
Physiotherapy in the Patients on Hemodialysis

S. Ufuk Yurdalan

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/53093>

1. Introduction

Today end-stage renal disease (ESRD) is still major health concern. ESRD, the deterioration of nephrons to an advanced stage resulting in the dysfunction of the kidneys for a long period, requires either dialysis treatment or transplantation in advance. ESRD results in a negative clinical status, which in turn results in both structural and functional changes in the musculoskeletal system. Consequently, the patient is faced with a sedentary life, making the patient even further dependent. Low functional capacity, exhaustion / fatigue and under nutrition was found to be prevalent among incident dialysis patients.

Complications such as uremia, anemia, myopathy, and neuropathy decrease muscular strength, cardio-pulmonary fitness, and quality of life, which is why this population is seen more frequently in physiotherapy practice currently.

Dialysis regulates the patients' general condition and fluid-electrolytes balance, assures the disposal of accumulated toxic substances in the body, facilitates the patient' continued healthy life, and prepares the patient for the transplantation. During this stage of treatment, there are two considerations: to increase both the quality of life and the life expectancy. To improve and enhance the quality of life through dialysis or transplantation, a well-planned exercise program also must be included. As the exercise program entails a risk in itself, the implemented program must be carefully planned, coordinated, and supervised based on health related fitness in this population.

There are many exercise training studies in patients with end-stage renal disease on hemodialysis, but exercise type and planning are open to discussion in this population. But it is clear that, physiotherapists are responsible from suitable exercise programs in inpatient and outpatient renal clinics.

2. Chronic kidney disease and physical activity

Chronic kidney disease is the progressive deficiency of renal function for months and years. When renal function decreases, the disease reaches life threatening (ESRD) stage which requires urgency replacement, in other words, dialysis or transplantation. Mortality can be delayed by these approaches [1].

The effects of intradialytic exercise programs on quality of life of chronic kidney disease (CKD) patients have been analyzed for the last three decades [1]. Quality of life is a consequence; in fact physical inadequacy issues affecting quality of life should be investigated in detail. Results of "Health, Aging and Body Composition Study" [2,3] and "Cardiovascular Health Study" [4] revealed that physical impairment can be detected at early stages of chronic kidney diseases. "Dialysis Morbidity and Mortality Wave 2 Study" [5] showed that poor self-physical performance, exhaustion and fatigue, low physical activity and inadequate nutrition were high among dialysis patients. Low physical performance indicates hospitalization and high mortality risk among dialysis patients [5,6]. Physiotherapists should follow physical function to monitor disease progression and to evaluate exercise programs.

Decrease in physical function is known to increase when combined with dialysis time, metabolic changes accompanying the disease and catabolic effects of dialysis [5,7]. Invasive studies evaluated physical performance by "International Classification of Function, Disability and Health (ICF)" [8]. 6 Minute Walking Test [9] and Timed Sit- to- Stand Test [7,10] are other approaches measuring physical performance. Although Timed Sit- to- Stand Test is realized at different durations and repetitions when compared to 10 sec Timed Sit- to- Stand or times 5-10 sit to stand maneuvers on the elderly living in nursing home 30 sec Timed Sit- to- Stand is more valid. Human Activity Profile (HAP) [8] developed by Fix and Daughton is another tool to evaluate physical performance in ESRD population. The HAP consists of 94 questions. The questions are graded according to oxygen consumption ratio of activities using metabolic equivalence. Thus, HAP involves various tasks from waking up to joggings. "have stopped doing this" response given to any HAP question is considered as a sign of inadequacy in terms of disease progression. Despite perfect validity and utility properties of all three tests, routinely at least two trials are recommended. A wide distribution can be observed between the real scores of individuals in the tests and repetitions can approximate to real score.

In addition to physical measurement of tests, it is also important to evaluate post invasive changes of individuals such as psychometric properties and reliability. Physiotherapists and clinicians should also be aware of the psychometric properties of the tests they will choose to monitor physical performance and capacity.

ESRD is characterized by anemia, decreased cardiac function, changes in skeleton muscle strength and decreased aerobic capacity which affect multiple organ system [8]. Therefore, in hemodialysis patients with ESRD with morphologic, electrophysiological and metabolic changes, weak muscles should be strengthened at early stage [11]. Apart from muscle weakness, low exercise tolerance is also a serious problem in ESRD patients which might result in

increased cardiovascular risk or even sudden death [12]. As a result of the above mentioned problems, physical activity and quality of life are low in these patients [13].

Small sampling size in studies on exercise and quality of life also made evaluations inadequate. Sampling size should be paid attention in study planning. However, in this population, planning of study is difficult as the patients' conditions are critical. Thus, available study results should be tried to derive clinical implications and to be adapted to practice.

Hemodialysis is a time consuming approach which is applied to ESRD patients as one of the basic renal replacement therapy with a frequency of 3-5 h /day and 2-3 times/week [13]. As a result, exercise programs in patients who received hemodialysis are structured as intradialytic and home exercise programs.

Exercise is reported to have a positive impact on anemia, functional capacity, cardiovascular risk factors, dyslipidemia and psychosocial problems in ESRD patients [14]. There is strong evidence that exercise is a part of medical treatment after renal transplantation [15]. It is suggested that similar to exercise, physical activity reduced renal cell cancer risk by decreasing body fat, blood pressure and growth factor concentration in circulation [16].

In patients who receive dialysis, muscle mass decreases as a response to mainly inflammation, physical inactivity and acidemia. Muscle mass can be protected by increasing dialysis frequency and giving nutritional support, regulation of acidemia and stimulation of physical activity [16].

Structural integration and functional continuity of postmitotic tissues such as mitochondrial biogenesis skeleton muscle [17]. Degradation of mitochondrial function is believed to cause decreases which play a role in changes (sarcopenia) in contractile functions appearing due to loss of skeleton muscle mass of DNA damage or age [1]. Muscle mass loss accompanied by mitochondrial dysfunction resembling sarcopenic changes due to age appears in chronic kidney disease [1,2,18]. Resistive exercise trainings are exercise modality reversing sarcopenia and increase mitochondrial function in aged muscle [11]. Yet, the effect of these exercises in increased mitochondrial biogenesis and cellular antioxidant protection were indicated [6].

It was argued that functional capacity, quality of life and survival increased in elder and hemodialysis patients with exercise training [19-21]. Despite the benefits of exercise, hemodialysis patients show low interest and participation to exercise. According to the results based on exercise barriers and facilitators, strategies to develop exercise participation were developed in patients receiving hemodialysis. In this context, Nonayama et al. [22]; evaluated applicability of combined hospital and home-based programs in elderly hemodialysis patients. Participation to hospital exercise programs in hemodialysis patients was found to be high (89%). High compliance was associated by the researchers with the fact that exercise program was formally included in dialysis program; the patient and their families were informed about the importance of exercise; exercise was supervised; exercise program was selected in accordance with the wish and preferences of the patient; a specially adapted equipment was provided for the patients who were unable to exercise in supine and prone position during hemodialysis and that exercise did not require extra time as it was per-

formed during dialysis [23,24]. The reasons for low participation of exercise at home programs were found to be lack of motivation of time constraint [23,25].

