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Nephrologists' Insights on Exercise in Renal Health

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Chronic kidney disease (CKD) is a rapidly growing worldwide non-communicable disease, contributing to a high rate of morbidity and mortality. Prevention and early detection of renal diseases is fundamental in reducing the risk of irreversible renal damage. The nephrology community has made significant efforts through initiatives like World Kidney Day to raise the awareness of kidney disease among the general population and to enhance early referrals to nephrologists [1–3]. Smart et al. [4] showed reduced mortality and hospitalization rates along with improved quality of life in CKD patients who were referred to nephrology services earlier rather than later. This underscores the importance of timely intervention, as in the paradigm of myocardial infarction, where "time is myocardium" [5]; similarly, in renal disease, "time is glomeruli."

Undoubtedly, nephrologists play a crucial role in initiating a holistic approach to promptly preserve renal health. Prescription of new pharmacological therapies (e.g., sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide 1 agonists, nonsteroidal mineralocorticoid receptor antagonists), on top of standard care, appears to yield more promising results in delaying CKD progression [6]. On the other hand, the more effective "drug" in renal disease management remains the prescription of lifestyle changes. Among non-pharmacologic approaches, physical activity and exercise training have garnered strong scientific interest over the last few decades in defining their benefits and potential risks in renal patients.

A great amount of literature has been published to assess the impact of physical activity and exercise, as a planned and structured type of physical activity, across the entire spectrum of CKD [7–11]. Observational and experimental studies have shown that regular physical activity has nephroprotective effects by positively influencing cardiovascular health and hemodynamic factors,

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Table 1. Summary of the main certainties, doubts, and barriers in the field of physical activity and exercise in CKD patients

Certainties	Doubts	Barriers
• Recommended for all CKD stages and KTRs • Recommended at least 150 min/w of moderate PA or at an intensity compatible with the patient's cardiovascular condition and tolerance • Improvement in quality of life, psychosocial outcome, functional capacity, muscle strength, and cardiorespiratory fitness • Effective if performed regularly • Safe with few side effects: moderate fatigue, dyspnea, leg and joint pain • Home-based training programs are not inferior to training performed on dialysis units • Personalization of prescription	• Benefits on dialysis efficiency • Mechanisms of nephroprotection • Cost-effectiveness • Effectiveness of gyms, online platforms, or the innovative technological tools • Strategies for increasing awareness of the exercise benefit • Strategies for increasing adherence	• Patient (physical, psychological, social, environment conditions) • Personnel (lack of knowledge, absence of counseling, lack of interest, lack of time) • Absence of a "renal rehabilitation team" • Slow operational translation of scientific evidence

KTR, kidney transplant recipient.

including blood pressure, cardiac output, and vascular tone [12]. Additionally, exercise has beneficial effects on CKD-related complications and metabolic status, such as improving insulin sensitivity, lipid profiles, inflammation, sarcopenia, renal anemia, and CKD-mineral bone disorders [13], all of which are associated with CKD progression. However, the pathophysiological mechanism of physical exercise in CKD patients is not fully understood. New molecules, known as myokines [14], which are expressed and released by skeletal muscle in response to physical activity, may help explain the effects of exercise on sarcopenia, malnutrition, metabolic dysregulation, and chronic inflammation [15]. Additionally, microRNAs have emerged as potential mediators. These microRNAs can alter their expression in response to exercise training, modulating osteogenic differentiation, a key mechanism in the development of vascular calcification that increases cardiovascular risk in CKD patients [16].

