Exercise to Improve Physical Function and Quality of Life in CKD

Manisha Jhamb* and Daniel E. Weiner†


It is estimated that one in 10 adults in the United States (>20 million people) may have CKD. Patients with advanced CKD have a comparable burden of patient-reported symptoms, including fatigue, poor sleep, depression, and poor overall health-related quality of life (HRQOL), as those with dialysis-dependent ESRD (1). Moreover, patients with CKD commonly have poor physical function and frailty, conditions that lead to poor outcomes, including falls and hospitalizations (2,3). Patient-reported and physical functioning outcomes are not only important indicators of morbidity and functional independence, but may also have prognostic significance in terms of mortality risk (4–6). Critically, these patient-reported outcomes may be modifiable, and exercise interventions in particular could improve these outcomes in people with CKD.

Although there are a large number of studies evaluating the effect of exercise on various outcomes in ESRD, fewer studies have evaluated the effects of exercise in people with nondialysis-dependent CKD (3), and these studies have typically examined varied outcomes in fairly small populations over relatively short treatment intervals (7). Reasons for the paucity of studies in CKD may include concerns about safety, specifically BP and glycemic control, as well as the only recent recognition of nondialysis CKD as a clinically important disease state (3). In this context, Rossi et al. conducted one of the largest clinical trials to date evaluating the safety and efficacy of a supervised exercise program in people with CKD, which is published in this issue of CJASN (8).

In this single-center randomized nonblinded trial, Rossi et al. randomized 119 individuals with CKD stages 3 or 4 to either a 12-week renal rehabilitation exercise program or usual care (8). The exercise program consisted of guided exercise twice weekly at local physical therapy or cardiac rehabilitation facilities, with the exercise program tailored to the individual’s capabilities at baseline in people with CKD. Exercise included both aerobic (treadmill and/or stationary cycling) and resistance (weight training) elements. In addition, exercise participants were given pedometers and encouraged to walk 5000–10,000 steps per day. The main outcomes were performance on physical function tests (6-minute walk test [6MWT], sit-to-stand test [STST], and gait speed test) and HRQOL assessed using the RAND Short Form-36 (SF-36).

Among the 119 randomized participants, six in each group did not receive the allocated intervention; in the exercise group, five of these reflected failure to obtain medical clearance to exercise. A total of 107 participants entered the study: 48 in the usual care group and 59 in the exercise group. The groups were similar in terms of age (68±12 years), but the exercise group had significantly more women (61% versus 31%) and patients with diabetes (47% versus 35%). There were 28 participants (26%) with stage 4 CKD, with the remainder having stage 3 CKD. As expected, patients in both groups had a low self-reported level of activity at baseline as well as physical functioning of only 60%–65% of that predicted for healthy individuals on the 6MWT and STST. Surprisingly, the exercise group had higher gait speed at baseline, differing significantly from the control group. At study completion, the exercise group but not the control group had significant improvements in the 6MWT (19% increase) and STST (29% improvement), whereas there was no change in gait speed. Patients in the exercise group reported significant improvements in the SF-36 physical measures, although neither study group experienced significant changes in SF-36 mental health measures. Importantly, the exercise program was well tolerated and no exercise-related adverse events were observed.

This study addresses an understudied problem of high clinical relevance in a chronically ill CKD population. It successfully demonstrated that a relatively brief supervised exercise intervention in patients with stages 3 and 4 CKD can have clinically meaningful improvements in physical function, especially lower extremity function and HRQOL. Moreover, it showed that moderate intensity supervised exercise was safe in these patients. The notable strengths of the study include the randomized design, use of validated and clinically relevant functional and patient-centered outcomes, and use of a multidisciplinary approach with involvement of the nephrologist, primary care physicians, and trained exercise/cardiac rehabilitation staff.

