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Research article

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Physical activity and exercise training in patients with chronic kidney Disease: A narrative review

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Abstract. *Physical activity (PA) is a non-pharmacological intervention that may improve cardiovascular risk, functional capacity, muscle strength, inflammation, and quality of life in patients with chronic kidney disease (CKD). However, practical use of PA remains limited because exercise prescription should differ according to CKD stage, dialysis status, comorbidity burden, and baseline physical capacity.*

The aim of this narrative review was to summarize mechanisms linking PA and CKD, evaluate clinical evidence for aerobic, resistance, balance, and low-intensity exercise, and formulate practical recommendations for non-dialysis and dialysis patients.

The reviewed evidence supports regular aerobic activity, resistance and balance training, and reduction of sedentary time in clinically stable non-dialysis CKD. Expected benefits include better cardiorespiratory fitness, muscle performance, endothelial function, inflammatory profile, and physical functioning.

For dialysis patients and patients with advanced CKD, individualized low-intensity activity, especially a home-based walking program with gradual progression, is a reasonable and safer starting strategy. Exercise should be prescribed as part of CKD care, monitored by symptoms, Borg scale, heart-rate response, gait speed, and the six-minute walk test.

Key words: *renal insufficiency, chronic; exercise therapy; exercise, aerobic; resistance training; ubiquitination; cardiorespiratory fitness.*

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Фізична активність і тренувальні вправи у пацієнтів з хронічною хворобою нирок: огляд літератури

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Резюме. *Фізична активність є важливою немедикаментозною складовою ведення пацієнтів з хронічною хворобою нирок (ХХН), оскільки може покращувати серцево-судинний ризик, функціональну здатність, м'язову силу, якість життя та показники запалення.*

Метою цього огляду було узагальнити механізми впливу фізичної активності при ХХН, проаналізувати докази щодо аеробних, силових, балансувальних та низькоінтенсивних вправ і сформулювати практичні рекомендації для пацієнтів з ХХН.

Для клінічно стабільних пацієнтів з ХХН G1-3 доцільними є регулярні аеробні навантаження середньої інтенсивності 150–300 хвилин на тиждень або високої інтенсивності 75–150 хвилин на тиждень у поєднанні з силовими та балансувальними вправами.

Для пацієнтів з ХХН G4,5 та осіб, які лікуються діалізною нирковою замісною терапією безпечнішим початковим підходом є індивідуалізована фізична активність низької інтенсивності, зокрема домашня програма ходьби з поступовим збільшенням навантаження та клінічним моніторингом.

Ключові слова: *хронічна хвороба нирок, фізичні вправи, аеробні тренування; тренування з опором; убіквітинування; кардіореспіраторний фітнес.*

Introduction. The benefits of physical activity (PA) in chronic kidney disease (CKD) are increasingly recognized, but implementation in routine nephrology practice remains insufficient. Many patients with CKD receive limited education about safe exercise and have low motivation or confidence to maintain regular activity [1, 2]. Exercise training (EXT) may reduce cardiovascular (CV) risk and improve health-related quality of life in patients with CKD, although the size of benefit depends on CKD stage, baseline frailty, comorbidities, and adherence [3, 4]. The potential CV benefits of PA include improved cardiorespiratory fitness, endothelial function, microvascular function, and arterial stiffness, which are relevant because CKD is strongly associated with vascular dysfunction and high CV mortality [5, 6].

Systemic inflammation, oxidative stress, endothelial dysfunction, immune dysregulation, insulin resistance, glucotoxicity, lipotoxicity, glomerular hemodynamic instability, vascular calcification, renin-angiotensin-aldosterone system imbalance, hyperuricemia, and sympathetic activation are common pathophysiological links between CKD, CV disease, and reduced physical capacity [7-12]. Metabolic disturbances in kidney damage also promote free radical production and structural-functional changes of cellular membranes, which may contribute to fatigue, muscle dysfunction, and reduced exercise tolerance [13].

