Physical dysfunction and muscle atrophy are common among patients with CKD; consequently, frailty and disability are also far more prevalent in this population than in unselected older individuals. Patients with ESKD report that maintaining independence and functional status is among their most important priorities. Although data are generally cross-sectional, these problems seem to develop and worsen as CKD progresses, with patients becoming less active and losing muscle mass and function.

Exercise improves functional status and cardiovascular outcomes among community-dwelling elders, and the extremely sedentary behavior observed in the dialysis population has been recognized as a potential contributor to functional limitations. Specifically, aerobic exercise increases aerobic capacity, leading to increased endurance, and it can also improve endothelial function, reduce resting BP and heart rate, and reduce cardiovascular mortality. Resistance exercise training increases muscle size and strength. Given the poor physical function of patients with CKD, even small increases in exercise capacity or strength have the potential to result in meaningful differences in functional status. Furthermore, it is conceivable that exercise could improve mortality or even slow the progression of CKD.

Hundreds of studies have examined exercise interventions in the CKD and ESKD populations, including aerobic exercise training delivered in a supervised rehabilitation center, at home, or during dialysis treatment. Interventions have varied in the form (e.g., stationary cycle or treadmill), intensity, and duration of training. Resistance exercise has been included in some of these studies, and it has also been examined as a primary form of therapy, including during dialysis. Most studies have reported beneficial effects of exercise in terms of improved exercise capacity, self-reported physical function, or physical performance as well as other effects, such as improved BP control or endothelial function.

On the basis of this extensive literature, it would be reasonable to suggest that exercise is more beneficial than many other treatments that we offer patients with CKD, at least for outcomes that they care about. However, it would also be fair to say that the evidence that exercise improves functional status among patients with CKD is weak. How is it possible for both of these views to be justified? The answer lies in heterogeneity among exercise interventions, patient populations, and outcomes along with small sample sizes and often, poor study quality. These issues have prevented investigators and clinicians from coming to a consensus about the value of exercise, the most beneficial form or forms of exercise, and the degree to which patients can be convinced to participate.

To be fair, these problems stem from the great challenges and barriers to studying patients with CKD and ESKD. Their extremely low baseline functional status and thrice weekly dialysis schedule make it challenging to deliver traditional moderate to vigorous exercise training intervention delivered in an exercise facility out of the question for most patients on dialysis. Even when intervention is tailored to patients’ initial exercise capacity and delivered in a dialysis facility, there are challenges related to safety and resources (equipment and ability of staff to deliver and supervise exercise). In addition, patients’ varying degree of volume overload and frequent hospitalizations also interfere with progression of exercise. Functional status and response to exercise are likely to be affected by non-CKD–related factors and comorbid conditions. Among patients with nondialysis-dependent CKD, there is further heterogeneity on the basis of level of eGFR and manifestations and treatment of complications of CKD. These issues have hindered the conduct and interpretation of exercise interventions.

Animal studies have a major advantage in that effects of kidney disease and exercise on muscle function and other outcomes can be isolated and that heterogeneity on the basis of age, cause of CKD, control of the complications of CKD, and comorbid conditions can be eliminated. In this issue of JASN, Avin et al. report on the effects of 10 weeks of voluntary wheel running among rats with and without progressive cystic CKD. The intervention consisted of housing rats in cages with a freely accessible voluntary activity wheel and was begun at 25 weeks of age, corresponding to stages 2–3 CKD. The results seem to be highly relevant to human CKD. Key findings were that rats with CKD ran less than normal litter mate rats without CKD and that the distance that they ran decreased with progression of disease. This is an important confirmation that CKD itself is associated with a progressive decline in volitional physical
activity independent of age (which was matched in this study) and comorbid conditions (which were absent).

Another important finding was that animals with CKD and access to a wheel were more active than those without access, although they were not compelled or incentivized to be more active. Obviously, the human environment is less easily controlled, and human motivations are complex, but this result suggests that providing access to physical activity is likely to increase it, even in the setting of CKD. Finally, wheel running improved serum creatinine concentration, cystic kidney weight, serum phosphorus, and parathyroid hormone in the rats with CKD, and it also increased muscle strength and exercise capacity. Thus, exercise slowed the progression of kidney disease, lessened manifestations of CKD-related mineral and bone disorder, and improved physical function, benefits that investigators have hypothesized might accrue to patients but have had difficulty studying.

How can we apply these results to patients with CKD? Although the intensity of exercise could not be precisely quantified in this study, it seems to have been moderate. Contrasting these results with those of the investigators’ prior work, in which forced, high-intensity treadmill exercise actually led to negative results, may be instructive. Overtraining may be an important consideration among animals and patients with CKD who have very low exercise capacity at baseline. Difficulty recruiting patients for exercise studies and high rates of dropout of enrolled participants could reflect patients’ fear of or actual negative experience with vigorous training.

The results of this study by Avin et al. serve as an exciting demonstration of the potential benefits of moderate-intensity exercise among patients with CKD. They align with a key message from the new 2018 physical activity guidelines for Americans that the greatest health benefits accrue by moving from no to even small amounts of physical activity. In a recent pilot study, patients on dialysis who were advised to walk more but allowed to determine the speed and timing of walking increased their activity, analogous to the rats’ volitional wheel running in the study by Avin et al. Larger studies of lower-intensity exercise requiring fewer resources and powered to examine important outcomes are urgently needed in the CKD and ESKD populations.

DISCLOSURES

Dr. Johansen is a member of the Steering Committee for GSK’s ASCEND study program.

REFERENCES


Transplantation of Kidneys from HCV Viremic Donors in the United States: A Missed Opportunity to Inform Clinical Decision Making and Health Policy

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In this issue of JASN, Potluri and colleagues report a marked increase in the availability and use of kidneys from HCV viremic deceased donors for transplantation as a result of the opioid epidemic and the advent of direct-acting antivirals (DAAs). Historically, transplantation of these kidneys was restricted to HCV-positive waitlist candidates and most were either not retrieved or discarded. DAAs now allow...