Although it is a rare complication, muscle infarction can develop in ESRD and diabetic patients. Since 1965 when reported for the first time, a total of 130 patients were reported. Of these patients, upper extremity involvement was the case of 2 patients. Muscle infarction whose pathogenesis is not exactly known is most common in femur; it appears with local edema, painful muscle mass and sudden pain. In upper extremity, edema and severe pain in posterior humeral lower half is determined. Shoulder and elbow joints are passively open [26]. It is a clinical process that prevents physiotherapy.

On the other hand, similar to low muscle mass, low bone mass is common in end stage renal disease patients, particularly in those who receive hemodialysis. As a result, fragility fracture incidence is high in ESRD patients with low bone mass [27].

Bone mass loss should be monitored in hemodialysis patients as it is asymptomatic and can be easily neglected. Since low bone density will increase fracture risk, if osteopenia is also present, the condition requires more attention. Detection of high risk patients which may develop fracture risk through regular bone mass density measurements can be considered as an effective healthy policy in decreasing mortality and medical spending. Approaches to optimize mineral metabolism, exercise trainings protective from falls and usage of hip protectors in risky patients are appropriate procedures [27,28]. A special attention should be shown to selection of appropriate exercises in patients with fracture risk.

Exercise is a non-pharmacological agent in preventing bone loss. Effective exercise that can load femoral neck was proved to increase bone mass in femur neck [29-31]. Huang et al. [27] emphasized that only regular exercise failed to prevent bone loss and that exercise type and duration that can be effective were also important factors. Exercise intensity is important in protecting involuntary bone loss particularly in ESRD patients. In this context, designing effective exercise programs in patients receiving ESRD and hemodialysis is also important [27]. Prospective studies evaluating the effects of exercise in hemodialysis patients on bone mass density are under way.

Fatigue is reported to be the most common symptom affected clinical status negatively in ESRD patients. Fatigue in patients receiving dialysis is a serious problem as it also indicates increased mortality risk. More importantly, since dialysis patients cannot find necessary energy in pursuing their daily life, increasing quality of life by exercise programs is given priority [32].

Causes of fatigue in dialysis patients can be listed as follows:

- i. Physiologic fatigue (decreased aerobic capacity and muscle strength)
- ii. Psychological and behavioral fatigue (anxiety, stress, depression, sleeping disorders)
- iii. Dialysis-related (dialysis frequency, changes in life styles which also cause physical limitations)
- iv. Socio-demographic issues (professional status, social support) [33].

Underlying cause of fatigue is mainly skeleton muscle weakness which is defined as a requirement for treatment by physiotherapy. Floyd et al, Lazaro and Kirshner and other researchers [34,35] explained progressive muscle weakness in ESRD patients who received hemodialysis as myopathy. Furthermore, sensorimotor neuropathy due to uremia and neuromuscular junction defects were also considered as potential outcomes of muscle weakness in this group of patients [36]. Recognition of the underlying mechanism of skeleton muscle weakness enables safe exercise application. Johanson et al. [37] observed no change in electrophysiological characteristics (CMAP) of skeleton muscle after a few exercise sessions in hemodialysis patients with ESRD accompanied by metabolic and electrophysiological changes [38].

Apart from muscle weakness, fatigue can be associated with inflammation, obesity, dialysis modalities, sleep, depression and cytokine levels. However, accurate understanding of these factors can help the clinician in terms of survival and quality of life of dialysis patients [32].

SF-36, which is a quality of life health survey to evaluate fatigue in clinic, is practical. The SF-36 vitality scale has good psychometric properties and internal consistency reliability in people with ESRD [13]. A higher score reflects more vitality and less fatigue. Patients were also asked about the number of good waking hours they had (In the past 4 week, on an average day, how many good working hours did you have?).

Studies on patients with myopathic changes showed oxygen deficiency in the muscles and decrease in VO_2 max. Myopathy related to uremia inflicts and lessening of oxidative enzyme activities cause fibrillary atrophy and capillary density loss in muscles [39,40].

In addition to proximal muscle weakness, distal muscle involvement was also reported in ESRD patients receiving hemodialysis. On the other hand, McElrey et al. [41] reported varying muscles weaknesses in these patients. Therefore, physiotherapists should make a complete muscle evaluation in all proximal and distal muscles and should also evaluate muscle strengthening resistance exercise skills and tolerance in the patients due to interaction of ESRD and hemodialysis with multiple organ systems, cardiovascular and nutrition status and comorbid interactions. It should be remembered that weak skeleton muscles together with Vitamin D anomalies and inadequate glycolytic mechanism.

A specific version of muscle loss in ESRD patients is termed as "protein energy wasting" (PEW). PEW is characterized by increased muscle protein catabolism related to protein synthesis. This condition is also related with metabolic disorder, hormonal anomalies and anomalies arising in time in muscle formation and has a strong mortality risk for ESRD patients [42]. For this reason, treatment of PEW or protection is important in maintenance of ESRD patients.

Exercise is one of protective approaches that reduce muscle protein loss or or muscle function muscle function. Exercise has a direct stimulating effect on synthesizing speed of muscle proteins ad also disturbs the balance between synthesis and destruction in favor of destruction [43-45]. Protective effects of regular physical activity or exercise have been determined in previous studies. Secondary gains of exercise include cardiovascular pro-

tection and improvement of some sudden cardiac death indicators in randomized controlled studies [46].

In ESRD patients treated with dialysis, peak oxygen uptake (VO_2 peak) is low. This decrease is affected from multiple factors including anemia, cardiac dysfunction (reduced contractility, increased anterior and posterior load); vascular dysfunction (limited reach of cardiac output to skeleton muscle); skeleton muscle anomalies (decreased fiber type, capillary density, mitochondrial density and increased diffusion distance) and/or metabolic anomalies and autonomic dysfunction. The only study in the literature examining peak VO_2 in hemodialysis patients is Moore et al.'s study. Moore et al. [47] found that cardiac output at rest and a- VO_2 difference were similar; both values decreased in peak exercise which resulted in changed oxygen provision to working muscles. In chronic kidney patients who underwent renal replacement, transplantation improved oxygen consumption; this parameter remained unchanged with hemodialysis. VO_2 changes after transplantation develops in relation to cardiac output due to peak heart rate rather than central mechanisms (oxygen distribution) and peak stroke volume. Thus, in contrast to hemodialysis patients with limited peak heart rate and exercise capacity, cardiovascular fitness is improved following the transplantation [48]. In fact, aerobic exercises are required for the combination of exercise with routine treatment after kidney transplantation, strengthening exercises to minimize sarcopenia and osteoporosis, cardiovascular disease risks and to reduce body weight [15].

Future studies should analyze the effects of physical activity on graft in kidney donors in evidence-based manner (15).

When ESRD patients are evaluated by subjective feedbacks, peak oxygen consumption, physical performance and muscle strength tests, their physical performances are found to be limited. One third of hemodialysis patients are unable to perform their normal daily life activities without getting help. Physical functionality is the major determinant of quality of life. As a result, attempts to improve functionality in these patients also have potential to improve quality of life [14]. Physical function and quality of life in patients receiving hemodialysis can be evaluated by 2 MWT, KDQoL, PCS. In addition, IIRS should be used to monitor the effects of exercise on general life style. Evaluation of the relationship between IIRS scores and attendance to exercise can be guide in clinic [17].