CKD negatively affects skeletal muscle structure and function through inflammation, metabolic acidosis, insulin resistance, and activation of catabolic pathways, including the ubiquitin-proteasome system [14-16]. Therefore, the relationship between CKD, muscle dysfunction, and PA has direct clinical importance, not only theoretical interest.

The aim of this narrative review was to synthesize current evidence on PA and EXT in CKD, with emphasis on: 1) mechanisms linking CKD with muscle and cardiovascular dysfunction; 2) methods for assessing exercise capacity and response; 3) clinical evidence by exercise type and CKD/dialysis status; and 4) practical recommendations for individualized PA prescription.

Materials and methods. This narrative review analyzed publications indexed in PubMed and Scopus during the previous 20 years, with priority given to clinical consensus statements, randomized controlled trials, systematic reviews, meta-analyses, and prospective cohort studies. The main keywords were "chronic kidney disease", "physical activity", "exercise training", "aerobic exercise", "resistance training", "dialysis", "cardiorespiratory fitness", and "six-minute walk test". Because this article is a narrative review, the search was not designed as a systematic review or meta-analysis.

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The review included studies involving adults with CKD, including non-dialysis CKD stages 2-5 and CKD G5D/hemodialysis, when they reported functional, cardiovascular, inflammatory, metabolic, renal, or patient-centered outcomes.

Studies in cancer, organ transplantation, recent stroke, acute kidney injury, or non-CKD populations were not considered central to the review. Because the goal was to formulate practical clinical recommendations, studies were interpreted according to CKD stage, dialysis status, intervention type, intensity, duration, and feasibility.

Effects of PA on skeletal muscle in CKD. Muscle wasting is one of the clinically important consequences of CKD. It contributes to weakness, reduced gait speed, lower exercise tolerance, falls, frailty, hospitalization, and mortality. CKD-related muscle loss is associated with inflammation, metabolic acidosis, insulin resistance, RAAS activation, and impaired insulin/insulin-like growth factor-1 signaling [14, 17, 18].

Exercise training, especially resistance training combined with aerobic activity, may counteract these changes by improving insulin sensitivity, stimulating anabolic signaling, preserving muscle strength, and improving functional performance [15, 16].

The adenosine triphosphate-dependent ubiquitin-proteasome system (UPS) is one of the central pathways of muscle protein degradation in CKD and other catabolic conditions [14]. The mechanism is presented in Fig. 1.

