

Physical exercise in CKD patients: when and how is it feasible?

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There is growing evidence suggesting that physical activity in chronic kidney disease (CKD) improves survival and may even prevent the decline in renal function. Still, CKD patients face many barriers to exercising, such as multiple comorbidities, fatigue, frailty, anxiety, and lack of support. Encouragement appears to be the greatest motivation to adhere to physical activity, but an individualized prescription by a physiotherapist, adapted to the patient's physical function, CKD, and end-stage renal disease treatment, plays an important role as well. Disease acceptance, self-care, perceived benefits of exercise, and increasing energy and strength, are other important motivators.

In exercise physiology VO_{2max} , which measures the maximum oxygen consumption rate during incremental exercise, is the gold standard for measuring and evaluating aerobic capacity. In clinical practice other methods to measure physical function are preferable, such as the six-minute walk test which indirectly assesses VO_{2max} during six minutes of walking on a hard, flat surface. Borg's scale of rating perceived exertion (RPE) is strongly associated with VO_{2max} and is a valuable technique for communicating the patient's perception of exercise intensity to the physiotherapist in order to titrate the exercise prescription. The intensity levels are classified as light (RPE 11-12), moderate (RPE 13-15) and vigorous (RPE>15).

A comparison of VO_{2max} between healthy subjects, patients with CKD stages 2-4, and on HD, all matched for sex and age, shows that CKD patients have poor baseline scores, suggesting that VO_{2max} might not be the best measure of aerobic capacity or physical function in this population. However, VO_{2max} correlates strongly with the six-minute walk test in a number of chronic diseases although CKD was not part of the evaluation.

Level of intensity	Activity	Bicycle ergometer, W	RPE
Light	Walking 2.5 km/h	<50	11-12
Moderate	Walking 3.0- 5 km/h; Cycling 16 km/h; Cycling stationary 100W	50-100	13-15
Vigorous	Jogging; Calisthenics (push-ups, sit-ups); Running in place	>100	>15

Figure 1. Measures of different levels of exercise intensity

Prescribing an individual exercise program for patients with CKD should include frequency, exercise intensity, duration of physical activity, and type of exercise (endurance, strength, flexibility, balance). The RENal EXercise (RENEXC) study, a randomized controlled trial of exercise in CKD, compared the effects of two exercise training programs on physical performance in 151 non-dialysis dependent patients with CKD stages 3 to 5 with an observation period of 12 months. Patients were randomized to endurance training in combination with either balance or strength training. The two exercise modalities required 150 minutes of total training time per week, divided over five days, comprising 60 minutes per week of endurance training and 90 minutes per week of either strength or balance exercises. Both groups were prescribed endurance training at an intensity of RPE 13 to 15, and strength and balance training at an intensity of RPE 13 to 17. The strength group's median total training time was 100 minutes per week and the balance group's 118, indicating that at least 50% of the patients did not complete the prescribed training time. Adherence rates were 62% in the strength group and 68% in the balance group. The training resulted in a highly significant improvement in endurance, assessed by the 6-minute walking test, muscular strength, measured with quadriceps strength, and balance, measured as functional reach, in both groups.

The EXercise Introduction To Enhance Performance in Dialysis (EXCITE) multicenter randomized trial followed patients on HD and peritoneal dialysis for 6 months to test whether a simple, personalized walking exercise program at home improves their functional status. The main study outcomes included change in physical performance assessed by the 6-minute walking test and the five times sit-to-stand test. Patients were randomized to normal physical activity (control) or an individually tailored prescription of walking exercise to fit their baseline ability. Patients in the exercise training group significantly increased their walking distance and improved their muscle strength and endurance compared to the control. group Additionally, a dose-response was observed, since patients who actively engaged in physical activity experienced a greater impact than those with a low rate of cooperation.

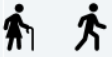
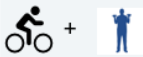

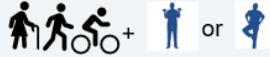






	EXCITE, 6 months	PEDAL, 6 months	CYCLE HD, 6 months	RENEXC, 12 months
Frequency/week	3	3	3	5
Intensity	According to 6MWD at baseline	40-75% of VO_{2max}	RPE 12-14	RPE 13-15(endurance) RPE 13-17 (strength/balance)
Duration/week, prescribed, min	60	90 (endurance) + resistance	90	150
Type of Exercise				
Adherence at end of study, %	83	42	61	 62  68
Outcome, physical function		=	=	  

Figure 2. Studies of exercise intervention in dialysis patients

Two trials followed the effects of intradialytic exercise in HD. The PrEscription of intraDialytic exercise to improve quALity of Life (PEDAL) multi-centre trial randomized patients to intradialytic exercise training (exercise group) and control group and followed them for 6 months.