Physical fitness, behavioral change and quality of life link with healthy were examined in a study [1]. Exercise program consisted of 12-week low-moderate intensity precondition exercises during dialysis for which exercise consultancy was provided; strengthening training and bisergo exercise before dialysis. Exercise was provided 2-3 times a week as 30 min training session within the first 2 hours of dialysis. Exercise intensity was personalized according to Borg Scale in patients. Motivational support was offered in addition to exercise consultancy to reduce dropout rate.

Physical fitness components were achieved by exercise capacity (VO_2 peak), reaction time, manual dexterity and lower extremity muscle strength (sit-to-stand test). MOS Short-Form General Health Survey (RAND-36) was used to evaluate general health quality of life of patients. In conclusion, physical and psychological benefits of exercise program were indicated. Vitality, general health perception and health behavior change, which are three elements of quality of life and lower extremity muscle strength significantly changed within the scope of physical benefits. Particularly patients' belief that health behaviors can change was strengthened [1].

Due to strong connection between HRQoL results and morbidity and mortality in ESRD patients, it is important to understand mostly affected quality of life elements in ESRD patients and to personally monitor the patients. Brennen et al. [49] found that in ESRD patients, physical issues were affected the most and the underlying cause of these effects were found to be nutrition biomarkers and Hct levels.

3. Exercise approaches in the patients on hemodialysis

Johansen et al. [50] sought to comprehend whether hemodialysis patients differ from healthy sedentary persons. To ascertain whether or not they were as active, they researched physical activity levels and clinical status. It was determined that hemodialysis patients were less active than healthy sedentary persons. The difference between the two increased in parallel to age. It was indicated that anemia and muscular weakness were key factors in diminishing functional capacity.



Figure 1. Exercise apparatus for hemodialysis patients



Figure 2. Dumbbells sets for strengthening exercise



Figure 3. Dumbbells for progressive resistance exercise

3.1. Intradialytic versus home based exercise training

Koh et al. examined the effects of supervised intradialytic exercise and non-supervised home-based exercise trainings on physical function and arterial stiffness. A total of 72 hemodialysis patients were randomized according to receiving intradialytic exercise training, home-based exercise training and standard treatment. In this controlled clinical study, hemodialysis patients were given bicycle ergometer while home-based exercise group was given walking program 3 days a week. As exercise intensity, the patients were expected to feel

fatigue corresponding to 12-13 intervals according to 6-20 Borg scale. Primary measurements were perceived as 6 MWD distance and aortic pulse wave (PWV) while secondary measurements consisted of augmentation index, peripheral and central blood pressures, physical activity and self- health evaluations. The evaluations were first conducted at 3. and 6. months.

“Active Australia Questionnaire” was used within the scope of physical activity and self-health evaluation [51,52]. Each patient was asked to give answers including any training they performed the week before. The survey evaluated frequency, intensity and duration of randomized and structured physical activity. Total duration for each activity was multiplied by 3.5 for light activity; by 4 for moderate level of activity and by 7 for intense activity as intensity value. Weekly physical activity of the participant was calculated as $\text{MET}\cdot\text{min}^{-1}$ by this formula.

“Medical Outcome Short-Form 36 (SF 36) Health Survey was used for health self-evaluation. Home-based exercise program in hemodialysis patients was found to be cost effective considering intense dialysis units. This result can guide development of exercise guide books. Future studies can analyze the effects of exercise on arterial stiffness in patients with cardiovascular morbidity marker [51].

3.1.1. Low intensity intradialytic exercises

Moderate level strengthening exercises is known to improve physical performance, nutrition level and quality of life in chronic kidney patients and hemodialysis patients. On the other hand, there is no evidence of the effect of low level strengthening trainings.

Chen et al. [53] randomized 50 patients with a mean age of 69 ± 13 years who received long term dialysis (3.7 ± 4.2 years) and divided the patients into low intensity strengthening exercise and stretching exercises (control group) groups. The study aimed to evaluate physical performance using “Short Physical Performance Battery (SPPB) Score” if the patients were fit after 24 sessions. Another aim of the study was to evaluate body composition, lower body strength and quality of life. The measurements were repeated at 36. session (post) and 48.session (final) apart from 24.session (mid).

Exercise sessions took place twice weekly during the second hour of haemodialysis for a total of 48 exercise sessions. Supervised sessions began with a 5-min warm-up and ended with a 5-min cool-down. Participants in the strength training group exercised their lower body only using ankle weights progressively in half-pound increments from 0.5 to 20 lbs (TKO, Houston, TX). Exercises included seated right/left knee extension with dorsi/plantar flexion (quadriceps muscle), seated leg curl with both legs keeping the heels pressed firmly against a chair while rolling the legs in and out (hamstrings), semirecumbent right/left inner leg raises (hip adductors), and semirecumbent dorsi/plantar flexion with straight legs (tibialis anterior, gastrocnemius and soleus muscles). Participants did a seated pelvic tilt (abdominal and lower back muscles) without using free weights. Two sets of eight repetitions were performed for each exercise with a 1.5s concentric phase, a 0.5s pause in the lifted position and a 3-s eccentric phase; assuring 1–2 min rest between sets. Exercise intensity was assessed by

the rate of perceived exertion (RPE) modified OMNI Scale [54], with a target moderate intensity of 6 (somewhat hard) out of 10 (extremely hard), equivalent to 60% of a one-repetition maximum [55]. The first eight exercise sessions were done with none or little weight and progressed based on participants' ability to complete two sets of eight repetitions with proper form and a RPE rating of 2–4 (easy to somewhat easy).

Attention-control participants did stretching exercises with light resistance bands (TKO, Houston, TX), using right/left dorsi/plantar ankle flexion, right/left ankle rotation, right/left calf stretch, right/left hamstring stretch and right/left inner thigh stretch. These exercises were done in the semi recumbent position, held for 20–30 s and repeated twice. All participants were asked to continue their usual activities, including physical activity and diet, and to report any changes in health status or medications.

As a result, progressive low intensity strengthening training was found to be an effective and safe approach in maintenance of hemodialysis patients. Majority of the study participants were chronic patients and elderly and in fact physically inadequate. Physical inadequacy was indicated with low SPPB scores "meaning that chi score is lower than 7". It was found that there was a strong correlation between low SPPB scores and old age. SPPB score change in the study is directly associated with knee extension strength which is strongly recommended to be improved by strength trainings. It is understood from this study that intradialytic low intensity strengthening trainings might reverse functional losses, which are also known as physical inadequacy and disability of hemodialysis patients and might protect their acquisitions. Future studies might concentrate on generalizability of strengthening exercises on hemodialysis patients and routine programming of dialysis units.

Similarly, Johansen et al. [50] obtained a significant increase in knee extension strength. They found that fat mass significantly increased while there was no significant change in non-fat body mass analyzed by Dual-Energy X-ray Absorbsiometry (DEXA) and physical performance. The two studies differ in terms of exercise durations, comorbidity and presence of more disabled patients. In fact since low intensity exercise group consisting of patients in a worse condition can show higher change when compared to the beginning, they seem to have made benefitted from exercise at a higher extent.

3.2. Flexibility and strengthening exercises

Based on the definitions of Painter et al., Nonoyama et al. concentrated on flexibility and muscle strength with a 12-week exercise program and cardiovascular fitness and functional capacity [56]. Patients diagnosed with ESRD, who were receiving > 6 month and 3 times / week hemodialysis, above the age of 55 who were ambulated with or without help and did not recently receive a structure exercise program were selected. Exercise program was prescribed by a physiotherapist and was personalized according to the skills, exercise preferences and individual aims of the patients. The patients were given 5 training sessions [57].

