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Review Article

# Physical activity and fitness in patients with end-stage renal disease: A review

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## Abstract

**Background:** End-stage renal disease (ESRD) is the final stage of chronic kidney disease, when the kidneys can no longer function on their own. Patients with dialysis-dependent kidney failure carry an additional burden of co-morbidities, such as, diabetes mellitus, hypertension, cardiovascular disease, infections, and many others. The incidence of dialysis is quite high. Approximately 10% of the world population is affected by chronic kidney disease (CKD). Exercise rehabilitation is a well-established therapy in patients with kidney disease. Despite more than three decades of exercise research in patients with kidney disease, its applications were not very common in practice.

**Objectives:** The objectives of this study are to review the benefits of physical activity and fitness, muscle strength and quality of life in patients with ESRD.

**Methods:** A total of 43 closely related references were reviewed on physical activity and fitness, and quality of life in patients with ESRD. These articles were consulted from databases such as PubMed, Google Scholar, and Web of Science considering the inclusion criteria of the study.

**Findings:** From the discussion of the study, it was found that supervised exercise therapy should be recommended to the ESRD patients in their rehabilitation.

**Conclusion:** From the findings of the present review, it was concluded that considering the physical status of the patients, the physical exercises should be encouraged by the nephrologists and physiotherapists to the patients undergoing hemodialysis, as one of the rehabilitation protocols.

**Keywords:** Renal rehabilitation, Exercise therapy, End-stage renal disease

## Introduction

Chronic kidney disease (CKD) is a major risk factor for dialysis, also increases the risk of cardiovascular diseases and is closely related to lifestyle-related diseases such as diabetes mellitus and hypertension. Moreover, dialysis patients develop complications including cardiovascular diseases, infections, and malignant neoplasms and have very poor prognosis. Approximately 10% of the world population is affected by CKD, and millions die each year because they do not have access to affordable treatment [1]. There is no doubt that lack of sufficient physical activity is a strong predictor of mortality among patients with end-stage renal disease (ESRD) and is associated with poor physical functioning. Globally, an estimated 144 out of every 1 million people are affected by ESKD, with a mortality rate varying between 20% and 50% within 24 months of starting renal replacement therapies [2]. In spite of number of scientific reports on the safety and effectiveness of physical exercise for patients with ESRD, the medical community still perceives it as a contraindication to physical exercise and fails to popularize it to the patients. Patients' fear of loss of vascular access, as well as frequent states of anxiety or depression, are also factors that limit the undertaking of physical exercise. The objectives

of the present study were to review the physical activity and fitness, muscle strength and quality of life in patients with ESRD to educate them about the benefit of the exercise therapies and to popularize the physical exercises by the nephrologists and physiotherapists in the patients undergoing hemodialysis, as one of the rehabilitation protocols to improve their quality of life (QoL).

In patients with ESRD, inadequate physical activity is a strong predictor of mortality. Though several reports suggested the benefits of physical exercise in ESRD patients, not much interest has been generated among these patients. Thus, the study reviewed to explore more information to popularize the exercise therapy among ESRD patients.

## Methods

A total of 43 references were reviewed which were closely related to physical activity and fitness, and quality of life in patients with ESRD. These articles were consulted from databases such as PubMed, Google Scholar, and Web of Science. The inclusion criteria were as followed: (1) articles containing the patients with ESRD, in which it is necessary to use renal replacement therapy, including hemodialysis, peritoneal dialysis or organ transplantation (2) administered of exercise therapies and fitness, and (3) reports regarding QoL of the ESRD patients.

