

## The Role of Physical Activity in the Management of Chronic Kidney Disease: A Historical Perspective

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### Introduction

Regular physical activity is an irreplaceable part of an active lifestyle not only in healthy but also in chronically ill patients. In those cases, exercise training of a certain volume and intensity becomes a tool for influencing the quality of life (QL) and could be a supporting non-pharmacological component of complex therapy.

Especially, patients with chronic kidney disease (CKD) and long-term dialysed patients suffer from decreased physical efficiency (sometimes on 50% of population standard specification), further from functional disturbances of moving system and their quality of life (QL) is getting worse together with the disease's progression. By one of sequels of reduced physical efficacy are sedentary lifestyle preferences. Owing to inactivity these patients lose their physical fitness, which in turn results in loss of self-sufficiency and gradually, they develop dependence on other persons' assistance.

The aim of this article is to present a brief overview of the methods, which are described and used in the area of different stages of CKD (pre-dialysis, dialysis and preparing for the transplantation), especially in the form of exercise rehabilitation. Research is done on this topic worldwide at the scientific and theoretical level, but there is still a lack of clear and validated implications for common use.

### Literature search

For this short review, PubMed, Medline and Scopus were searched for studies (from 1970 up to 2016) investigating elements of exercise rehabilitation in the area of different stages of CKD (pre-dialysis, during and outside the haemodialysis, prepare for the kidney transplantation). From the huge number of research studies we only chose those with focus on the effect of exercise programs using rehabilitation exercise methods for improving: flexibility, muscular strength, endurance, and balance in CKD patients in pre-dialysis stage and on haemodialysis treatment. Search terms "exercise during haemodialysis", "exercise and CKD", "intradialytic exercise".

### Exercise rehabilitation in patients with CKD

Exercise rehabilitation is part of a multidisciplinary approach to the patient and it is considered as one of the components of non-pharmacological treatment. The main objective is to maintain or increase patient's physical and mental fitness and to promote their longstanding self-sufficiency and independence from helping others. In addition it reduces the financial costs of nursing care.

The positive effect of a regular exercise on the general condition of CKD and in end-stage renal disease (ESRD) patients has been described in a number of studies over for last 40 years.

It is well known, that sedentary dialysis patients are at higher risk of death as compared to non-sedentary ones [1]. In the last twenty years, in the frame of renal replacement therapy (RRT), there is a rising number of senior's age patient's. Examination of the physical, mental and social status on renal dialysis therapy (RDT) is a worldwide high current issue. Senior's dialysed patients have a longer anticipated life expectancy and incidence of musculoskeletal complications is growing. Musculoskeletal disorders contribute to the deterioration

of their functional capacity along with other health complications. It reduces the overall quality of life of dialysed patients in the field of self-sufficiency impact on the psycho-social aspect of life.

Changes in kidney function in old age reflect pathophysiological processes that significantly affect not only the kidneys, but also the cardiovascular system, water and electrolyte management, hormonal regulation and metabolism. Sarcopenia is a chronic condition associated with physiological aging process and is defined by reduction of the mass, muscle strength and function. In CKD, sarcopenia is prevalent and is associated with increased morbidity and mortality and occurrence of cardiovascular complications [2,3]. There is also another common health problem of patients on RDT – diabetes mellitus. Diabetes mellitus is one of the major risk factors for the emergence and development of CKD. The number of diabetics, especially older than 60 years, on dialysis is worldwide increasing [4,5]. Above all it concerns demands of nursing and rehabilitative care. According to Farragher and Jassal rehabilitation should be an important part of traditional treatments for the elderly dialysed patients [6].

Basic characteristics of studies listed below can be found in Table 1. From this table we have excluded theoretical survey studies. For information we selected the aim of the study, exercise design, type of exercise programme and used exercise equipment.