In flexibility and strengthening exercises, exercise intensity was determined according to definition of the exercises by the patient as painless and "slightly difficult" according to rated perceived exertion (RPE). Upper and lower extremity strengthening exercises were com-

pleted using exercise bands and 0.5-2 lb dumbbells in such a way not to exceed 6 different exercises at each session. Each exercise was started with 10 repetitions; one set was increased to 15 as the patient tolerated and then progressed to 2 or 3 sets with 15 repetitions. Resistance and dumbbells was increased by 0.5- 2 lb when this frequency was reached.

To provide cardiovascular fitness by this program, exercise intensity was based on patients' level from "mild" to "slightly difficult" according to RPE during pedaling; patients ability to speak without difficulty during exercise; patients level at training heart rate according to heart rate reserve for very low exercise intensity; blood pressure values, presence of other symptoms and patient feedbacks [58,59]. Workload was increased by 1-5 watts if the patients managed adequate duration after 20-30 minutes aerobic exercise [57].

The patients were analyzed by ESRD-modified version of Charlson Index for Comorbidity [60]. Initial and 12-week Duke Activity Status Index (DASI) [61] was evaluated by 2 Min Walking Test (2 MWT) [62], Timed-Up-and-Go Test (TUG) [63], Illness Intrusiveness Ratings Scale (IIRS) [64] and The Kidney Disease Quality of Life Questionnaire (KDQoL) [65].

The study proved the applicability of exercise programs in hemodialysis patients with over the age of 55 with low functional level. Randomized studies with larger sampling should analyze exercise effectiveness during hemodialysis.

3.3. Resistance training

Balakrishan et al.[66]. analyzed aerobic effects of 12-week high intensity training in randomized controlled chronic kidney disease stage 3 and 4 patients with low protein diet (approximately 0.6 g/kg/day) to examine the effect of resistance training on mtDNA copy number and to identify combination with skeleton muscle phenotype (measurement of muscle mass and strength).

Resistance Exercise Training Group

Participants exercised three times per week under supervision. Each session lasted approximately 45 minutes and included the following: 5 minutes warm-up, 35 minutes resistance training on chest and leg press, M.latissimus pull-down, knee extension, and flexion pneumatic resistance training machines (Keiser Sports Health Equipment Inc., Fresno, CA), and 5 minutes cool-down. Participants performed three sets of eight repetitions on each machine per session. Training intensity was targeted at 80% of one repetition maximum (1RM) and progressively increased per participants' self-perceived level of exertion using a Rating of Perceived Exertion Scale [54]. Cool-down included five to eight upper and lower body-stretching and flexibility exercises.

Attention-Control Group

Participants met and performed the same stretching and flexibility exercises as those used during cool-down in the resistance exercise training group.

In conclusion it was found that oxidative metabolic capacity increased in uremic skeleton muscle. There was no relationship between mitochondrial content and insulin resistance.

The factors affecting anabolism such as energy intake and IGF⁻¹ concentrations in circulation were found to be positively correlated with the changes in mtDNA copy number. Therefore, mechanisms of anabolic and genomic factors on mitochondrial functions should be analyzed and well understood [67].

3.3.1. Resistance exercise protocol example Jie Dong, et al. [68]

Subjects randomized to receive exercise (NS+EX) performed the prescribed resistance exercise, under supervision of study personnel, within 30 minutes prior to each dialysis session and ingestion of at least one can of Nepro®. A pneumatic leg press machine (Keiser®, Fresno, CA) was used, mainly focused at exercising the quadriceps, hamstring, and gluteus muscles. Subjects sat on the leg press machine with their feet placed on a platform, their legs at a 90 degree angle, and were instructed to push the platform forward, leaving their knees slightly bent. For the first month, exercise was set at approximately 70% of the subject's 1-RM established at the baseline control visits. An initial leg press weight approximately equal to the participant's body weight was used. Additional weight (~25-50 lb) was added at each repetition until the participant could no longer push the platform. Once the 1-RM was determined, 70% of this weight was used for participants in the NS+EX arm performing 3 sets of 12 repetitions prior to each dialysis session. At the month 3 and month 6 assessments, 1-RM was repeated in all subjects to evaluate progress and determine a new 1-RM for those in the NS+EX arm.

4. The effects of aerobic and resistance exercises on lipid profiles and inflammation level

In ESRD patients, exercise results in entrance of higher amounts of uremic toxins into vascular compartment by increasing muscle blood flow. Afshar et al. [14] investigated the effects of intradialytic aerobic exercise and resistance training on lipid profile and inflammation status in hemodialysis patients.

The training program consisted of a 5-min warm up, a 10–30min aerobic or resistance training and a 5 min cool down period during the first 2 h of each dialysis session in recumbent position, within 8 weeks. According to primary results of Baecke Questionnaire on physical activity which was filled for all participants at baseline, aerobic training participants should perform stationary cycling at an intensity of 12–16 out of 20 at the rate of perceived exertion of Borg scale so that intensity involved 65–85% of an individual's maximal capacity, a level at which cardiovascular health can be obtained.

Resistance exercise training of the lower extremities was performed in three sets and under the supervision of a physician by applying ankle weights for knee extension-flexion and hip abduction-flexion at an intensity of 15–17 out of 20 at the RPE scale. Starting weights were determined from a three-repetition maximum (3RM) using ankle weights that can be adjusted in 0.5⁻¹ kg/week increments. A 3RM is the maximum weight that can be lifted three times

with a proper technique. Training started at approximately 60% of 3RM for two sets of eight repetitions and was increased to three sets as tolerated. When patients could perform three sets successfully, the weight was increased. Blood pressure and heart rate of the participants were monitored each 5 min during exercise. Fasting venous blood samples were obtained from patients before mid-week dialysis session in order to measure serum urea, creatinine, albumin, hemoglobin, lipid levels [low density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride], and CRP (turbidometric technique with normal range below 10 mg/L), at baseline and 8 weeks.

In this study, 8-week aerobic and resistance training had a significant effect on chronic inflammation; hs-CRP levels increased by 83.4% or 67.9% by aerobic exercise when compared to resistance training. These two approaches are not effective on lipid profiles. Intradialytic aerobic exercise is accompanied by triglyceride decrease and HDL elevation; it improved lipid profile due to weight loss. However, 8 week is a short period in terms of lipid effect. Besides, secondary hyperparathyroidism which inhibits type, nutrition status and more complicated lipolytic activity should not be ignored. The fact that number of male patients in whom lipid change was observed was low affected the result.

5. Exercise as an anabolic intervention

Although the effectiveness of resistance training as an anabolic intervention have been shown in healthy and chronic patients, long term improvement results on muscle mass markers in chronic hemodialysis patient have not been shown. Follow-up studies showed that peak torque value increased in response of dominant leg extensions to exercise in type I and II muscle fiber hypertrophy and hemodialysis patients.