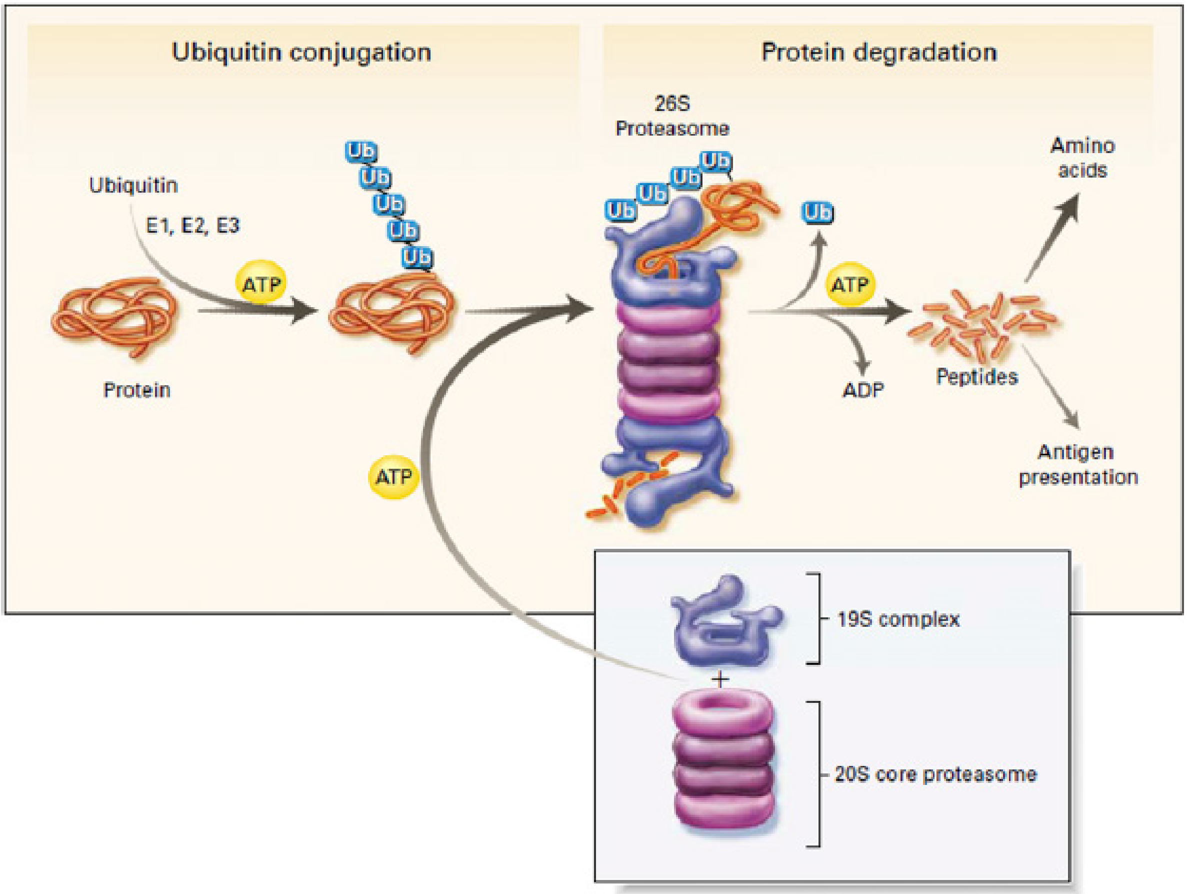

Fig. 1. The adenosine triphosphate-dependent ubiquitin-proteasome system.

In the UPS pathway, proteins are tagged by ubiquitin through ATP-dependent enzymatic steps and then degraded by the 26S proteasome [14, 17]. This catabolic process contributes to CKD-related muscle wasting and should be clearly separated from the beneficial adaptive effects of exercise. The final products of this degradation are small peptides and amino acids that leave the cell and may be used for energy or other metabolic needs [14].

Caspase-3 activation can increase proteasome activity and contribute to muscle protein breakdown. Excess angiotensin II, metabolic acidosis, inflammation, and impaired insulin/IGF-1 signaling can activate these catabolic processes in CKD [14, 18, 19]. Reduced Akt phosphorylation is linked to impaired anabolic signaling and activation of transcriptional pathways involved in muscle atrophy [14, 19]. Thus, the clinical message is that exercise may partly oppose CKD-related muscle catabolism by improving insulin sensitivity, muscle performance, and physical function, not that exercise itself activates caspase-3.

Classification and prescription of PA. PA should be classified by intensity, type, frequency, duration, and setting. This classification is clinically useful because patients with early non-dialysis CKD, advanced CKD, and dialysis dependence have different safety profiles and functional limitations [20].

According to intensity, PA may be light-intensity (LPA), moderate-intensity (MPA), vigorous-intensity (VPA), moderate-to-vigorous physical activity (MVPA), or total daily activity [21]. Resistance training may be static/isometric or dynamic. Dynamic resistance exercise is especially useful in CKD rehabilitation because it can be adapted to large and small muscle groups and progressed gradually [22].

Static balance exercises include standing on one leg, standing with the feet together, tandem stance, standing on a balance board, planking, or maintaining balance using a Pilates ball [20].

Dynamic balance exercises include heel-to-toe walking, arm reaches in a double- or single-leg stance, side-shuffles with turns, lunges with rotation, and single-leg dead lifts [20].