The first mention of the importance of physiotherapy and physical therapy in CKD patients was found in the 1970s [7]. This paper described the physiotherapy procedures for acute (AKD) and chronic kidney disease (CKD) in haemodialysis and peritoneal dialysis. It emphasized the techniques of respiratory physiotherapy, exercises to maintain or restore the joint range, to prevent muscle atrophy and to maintain or increase muscle strength. The importance of regular physiotherapy in CKD was associated with therapy of uremic polyneuropathy. Recommended practices were both individual and group forms of exercise. A bicycle ergometer was mentioned in the exercise aids.

During this period (in the 1970s and 1980s), the research was mainly focused on physical fitness testing [8]. We can see the first mention of the application of physical activity as a way of improving the functional and psychological condition, even alleviating of the symptoms of some CKD associated diseases - arterial hypertension, anaemia, hyperlipidaemia, psychiatric disorders [9-17]. In most of the above studies, we encountered the application of aerobic physical activity during haemodialysis (HD) using a specially modified bicycle

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References	Aim of the exercise intervention	Type of the exercise programme/Exercise equipment	Exercise design
1970-1980 Bradford [7]	To maintain or restore the joint range To prevent muscle atrophy To maintain or increase muscle strength	Aerobic - cyclic Ergo cycle	Supervised Intradialytic
1981-1990 Carney et al. [9] Carney et al. [10] Goldberg et al. [11] Gutman et al. [12] Hagberg et al. [13] Krause [14] Krause [15] Painter and Zimmermann [16] Zabetakis et al. [17] Painter et al. [18]	To improve the functional and psychological condition To alleviate the symptoms of some CKD associated diseases	Aerobic - cyclic Modified ergo cycle (bed side ergometer)	Supervised Intradialytic 4 weeks to 14 months; 2-3x/week; 15-90 min; 50-80% $VO_{2max}$ *
Since the 1990s Castaneda et al. [20] Curtin et al. [21] Painter et al. [22] Oh-Park et al. [23] Fuhrmann and Krause [24] Moinuddin and Leehey [26] Samara et al. [27]	To improve joint mobility, muscle strength and endurance To develop coordination of movement To coordinate breath and exercising To practise relaxation techniques To improve psychological status To improve the health related quality of the life To improve nutritional status	Resistance training – resisting, lifting and lowering weights	Supervised x home based Pre-dialysis Intradialytic 8-12 weeks
Segura-Ortí et al. [31] Segura-Ortí et al. [33]	Supervised: To improve exercise capacity, muscle strength, physical functioning and health-related quality of the life	Resistance training/low intensity aerobic training Elastic rubber belts Dumbbells Leg press machines Ergo cycle Treadmill	Intradialytic, supervised by a physiotherapist; Resistance training or low-intensity aerobic training versus resistance training consisted of three sets of 4 exercises at an intensity of RPE scale 12-15 (Borg scale) Every session during 24 weeks.
Bulckaen et al. [36]	To evaluate the effects of different 6-month programs of physical activity	Intradialytic/home based aerobic cyclic exercises and strengthening exercises None equipment (only own body weight)	Supervised Intradialytic exercises - 30 min plus home exercise walking training or the advised home training program plus an additional supervised gym training session, twice weekly. Combination of flexibility, strengthening and coordination and aerobic training for the lower limbs
Bullani et al. [37]	To evaluate the effect of intradialytic resistance band exercise training on physical function in HD patients.	Resistance exercise programme Elastic rubber bands	Supervised Intradialytic resistance band exercise training. Thirty-six exercise sessions of moderate intensity (twice a week, mean duration 40 min each, during 4.5 to 6 months), mainly involving leg muscles against an elastic resistance, were performed.
Oliveros et al. [38]	To evaluate the effects of an exercise training program in patients undergoing chronic haemodialysis.	Aerobic cyclic exercises Ergo cycle Rubber bands – Thera-Band™; Loops	Supervised Intradialytic; each dialytical procedure; 16 weeks
Reboredo et al. [39]	To assess the effectiveness of intradialytic aerobic training in ESRD patients	Aerobic cyclic exercise programme None equipment	Supervised Intradialytic, moderate-intensity aerobic training program, 3 times per week for 12 weeks
Besnier et al. [40]	To evaluate exercise training program with ergo cycle at the anaerobic threshold (AT) during dialysis sessions on effort tolerance, quality of life, blood pressure and lipid disorders.	Aerobic/anaerobic cyclic exercise programme Ergo cycle	Supervised Intradialytic 3 months, each dialysis procedure
Orcy et al. [43]	To compare the effects of combined resistance and aerobic exercise with a resistance programme alone on functional performance among haemodialysis patients.	Aerobic cyclic and strengthening exercises None equipment (only body weight)	Supervised Combined resistance and aerobic exercise versus ongoing resistance programme alone; 10 weeks
Bohm et al. [44]	To compare the effects of intradialytic cycling versus a pedometer program on physical function, physical activity and quality of life.	Ergo cycle Pedometers	Supervised Intradialytic cycling during each dialysis/home based pedometer program 24 weeks