### Physical activity and fitness in patients with end-stage renal disease

It is now well established that patients with ESRD have a much lower level of physical activity and related physical capacity than the normal population. The process of physical impairment begins with the initial changes in kidney function [3-5]. The daily life of patients is reflected by the level of their physical activity and is closely related to their quality of life, level of satisfaction, mental condition and social relationships [6]. The physical fitness of the patients is also correlated with their quality of life and is independently associated with mortality rate [2,3,7]. For the measurement of the body's physical fitness level, the $VO_2$ max index is widely used. It is called maximum oxygen uptake, also it expresses the body's ability to absorb oxygen used for metabolic changes during exercise [8]. As in dialysis patients, the onset of fatigue is reported faster, the $VO_2$ max is often replaced by $VO_2$ peak. This value depends on central and peripheral factors. Its value is the resultant of the efficiency of many systems including circulatory, respiratory and musculoskeletal (joint-ligament and muscular) and the ability to transfer oxygen through the blood. The decrease in $VO_2$ max level is already observed at the earlier stages of CKD, and obviously, in patients with ESRD, it is significantly reduced, ranging from 15-21 ml/min/kg on average. Whereas the normal population averages it as 30-40 ml/min/kg [9,10]. Oxygen carrying capacity correlates with a number of simple tests with broader clinical applications in various patient groups. Of them, the 6-Minute Walk Test (6-MWT) is widely used to indirectly assess the body's efficiency and positively correlates with $VO_2$ max, both in the healthy and patients' groups [11,12].

### Muscle strength in patients with end-stage renal disease

The primary task of the muscles is to generate the strength to overcome external resistance during work. Thus, muscle strength is the most important characteristic of life. The muscle strength reaches its maximum at the age of 20-30 years. After that, it gradually decreases with age [13,14]. Initially, the loss of strength is noted and later, the loss of muscle mass. Muscle strength is also a unique indicator of muscle function, more important than mass, cross-section or circumference [15]. The age-related phenomenon of loss of muscle mass, and more importantly muscle strength, are closely related to sarcopenia [16].

In a number of studies, a high correlation has been reported between muscle strength and many factors significantly affecting the efficiency of: gait speed [10,15], balance disorders, risk of falls and fractures [10,17], as well as the frequency of hospitalization [15,17] of an individual. The decrease in muscle strength is responsible for the decrease in physical activity of patients [13,18] and is an important factor in the development of disability [15,17,18]. Patients with CKD experience a reduction in muscle strength at the early stages of the disease. The decrease in muscle strength correlates with the decrease in the GFR index, and its greatest impairment is observed in the ESRD [19]. The mechanism of these changes can be either primary, caused by myopathy or uremic sarcopenia, which is characterized by changes in the structure and function of muscles in the so-called uremic environment. The secondary changes are related to a number of factors, including comorbidities, lifestyle and age-related sarcopenia [16]. Though the pathogenesis of uremic sarcopenia is not fully understood, but a synergistic effect of many factors is assumed [20,21], these are metabolic acidosis, hormonal disorders, chronic inflammation increasing catabolism, impaired cell function and trophic changes in muscle fibers [20,22].

In patients with ESRD, a reduction in the number of muscle fibers, especially types IIa and IIb, reduction in the cross-section of the fibers and a decrease in their capillarization, has been reported [20,22]. A reduction in the number and impairment of mitochondria function has also been reported in ESRD patients, and consequently impairment of aerobic metabolic pathways, slowing down of cellular ATP renewal processes, excessive depletion of cellular phosphagen reserves, impairment of sarcoplasmic reticulum function and the process of calcium ion release or disorders of potassium ion management [20,22]. Chronic malnutrition is another significant factor responsible for uremic sarcopenia [23,24], which is associated with increased inflammation of the body [25] and increased catabolic processes causing degradation of muscle proteins [26]. Significant changes in the vascularization of muscle tissue are also observed, which translate into inadequate supply of cells with energy substrates and elimination of cellular transformation end-products [27].

The uremic neuropathy, the changes in the central and peripheral nervous systems, is also observed. A considerable reduction in the innervation of muscle tissue is emphasized which is evident in reduction of motor units, impaired function of neuromuscular connections and neuromuscular spindles, reduction of action potential, increased latency of motor neurons or reduction of excitability within central systems [28,29].

In the context of physiotherapy, a very important factor influencing the development of sarcopenia is lifestyle of the patients, including the level of physical activity. According to the concept of mechano-transduction, sufficient mechanical stress is needed for the body to function optimally. Insufficient physical load on the muscle tissue is associated with the lack of proper stimulation, which manifests itself in the dysregulation of cellular processes and the activation of atrophic processes [29,30]. With regard to muscle tissue, the lack of sufficient load may result in insufficient stimulation of the molecular mechanisms among muscle cells. As a

result, insufficient development of muscle structure, its composition and muscle fiber ratio, development of insulin resistance and excessive infiltration of adipose tissue occur [29-31]. Patients with ESRD usually lead a sedentary lifestyle [32], which, according to the concept of mechano-transduction, results in insufficient mechanical stimulation of cells, initiating muscle cell reduction processes.