Although exciting, the results of this study should be interpreted in the context of some limitations. As is a problem with most lifestyle modification studies, adherence to the exercise program was an issue and 18.6% of the patients in the exercise group did not complete the program. Although this may seem like a high dropout rate over a relatively brief study, it is comparable to reported adherence rates in other lifestyle intervention studies in elderly patients and patients with CKD. For example, the recently competed Lifestyle Interventions and Independence for Elders (LIFE) study, which randomized 1635 sedentary men and women aged 70–89 years who had physical limitations to either exercise or

*Renal-Electrolyte Division, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; and †Division of Nephrology, Tufts-New England Medical Center, Boston, Massachusetts

Correspondence: Dr. Manisha Jhamb, Renal-Electrolyte Division, University of Pittsburgh School of Medicine, 200 Lothrop Street, P/UH C-1101, Pittsburgh, PA 15213. Email: jhambm@upmc.edu
education interventions for an average of 2.6 years, noted 63% attendance at scheduled exercise sessions after excluding missed sessions for medical reasons, whereas health education participants attended 73% of scheduled sessions (9). Important to note is that of the 48 participants randomized to the rehabilitation program who completed the study, 35 (73%) attended all 24 sessions. Second, this study required travel to an exercise/cardiac rehabilitation facility; accordingly, more infirm individuals who were less likely to travel may not have participated, resulting in modest selection bias. Third, eGFR was not reported, and it is possible that many of the participants with CKD stage 3 had only very modest kidney disease. Finally, this study either failed to capture or did not report several potential confounding factors such as hemoglobin, albumin levels, and race/ethnicity, possibly limiting generalizability.

In studies measuring patient-reported outcomes and subjective well-being, including in studies where blinding is not possible because of the nature of the intervention, results may be confounded by the attention received from being in the treatment group of the study rather than the true effect of the intervention itself. To determine the true effect of exercise on HRQOL measures, it would be optimal to have an attention control group as the comparator, as was done in the LIFE study (9). This group would receive an intervention that approximates the amount of time and attention received by the exercise group, and thus could help tease out the true effect of exercise. Despite its limitations, the results of this study add substantially to the current knowledge of the effects and efficacy of exercise in people with CKD and have important clinical and research implications.

Several questions remain. First, can exercise interventions be translated and integrated into routine clinical care? Second, will (and should) theoretical safety issues, including concerns over cardiac clearance, affect the willingness of physicians and other providers to suggest exercise and patients to undertake exercise? Third, can benefits seen in a 12-week study be maintained over longer periods of time, particularly in settings with less attention from exercise staff? Finally, is the infrastructure available to provide supervised exercise training, at least initially, to patients with advanced CKD, many of whom have other medical comorbid conditions? Future research is needed in this field to address these and other questions, focusing on longer studies assessing adherence, safety, and efficacy as well as evaluating the mediators of any benefits of exercise in people with CKD. In this area, the ongoing Aerobics, Weights and Renal Disease (AWARD) study is randomizing 210 individuals with CKD stages 3–4 to a 1-year exercise versus education intervention, similar to that done in the LIFE study. The AWARD study will focus on physical and cognitive function outcomes and will evaluate the potential mediating role of microvascular disease (ClinicalTrials.gov identifier NCT01462097).

Current guidelines for management of patients with CKD, on the basis of very limited data, suggest exercise for the CKD population. Specifically, the Kidney Disease Improving Global Outcomes 2012 Clinical Practice Guideline for the Evaluation and Management of CKD recommends that patients with CKD undertake regular exercise, compatible with cardiovascular health, aiming for at least 30 minutes, 5 times per week (10). Interestingly, the Kidney Disease Outcomes Quality Initiative (KDOQI) guideline notes that “implementation of this recommendation has no public health cost” (10). This KDOQI guideline likely understates the infrastructure investments needed to make exercise rehabilitation programs a readily available resource for patients with CKD (11), although resources for and acceptance of exercise as a treatment continue to expand. Ultimately, the key to any exercise intervention is to apply it widely to reinforce a culture of exercise and healthy living, even to people with advanced comorbid conditions such as CKD, and to continuously highlight patients’ successes, including their ability to transition exercise into their daily home routines. In this regard, the widespread proliferation of home fitness trackers, like Fitbit, Nike+, Jawbone, and other systems, with their ability to remotely communicate activity data, presents a tremendous theoretical opportunity to promote and reinforce exercise in people with CKD. In summary, with their rigorous study of a practical exercise intervention, Rossi and colleagues highlight that the time has come for the nephrology community to catch up to our cardiology and pulmonary colleagues by adding renal rehabilitation programs to the list of widely available and frequently accessed resources for patients with chronic medical conditions.

Disclosures
None.

References

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See related article, “Effects of a Renal Rehabilitation Exercise Program in Patients with CKD: A Randomized, Controlled Trial,” on pages 2052–2058.