Howden et al. [45]	To analyse secondary outcomes of a randomized controlled trial, with participants randomly assigned to either lifestyle intervention or usual care (control).	Combination of aerobic and resistance training: Ergo cycle Treadmill Rowing simulator Resistant bands (Theraband) Hand weights	Outside the dialysis Two faced exercise program: 8 weeks supervised/10 months home-based. Combination of aerobic and resistance training Aerobic training: walking, jogging, cycling or rowing; intensity on RPE 13-15; 30 min. Resistance training: 3 sets of 10-15 repetitions of 6-8 functional resistance exercises (e.g. Wall squats, bench press, lunges, pushups, bicep/triceps extension, bridge holds, etc.) Home based exercise programme: continue to perform a combination of aerobic and resistance exercise training.
Watson [46]	To determine the feasibility of delivering a supervised progressive resistance exercise program in CKD. To investigate effects on muscle size, strength and physical functioning.	Fixed fitness resistance machine	Progressive resistance exercise program - 3 sets of 10 to 12 leg extensions at 70% of estimated 1-repetition maximum. 8 week/3x week.
Thompson et al. [47]	To evaluate the feasibility of a main study evaluating the efficacy of cycling and resistance exercise during the haemodialysis treatment on QoL.	Aerobic cyclic and strengthening exercises Ergo cycle Weights	Supervised, intradialytic Combination of cycling and resistance training (only cycling, only weights, cycling+weights, control) 12 weeks, each dialysis procedure
Gordon et al. [48]	To investigated the impact of Hatha yoga exercise on lipid parameters in patients with ESRD on haemodialysis.		
Gordon et al. [49]	To investigated the impact of Hatha yoga on oxidative stress indicators and oxidant status in patients with ESRD on haemodialysis	Hatha yoga	Outside dialysis 4 months
Yurtkuran et al. [50]	To evaluate the effects of a yoga-based exercise program on pain, fatigue, sleep disturbance and biochemical markers in haemodialysis patients.	Yoga based exercises	Yoga-based exercises were done in groups for 30 min/day twice a week for 3 months.
Dobsak et al. [51]	To compare the effect of rehabilitation (RHB) training on a bicycle ergometer and electromyostimulation (EMS) of leg extensors in HD patients with ESRD.	Aerobic cyclic exercise Ergo cycle Electro stimulation	Exercise training 2 x 20 min; EMS - stimulation (10 Hz) of leg extensors was applied for 60 min; 20 weeks; 3x/week.

CKD: Chronic Kidney Disease; RPE scale: Rating Perceived Exertion; HD: Haemodialysis/Haemodialysed; ESRD: End-Stage Renal Disease; QoL: Quality of Life

**Table 1:** Short characteristics of the overviewed studies

ergometer, the bed-side bicycle ergometer. The length of the exercise program ranged from 4 weeks to 14 months, with a frequency of 2-3 times a week. The session lasted 15-90 minutes and a loading intensity was 50-80%  $VO_{2max}$ . The studies mainly described the improvement of cardiorespiratory performance, as well as lowering blood pressure of some hypertensive patients [13,18]. The implications of these studies have been transferred further into future research, e.g. Miller et al. [19].