Johansen et al. [69] carried out a controlled study consisting of 12-week moderate intensity lower extremity resistance exercise training and found no change with DEXA; however they found that quadriceps muscle area measured by magnetic resonance imaging (MRI) have improved. This change accompanies increases in body weight and fat mass. In another controlled study, Cheema et al. [70] found no improvement in computerized tomography (CT) scan in skeleton muscle amount with 12-week high intensity progressive resistance training routinely applied during hemodialysis. Similarly, the follow-up after 24 weeks found no additional benefit. Kopple et al. [71] examined the effects of different exercise training (strength, endurance and combination of both) in RNA levels in muscle genes. Although there was no significant difference in non-fat body mass (LBM) at the end of 6 month individual exercises, it was observed that exercise training in hemodialysis patients increased m RNA changes in skeleton muscle and muscle insulin-like growth factor-1 (IGF-I) protein. This factor is important as it accelerates protein anabolism.

On the other hand, although the effects of resistance exercise on muscle quantity and quality in hemodialysis patients have been shown, strength and physical function cannot be main-

tained in these patients. Although the causes are not clear, lack of nutritional support particularly during hemodialysis is held responsible.

6. Do muscle contraction types affect differently?

Koudi et al. [40] reported increase in proportion of type I fibers and muscle fiber hypertrophy following a 6-month low intensity resistance exercise program in ESRD patients receiving hemodialysis. Isometric contractions in contracted muscle position are more effective than dynamic training in maintenance of type II fibers [72,73]. However, this issue could not be customized in ESRD patients. Although eccentric muscle contractions have a protective effect on muscle with progressive weakness, the effects of eccentric contraction in muscle with myopathic changes could not be determined.

Reduced muscle mass and metabolic deficiencies of anaerobic metabolism require specific exercises. In this manner, we can discuss low intensity resistance exercises.

7. Assessment of isometric muscle strength

In the literature, grip strength studies are related mostly dominant or non-dominant hand strength in the healthy population [74]. For Yurdalan et al. study [75], the arm without fistula was considered dominant. In their study, they also measured the non-dominant arms at elbow flexion and extension. The results in elbow flexion were lower than those of extension. Though they didn't encounter a statistical difference, this result indicated that force distribution occurred from powerful muscles to weaken muscles. The arm with fistula was checked also against the values of the arm without fistula, and all cases were dramatically lower. This may be evidence of the nonuse of the arm with fistula in their daily living activities, which have been outlined in the literature.

8. Evaluation of functional capacity

Peak oxygen consumption (VO_2 peak) is the most commonly used parameter to evaluate functional capacity in ESRD patients. In addition, 6 MWT is one of clinical tools to determine functional capacity in almost all chronic diseases. This is a submaximal test, low-cost and easily applied. In addition, it is an alternative VO_2 peak determinant in patients who cannot tolerate ergometric tests.

In Yurdalan et al. study [75], the limited walking distance can be due to cardiopulmonary and musculoskeletal origins. The result exemplifies the lower functional capacity of the hemodialysis cases.

6 MWT was used to evaluate functional capacity in chronic kidney patients however was not adequately investigated as a mortality factor [76-78]. In the study of Kohl et al. [76]; walked distance was found as an independent predictor in ESRD patients in terms of mortality. Each 100 m walked was approximately 5.3% protective factor in relation to life expect-

ancy and it was at the same time found to be correlated with peak oxygen consumption. For this reason, 6MWT can be used as a strategy to define progression and aggravation of disease. In patients with terminal renal insufficiency it can be used to determine death risk. In other words, it is recommended to be used during treatment programs and follow-ups of hemodialysis patients.

Please visit <http://cin2011.uninet.edu/es/trabajos/346.html>. You will find ppt file titled " Evaluation of functional capacity in patients on hemodialysis,what is new?"

9. Assessment of health related fitness: Using eurofit test battery

There are many exercise training studies in patients with end-stage renal disease on hemodialysis, but few, if any, health-related fitness assessment in the literature. For this reason, Yurdalan et al. hypothesize the suitability of Eurofit for adults in this group of patients and sought to evaluate the hemodialysis patients relevant to health-related physical fitness using Eurofit Test Battery, which tests all approved, valid, and reliable measures of these components for adults [79,80].

From the 25 end-stage renal disease patients in the maintenance hemodialysis program at the Renal Unit, 18 without exclusion criteria (*pre-dialysis potassium* > 5.5 mmol l, *Hb* < 10 g/dL, *unstable hypertension*, *congestive heart failure* (grade > u according to NYHA), *cardiac arrhythmias* (< u according to Lown), recent myocardial infarction or unstable angina, persistent hyperkalemia before dialysis, peripheral vascular disease, arthritic or orthopedic problems limiting functional capacity) and 22 aged-matched healthy subjects volunteered to participate in the study. The hemodialysis patients had all been undergoing regular HD, three sessions a week, four hours each session.

Aerobic Fitness

A six-minute walking test (6MWT) was used in the determination of aerobic fitness in place of 2 km walking test, ergometer test, or multistage shuttle run test in original Eurofit Battery. Because 6MWT is more suitable for chronic patient groups, aerobic fitness was tested within this protocol according to American Thoracic Society (ATS) 6 MWT statement (81). Blood pressure (systolic/diastolic blood pressures (SBP/DBP) and heart rate (HR) were measured before and after test. The perception of exercise intensity was assessed by Original Borg Scale. At the end of test, the distance walked was recorded. The following formula was used determine $VO_2 \max$ (ml.min⁻¹.kg⁻¹):

$$70.2 \times \text{distance(m)} - 0.191 \times \text{age(year)} - 0.07 \times \text{weight(kg)} + 0.09 \times \text{height(cm)} + 0.26 \times \text{rpp} (\times 10^{-3}) + 2.45$$

Where RPP is the rate-pressure product (HR×SBP).

Musculoskeletal Fitness

The musculoskeletal fitness of the patients was assessed by the components of muscle strength and endurance and flexibility of Eurofit Test Battery for Adults.

The grip strength for the hand muscle strength was performed with JAMAR dynamometer, once with each elbow in flexion, once with each elbow extension. Each measurement was repeated twice and the higher score was recorded.

The vertical jump test was used in order to measure the lower extremity muscle strength. The subject jumped as high as possible at a 20 cm distance from the wall and the distance he/she jumped was measured.

Side-bending test was used for evaluating the spinal flexibility. The patients stood upright against a wall on two parallel lines at right angles to the wall and 15 cm apart. The patients held their arms straight against the sides of their body. The position of the middle finger on each side was marked with a horizontal line on the lateral thigh. The subject was then asked to bend sideways as far as possible while maintaining contact between the back and the wall. The distance between the first and last position of the middle finger was recorded.

Motor Fitness

In the assessment of motor fitness, the single leg balance test was used with eyes open and closed. At the end of the test total time was recorded.

Anthropometry (Body Composition)

In order to assess body composition, height, body weight, body mass index, skinfold thickness, and percentage of body fat (PBF) were measured. Body mass index (BMI) was calculated as body weight in kg divided by square of height in meters (kg/m^2).

The skin fold thickness measurements were carried out in Holtain Calipers with 0.2 mm spaces, and the measurements have been applied on the right side of the body. Measurement sites were the biceps, triceps, subscapular, suprailiac, abdominal, and thigh. Four sites (biceps, triceps, subscapular, suprailiac) are measured to calculate the percentage of body fat.

