J Nephrol (2015) 28:143–150
DOI 10.1007/s40620-014-0169-6

REVIEW

Physical excercise programs in CKD: lights, shades and perspectives: a position paper of the "Physical Exercise in CKD Study Group" of the Italian Society of Nephrology

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Received: 18 September 2014 / Accepted: 3 December 2014 / Published online: 3 February 2015

Abstract In the general population, moderate exercise is associated with several health benefits including a decreased risk of obesity, coronary heart disease, stroke, certain types of cancer and all-cause mortality. In chronic kidney disease (CKD), physical inability is an independent risk of death. Health benefits of regular exercise in CKD patients include improvements in functional and psychological measures such as aerobic and walking capacity and health-related quality of life. Nonetheless, in CKD patients exercise rehabilitation is not routinely prescribed. Renal patients are heterogeneous across the different stages of CKD so that the assessment of physical capability is mandatory for a correct exercise program prescription. To plan appropriate exercise programs in the CKD setting, targeted professional figures should be actively involved as many psychological or logistic barriers may hamper exercise implementation in these subjects. Different approaches, such as home exercise rehabilitation programs, supervised exercise training or in-hospital gym may theoretically be proposed. However, physical exercise should always be tailored to the individual capacity and comorbidities and each patient should ideally be involved in the decision-making process.

Keywords Physical activity · Chronic kidney disease · Exercise training · Physical functioning · Quality of life

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Introduction

It has been estimated that, worldwide, one in every five adults is physically inactive [1]. Large prospective cohort studies have clearly demonstrated that sedentary behavior is associated with a variety of poor health outcomes ranging from obesity to increased mortality [2]. Moderate exercise is associated with several health benefits, including a decreased risk of obesity, coronary heart disease, stroke, certain types of cancer and all-cause mortality. Exercise may also increase the likelihood of quitting tobacco use, reduce disability for daily living activities in older persons, delay cognitive decline in older adults, and reduce stress, anxiety and depression. Regular physical activity and higher cardiorespiratory fitness decrease overall mortality in a dose–response fashion [3]. The benefits of exercise rehabilitation are clearly recognized in patients with chronic cardiac, pulmonary or neurologic diseases. Notably, although persons with chronic kidney disease (CKD) may also benefit from physical rehabilitation for improving health status, exercise rehabilitation is not yet routinely prescribed to these patients [4]. Despite the recommendation of the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines to undertake aerobic physical activity, physical functioning of renal patients is even worse than that of sedentary healthy subjects [5–7] and, regardless of age, it can be rather comparable to that of older individuals in the general population [8, 9].

Physical performance and outcomes in CKD

Many predisposing factors have been called into question to explain the poor physical function in the CKD population, including physical inactivity, anemia, abnormal cardiac function and structural and skeletal muscle abnormalities [10]. Padilla et al. [11] showed that physical performance and self-reported physical functioning [based on the Physical Functioning scale and the Physical Component Summary (PCS) measure of the SF-36 questionnaire] are reduced in patients with mild to moderate CKD. Similar evidence was reported in a Swedish cohort [12] and in the African American Study of Kidney Disease and Hypertension (AASK) [13]. The functional capacity of persons with CKD, as measured by the peak oxygen consumption (VO_2 peak), is about 50–80 % of healthy levels [14]. Recently, a comprehensive study [9] of pre-dialysis CKD patients showed a substantially diminished performance in lower extremity function, but relatively preserved upper extremity muscle strength. In a corollary analysis of the Exercise Introduction to Enhance Performance in Dialysis (EXCITE) trial [15], the crude risk-excess of death in dialysis patients non-eligible versus those eligible for a simple fitness program [hazard ratio (HR) 1.96; $p < 0.001$] was almost nullified after including in a multivariate model the presence of deambulation impairment (HR 1.16; $p = 0.513$). Furthermore, an increase of 20 walked meters at the 6-min walk test (6MWT) was associated to a 6 % reduction of the risk for the composite end-point of death, cardiovascular events and hospitalizations ($p = 0.001$) regardless of classical and non-classical risk factors [16]. This indicates that physical inability conveys per se an important excess risk of mortality also in frail end-stage kidney disease (ESKD) patients on chronic renal replacement therapy. Also in renal transplanted patients physical activity and related cardio-respiratory fitness are impaired and such reductions seem associated with increased risk of mortality [17].