Since the 1990s, studies have started describing therapeutic programs that focused on joint mobility, muscle strength and endurance and developing coordination of movement. It emphasizes coordination of breathing and practising of relaxation techniques in the exercise program during the HD procedure [20-28]. Again we can read some studies in which renal specialists cooperating with physiotherapists within the exercise rehabilitation during haemodialysis [29-34].

"Renal Rehabilitation" is a term used for rehabilitation of dialyzed patients and patients in pre-dialysis [25]. This term was created in 1994, when the Life Options Rehabilitation Advisory Council published a document called "Renal Rehabilitation - Bridging the Barriers" in the USA [35]. The material described how to create a rehabilitation plan for dialyzed patients. It was a "coordinated program of treatment, education, counselling, nutritional and physical intervention to maximize the work potential and quality of life of dialyzed patients". It emphasized the support of self-sufficiency and the maintenance of self-service with the minimization of dependence on the help of others due to the integration of the physiotherapy into the multidisciplinary treatment of CKD patients.

The European Association of Rehabilitation in Chronic Kidney Disease (EURORECKD) was established in the same year. This association brought together experts in the field of nephrology, physiology of physical stress, rehabilitation and physiotherapy, metabolism and nutrition.

The exercise program that combines resistance exercises - exercise aids are mostly elastic rubber belts and dumbbells; leg press machines and aerobic training - use of a bicycle ergometer, treadmill, or simply walking with pedometers using has appeared more and more often since 2000 [31,33,36-47].

There are also studies of CKD patients using yoga exercises (Hatha yoga) to influence lipid metabolism [48]. Modified yoga exercises can prevent and treat the oxidative stress which causes endothelial dysfunction and can cause atherosclerosis [49]. Yurtkuran et al. applied a three-month exercise program of modified yoga exercises to a group of haemodialysis patients, monitoring the effect on pain, fatigue, sleep quality, and blood parameters. The results showed a significant improvement of all the variables observed in comparison with the control group [50].

Dobsak et al. compared the effect of aerobic training on the bicycle ergometer and electro-stimulation (EMS) of the lower limb extensions of CKD patients [51]. One group of CKD patients exercised and the second group was electro stimulated between the 2nd and the 3rd hour of haemodialysis, 2-3 times a week. The groups were observed for 20 weeks. Significant positive effects on physical fitness and quality of life

were demonstrated in both groups. The EMS method may be used as the major therapeutic part of rehabilitation for HD patients.

There are less overviews of assessing the effect of regular physical exercise on patients with renal disease in the pre-dialysis stage, i.e., at the stage of chronic kidney disease 1-3.

Authors Johansen and Painter have dedicated their research to physiology and pathophysiology of physical activity of CKD patients [52]. They published an overview study of the effect of physical exercise on physical function and physical fitness of CKD patients in the pre-dialysis period [52]. They confirmed the strong positive effect of regular physical activity in dialyzed individuals. We show the results of individual randomized and experimental studies that support their report. The value of  $VO_{2max}$  improved of 17-23% in average after graduating physical activity during the intervention program. The improvement was proved in physical fitness tests (Up-Go test, 6 min walk test, Sit to stand test) and in the area of quality of life, specifically in domains evaluating the physical condition.

In randomized studies by other authors, their results are confirmed. The aerobic and strength exercises were applied in the treatment program separately or combined. The aerobic activities have been described as walking - on a treadmill, riding a bicycle trainer aerobic fitness exercises at home and swimming [53-58]. Activities included mainly strengthening of large muscle groups of the lower limbs - extensors and flexors of the knee joint, flexors and extensors of hip. The used fitness gear was booster gums or fitness device [59]. Intensity of physical load was from 60% to 80% 1RM [60-63].