In conclusion, two results were obtained from this research. First, it was seen that health-related physical fitness in hemodialysis patients resulted in a significant decrease in all aspects. Thus, limited health-related physical fitness should be taken into consideration during daily hemodialysis treatment, and must be improved regular fitness program. Second, the Eurofit Test Battery may be useful instrument to ascertain the specific aspects related to hemodialysis cases in terms of health-related fitness; a well-planned exercise program that was tailored to hemodialysis patients' needs can be set through the Eurofit Test Battery. On the other hand, the Eurofit Test Battery was not employed in this group previously, and its novelty itself assured total originality in the process.

10. Accelerometric evaluation for physical activity

Accelerometer based technology is mainly used to measure physical activity. Accelerometer can objectively predict exercise frequency, duration and intensity; however its validity and reliability is controversial.

Although the study of Sloane et al. [82] did not include hemodialysis patients, it can be used to follow-up home-based exercise programs. Knowledge of energy consumption of moderate and high intensity activity can ensure more comprehensive evaluation of exercise program in terms of oxygen consumption.

11. Conclusion

The role of physiotherapist and physiotherapy and effectiveness of exercise programs is clear in hemodialysis patients. However, it is imperative to select correct patients and to re-evaluate their suitability to exercise at each session with a multidisciplinary team. Although patients with lower capacity make more benefit from due to the nature of exercise training, we should make sure that exercise is not contraindicated in patients with poor clinic. In fact exercise is an approach that is harmful for homeostasis; it might not create sequelae in healthy or other clinical patients. On the other hand, in renal patients with difficult clinical compensation internally it might cause irreversible damage.

Addition to above statement, positive impact of medical treatment on survival in hemodialysis patients helps long term maintenance of physiotherapy with the treatment and protection of physical gains. Follow up of patients during hemodialysis and through programs increasing clinical effectiveness by home-based programs can only be realized by patient follow-up record and electronic or face-to-face feedback from the patient and families the fact that the patients were young adults might require diversification or intensification of programs of the patients by the physiotherapist as much as clinical status allows in case they need more active life style in terms of work and social status.

The literature contains a growing number of studies analyzing different renal clinical problems. However, exercise evaluation and training protocols in hemodialysis patients could not be adequately defined. The research should give priority to physiotherapy approaches to address physical and functional improvement of hemodialysis patients to pursue their daily lives which can guide particularly clinicians. In addition, the fact that exercise approaches clarify effect mechanisms in parallel to pathophysiology will contribute to deciding on the need for exercise, preparing the content of exercise and clinical follow-up of patients doing exercise by the health professionals in nephrology particularly to physiotherapists.

Author details

S. Ufuk Yurdalan

Professor of Physiotherapy, Physiotherapy and Rehabilitation Department, Health Sciences Faculty, Marmara University, Turkey

References

- [1] Takhreem M. The Effectiveness of Intradialytic Exercise Prescription on Quality of Life in Patients with Chronic Kidney Disease. *The Medscape Journal of Medicine* 2008;10(10):226.
- [2] Chen JLT, Godfrey S, Ng TT, Moorthi R, Liangos O, Ruthazer R, Jaber BL, Levey AS, Castaneda-Sceppa C. Effect of Intra-dialytic, Low-intensity Strength Training on Functional Capacity in Adult Hemodialysis Patients: A Randomized Pilot Trial. *Nephrology Dialysis Transplant* 2010;25(6):1936-1943.
- [3] Fried LF, Lee JS, Shlipak M, Chertow GM, Green C, Ding J, Harris T, Newman AB. Chronic Kidney Disease and Functional Limitation in Older People: Health, Aging and Body Composition Study. *J Am Geriatr Soc* 2006, 54:750-756.
- [4] Shlipak MG, Stehman-Breen C, Fried LF, Song X, Siscovick D, Fried LP, Psaty BM, Newman AB. The Presence of Frailty in Elderly Persons with Chronic Renal Insufficiency. *Am J Kidney Dis* 2004; 43: 861-867.
- [5] Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of Frailty Among Dialysis Patients. *J Am Soc Nephrol* 2007; 18: 2960-2967.
- [6] Overend T, Anderson C, Anuradha S, Perryman B, Locking-Cusolito H. Relative and Absolute Reliability of Physical Function Measures in People with End-stage Renal Disease. *Physiother Can* 2010; 62(2):122-128.
- [7] Sterky E, Stegmayr BG. Elderly Patients on Hemodialysis Have 50% Less Functional Capacity than Gender- and Age-matched Healthy Subjects. *Scand J Urol Nephrol* 2005; 39:423-30.
- [8] International Classification of Functioning, Disability and Health [document on the Internet] Geneva: World Health Organisation; 2001. [cited 2009 Feb 2]. Available from: http://www.handicapincifre.it/documenti/ICF_18.pdf.
- [9] Laupacis A. A Randomized Double-Blind Study of Recombinant Human Erythropoietin in Anaemic Hemodialysis Patients (Canadian Erythropoietin Study Group). *Transplant Proc* 1991;23:1825-6.
- [10] Levendođlu F, Altintepe L, Okudan N, Ugurlu H, Gokbel H, Tonbul Z, Güney İ. A Twelve Week Exercise Program Improves the Psychological Status, Quality of Life and Work Capacity in Hemodialysis Patients. *J Nephrol* 2004;17:826-32.
- [11] Anuradha S, Garland SJ, House AA, Overend TJ. Morphological, Electrophysiological and Metabolic Characteristics of Skeletal Muscle in People with ESRD: A Critical Review. *Physiother Can* 2011;63(3):355-376.
- [12] Park J, Campese VM, Middlekauff HR. Exercise Pressor Reflex in Human with End-stage Renal Disease. *Am J Physiol Regul Integr Comp Physiol* 2008; 259(4):1188-1194.

- [13] Tae DJ, Park SH. Intradialytic Exercise Programs for Hemodialysis Patients. *Chonnam Medical Journal* 2011;47(2):61-65.
- [14] Afshar R, Shegarfy L, Shavandi N, Sanavi S. Effects of Aerobic Exercise and Resistance Training on Lipids Profiles and Inflammation Status in Patients on Maintenance Hemodialysis. *Indian J Nephrol* 2010; 20(4):185-9.
- [15] Gordon EJ, Prohaska T, Siminoff LA, Minich PJ, Sehgal AR. Needed: Tailored Exercise Regimen for Kidney Transplant Recipients. *Am J Kidney Dis* 2005; 45 (4):769-774.
- [16] Moore SC, Chow WH, Schatzkin A, Adams KF, Park Y, Ballard-Barbash R, Hollenbeck A, Leitzman MF. Physical Activity during Adulthood and Adolescence in Relation to Renal Cell Cancer. *Am J Epidemiol* 2008; 168 (2):149-157.
- [17] Nonoyama ML, Brooks D, Ponikvar A, Jassal SV, Kontos P, Devins GM, Spanjevic L, Heck C, Laprade J, Nagle G. Exercise Program to Enhance Physical Performance and Quality of Life of Older Hemodialysis Patients: A Feasibility Study. *Int Urol Nephrol* 2010; 42(4):1125-1130.
- [18] Kelly A. Musculoskeletal Pain in Dialysis-Related Amyloidosis. *Can J Surg* 2007; 50(4):305-306.
- [19] Painter P, Carlson L, Carey S, Paul SM, Myll J. Physical Functioning and Health-Related Quality-of-Life Changes with Exercise Training in Hemodialysis Patients. *American Journal of Kidney Diseases* 2000;35:482-492.
- [20] Cheema BS. Review Article: Tackling the Survival Issue in End-stage Renal Disease: Time to Get Physical on Hemodialysis. *Nephrology* 2008;13:560-569.
- [21] Pianta TF, Kutner NG. Improving Physical Functioning in the Elderly Dialysis Patient: Relevance of Physical Therapy. *American Nephrology Nurses' Association Journal* 1999;26:11-21.
- [22] Cheema BSB, Singh MAF. Exercise Training in Patients Receiving Maintenance Hemodialysis: A Systematic Review of Clinical Trials. *American Journal of Nephrology* 2005;25:352-364.
- [23] Kontos PC, Miller KL, Brooks D, Jassal SV, Spanjevic L, Devins GM, Souza MJ, Heck C, Laprade J, Naglie G. Factors Influencing Exercise Participation by Older Adults Requiring Chronic Hemodialysis: A Qualitative Study. *International Urology and Nephrology* 2007;39:1303-1311.
- [24] Painter P, Carlson L, Carey S, Myll J, Paul S. Determinants of Exercise Encouragement Practices in Hemodialysis Staff. *Nephrology Nursing Journal* 2004;31:67-74.
- [25] Williams A, Stephens R, McKnight T, Dodd S. Factors Affecting Adherence of End-stage Renal Disease Patients to an Exercise Programme. *British Journal of Sports Medicine* 1991;25:90-93.

