)
Systolic blood pressure, mmHg	138.4 ± 21.6	134.3 ± 21.2	133.9 ± 20.4
Hemoglobin, g/dl	13.9 ± 1.4	14.1 ± 1.4	14.3 ± 1.3

Characteristic	Physical activity score		
	2 – 3 (N=896)	4 – 6 (N=2137)	7 – 8 (N=978)
LDL, mg/dl	130.9 ± 36.9	130.5 ± 35.1	129.2 ± 34.2
HDL, mg/dl	54.1 ± 15.1	54.5 ± 15.5	54.8 ± 16
Triglycerides, mg/dl	144.4 ± 73.8	139 ± 72.9	132.3 ± 69.2
C-reactive protein, mg/dl	5.3 ± 8.4	4.3 ± 8.5	3.3 ± 5.8
Common cIMT, mm	1.07 ± 0.2	1.04 ± 0.2	1.03 ± 0.2
Ankle arm index	1.05 ± 0.2	1.08 ± 0.1	1.12 ± 0.1
Baseline kidney function			
Estimated GFR _{cystatin C} mL/min/1.73 m ²	75.1 ± 18.3	78.9 ± 17.2	81.1 ± 16.2
Estimated GFR _{MDRD} mL/min/1.73 m ²	78.0 ± 23.5	79.1 ± 21.8	79.3 ± 19.9
Forced expiratory volume 1-second, L	1.9 ± 0.6	2.1 ± 0.6	2.4 ± 0.9

Entries are *N*(%) for categorical variables and mean (± standard deviation) for continuous variables.

^{†*} Sum of leisure-time activity (ordinal score for quintiles) and walking pace (ordinal score for 3 categories)

LDL = low density lipoprotein; HDL = high density lipoprotein; GFR= glomerular filtration rate

Table 2Examples of physical activities to achieve specific leisure-time activity quintiles..[†]

Kilocalories of leisure-time activity per week	Example activities
<105	Walking 20 minutes per week, or Bowling 30 minutes per week, or Low-impact aerobics 15 minutes per week
105–479	Walking 10 minutes per day, or Bowling 2 hours per week, or Low-impact aerobics 30 minutes per week
480–1012.4	Walking 20 minutes per day, or Golf using a cart 4 hours per week, or Swimming laps 60 minutes per week
1012.5–2088	Walking 40 minutes per day, or Golf walking and pulling clubs 4 hours per week, or Tennis (singles or doubles) 2 hours per week
2089	Walking 90 minutes per day, or Golf walking and pulling clubs 8 hours per week, or Swimming laps 3 hours per week

[†]For a person of average weight of 159 pounds

Table 3

Association of physical activity variables with rapid kidney function decline.

Physical activity variable	Rapid kidney function decline	Model 1 [€]	Model 2 [¥]	Model 3 [£]
Physical Activity Score [‡]				
2–3	107/338	1.0 (reference)	1.0 (reference)	1.0 (reference)
4–6	153/558	0.85 (0.75,0.97)	0.86 (0.74,0.99)	0.86 (0.73,1)
7–8	148/635	0.7 (0.59,0.83)	0.72 (0.59,0.87)	0.72 (0.59,0.88)
p-for trend		<0.001	0.001	0.002
Kilocalories leisure time expended per week				
<105	239/830	1.0 (reference)	1.0 (reference)	1.0 (reference)
105–479	177/776	0.81 (0.68,0.95)	0.82 (0.68,1)	0.77 (0.63,0.94)
480–1012.4	201/803	0.9 (0.76,1.05)	0.91 (0.76,1.09)	0.91 (0.75,1.09)
1012.5–2088	177/800	0.8 (0.67,0.95)	0.86 (0.71,1.05)	0.83 (0.68,1.01)
2089	164/802	0.74 (0.62,0.88)	0.72 (0.58,0.89)	0.71 (0.57,0.88)
p-for trend		0.002	0.012	0.012
Walking pace (miles per hour)				
<2	269/951	1.0 (reference)	1.0 (reference)	1.0 (reference)
2–3	441/1787	0.9 (0.79,1.02)	0.95 (0.82,1.11)	0.98 (0.84,1.15)
>3	248/1273	0.74 (0.64,0.86)	0.78 (0.66,0.93)	0.82 (0.68,0.99)
p-for trend		<0.001	0.006	0.029
Exercise intensity				
No exercise	71/249	1.0 (reference)	1.0 (reference)	1.0 (reference)
Low intensity	475/1856	0.95 (0.77,1.17)	1.11 (0.85,1.45)	1.08 (0.82,1.42)
Moderate	341/1471	0.86 (0.7,1.07)	1.06 (0.81,1.39)	1.01 (0.76,1.33)
High intensity	71/435	0.64 (0.48,0.85)	0.73 (0.51,1.03)	0.68 (0.48,0.98)
p-for trend		<0.001	0.021	0.008
Number of blocks walked per week				
<6	261/919	1.0 (reference)	1.0 (reference)	1.0 (reference)
6–11	176/753	0.87 (0.74,1.03)	0.89 (0.74,1.07)	0.9 (0.74,1.09)
12–29	151/736	0.77 (0.64,0.92)	0.81 (0.66,0.99)	0.84 (0.68,1.02)
30–71	194/848	0.86 (0.73,1.01)	0.86 (0.72,1.04)	0.86 (0.71,1.05)
72	164/717	0.88 (0.74,1.04)	0.86 (0.71,1.06)	0.9 (0.73,1.1)
p-for trend		0.114	0.144	0.236