**Physiotherapy assessment methods in chronic hemodialysis patients**

The patients undergoing hemodialysis require some qualifications for participation in exercise therapy, the cooperation of an interdisciplinary team consisting of leading nephrologists, cardiologists, physiotherapists, and diabetologists. Some physiotherapy assessment techniques used for chronic hemodialysis patients are given below: evaluation of anthropometric parameters, evaluation of circulatory system function, cardiopulmonary exercise test, evaluation of limb muscle strength, handgrip strength test, measurements of lower limb muscle strength, the sit to stand test, the arm curl test, accelerometers, pedometer, the International Physical Activity Questionnaire (IPAQ), the Barthel Index (BI), The Kidney Disease Quality of Life – Short Form (KDQoL) and the Beck Depression Inventory (BDI).

So far, the intervention strategies are concerned, it depends upon the conditions of each case, i.e. exclusively case specific, and reported earlier in detail [33].

**The anti-aging gene critical for muscle strength and the prevention of kidney disease**

Appetite regulation by nutritional intervention is required early in life that involves the anti-aging gene Sirtuin 1 (*SIRT1*) with Sirt 1 maintenance of other cellular anti-aging genes involved in cell circadian rhythm, senescence and apoptosis. Nutritional aspect is important for ESRD patients for their overall improvement. Exercise therapy is important to the activation of Sirt 1 with relevance to rehabilitation of ESRD patents. Appetite dysregulation is connected to the anti-aging gene *SIRT1* that is connected to the circadian rhythm with effects on the endocrine and metabolic systems that involve diseases of the adipose tissue, heart, liver, pancreas and brain [34]. Neuron apoptosis and survival is determined by *SIRT1* and other anti-aging genes and interventions that prevent down regulation of anti-aging genes may allow appetite regulation with prevention of other chronic diseases. Interests in the calorie restriction with stabilization of anti-aging genes have accelerated in recent years to delay and prevent programmed cell death linked to the various chronic diseases. The consumption of Sirt 1 activators versus inhibitors may need to be assessed with relevance to the success of exercise therapy in ESRD patients [35].

## Quality of Life in Patients with End-Stage Renal Disease

In the course of ESRD, depression and anxiety are very common [36]. In approximately 30% of patients with CKD, depression is diagnosed [37]. The cause of such disorders is undoubtedly specific factors, like disease-dependent biochemical changes [38], as well as non-specific, behavioral variables resulting from the patient's attitude towards the disease, treatment prospects and life situation. As CKD is a progressive disease, the source of anxiety in the patients is undoubtedly their current state of health [39]. Long-term dialysis also distorts the self-image of the patients, leading to unfavorable self-perception, causing number of negative emotions. The presence of depression and anxiety disorders may reduce the patient's involvement in the treatment process, as well as negatively affect the acceptance of additional interventions, e.g. rehabilitation [40]. Physical therapy included supervised regular physical exercises, can improve quality of life among patients with ESRD, as well as reduce the severity of depressive and anxiety disorders [41-44].

In the subjective assessment of the quality of life among dialysis patients, validated and standardized multidimensional questionnaires are used. Examples of those generic are "The Short Form 36 Health Survey Questionnaire (SF-36)", "EuroQol 5-Dimension (EQ5D)", and "The Kidney Disease Quality of Life (KDQoL)". In the evaluation of anxiety-depressive symptoms, the "Beck scale" and "The Hospital Anxiety and Depression Scale (HADS)" are used.

## Conclusion

From the study we conclude that supervised exercise therapy should be recommended to the ESRD patients (considering the cases) in rehabilitation of the patients. In the absence of guidelines specific to the ESRD population, recent guidelines developed for older individuals and patients with chronic disease should be applied to this population too. In sum, exercise appears to be safe in this patient population if begun at moderate intensity and increased gradually. The evidence suggests that the risk of remaining inactive is higher. Patients should be advised to increase their physical activity when possible and be referred to physical therapy or cardiac rehabilitation programs when appropriate.

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