In 2014 was published narrative review about exercise in pre-dialysis patients with CKD [64]. This article chronologically included studies from years 1990-2014 and clearly describes physiological effect and highlights the importance of exercise training for patients in pre-dialysis.

Certain degree of physical performance is indispensable also for dialysed patients subscribed to the kidney transplantation waiting list, not only because of the rather exhausting operation but also for a better life with the transplanted kidney [65-67]. Long term inactivity especially before the transplantation and during the dialysing period leads to a regression of the recipient's fitness level which leads further to the muscular atrophy, reduced capacity of the musculoskeletal system, bone, neural and articulation diseases [68]. Working capacity and PA tolerance after transplantation increase quite fast when maintaining a regular PA especially in the first year that follows the transplantation [69,70]. Rehabilitation after kidney transplantation help to renew patient's physical as well as mental condition and support the family, working and social life as well [71,72].

According to Manfredini et al. [73] and Cupisti et al. [1] exercise programs still rarely occurs in nephrology and/or dialysis units. Nephrology departments represent the crossroad between care and therapy, patient counselling and possible integration of competences.

### Objectives of exercise programs for patients with CKD

The main goal of exercise programs (EP) is to maintain or improve physical fitness, thereby preserving general self-sufficiency and independence from others, returning to society, living the same level as a healthy person and reintegration into work place if the patient is still in productive age [24,74-79]. Individual or group EPs must respect the individuality of each patient, their previous physical experience, and the current level of physical fitness and the recommendation of the attending physician. It must not endanger the health of the patient.

The main focus of EP should be: to maintain or develop joint mobility, muscle strength for compensating muscle imbalances, restoring dynamic stereotypes, which are necessary for self-care, correcting disorders of movement coordination and improving cardiorespiratory fitness [24,74-79]. Accompanying effects of physical activity are benefits in the psychosocial area, i.e., increased psychological resilience (self-confidence, self-esteem, coping with stress situations). It contributes to general self-sufficiency and independence from another person. It reduces the complications of the illness and supports the treatment (shorter hospitalization, morbidity and mortality). It helps the patient with work and leisure activities and assists the cope with social roles in the family, at work and in society [24,74,75]. These demands are especially important in elderly patients who are CKD predominant [6]. The exercise rehabilitation can ensure those [6].

Very important for adherence to the EP and to go through is patient's motivation [80]. There is necessary communication between the whole multidisciplinary staff, especially with the physician and dialysis nurses. The professional staffs have to explain to the patient benefits and possible risks of exercise activities and to emphasize their significance for complex treatment. Study of Thompson et al emphasizes the importance of involvement of HD unit staff for supporting the patient implementation to the regular exercise programme [47]. They propose to use a pre-study demonstration phase to introduce the intervention to the cooperating HD staff.

External resources summarizing recommendations for choosing and applying physical activity to individuals with CKD are available on the company's website Life Options website in the brochure form "Exercise for the Dialysis Patient", or website of National Institutes for Health in the brochure form "Exercise and Physical Activity" [81,82].

### Conclusions and Recommendations

From the above reviewed studies is obvious that an acceptable choice of regular exercise activity for patients with CKD and ESRD together with another treatment methods could be the best way of non-pharmacological character, that offers to the patient an opportunity to achieve an optimal functioning and psychosocial level for each one almost equal to pre-morbid state [74-79]. Particularly in elderly patients, should be their functional independence supported by various types of exercise activities [6].

Application of exercise rehabilitation should be safe and focused on individual's possibilities of the each one patient. Based on the references above, it seems to be more effective to combine aerobic and resistance training for improving functional performance. Success rate in adaptation or improvement of physical and psychical functions mediated by the exercise therapy undoubtedly depends on total length of exercise program, its content, volume, load intensity and on its time incorporation during or outside the haemodialysis [83].

Using different types of intervention programs can affect the level of physical functioning and psycho-social integrity of patients. Building and integrating the complex of rehabilitation program into the medical care for seniors in pre-dialysis and on dialysis could be the way how to improve patients' lives and reduce the financial cost of care [83].

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