Despite this encouraging experimental and clinical data, few large, long-term randomized clinical trials (RCTs) have been published, particularly in patients on hemodialysis [17–19]. Among these, the milestone EXerCise Introduction To Enhance performance in dialysis patients (EXCITE) trial [18] stands out. This multicenter Italian RCT demonstrated that improved physical performance, assessed by the 6-min walking test (6MWT) and five times sit-to-stand test (5STS), in patients who engaged in home-based, low-intensity walking exercise compared to controls over 6 months. Additionally, a significant reduction in the long-term risk for a composite endpoint, including death from any cause, cardiovascular events, and hospitalizations, was also observed [20]. These findings are consistent with another RCT, the dialysis training therapy (DiaTT) [19], which tested exercise interventions during hemodialysis sessions. After 1 year of thrice-weekly supervised endurance and resistance exercise training, improvements were found in walking performance and lower body strength, as assessed by 6MWT and 60-s sit-to-stand test (60STS), respectively. A recent meta-analysis and systematic review confirmed that home-based exercise programs for 3–6 months in patients on dialysis have a beneficial impact on physical function, superior to usual care and not inferior to intradialytic training [21].

In 2022, the clinical practice guidelines developed by the UK Kidney Research Consortium Clinical Study Group for exercise and lifestyle [22] summarized the latest evidence regarding physical activity and exercise in patients on conservative treatment, those on dialysis, or kidney transplant recipients. These guidelines recommended physical activity and exercise in renal patients with a 1B or 1C grade, if it is not contraindicated. Similarly, KDIGO 2024 guidelines [6], which update the 2012 KDIGO guidelines [23], extended their recommendation to engage in moderate-intensity physical activity for at least 150 min per week for all CKD populations, based on their cardiovascular and physical tolerance.

Despite these recommendations, surveys conducted across Spain, Canada, New Zealand, and Australia showed that nephrologists did not provide any exercise programs to CKD patients in 42%–81% of cases [24, 25]. Similarly, a recent Italian survey [26] revealed that only

26% of nephrology centers offered exercise programs to renal patients.

This discrepancy between the growing evidence of the exercise benefits and its limited implementation in clinical practice is due to several doubts and uncertainties, as well as disease-specific (e.g., comorbidities) and patient-specific (e.g., psychological, physical, and economic constraints) barriers to physical activity (Table 1) [27]. Additionally, Regolisti et al. [28] revealed that barriers related to health-care personnel, such as negative attitude, insufficient time to discuss with patients, or lack of interest, also play a fundamental role in the inactivity of hemodialysis patients. Although nephrologists appear to be aware that exercise counseling and prescription should be their prerogative, there is a lack of guidance on how to implement the physical activity and exercise into routine treatment of renal patients. To address this gap, an Italian consensus paper by the Working Group (WG) on Physical Exercise in CKD of the Italian Society of Nephrology has provided practical advice through 16 statements [29]. These statements cover a range of topics, from conducting a thorough physical function assessment to prescribing an appropriate diet plan with protein restriction and dietary supplements to prevent sarcopenia during exercise training. The consensus suggests engaging in aerobic and resistance exercises for at least 12 weeks, with the intensity gradually increased according to the CKD patient's tolerance. This exercise training can be undertaken individually or in a group setting, at home, in a dialysis unit, or in a sports facility. Furthermore, in order to improve the patient compliance and awareness regarding physical activity and exercise, the Italian WG suggests integrating new technologies, such as virtual reality gaming or social networks, in the clinical practice. To reach this goal, ecological strategies have been proposed, such as replicating a natural environment in the dialysis center through biophilic design [30].

Nephrologists have the necessary "know-how" in managing renal patients to tailor personalized physical activity and exercise programs, ensuring patient safety and adherence, in collaboration with exercise experts. In line with this, an ongoing pragmatic nonrandomized trial [31] will test having an exercise facilitator regularly present in the dialysis unit alongside with nephrologist. This study could provide valuable insights into patients' willingness to participate in and their preferences for a 3-month exercise program. Specifically, four different exercise options will be available: (a) unstructured physical activity; (b) structured home-based low-intensity exercise; (c) in-hospital (pre/post dialysis) structured supervised low intensity exercise; (d) performance assessment only.

In conclusion, a multidisciplinary approach [32], involving nephrologists, nurses, dietitians, and exercise professionals, should be adopted to implement physical activity and exercise programs for CKD patients in clinical practice. This approach can help alleviate the physical and mental effects [33] of renal disease and dialysis therapy, prolong life expectancy, improve socialization, reduce fatigue stress, and enhance health-related quality of life.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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