[€]Model 1 adjusted for age, sex, race and number of cystatin C measurements. 100% complete.

[¥]Model 2 adds smoking status (never, former, current), alcohol use (number of drinks per week), education level, diabetic status, body mass index, prevalent cardiovascular disease (any of heart failure, stroke, claudication, coronary heart disease, atrial fibrillation, transient ischemic attack), medication use (ace inhibitors, non-steroidal anti-inflammatory drugs), systolic blood pressure, serum levels of hemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and c-reactive protein. 97.4% complete.

[£]Model 3 adds ankle arm index (<1, 1–1.4, 1.4), forced expiratory volume in one second, common carotid intima-media thickness and self-reported health status. 94.8% complete.

[‡]Sum of leisure-time activity (ordinal score of 1–5 for quintiles) and walking pace (ordinal score of 1–3 for 3 categories)

Table 4

Association of physical activity score with rapid kidney function decline in selected subgroups of participants

	Participants with no prevalent cardiovascular disease (N=2904)	Participants with self- reported health status of “good”, “very good” or “excellent” (N=3111)	Participants with no more than one component of the frailty phenotype² (N=3845)
Physical activity score			
2–3	1.0 (reference)	1.0 (reference)	1.0 (reference)
7–8	0.7 (0.56,0.83)	0.67 (0.55,0.82)	0.74 (0.58,0.95)

¹ Adjusted for variables in model 3: age, sex, race, smoking status (never, former, current), alcohol use (number of drinks per week), education level, body mass index, prevalent cardiovascular disease (any of heart failure, claudication, coronary heart disease, atrial fibrillation, transient ischemic attack), medication use (ace inhibitors, non-steroidal anti-inflammatory drugs), systolic blood pressure, serum levels of hemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, c-reactive protein, ankle arm index (<1, 1–1.4, 1.4), forced expiratory volume in one second, common carotid intima-media thickness, diabetic status, and self-reported health status. Model is 94.8% complete.

² Components of the frailty phenotype: (1) shrinking, 10 pounds unintentional weight loss in the previous year (or >5% loss in body weight); (2) poor endurance and energy, based on 2 questions from the Center for Epidemiologic Studies Depression scale; (3) weakness, grip strength in the lowest 20% (adjusted for sex and body mass index (BMI)); (4) slow walking speed, the slowest 20% in a 15-foot walk (adjusted for sex and height)).

Table 5Physical activity score and rapid kidney function decline by baseline kidney function[/].

	Baseline estimated GFR _{cystatin C} mL/min per 1.73 m ²		
	<60 (N=558)	60–89 (N=2434)	90–119 (N=1019)
Physical activity score			
2–3	1.0 (reference)	1.0 (reference)	1.0 (reference)
4–6	0.75 (0.45,1.27)	0.88 (0.71,1.09)	0.72 (0.56,0.92)
7–8	0.78 (0.40,1.51)	0.63 (0.47,0.85)	0.69 (0.51,0.94)
p-for trend	0.438	0.002	0.044

[/] Adjusted for variables in model 3: age, sex, race, smoking status (never, former, current), alcohol use (number of drinks per week), education level, body mass index, prevalent cardiovascular disease (any of heart failure, claudication, coronary heart disease, atrial fibrillation, transient ischemic attack), medication use (ace inhibitors, non-steroidal anti-inflammatory drugs), systolic blood pressure, serum levels of hemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, c-reactive protein, ankle arm index (<1, 1–1.4, 1.4), forced expiratory volume in one second, common carotid intima-media thickness, diabetic status, and self-reported health status. Model is 94.8% complete.