- [26] Raman J, Bajinder R, Hilarie S. Upper Extremity Diabetic Muscle Infarction in Three Patients with End-stage Renal Disease: A Case Series and Review. *Journal of Clinical Rheumatology* 2009;15(2):81-84.
- [27] Huang GS, Chu TS, Lou MF, Hwang SL, Yang RS. Factors Associated with Low Bone Mass in the Hemodialysis Patients- A Cross-Sectional Correlation Study. *BMC Musculoskeletal Disord* 2009; 10:60.
- [28] Jadoul M: Towards the Prevention of Bone Fractures in Dialysed Patients? *Nephrol Dial Transplant* 2007, 22(12):3377-80.
- [29] American College of Sports Medicine: ACSM Position Stand on Osteoporosis and Exercise. *Med Sci Sports Exer* 1995, 27(4):i-vii.
- [30] French SA, Fulkerson JA, Story M: Increasing Weight-Bearing Physical Activity and Calcium Intake for Bone Mass Growth in Children and Adolescents: A Review of Intervention Trials. *Prev Med* 2000, 31:722-731.
- [31] Heinonen A, Kannus P, Sievanen H, Oja P, Pasanen M, Rinne M, Uusi-Rasi K, Vuori I: Randomised Controlled Trial of Effect of High-impact Exercise on Selected Risk Factors for Osteoporotic Fractures. *Lancet* 1996, 348(9038):1343-7.
- [32] Jhamb M, Argyropoulos C, Steel JL, Plantinga L, Wu AW, Fink NE, Powe NR, Meyer KB, Unruh ML. Correlates and Outcomes of Fatigue among Incident Diaysis Patients. *Clin J Am Soc Nephrol* 2009; 4(11):1779-1786.
- [33] Jhamb M, Weisbord SD, Steel JL, Unruh M. Fatigue in Patients Receiving Maintenance Dialysis: A Review of Definitions, Measures, and Contributing Factors. *Am J Kidney Dis* 2008;52:353-65.
- [34] Floyd M, Ayyar DR, Barwick DD, Hudgson P, Weightman D. Myopathy in Chronic Renal Failure. *Q J Med* 1974;43:509-24.
- [35] Lazaro R, Kirshner H. Proximal Muscle Weakness in Uremia. *Arch Neurol* 1980;37:555-8.
- [36] Griggs RC, Mendell JR, Miller RG. Myopathies of Systemic Disease. In: Griggs RC, Mendell JR, Miller RG (eds). *Evaluation and Treatment of Myopathies*. Philadelphia: FA Davis Co.; 1995. pp. 355-85.
- [37] Bilodeau M, Yue GH, Enoka RM. Why Understand Motor Unit Behavior in Human Movement? *Neurol Rep* 1994;18:11-4.
- [38] Johansen KL, Doyle J, Sakkas GK, Kent-Braun JA. Neural and Metabolic Mechanisms of Excessive Muscle Fatigue in Maintenance Hemodialysis Patients. *Am J Physiol* 2005;289:R805-13.
- [39] Painter P. The Importance of Exercise Training in Rehabilitation of Patients with ESRD. *Am J Kid Dis* 1994;24(19):52-59.

- [40] Koudi E, Albani M, Natsis K, Magalopoulos A, Gigis P, Guiba-Tzianing O. The Effects of Exercise Training on Muscle Atrophy in Hemodialysis Patients. *Nephrology Dial Transplant* 1998;13(3):685-699.
- [41] Pupim LB, Cuppari L, Ikizler TA. Nutrition and Metabolism in Kidney Disease. *Semin Nephrol* 2006;26(2):134-157.
- [42] Carrero JJ, Chmielewski M, Axelsson J, Snaedal S, Heimbürger O, Bárány P, Suliman ME, Lindholm B, Stenvinkel P, Qureshi ARR. Muscle Atrophy, Inflammation and Clinical Outcome in Incident and Prevalent Dialysis Patients. *Clin Nutr* 2008;27:557-564.
- [43] İkizler TA. Exercise as an Anabolic Intervention in ESRD Patients. *J Ren Nutr* 2011; 21 (1) :52-56.
- [44] Biolo G, Maggi SP, Williams BD, Tipton KD, Wolfe RR. Increased Rates of Muscle Protein Turnover and Amino Acid Transport After Resistance Exercise in Humans. *Am J Physiol* 1995;268:E514-20.
- [45] Wolfe RR. Protein Supplements and Exercise. *American Journal of Clinical Nutrition* 2000;72:551S-7S.
- [46] Kouidi EJ, Grekas DM, Deligiannis AP. Effects of Exercise Training on Noninvasive Cardiac Measures in Patients Undergoing Long-term Hemodialysis: A Randomized Controlled Trial. *Am J Kidney Dis* 2009;54: 511-521.
- [47] Moore GE, Brinker KR, Stray-Gundersen J, Mitchell JH. Determinants of VO₂ peak in Patients with End-Stage Renal Disease: On and Off Dialysis. *Med Sci Sports & Exerc.* 1993;25:18-23.
- [48] Painter P. Effects of Modality Change and Transplant on Peak Oxygen Uptake in Patients with Kidney Failure. *Am J Kidney Dis* 2011; 57(1): 113-122.
- [49] Spiegel BMR. Biomarkers and Health-related Quality of Life in End-stage Renal Disease: A Systematic Review. *Clin J Am Soc Nephrol* 2008;3(6):1759-1768.
- [50] Johansen KL. Physical Functioning and Exercise Capacity in Patients on Dialysis. *Adv Ren Replacement Therapy* 1996;6(2):141-148.
- [51] Koh KP, Fasset RG, Sharman JE, Coombes JS, Williams AD. Intradialytic Versus Home Based Exercise Training in Hemodialysis Patients. A Randomized Controlled Trial. *BMC Nephrol* 2009;10 :2.
- [52] Chan CT. Determinants of Cardiac Autonomic Dysfunction in ESRD. *Clin J Am Soc Nephrol* 2010;5(10):1821-1827.
- [53] Chen JLT, Godfrey S, TT Ng, Moorthi R, Liangos O, Ruthazer R, Jaber BL, Levey A, Castenada-Sceppa C. Effect of Intra-dialytic, Low-Intensity Strength Training on Functional Capacity in Adult Hemodialysis Patients: A Randomized Pilot Trial. *Nephrol Dial Transplant* 2010 ;25(6):1936-1946.

