Lower Physical Activity and Depression Are Associated with Hospitalization and Shorter Survival in CKD

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Clin J Am Soc Nephrol 9: 1669–1670, 2014. doi: 10.2215/CJN.08400814

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Physical activity or exercise training helps improve muscle strength and physical and mental function, including benefits on depressive symptoms, which affects at least 20%–30% of patients receiving maintenance hemodialysis (MD) (1). Depression contributes to low quality of life and restricted living among patients with CKD. Thus, exercise can be an interesting intervention to reduce depression and hospitalization and improve quality of life in these patients. Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure. Exercise is a subset of physical activity that is planned, structured, and repetitive and has a final or intermediate objective to improve or maintain physical fitness (2). These activities cannot be measured in the same ways: Physical activity can be estimated by self-reported instruments, such as scales, questionnaires, or pedometers, whereas exercise needs more objective measures, such as motion sensor recording.

Exercise is complex in that it can specifically train certain muscles. Different types of solicitation are proposed: continuous versus sequential and resistance versus endurance. These differences may confound the analysis of benefits between rehabilitation programs. Another important question is the purpose for which patients are trained: For the most active patients, the goal may be to ensure they have muscles strong enough to allow them to walk or run; for the elderly, to maintain their balance; and for patients with heart disease, to perform regular protective cardiovascular training.

Physical activity is extremely low in patients with CKD and those undergoing MD (3). In a 2012 cohort from France in >1100 patients receiving MD, the median number of steps was 3700 per day (4); in contrast, routine physical activity in healthy adults should reach 10,000 steps per day. Of note, whereas age is a determinant of the daily step number, some phenotypes may be associated with different levels of physical activity independent of age: Patients with a prior renal transplant had greater physical activity (>5000 steps per day), and those with chronic inflammation and a history of cardiovascular events, even at a younger age, had the lowest level of physical activity (<2700 steps per day). Thus, physicians should be aware of particular conditions associated with very low physical activity and may first target rehabilitation program in these subgroups of patients. Also remarkable is that <10% of MD patients had a regular exercise program (4). When MD patients did wear a pedometer, they significantly increased their level of physical activity (5).

Obviously, physicians taking care of patients with CKD encounter physical inactivity, and a growing literature demonstrates that physical inactivity is a cardiovascular risk factor in CKD. Indeed, survival rates are lower in patients with lower physical activity: Roshanravan *et al.* reported that patients with stages 2–4 CKD had an increasing mortality rate of 26% for each 0.1 m/s–decrease in gait speed test (6). Furthermore, patients who engaged in physical activity 2–5 times weekly had a lower mortality rate than those who were physically active only once a week (7). In a cohort of 2264 hemodialysis patients, mortality among those who said they engaged in physical activity was 5% compared with 11% in sedentary patients (8). Thus, in CKD there seems to be compelling evidence that low physical activity is a risk factor.

Overall, is exercise beneficial to patients with CKD? The answer is yes. Both physical activity and exercise are associated with improved outcomes in these patients. Although a limited number of studies have been reported, all differing by protocol, they show that aerobic and resistance training can improve physical functioning, quality of life, depressive symptoms, survival, or hospitalization (1,9,10).

Providing more insight on this topic are three studies published in this issue of *CJASN*. The first one, by Bowling *et al.* (11), used the Short-Form (SF)-12 in 3557 elderly individuals (age >75 years) who were among the 30,239 United States volunteers in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. They compared participants with normal renal function (≥60 ml/min per 1.73 m^2 based on CKD-Epidemiology Collaboration formula) to those with lower eGFR and higher albumin-to-creatinine ratio. Elderly patients with more nonspecific symptoms (including exhaustion and impaired mobility) were more frequently hospitalized and had a lower 5-year survival rate if they had impaired renal function or higher albumin-to-creatinine ratio. This study analyzed neither physical activity nor exercise because SF-12 evaluates only mobility, exhaustion, and history of falls. Although not specifically investigating this question, the study suggests that elderly patients with CKD presenting with exhaustion and impaired mobility, who probably are the most inactive, have a lower survival rate and are more often hospitalized.

In a second report focused on depressive affect, Lacson *et al.* (12) retrospectively evaluated 8776 incident adult hemodialysis patients from a large United States cohort. Using the SF-36 survey administered shortly after dialysis inception, they observed that approximately 40% of patients had depressive symptoms and that depression was associated with a higher risk of hospitalization and more hospitalization days during the subsequent 12 months of treatment. This observation was made from data obtained 8 years ago, and there was no information on potential treatment or absence of treatment during the subsequent year. In addition, causes of death and follow-up of SF-36 survey were not available to allow the investigators to estimate the progression of depressive symptoms over time.

The third study, from Lopez *et al.* (13), may be the link between the first two studies. A total of 5763 MD patients from 12 countries participating in the 2009–2012 Dialysis Outcomes and Practice Patterns Study(DOPPS) were assessed by the Rapid Assessment of Physical Activity (RAPA) questionnaire, which evaluates aerobic activity. Another component of physical exercise (strength/flexibility activity) was also measured. RAPA responses were positively associated with quality of life and inversely related to depression symptoms and mortality (13).

If we could aggregate these three studies, we would find that elderly patients with CKD would have higher risk of depressive symptoms (11), depression is associated with more hospitalization when patients start MD (12), and greater physical activity during hemodialysis is associated with better quality of life and fewer depressive symptoms. These finding suggest that physical activity should be enforced in all dialysis facilities. However, these results are from observational studies—they can only suggest facts, not prove them. Randomized controlled trials are needed to ascertain causality and prove efficacy of these measures.

Is it easy to record physical activity? Not really, based on the high number of dropouts and incomplete recording observed in routine practice. In the study by Lopes *et al.* (13), 11,733 patients were enrolled and sufficient information was obtained for only 5763 (49.1%). In prospective studies specifically designed to measure physical activity, records were incomplete for 8% of enrolled patients (4). Thus, as for nutritional status, physical activity is still a tricky performance to monitor, and research should continue to improve data collection and reliability.

Physical activity or exercise seems to be an effective treatment for depression and consequently may reduce mortality and hospitalization. Aerobic exercise is the most common form of training in patients with CKD and appears to be effective in improving CKD complications; however, resistance exercise may also be an alternative. Not only is the nature of exercise important, but also the duration of intervention and the frequency and intensity of sessions are crucial points to be discussed.

Acknowledgments

We wish to thank Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and le Comité Français d´Evaluation de la Coopération Universitaire avec le Brésil (COFECUB).

Disclosures

None.

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Published online ahead of print. Publication date available at www.cjasn.org.

See related articles, "Nondisease-Specific Problems and All-Cause Mortality among Older Adults with CKD: The REGARDS Study," "Depressive Affect and Hospitalization Risk in Incident Hemodialysis Patients," and "Associations of Self-Reported Physical Activity Types and Levels with Quality of Life, Depression Symptoms, and Mortality in Hemodialysis Patients: The DOPPS," on pages 1737–1745, 1713–1719 and 1702–1712 respectively.