Key messages

- Daily physical activity is reduced in CKD patients of all stages.
- In chronic diseases including CKD, physical inability represents a major disease risk factor.
- Physical functioning capacity in CKD populations is reduced, averaging 50–80 % of that of healthy people.
- Physical inability increases the risk of mortality in dialysis patients.

Methods to assess physical performance

Objective measures to assess physical performance are crucial to frame the single-patient risk profile and to tailor exercise programs to the individual's capacity (Table 1). Measurements of lower extremity function are relatively easy to perform and may capture a complex set of skeletal muscle and neurologic impairments that develop in CKD patients. The 6MWT measures the distance an individual is able to walk over a total of 6 min on a hard, flat surface. The goal is for the individual to walk as far as possible in 6 min. The individual is allowed to self-pace and rest as needed while traversing back and forth along a marked path. The 6MWT was initially developed to evaluate functional capacity in frail elderly patients referred to a geriatric hospital [18], but it has been subsequently validated in a variety of other chronic diseases as it is useful to predict hospitalization and mortality as well as to detect changes following interventions to improve exercise tolerance [19].

The Chair Stand test (also known as the Sit-to-Stand or STS test) was also designed to test leg strength and endurance, particularly in aged patients who may not be able to do traditional fitness tests [20]. The only equipment required to perform such test is a straight-back or folding chair without arm rests (seat 44 cm high) and a stopwatch. The subject sits in the middle of the seat, with the feet shoulder-width apart, flat on the floor. The arms are crossed at the wrists and held close to the chest. From sitting position, the subject stands completely up, then sits back down, repeating this procedure for 30 s. The total number of complete chair stands is counted and if the subject has completed a full stand from the sitting position when the time is elapsed, the final stand is counted in the total. The final score is the number of completed chair stands in 30 s.

The Timed Get Up and Go Test (TUS) is another test for measuring mobility in people who are able to walk on their own. Persons are seated in the chair with their back to the chair and arms resting on the arm rests. They are then asked to stand up and walk a distance of 3 m, turn around, walk back to the chair and sit down again. Timing begins when they start to rise from the chair and ends when they return to the chair and sit down. The times from the three actual trials are averaged.

Finally, submaximal cycle ergometer testing is used in place of a maximal exercise test to assess (sub)maximal

Table 1 Main tests for assessing physical fitness in CKD patients

Test/ parameter	Details	Outcome measures	Fitness index	Population targets	Data in CKD
Six-minute walk test (6MWT)	Distance an individual is able to walk over a total of 6 min on a hard, flat surface (marked pathway). The individual is allowed to self-pace and rest as needed	Distance covered in meters over 6 min. To measure functional aerobic capacity or general fitness, this test may be used in conjunction with VO_2 testing. Fatigue perceived may be assessed by the BORG scale	Functional capacity/ fatigue	Chronic diseases (heart failure, chronic obstructive pulmonary disease, stroke) To predict hospitalization and mortality in elderly subjects	Usually reduced 6MWT distance covered as compared to healthy, age-matched subjects
Chair stand, or Sit-to-Stand (STS), test	From sitting position, the subject stands completely up, then sits completely down, repeating this procedure for 30 s	The final score equals the number of completed chair stands in 30 s	Leg strength and endurance	Elderly with limited functional capacity who are not able to do traditional fitness tests	Lower number of chair stands as compared to healthy subjects
Submaximal cycle ergometer testing	Subject pedals a stationary cycle ergometer with an initial exercise intensity that is set below the anticipated maximal capacity and then progressively increased	Heart rate, blood pressure and ECG data are recorded during and at the end of the test	Submaximal aerobic- or functional work-capacity	Persons with reduced reserve capacity	Reduced exercise tolerance in mildly impaired ESKD patients
Timed Get Up and Go Test (TUS)	Subject sitting in a chair is asked to stand up and walk 3 meters, turn around, walk back to the chair and sit down again	Timing begins when the person starts to rise from the chair and ends when the person returns to the chair and sits down. The times from the three actual trials are averaged	Mobility/ functional capacity	People able to walk	No evidence

VO_2 oxygen consumption, *ECG* electrocardiogram, *ESKD* end-stage kidney disease

aerobic- or functional work-capacity in persons with reduced reserve capacity of the cardiopulmonary and musculoskeletal systems, such as ESKD patients [21]. Subjects are asked to pedal a stationary cycle ergometer with an initial exercise intensity that is set well below the anticipated maximal capacity and then progressively increased. Heart rate, blood pressure and electrocardiogram (ECG) data are usually recorded during and after the test.

