Exercise Capacity and Risk of Chronic Kidney Disease in US Veterans: A Cohort Study

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Abstract

Objective: To assess the association between exercise capacity and the risk of developing chronic kidney disease (CKD).

Patients and Methods: Exercise capacity was assessed in 5812 male veterans (mean age, 58.4±11.5 years) from the Veterans Affairs Medical Center, Washington, DC. Study participants had an estimated glomerular filtration rate of 60 mL/min per 1.73 m^2 or more 6 months before exercise testing and no evidence of CKD. Those who developed CKD during follow-up were initially identified by the *International Classification of Diseases, Ninth Revision* and further verified by at least 2 consecutive estimated glomerular filtration rate values of less than 60 mL/min per 1.73 m^2 3 months or more apart. Normal kidney function for CKD-free individuals was confirmed by sequential normal eGFR levels. We established 4 fitness categories on the basis of age-stratified quartiles of peak metabolic equivalents (METs) achieved: least-fit (≤25%; 4.8±0.90 METs; n=1258); low-fit (25.1%-50%; 6.5±0.96 METs; n=1614); moderate-fit (50.1%-75%; 7.7±0.91 METs; n=1958), and high-fit (>75%; 9.5±1.0 METs; n=1436). Multivariable Cox proportional hazard models were used to assess the association between exercise capacity and CKD.

Results: During a median follow-up period of 7.9 years, 1010 developed CKD (20.4/1000 person-years). Exercise capacity was inversely related to CKD incidence. The risk was 22% lower (hazard ratio, 0.78; 95% CI, 0.75-0.82; $P<.001$) for every 1-MET increase in exercise capacity. Compared with the least-fit individuals, hazard ratios were 0.87 (95% CI, 0.74-1.03) for low-fit, 0.55 (95% CI, 0.47-0.65) for moderate-fit, and 0.42 (95% CI, 0.33-0.52) for high-fit individuals.

Conclusion: Higher exercise capacity attenuated the risk of developing CKD. The association was independent and graded.

 ■ Mayo Clin Proc. 2015;90(4):461-468

Chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m^2 for 3 months or more (stages 3-5), substantially increases mortality risk.[1] The prevalence of CKD worldwide is rising.[2] Thus, ways to prevent the incidence of CKD should be explored.

The findings of large epidemiologic studies from diverse populations support that increased cardiorespiratory fitness, estimated by exercise capacity derived from a standardized exercise test, attenuates the progression to chronic diseases.[3,4] It is also inversely and independently associated with lower mortality risk regardless of age,[4-6] race,[7] sex,[8-11] documented cardiovascular disease (CVD),[12] or other comorbidities.[13-16]

The effect of cardiorespiratory fitness on the risk of developing CKD has not been studied extensively. However, findings of the few available studies suggest that physical activity status may affect kidney function. Physical inactivity was strongly and directly associated with CKD prevalence,[17] whereas even mild physical activity was positively associated with better kidney function.[18] In subjects with established CKD, higher physical activity was associated with slower rates of eGFR decline[17,19] and higher hand grip strength and gait speed were associated with lower risk of death in 347 individuals with CKD followed for 3 years.[20] Thus, the objective of the present study was to evaluate the effects of cardiorespiratory fitness, as assessed by exercise capacity achieved during a standardized exercise test, on the development of CKD.

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PATIENTS AND METHODS

Design and Sampling

This prospective cohort study included individuals from a larger database, established at the Veterans Affairs Medical Center in Washington, DC, to assess the association between exercise capacity and health outcomes in veterans. All participants (n=7733) had a symptom-limited exercise test between January 12, 1987, and December 30, 2012. The test was administered either as part of a routine assessment, clearance to participate in exercise, or to assess exercise-induced ischemia. In case of multiple exercise tests, the first test was used.

From this database, we excluded individuals without eGFR data or an eGFR of less than 60 mL/min per 1.73 m^2 before the exercise test (n=898). We also excluded all women (n=454) and those with the following conditions at the time of the exercise test: (1) body mass index (BMI; calculated as the weight in kilograms divided by the height in meters squared) of less than 18.5 kg/m^2, to minimize the potential effect of low body weight on mortality due to cachexia (n=116); (2) an exercise capacity of less than 2 metabolic equivalents (METs), unable to complete the test, or required emergent intervention (n=185); (3) those with an implanted pacemaker (n=145); (4) those with chronic failure New York Heart Association class II or higher (n=58); and (5) those with chronic obstructive pulmonary disease (n=65). After these exclusions, the cohort comprised 5812 participants (mean age, 58.4±11.5 years). Of these, 4287 (73.8%) were black (mean age, 58.0±11.3 years) and 1525 (26.2%) were white (mean age, 59.5±12.0 years).

CKD Determination

Preexercise eGFR (baseline eGFR) was estimated for each participant, using serum creatinine measurements performed within 6 months before the exercise test, available in the electronically stored medical records known as the Computerized Patient Record System (CPRS). When more than 1 serum creatinine measurement was available, the one carried out closest to the exercise test was used. Participants who developed CKD during the follow-up period were initially identified by using the *International Classification of Diseases, Ninth Revision* (*ICD-9*) and further verified with at least 2 consecutive eGFR values of less than 60 mL/min per 1.73 m^2 3 months or more apart. Follow-up eGFR level for these individuals was estimated on the basis of serum creatinine measurements at the time CKD diagnosis was recorded. Normal kidney function for those who did not develop CKD was confirmed by sequential normal eGFR levels. Follow-up eGFR was assessed using the last available serum creatinine measurement. All eGFR values were estimated by using the Chronic Kidney Disease Epidemiology Collaboration equation.[21] The study was approved by the institutional review board of the Veterans Affairs Medical Center, Washington, DC, and all subjects gave written informed consent before their exercise test.

Details on relevant demographic, clinical, and medication information, risk factors, and comorbidities as defined by the *ICD-9* coding for all participants were obtained from the CPRS at the time of the exercise test. Body weight and height were assessed using a standardized scale and recorded before the test and the BMI was calculated. In addition, risk factors and comorbidities as defined by the *ICD-9* coding for all participants were recorded from electronic medical records.

Exercise-Related Assessments

Cardiorespiratory fitness was assessed by a standard treadmill test using the Bruce protocol. Peak exercise capacity (in METs) was estimated using standardized equations.[22] One MET is defined as the energy expended at rest, which is approximately equivalent to an oxygen consumption of 3.5 mL of O_2 per kg body weight per minute. Subjects were encouraged to exercise until volitional fatigue in the absence of symptoms or other indications for stopping.[23] The use of handrails was allowed only if necessary for balance and safety. Medications were not altered before testing.

We stratified the cohort into 3 age categories: younger than 50 years, 50 to 69 years, and 70 years or older. We then identified those with a MET level of 25% or less, more than 25% to 50%, more than 50% to 75%, and more than 75% of METs achieved within their respective age category, as described previously.[13,24] We then established the following 4 fitness categories on the basis of age-stratified quartiles of peak METs achieved: least-fit category (4.8±0.90 METs;