- [54] Robertson RJ, Goss FL, Rutkowski J, Lenz B, Dixon C, Timmer J, Frazee K, Dube J, Andreacci J. Concurrent Validation of the OMNI Perceived Exertion Scale for Resistance Exercise. *Med Sci Sports Exerc* 2003, 35:333-341.
- [55] Lagally KM, Robertson RJ. Construct Validity of the OMNI Resistance Exercise Scale. *J Strength Cond Res* 2006;20:252-256.
- [56] Painter P, Blagg C, Moore GE. Exercise: A Guide for the People on Dialysis Patient. A Comprehensive Program. *Geriatric Nephrology and Urology* 1996;5:157-165.
- [57] Exercise Prescription for Other Clinical Populations: Renal Disease. In: Thompson W, Gordon N, Pescatello L. (eds). *ACSM's Guidelines for Exercise Testing and Prescription*. Lippincott Williams & Wilkins; Philadelphia: 2009. pp. 264-271.
- [58] Borg GA. Psychophysical Bases of Perceived Exertion. *Medicine & Science in Sports & Exercise* 1982;14:377-381.
- [59] Swain DP, Leutholtz BC. Heart Rate Reserve is Equivalent to % VO₂ Reserve, Not to % VO₂ max. *Medicine & Science in Sports & Exercise* 1997;29:410-414.
- [60] Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity Index for Use in Patients with ESRD. *American Journal of Kidney Diseases* 2003;42:125-132.
- [61] Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB. A Brief Self-Administered Questionnaire to Determine Functional Capacity (The Duke Activity Status Index). *American Journal of Cardiology* 1989;64:651-654.
- [62] Finch E, Brooks D, Stratford PW, Mayo NE. *Physical Rehabilitation Outcomes Measures: A Guide to Enhanced Clinical Decision-Making*. B.C. Decker, Inc; 2002. Walk Test (2-Minute) (2MWT) pp. 246-247.
- [63] Rockwood K, Awalt E, Carver D, MacKnight C. Feasibility and Measurement Properties of the Functional Reach and the Timed Up and Go Tests in the Canadian Study of Health and Aging. *Journals of Gerontology Series A Biological Sciences & Medical Sciences* 2000;55:M70-M73.
- [64] Devins GM. Illness Intrusiveness and the Psychosocial Impact of Lifestyle Disruptions in Chronic Life-Threatening Disease. *Advances in Renal Replacement Therapy* 1994;1:251-263.
- [65] Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB. Development of the Kidney Disease Quality of Life (KDQOL) Instrument. *Quality of Life Research* 1994;3:329-338.
- [66] Balakrishnan VS, Rao M, Menon V, Gordon PL, Pilichowska M, Castenada F, Castenada-Sceppa C. Resistance Training Increases Muscle Mitochondrial Biogenesis in Patients with Chronic Kidney Disease. *Clin J Am Soc Nephrol* 2010; 5(6):996-1002.

- [67] Rao M, Li L, Demello C, Guo D, Jaber BL, Pereira BJ, Balakrishnan VS.: Mitochondrial DNA Injury and Mortality in Hemodialysis Patients. *J Am Soc Nephrol* 2009; 20: 189-196.
- [68] Dong J, Sundell MB, Pupim LB, Wu P, Shintani A, İkizler A. The Effect of Resistance Exercise to Augment Long-term Benefits of Intradialytic Oral Nutritional Supplementation in Chronic Hemodialysis Patients. *Journal of Renal Nutrition* 2011 ;21(2): 149-159.
- [69] Johansen KL, Painter PL, Sakkas GK, Gordon P, Doyle J, Shubert T. Effects of Resistance Exercise Training and Nandrolone Decanoate on Body Composition and Muscle Function among Patients Who Receive Hemodialysis: A Randomized, Controlled Trial. *J Am Soc Nephrol* 2006;17:2307-14.
- [70] Cheema B, Abas H, Smith B, O'Sullivan A, Chan M, Patwardhan A, Kelly J, Gillin A, Pang G, Lloyd B, Singh MF. Progressive Exercise for Anabolism in Kidney Disease (PEAK): A Randomized, Controlled Trial of Resistance Training during Hemodialysis. *J Am Soc Nephrol* 2007;18:1594-601.
- [71] Kopple JD, Wang H, Casaburi R, Fournier M, Lewis MI, Taylor W, Storer TW. Exercise in Maintenance Hemodialysis Patients Induces Transcriptional Changes in Genes Favoring Anabolic Muscle. *J Am Soc Nephrol* 2007;18:2975-86.
- [72] Duchateau J, Hainaut K. Isometric or Dynamic Training: Differential Effects on Mechanical Properties of a Human Muscle. *J Appl Physiol* 1984;56:296-301.
- [73] Hurst JE, Fitts RH. Hindlimb Unloading-induced Muscle Atrophy and Loss of Function: Protective Effect of Isometric Exercises. *J Appl Physiol* 2003;95:1405-17.
- [74] Branz NR, Newton RA. Hand Function in Patients on Maintenance Hemodialysis. *Physical Therapy* 1998;68(7):1092-1097.
- [75] Yurdalan SU, Kondu S, Malkoç M. Assessment of Health-Related Fitness in the Patients with End-Stage Renal Disease on Hemodialysis: Using Eurofit Test Battery. *Renal Failure* 2007; 29:955-960.
- [76] Kohl LM, Signori LU, Riberio RA, Silva AMV, Moreira PR, Dipp T, Sbruzzi G, Lukrafka JL, Plentz RDM. Prognostic value of the Six-minute Walk Test in End-stage Renal Disease Life Expectancy: A Prospective Cohort Study. *Clinics* 2012;67(6):581-586.
- [77] Painter P. Physical Functioning in End-stage Renal Disease Patients: Update 2005. *Hemodial Int* 2005;9(3):218-35.
- [78] Hsieh RL, Lee WC, Chang CH. Maximal Cardiovascular Fitness and Its Correlates in Ambulatory Hemodialysis Patients. *Am J Kidney Dis* 2006;48(1):21-7.
- [79] Eurofit for Adults. Assesment of Health-Related Fitness. In Oja P, Tuxworth B, eds. Council of Europe, Committee for the Development of Sport and UKK Institute for Health Promotion Research 1995. Tampere, Finland; 1995:5-104.

- [80] Committee of Experts on Sports Research Eurofit. Handbook for Eurofit Tests of Physical Fitness. 2nd ed. Strasbourg: Council of Europe; 1993.
- [81] ATS Statement. Guidelines for the Six-Minute Walk Test. *Am J Respiratory Critical Care Medicine* 2002; 166:111-117.
- [82] Sloane R, Snyder DC, Demark-Wahnefried W, Lobach D, Kraus W. Comparing the 7-Day PAR with a Triaxial Accelerometer for Measuring Time in Exercise. *Med Sci Sports Exerc* 2009; 41(6):1334-1340.