Resistance exercise may include quadriceps extensions, hamstring curls, squats, step-ups, sit-ups, push-ups, back extensions, biceps curls, overhead press, lat-pulldowns, chest press, or dumbbell rows, depending on the patient's functional level and comorbidities [20]. Each type of PA can be progressed, but progression should be gradual and individualized.

Balance exercise intensity can be increased by prolonging static positions, closing the eyes, adding upper-body movement or light weights, increasing the pace of dynamic exercises, using an unstable surface, or progressing to more complex activities [20].

Resistance exercise intensity can be increased by changing weight, repetition number, body position, or exercise difficulty [20].

Aerobic exercise involves large muscle groups and dynamic movement with an increase in heart rate. Typical examples include walking, cycling, swimming, jogging, and elliptical training [16, 22].

Vigorous-intensity or anaerobic exercise requires greater caution in CKD and should usually be reserved for clinically stable and adequately assessed patients [22].

Frequency is usually described as the number of exercise sessions per week. For many adults, at least 150 min/week of moderate-intensity activity is a practical target, but patients with CKD may need a lower starting dose and slower progression [22].

Assessment of exercise effect and safety. Aerobic capacity, muscular strength, endurance, balance, gait speed, and daily functioning are key indicators of physical fitness and physical functioning in CKD [23]. Walking capacity, stair-climbing capacity, and activities of daily living should be assessed because they directly reflect the patient's ability to benefit from rehabilitation [23].

Peak oxygen consumption (VO2peak) measured during cardiopulmonary exercise testing is the gold standard for cardiorespiratory fitness. The six-minute walk test (6MWT) is a simpler practical tool and is often correlated with VO2peak [3, 24]. Exercise intensity can be expressed as a percentage of maximal heart rate or heart-rate reserve, when this information is clinically available [22]. The Karvonen formula and Borg scale are useful for prescribing and monitoring exercise intensity, especially when direct cardiopulmonary testing is not available [20, 22].

Clinical evidence and interpretation. Prospective cohort data suggest that moderate-intensity PA is associated with a lower incidence of CKD during long-term follow-up, supporting the preventive value of regular activity [21].

Physical performance also has prognostic value. In a cohort of patients with CKD stages 2-4, slower gait speed and worse timed up-and-go performance were associated with higher all-cause mortality, indicating that functional measures should be considered clinically meaningful outcomes [25].

Physical activity may influence metabolic risk factors, but these outcomes should be interpreted together with functional capacity, cardiovascular risk, inflammation, and safety. Resistance training for 12 weeks reduced serum CRP and IL-6 and improved muscle strength in non-dialysis CKD, suggesting that resistance exercise may improve both functional and inflammatory status [26].

Inflammation, lipid abnormalities, and cardiometabolic comorbidity often coexist in diabetes, CKD, and dialysis populations and may influence exercise tolerance and cardiovascular risk [27-29].

Dyslipidemia is an important component of cardiovascular risk in patients with CKD, especially in those receiving dialysis. In dialysis patients, lipid abnormalities are often characterized not only by elevated triglycerides but also by qualitative changes in lipoproteins, reduced anti-inflammatory function of HDL, and a close relationship between lipid disturbances, oxidative stress, inflammation, and vascular calcification [30]. Therefore, when discussing the benefits of physical activity in CKD, it is reasonable to consider not only exercise tolerance and muscle strength, but also possible effects on triglycerides, HDL function, insulin resistance, and chronic inflammation. However, available data suggest that exercise programs in dialysis patients may improve functional capacity more consistently than lipid parameters; therefore, lipid outcomes should be interpreted as secondary and not as the main expected effect of exercise training [31].

CKD progression is also associated with impaired fatty-acid oxidation and triglyceride accumulation; therefore, exercise studies should interpret metabolic markers together with functional and CV outcomes [32].