Key messages

- Physical capacity can be evaluated by several simple tests that do not require any special devices and may capture skeletal muscle and neurologic impairments (see Table 1).
- Simple tests evaluating physical capacity should be implemented in clinical practice.

Effects of exercise in the CKD population

Health benefits of regular exercise may extend also to patients with CKD. These mostly include improvements in functional and psychological measures such as aerobic and walking capacity and health-related quality of life (HRQoL) [22]. Regular exercise may also slow the decline in renal function [23]. Pre-dialysis patients may have a rapid improvement in physical function, even after short-term exercise regimens [24, 25]. Exercise may also help to preserve muscle mass and improve strength in pre-dialysis patients on a low-protein diet [26]. Improved walking and aerobic capacities by regular fitness in pre-dialysis as well as in dialysis CKD patients have been reported in several studies [22, 27–31]. In addition, muscle strength and muscular area may also be improved [26, 28, 32, 33]. Regular exercise may somewhat ameliorate HRQoL of CKD and dialysis patients [29, 30, 32, 34–42]. Some evidence also exists that in HD patients regular training may improve parameters of nutritional status such as serum albumin levels and creatinine generation rate [37] as well as left ventricular mass [27, 29]. Unfortunately, no longitudinal data on the impact of physical exercise on hard outcomes, such as fatal and non-fatal cardiovascular events, are yet available. Sparse data are also available in renal transplanted patients with CKD. In a prospective, controlled study in renal transplanted children, exercise sessions of 3–5 h per week normalized indexes of cardio-respiratory fitness [43]. In a systematic review focused on renal transplanted patients, habitual physical activity was associated with better quality of life and aerobic fitness, and exercise interventions had beneficial effects on aerobic capacity and muscle strength [44].

Physical exercise could, theoretically, be dangerous in some CKD patients, particularly the most frail (such as ESKD patients). Sustained exercise, for instance, might transiently increase the risk of fatal or nonfatal cardiovascular events, particularly in individuals with structural cardiac diseases, hereditary or congenital cardiovascular abnormalities [45] or in older individuals at high risk of thrombosis [46]. However, in a 4-year study of 48 hemodialysis (HD) patients randomly assigned to a supervised outpatient exercise training program on the non-dialysis days or to exercise with stationary bicycles during the dialysis session, no adverse effects were reported [47].

Unfortunately, additional evidence confirming the safety of exercise programs in the CKD setting is lacking. In the absence of such evidence, low-intensity exercise schedules tailored to the individual's functional status and comorbidities (see below) represent the most rational and pragmatic approach to this issue.

Key messages

- Regular physical activity and good cardio-respiratory performance are associated with health benefits in CKD patients.
- Stable, uncomplicated CKD patients would benefit from at least 30 min of moderate-intensity physical activity (i.e. 3.0–6.0 METs: housekeeping, cycling at a slow pace, walking at 5–6 km/h, gardening, swimming, playing golf, handwork, etc.) four to five times per week.

Implementation of physical activity in renal patients not on dialysis

Renal patients are clinically heterogeneous across the different stages of CKD and, therefore, assessment of physical capability and cardiopulmonary status and function are mandatory for a correct exercise program prescription [48]. According to KDOQI guidelines, people with CKD should undertake at least 30 min of low/moderate-intensity physical activity 4–5 times per week [49], i.e. an exercise program very similar to those recommended by the U.S. Department of Health and Human Services (HHS)/American College of Sports Medicine (ACSM)/American Heart Association (AHA) Guidelines on Physical Activity [50] and the European Society of Cardiology (ESC) European Guidelines on Cardiovascular Disease Prevention in Clinical Practice [51]. Implementation of exercise and encouragement of physical activity might become part of the routine care of patients with CKD [52]. Greenwood et al. [53] evaluated the feasibility of a pragmatic, supervised, outpatient exercise program based on self-management education and exercise training for 12 weeks. The program was delivered by a team consisting of a lead renal physiotherapist, a specialist physiotherapist and a technical instructor. Patients were required to attend a twice-weekly supervised outpatient exercise program and education sessions before entering a once-weekly home-based exercise program. The exercise prescription and its intensity were individualized according to the patient's functional abilities and needs. Overall results were encouraging and the approach was effective in improving functional capacities in all CKD patients.