The intervention consisted of intradialytic cycling and resistance training of moderate intensity based on the VO_{2max} at baseline with the workload set to between 40 to 70 % of the VO_{2max} reserve. The starting point was 20 minutes per exercise session, and at 8 weeks, the patients gradually increased their cycling time. Patients also engaged in resistance training twice a week, under the supervision of a physiotherapist. The primary outcome was the Kidney Disease Quality of Life Instrument (KDQOL) – SF36 physical component score, which did not reach statistical significance, nor did any of the measures of aerobic capacity or physical function. The compliance with the exercise program was 47%, and the adherence to the prescribed exercise type, intensity, and duration was 18%. Many patients withdrew from the study or were too unwell to complete all physiological outcome assessments.

The prospective, open-label, single-blinded cluster-randomized CYCLE-HD trial assessed the effects of an intra-dialytic cycling regimen during 6 months on left ventricular mass as evaluated by cardiac magnetic resonance imaging. Patients were prescribed 30-minute of cycling thrice weekly during dialysis, with RPE 12-14. Although the functional tests showed no statistically significant results, there was a significant reduction in left ventricular mass after 6 months of follow-up in the exercise group.

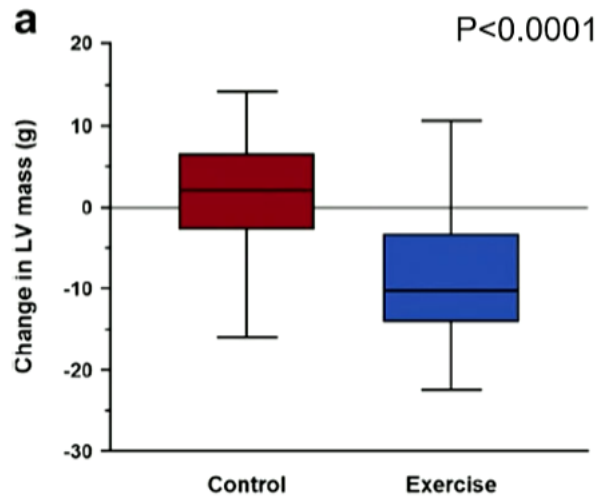


Figure 3. The primary aim of CYCLE-HD study: changes in left ventricular mass

The World Health Organization’s recommendation for 150 minutes of physical activity per week is also included in The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Management of CKD. Nevertheless, recent research questions the feasibility and necessity of adherence to this recommendation. 150 minutes of weekly exercise is highly unattainable and unrealistic for patients unaccustomed to physical activity, elderly individuals, and people with chronic medical conditions, as demonstrated by the low adherence levels in some medical trials. Importantly, there is overwhelming evidence in the RENEXC, EXCITE and Cycle-HD trials that marked benefits can be observed in people living with disability and/or chronic disease, with volumes of activity well below 150 minutes per week.

Key points

1. There is mounting evidence that physical activity improves survival and may even delay the deterioration of kidney function in CKD patients.
2. Although VO_{2max} , is recognized as the gold standard, other methods for measuring and assessing aerobic capacity in people with chronic disease are preferable such as the six-minute walk test and Borg's scale of rating perceived exertion (RPE).
3. The RENEXC, EXCITE, PEDAL and CYCLE-HD trials observed the effects of exercise training in patients with non-dialysis dependent CKD and patients on dialysis and showed beneficial effects on physical performance and some health parameters.
4. WHO and KDIGO recommendations for 150 minutes of physical activity per week are seldom attainable in patients with CKD. Nevertheless, patients should be advised on the beneficial effects of any physical activity and receive prescriptions tailored to their ability.

Further reading

- (1) Hellberg M, Höglund P, Svensson P, Clyne N. Randomized controlled trial of exercise in chronic kidney disease - the RENEXC study. *Kidney Int Rep* (2019) 4, 963–976; <https://doi.org/10.1016/j.ekir.2019.04.001>.
- (2) Manfredini F, Mallamaci F, D'Arrigo G, et al. Exercise in Patients on Dialysis: A Multicenter, Randomized Clinical Trial. *J Am Soc Nephrol*. 2017;28(4):1259-1268. doi: 10.1681/ASN.2016030378. Epub 2016 Dec 1. Erratum in: *J Am Soc Nephrol*. 2018 Jul;29(7):2028. PMID: 27909047; PMCID: PMC5373448.
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- (4) Graham-Brown MPM, March DS, Young R, et al. A randomized controlled trial to investigate the effects of intra-dialytic cycling on left ventricular mass. *Kidney Int*. 2021;99(6):1478-1486. doi: 10.1016/j.kint.2021.02.027. Epub 2021 Apr 8. PMID: 34023029.
- (5) Warburton DER, Bredin SSD. Reflections on Physical Activity and Health: What should we recommend? *Can J of Card* 2016,32:495-504.