A systematic review and meta-analysis reported that cardiovascular exercise and combined cardiovascular plus resistance exercise can improve aerobic capacity in adults with CKD, whereas resistance training alone appears more important for strength than for aerobic capacity [23]. For clinically stable non-dialysis CKD patients, current recommendations support at least 150-300 min/

week of MPA, 75-150 min/week of VPA, or an equivalent combination, together with resistance and balance training on most days of the week [3].

Daily reduction of sedentary time and the inclusion of LPA throughout the day are recommended for all CKD patients, especially those who cannot initially reach moderate-intensity targets [3]. Svensson et al. evaluated self-administered balance and resistance exercise in patients with CKD stages 3-5 not receiving kidney replacement therapy [20].

The program used the Borg scale to guide intensity and included static balance, dynamic balance, and resistance exercises. The results support the feasibility and safety of self-administered balance and resistance training when intensity is individualized and monitored [20]. Kirkman et al. studied moderate-to-vigorous aerobic exercise for 12 weeks in non-dialysis CKD. The intervention was performed three times weekly and progressed to 45 minutes per session [6]. This trial assessed cardiorespiratory fitness, microvascular function, endothelial function, and arterial stiffness using objective vascular and exercise measurements [6].

In non-dialysis CKD, aerobic exercise improved cardiorespiratory fitness, endothelial function, and microvascular function, probably through improved redox balance; however, arterial stiffness did not significantly improve [6]. These findings support aerobic exercise as one part of cardiovascular risk reduction in CKD, while comorbid hypertension, obesity, atrial fibrillation, and CKD-related medication issues should also be considered when prescribing exercise [33, 34].

Overall, available evidence suggests that exercise may reduce oxidative stress and improve endothelial function in CKD, but the strength of evidence differs across outcomes and study designs.

Ikizler et al. examined aerobic PA combined with dietary calorie restriction for four months in patients with moderate to severe CKD and showed reductions in body weight, fat mass, IL-6, and F2-isoprostane [35]. However, significant changes in VO2peak, kidney function, and urine albumin-to-creatinine ratio were not observed, indicating that short-term interventions may improve metabolic and inflammatory status without producing measurable changes in kidney function [35]. Exercise modalities used in this trial included treadmill, elliptical cross-trainer, and recumbent stationary bicycle training [35].

Headley et al. evaluated exercise training in patients with CKD stages 2-4 and measured VO2peak using a computerized metabolic cart [36]. The intervention lasted 48 weeks and included progressive aerobic training followed by resistance exercise during the second half of the program [36]. Resistance exercises included machine-based exercises such as leg curl, compound row, triceps or lat pull-down, leg press, and chest press [36]. VO2peak improved in the exercise group and declined in the control group, supporting the benefit of long-term supervised training for cardiorespiratory fitness in pre-dialysis CKD [36]. Heart rate also decreased after exercise training, while significant improvement in GFR was not demonstrated. Thus, the main benefit of long-term exercise in this trial was functional and cardiorespiratory rather than a direct short-term improvement in GFR [36].

Duration of PA is also important. Short-term exercise programs may not change central arterial stiffness, and vascular changes in advanced CKD may be partly irreversible; therefore, earlier initiation and longer follow-up may be needed to demonstrate vascular benefits [37].

Because evidence differs between pre-dialysis and dialysis populations, exercise recommendations should be separated according to dialysis status. In hemodialysis and advanced CKD, cardiovascular comorbidity, hyperuricemia, and cardiac remodeling pathways may influence exercise tolerance and safety [38, 39]. Dialysis-specific exercise evidence should therefore be interpreted separately from non-dialysis CKD evidence [31, 40].

Manfredini et al. evaluated a personalized low-intensity home-based walking program for patients with CKD stage 5 receiving dialysis over six months [40].

