AJKD
Original Investigation

# Exercise Training in CKD: Efficacy, Adherence, and Safety

Erin J. Howden, PhD,[1,2] Jeff S. Coombes, PhD,[1] Haakan Strand, PhD,[2] Bettina Douglas, MN, NP,[2,3] Katrina L. Campbell, PhD,[2,3] and Nicole M. Isbel, MBBS, PhD[2,3]

**Background:** Exercise training increasingly is recommended as an important part of the management of cardiovascular disease. However, few studies have evaluated the effectiveness of exercise training in patients with chronic kidney disease (CKD), and those that have included very selective populations.

**Study Design:** Analysis of secondary outcomes of a randomized controlled trial, with participants randomly assigned to either lifestyle intervention or usual care (control).

**Setting & Participants:** Patients with CKD stages 3 to 4 and one or more uncontrolled cardiovascular risk factor were recruited from an outpatient clinic at a large tertiary hospital.

**Intervention:** Lifestyle intervention included access to multidisciplinary care through a nurse practitioner–led CKD clinic, exercise training, and a lifestyle program. The exercise training was a 2-phased program in which participants received 8 weeks of supervised training before commencing 10 months of home-based training.

**Outcomes & Measurements:** Efficacy, as assessed by metabolic equivalent tasks (METs), 6-minute walk distance, Timed Get-Up-and-Go test, grip strength, and anthropomorphic measures; adherence, as assessed by self-reported physical activity; and safety, as assessed by reported serious adverse events, were recorded.

**Results:** 83 patients were randomly assigned and 72 patients completed follow-up testing (intervention, n = 36; control, n = 36). The intervention resulted in a significant improvement in METs (pre, 7.2 ± 3.3; post, 9.7 ± 3.6), 6-minute walk distance (pre, 485 ± 110 m; post, 539 ± 82 m), and body mass index (pre, 32.5 ± 6.7 kg/m$^2$; post, 31.9 ± 7.3 kg/m$^2$). Reported physical activity levels significantly increased in the intervention group at 6 months, but decreased at 12 months. There were no serious adverse events related to the exercise training.

**Limitations:** This study was not powered to evaluate the safety of exercise training on serious adverse events.

**Conclusions:** The findings from the present study suggest that an exercise program that includes a supervised and home-based training phase is effective, adhered to, and safe in patients with CKD.

*Am J Kidney Dis.* 65(4):583-591. 

***INDEX WORDS:*** Physical activity; exercise capacity; physical functioning; muscle strength; cardiovascular risk; lifestyle; exercise training; aerobic exercise; resistance training; modifiable risk factor; chronic kidney disease (CKD).

Sedentary behavior increases the risk of developing cardiovascular disease, type 2 diabetes, hypertension, obesity, and premature death and is the fourth leading risk factor for global mortality.[1] To ease the health burden associated with sedentary behavior, effective strategies to increase physical activity and reduce cardiovascular risk are urgently required, especially among high-risk individuals. Patients with chronic kidney disease (CKD) are sedentary[2] and have poor cardiorespiratory fitness[3] and disproportionately high cardiovascular risk.[4]

Sedentary behavior is both a determinant and consequence of disease progression in CKD, with physical inactivity and low physical functioning associated with increased mortality in dialysis patients.[5] Moreover, in patients with CKD, low physical functioning limits activities of daily living and is associated strongly with all-cause mortality.[6] Physical functioning, quantified as maximum exercise capacity (peak $V_{O_2}$) and/or metabolic equivalent tasks (METs) during a maximal exercise test are powerful predictors of morbidity and cardiovascular mortality in the general population[7,8] and in patients with end-stage kidney disease.[9] Public health recommendations aimed at increasing physical activity levels assume that adopting regular activity will increase exercise capacity and physical function and therefore reduce the risk of premature death from cardiovascular causes. Secondary benefits may include improved ability to perform

*From the [1]Schools of Human Movement Studies and [2]Centre for Clinical Research Excellence–Cardiovascular Disease and Metabolic Disorders, University of Queensland; and [3]Department of Renal Medicine, Princess Alexandra Hospital, Brisbane, Queensland, Australia.*

*Received May 2, 2014. Accepted in revised form September 26, 2014. Originally published online November 13, 2014.*

*Address correspondence to Nicole M. Isbel, MBBS, PhD, Renal Research, Department of Nephrology, Princess Alexandra Hospital, Ipswich Road, Brisbane, Queensland, 4102 Australia. E-mail: nikky.isbel@health.qld.gov.au*



*0272-6386*
*http://dx.doi.org/10.1053/j.ajkd.2014.09.017*

activities of daily living and better quality of life.[10] There has been less focus on incorporating strategies to boost physical activity and physical function in moderate kidney disease, for which increasing physical activity levels could be most beneficial. It recently was reported that patients with moderate CKD who walk 5 or more times per week were ~58% less likely to die and 43% less likely to need dialysis or a transplant during the study.[11] Whether interventions aimed at increasing physical activity levels in patients with CKD translate to decreased cardiovascular risk or improved physical functioning is unclear.

We recently have reported that 12 months of exercise training improves cardiorespiratory fitness and left ventricular diastolic function and preserves arterial function in patients with CKD.[3] We sought to further examine the efficacy of, adherence to, and safety of the lifestyle intervention that included gym-based followed by home-based exercise training in patients with CKD.