Implementation of physical activity in dialysis patients

Increasing physical fitness in dialysis patients might be helpful to reduce comorbidities and hospitalizations, hence contributing to cost-saving [54].

In peritoneal dialysis (PD) patients exercise implementation may improve the control of dyslipidemia, glucose metabolism and weight excess [55]. However, careful attention should be paid to activities that could increase the intra-abdominal pressure (i.e. strong isometric-resistance exercises).

In stable HD patients, different programs such as home exercise rehabilitation, supervised exercise training, in-hospital gym and exercise activity during the hemodialysis session, might be proposed.

Home exercise-training programs basically consist in encouraging the patient to progressively increase the time and intensity of usual daily life activities such as walking, cycling, dancing, and so on. Diary reporting or pedometers may be simple tools to check and supervise these activities. More structured exercise programs need a pre-evaluation of performance capacity before prescribing the duration and intensity of exercise [56]. In the EXCITE trial [57], patients were divided into three different levels of physical capability (low–moderate–good) and assigned to an exercise program on the basis of their baseline functional performance. Supervised exercise-training programs consist in training sessions twice/thrice a week in an in-hospital gym, including a treadmill or a workout with an upper limb ergometer crank. High-performance and low-comorbidities patients, such as younger dialysis patients awaiting kidney transplantation, may be addressed to mild to moderate training and provided full nutritional status examinations, echocardiography and cardiopulmonary exercise test by a sports medicine physician or cardiologist. A feasible schedule might consist in training sessions performed twice a week, on non-dialysis days [42, 58], based on aerobic activities below the anaerobic threshold. Duration of each session could be up to 90 min including a warm-up phase of stretching exercises (15–20 min) followed by 20–50 min of cycling on an electronically braked cycle ergometer and finally followed by a recovery phase. The intensity of the exercise would be submaximal, i.e. under the anaerobic threshold, not exceeding 60 % of peak VO_2. The sessions may be held in a gym inside or outside the hospital, with the supervision of a skilled exercise physiologist. In another experience [58], the exercise session schedule consisted of 30–60 min of continuous moderate-intensity walking with a variable load (velocity from 2 to 3 km/h on a slope from 0 to 10 %). The training session began after a brief warm-up of 2 min at a speed of 2 km/h with no slope and was supervised by a physiotherapist and a physician who monitored heart rate, arterial blood pressure, oxygen partial pressure (pO_2) saturation and Borg scale.

Intra-dialytic cycling training is another option, consisting in exercise of variable intensity and time (usually 30 min) during the first 2 h of the HD session [59]. An intra-dialysis exercise training strategy would be possible also without cycles. Patients can perform low-intensity exercises for coordination, muscle strengthening and flexibility and can be trained to adjust exercise intensity using the Borg scale for muscle fatigue. The more frequently used tools are roller and rubber balls placed under the knees for isometric exercises [58]. A recent pilot, randomized trial [60] examined the impact of a novel intra-dialytic progressive resistance exercise training (PRET) program on muscle volume, strength, and physical function in HD patients. PRET consisted of thrice-weekly high-intensity leg press exercises (three sets of 8–10 repetitions at 80 % of their predicted one-repetition maximum) and, after 12 weeks, resulted in a significant increase in thigh muscle volume and knee extensor strength. The intra-dialytic exercise training has the advantage of reducing costs, time and transport of patients. In addition, it may improve dialysis efficiency, enhance solute removal and ameliorate protein metabolism and nutritional status [61, 62].

As a whole, data from the literature would encourage intra-dialysis exercising as a significant aspect of patient care rather than an optional adjunct [4]. However, exercise sessions should be performed under supervision by appropriately qualified staff. Exercise led by a physiotherapy assistant/technical instructor may be the most effective approach, but some programs can be delivered successfully also with the "nurse-led" approach [63]. Three crucial elements of clinical care may contribute to a successful intra-dialytic exercise program: (a) involvement of exercise professionals; (b) real commitment of nephrologists and dialysis professionals; (c) an exercise program adapted to the individual's conditions and needs [64]. The engagement of experts in physical therapy is also crucial as it may help reduce the workload of the hemodialysis staff, who often look upon intra-dialysis exercise as a factor disturbing their clinical duties [65], and it may increase patients' personal confidence with exercise [66].