The absence of major changes in blood pressure and biochemical markers may reflect advanced vascular and renal damage, low exercise intensity, limited intervention duration, or insufficient power for these endpoints. The main positive result was improved six-minute walking distance among patients who completed the program, supporting walking distance as a realistic outcome in dialysis rehabilitation [40].

However, serum creatinine, urea, total cholesterol, triglycerides, and glucose did not significantly decrease, so functional improvement should not be interpreted as biochemical improvement in advanced CKD [40].

The 6MWT is a practical monitoring tool in hemodialysis because it correlates with VO2peak and is feasible in routine clinical settings [3, 24].

Therefore, exercise training should be individualized according to CKD stage, dialysis status, frailty, cardiovascular risk, symptoms, and patient preference. In clinically stable non-dialysis patients, moderate-intensity aerobic activity, resistance exercises, balance training, and reduction of sedentary time are appropriate targets. In patients with advanced CKD or dialysis dependence, low-intensity activity, short walking sessions, and simple home-based exercises are safer initial options. Functional outcomes such as walking distance, gait speed, fatigue, Borg scale, and quality of life should be prioritized because short-term changes in serum creatinine, eGFR, lipid levels, or other biochemical markers may be limited [3, 31, 40, 41].

Practical recommendations for clinical use:

1. Before prescribing PA, clinicians should assess CKD stage, dialysis status, CV symptoms, blood pressure control, anemia, frailty, neuropathy, musculoskeletal limitations, fall risk, and previous activity level.

2. For non-dialysis CKD, the preferred target is gradual progression toward 150-300 min/week of moderate-intensity aerobic PA or 75-150 min/week of vigorous-intensity PA, combined with resistance and balance exercises when clinically safe [3].
3. For patients with low baseline capacity, frailty, advanced CKD, or dialysis dependence, PA should begin with LPA, short walking sessions, sit-to-stand exercises, and simple balance tasks, with gradual progression based on symptoms and Borg scale.
4. Functional outcomes should be prioritized. Gait speed, 6MWT, stair-climbing ability, Borg scale, heart-rate response, adherence, fatigue, and quality of life may be more sensitive than serum creatinine or eGFR for short-term evaluation of exercise benefit [3, 20, 23, 24].
5. Exercise should be stopped or modified in the presence of chest pain, severe dyspnea, dizziness, symptomatic hypotension or hypertension, acute infection, unstable cardiac disease, or post-dialysis exhaustion.
6. The main practical conclusion is that PA in CKD should be prescribed as individualized rehabilitation, not as a general instruction to "exercise more".

Conclusions. Physical activity should be considered an important part of care for patients with chronic kidney disease. Its main benefits are improvement of physical function, cardiorespiratory fitness, muscle strength, exercise tolerance, quality of life, and possibly inflammatory and vascular status.

Exercise should not be prescribed in the same way for all patients. In clinically stable non-dialysis patients, regular aerobic activity can be combined with resistance and balance exercises. The intensity and duration should be increased gradually according to the patient's condition and tolerance.

In patients with advanced chronic kidney disease or those receiving dialysis, the safest approach is to start with low-intensity activity, especially walking and simple home-based exercises. In these patients, the main expected benefit is better walking capacity and daily functioning, while changes in kidney function, lipid levels, or other laboratory markers may be small or absent.

Exercise programs should be individualized and monitored by symptoms, blood pressure, heart-rate response, Borg scale, gait speed, and the six-minute walk test. Physical activity in chronic kidney disease should be presented as supervised and individualized rehabilitation, not only as a general recommendation to exercise more.

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Author Contributions.

O. Chernatska: conceptualization, methodology, literature search, visualization, data curation, formal analysis, writing – original draft.

N. Demikhova: conceptualization, methodology, literature search, writing – review & editing, supervision.

O. Vlasenko: data curation, interpretation of literature data, writing – review & editing.

I. Dehtyarova: literature search, data curation, writing – review & editing.

A. Demikhov: literature search, data curation, writing – review & editing.

All authors have read and approved the final version of the manuscript.

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