## METHODS

### Participants

This study was a prespecified substudy of an open-label randomized controlled trial in cardiovascular risk factor modification in CKD (LANDMARK 3 [Longitudinal Assessment of Numerous Discrete Modifications of Atherosclerotic Risk Factors in Kidney Disease 3]). The study received approval by the Princess Alexandra Human Research Ethics Committee (HREC 2007/190) and University of Queensland Medical Research Ethics Committee (MREC 2008000184) and was registered at the Australia New Zealand Clinical Trials Registry (www.anzctr.org.au; study number 12608000337370). Patients were eligible for inclusion if they were aged 18 to 75 years, had moderate CKD (estimated glomerular filtration rate [eGFR] calculated using the MDRD [Modification of Diet in Renal Disease] Study equation of 25-60 mL/min/1.73 $m^2$), and had one or more uncontrolled cardiovascular risk factor, such as blood pressure [BP] exceeding target, overweight (body mass index [BMI] > 25 $kg/m^2$), poor diabetic control (hemoglobin $A_{1c}$ > 7%), or lipid levels exceeding target. Exclusion criteria for the study were intervention for or symptomatic coronary artery disease (within 3 months), current heart failure (New York Heart Association classes III and IV), or significant valvular heart disease; pregnant or planning to become pregnant; or life expectancy or time to dialysis or transplantation less than 6 months. Participants provided written informed consent, and the study complied with the Declaration of Helsinki.

### Study Procedure

Before randomization, all eligible patients were screened by exercise stress echocardiogram for exercise-inducible myocardial ischemia. Patients identified as having an abnormal stress test result suggestive of ischemia were reviewed by a cardiologist prior to randomization to the study.

After completion of screening and baseline testing, the study nurse used a computer random assignment program to allocate patients to either the lifestyle intervention (intervention) group or a usual-care (control) group in a ratio of 1:1. The groups were stratified by kidney function (high or low eGFR: >44 or ≤44 mL/min/1.73 $m^2$, respectively), sex, and diabetes status.

Patients attended the laboratory early in the morning for baseline and 6- and 12-month assessments, after an overnight fast and prior to taking antihypertensive or diabetes medication. Fasting blood and urine samples were collected, as well as anthropometric (weight and height), clinic BP, physical activity, and physical performance measurements. Patients medicated with heart rate–limiting medication were advised to withhold the medication for more than 24 hours prior to maximal exercise testing.

### Usual-Care Group

The control group received treatment according to best practice guidelines.[12,13] At our site, this includes attending a consultation with a nephrologist and lifestyle modification being recommended, but no detailed information or education, and referral on an ad hoc basis to an allied health practitioner.

### Exercise Training and Lifestyle Intervention

In addition to the usual care provided by a nephrologist, assistance in managing cardiovascular risk was provided by a nurse-led multidisciplinary team to patients in the intervention group. The multidisciplinary team included a nurse practitioner, exercise physiologist, dietitian, psychologist, credentialed diabetes educator, and social worker. The team monitored risk factors regularly according to a standard protocol, with the aim of improving the attainment of risk factor targets.[12,13]

Prior to commencing exercise training, patients were reviewed by the nurse practitioner. A detailed medical and surgical history was taken and current medications were recorded. In particular, medical conditions that could potentially affect the ability to exercise safely, such as prior cardiovascular disease, peripheral vascular disease, or peripheral neuropathy and musculoskeletal injuries, were assessed. Patients were educated about exercising safely, in particular, the importance of maintaining hydration in a subtropical climate, and signs and symptoms of an abnormal response to exercise. Patients who experienced angina during exercise were instructed to cease activity and medicate with nitroglycerin, rest until pain resolves, and when able, continue with exercise. Patients with severe arthritis, which limited their mobility, were trained in a swimming pool to minimize stress on joints and build strength.

All patients with diabetes had a baseline assessment by a diabetes educator, who ensured that the patient had a functioning blood glucose meter, was self-monitoring appropriately, and was educated on how to identify and treat hypoglycemia correctly.

Exercise prescription was individualized based on patient comorbid conditions using the guidelines of the American College of Sports Medicine.[14] The exercise training component of the intervention aimed to have patients complete 150 min/wk comprising moderate intensity aerobic and resistance exercise, starting with 8 weeks of supervised exercise training followed by 10 months of home-based training. The initial supervised phase included a combination of aerobic and resistance training. Aerobic activities included walking or jogging, cycling, or rowing at an exercise intensity of rating of perceived exertion of 13 to 15 for up to 30 minutes. Participants then performed 3 sets of 10 to 15 repetitions of 6 to 8 functional resistance exercises, using hand weights or resistant bands (Theraband), that focused on whole-body activities, including wall squats; bench press; lunges; wall pushups; seated row, bicep, and tricep extension; "supermans"; and bridge holds.

Follow-up with the nurse practitioner was scheduled at week 4 to monitor the impact of exercise on BP and blood glucose levels. BP and blood glucose levels (in participants with diabetes only) were assessed by the exercise physiologist prior to each gym session and monitored closely throughout the supervised intervention. The nurse practitioner was consulted and additional review was sought if the patient required medication modification or further counseling on hypoglycemia management or if other issues were identified during the exercise session. During the home-based