Key messages

- Promoting and counseling on physical activity as well as implementing exercise training should become part of the routine care of CKD patients.
- Most CKD patients should be encouraged to progressively increase the time and intensity of their usual daily life activities such as walking, cycling, dancing, and so on.
- An ideal exercise program should include both resistance and aerobic activities with single-patient-adjusted duration and intensity, coupled with flexibility, mobility and stretching exercises.
- Exercise programs should be tailored to the existing comorbidities and physical capacity of each patient, who must participate in the decision-making process.

Barriers to physical activity planning in renal patients

Three main barriers make the implementation of exercise programs in the CKD setting extremely challenging: (1) therapeutic nihilism or lack of awareness on the part of healthcare providers, (2) low patient motivation, and (3) multiple comorbidities that may affect the patients. Two studies [67, 68] clearly showed that a complex mix of disease- and patient-specific reasons (socio-economic, psychological, cultural, and clinical) plays a key role in determining physical inactivity. Moreover, also health personnel (e.g. staff of dialysis units) attitudes could significantly contribute to sedentary habits in CKD patients. As a proof, a very low level of exercise counseling has been documented among nephrologists and only a small proportion of them habitually assess patients' level of physical activity [69]. For many years, nephrologists were particularly afraid about the prescription of physical exercise in view of the reduced exercise tolerance of their patients [67]. Recently, the National Kidney Foundation recommended counseling by nephrologists to increase patients' levels of physical activity [70]. Unfortunately, despite the new guidelines, counseling behavior has not increased [67]. These being the facts, one concept stands out: motivating CKD (particularly dialysis) patients to exercise is not a high priority. However, does this lack of consideration stem from a lack of knowledge and rudimentary training in exercise physiology or from a lack of nephrologists' motivation? It is therapeutic nihilism to state that renal patients are insufficiently driven to improve their fitness level. Furthermore, it becomes a fait accompli that CKD patients will not enhance their exercise tolerance if such an attitude prevails [71]. Barriers to the development of dynamic, metric-based exercise programs for CKD patients exist and include inertia on the part of healthcare providers as well as patients. Psychological barriers (e.g. motivation) or logistic barriers (e.g. availability of places to exercise, tutoring availability) would require the involvement of other specific expert professionals, ideally working together with the dialysis team. Recently, the ACSM and AHA published focused guidelines for subjects with chronic diseases, stating that at least 30 min of continuous or intermittent (for at least 10 min at a time) moderate-intensity exercise, 5 or more days per week, is associated with a reduced risk of major cardiovascular events [72]. These guidelines were not specifically designed for patients with CKD, but they may provide an initial framework for prescribing therapeutic exercise also in this setting.

Key messages

- A number of clinical, economic, psychological and logistical barriers exist to the implementation of physical activity in CKD patients.
- Physical activity and exercise rehabilitation are not routinely prescribed in CKD patients, and counseling by nephrologists on physical activity is inadequate as well.
- Patient- and center-specific barriers to physical activity should be identified and overcome.
- An optimal implementation of exercise programs in dialysis units requires the creation of an exercise dialysis team including a nephrologist, physiotherapist, nurse, exercise physiologist and sports medicine clinician.

Conclusions

Patients with CKD are physically inactive, often have difficulties in performing daily activities and occupational tasks, and report a lower HRQoL compared to healthy controls. It is now clear that physical inability conveys *per se* an important excess risk of morbidity and mortality in patients with CKD, particularly in frail ESKD patients. Nowadays, the promotion of physical activity should become part of the routine workflow of the nephrologist community [73, 74], that needs to be aware of the benefits that regular exercise may confer to their patients. These mostly include improvements in functional and psychological measures, such as aerobic and walking capacity and HRQoL, but also a reduction of all-cause mortality across the spectrum of CKD. Exercise planning in CKD patients should aim at inducing favorable physiological adaptations. The exercise program should be tailored to the individual's functional capacity and comorbidities. Because there are numerous barriers for planning adequate exercise programs in the CKD setting, a multidisciplinary team is the main prerequisite for success. Building an effective exercise team, promoting the culture of exercise and increasing physical activity levels may lead to a more complete and modern clinical care management of CKD patients.

Conflict of interest The authors declare that they have no conflict of interest.

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