

Invited Editorial

Exercise Training in Dialysis Patients: Why, When, and How?

Treatment of patients with end-stage renal disease has evolved considerably over the past decade. Reported mortality rates have fallen because of a variety of factors, including prevention; earlier diagnosis and treatment of the acute event; improved management of complications such as anemia, secondary hyperparathyroidism, hypertension, cardiac disorders etc.; and widespread availability of therapeutic methods, such as hemodialysis, continuous ambulatory peritoneal dialysis (CAPD), and transplantation. In addition, for each of these three strategies new technical developments have been helpful to improve mortality further (1). Despite the progress made, an aspect that has all too much been neglected until now is the enhancement of rehabilitation and quality of life (2,3).

Dialysis patients commonly have poor exercise tolerance and debilitation symptoms and impaired quality of life (4). Functional capacity is mainly limited by fatigue, but dyspnea on exertion is also a contributing factor (5). Aerobic capacity, peripheral skeletal muscle strength, and endurance in hemodialysis patients are approximately half that of the corresponding healthy sedentary aged-matched men (4). Moreover, hostility, psychological disorders, dependency, and social isolation deteriorate their health-related quality of life (6). Anemia, deconditioning, cardiac dysfunction, impairment of autonomic balance, and mainly skeletal muscle weakness and fatigue, primarily because of uremic myopathy and neuropathy, are the main predisposing factors for their low functional ability (4,5,7). Moreover, the deleterious influence of both small and middle molecular weight uremic retention solutes, known as *uremic* toxins, plays an important role in these morphological and functional abnormalities (8).

Recently, several reports have shown that there are functional and psychological benefits from using regular exercise training as adjunctive therapy in the treatment of dialysis patients (2,7,9,10). The underlying mechanisms responsible for the beneficial effects of exercise training are becoming apparent. Therefore, we offer in this review a summary of the

current knowledge about the effects and benefits of exercise training in hemodialysis patients.

WHY TRAIN DIALYSIS PATIENTS?

A well-accepted observation in dialysis patients is that exercise training produces beneficial effects on exercise capacity. Exercise duration and VO_{2peak} improve significantly, by 15–20% and 15–40%, correspondingly, in both hemodialysis and CAPD patients who are trained for 6–12 months (2,7,9,11,12). Furthermore, previous studies in our laboratory, after a 6 year exercise-training program in a group of 10 hemodialysis patients, have shown an increase in both VO_{2peak} by 76% and exercise capacity by 60% (13). A reduction in blood lactate production at peak exercise was also found (14). However, lactate production has been shown to be independent from VO_{2peak} improvement, probably because of altered carbohydrate metabolism in uremia (14).

Importantly, the increase in exercise tolerance seems to be correlated with symptomatic improvements and enhancements in health-related quality-of-life measurements (9,10). Improvements in measures of fatigue, activities of daily living, symptoms of peripheral neuropathy and myopathy, breathlessness, depression, and anxiety, as well as general well-being after exercise training are also reported (9,10,14). Interestingly, in chronic uremia, subtle improvements in overall nutritional status were found after training, especially with resistance exercises (15,16). A trend toward improved diabetic control in trained hemodialysis patients was also noted (15). Before the widespread use of erythropoietin (EPO), exercise training was shown to increase the level of hematocrit (11). Subsequently, it seems obvious that training plus EPO are beneficial in improving exercise capacity and quality of life in dialysis patients (17).

It seems that functional improvements are primarily caused by peripheral and metabolic adaptations although improved resting and submaximal exercise ejection fraction and cardiac output were also reported after training (7,10,15,18). Although there is some evidence that exercise training causes left ventricular anatomical adaptations (eccentric type hy-

perrophy), this was not found to be harmful but was associated with a subtle improvement in cardiac function (18). Also a reduction of heart rate at rest and submaximal exercise and a decrease in arterial blood pressure in hypertensive hemodialysis patients were found, mainly by reduction of the peripheral vascular resistance (11,18). However, others have not demonstrated significant beneficial effects of training on blood pressure (15). It is likely that the decrease in resting heart rate after exercise training is caused by an increase in cardiac parasympathetic activity and a reduction in sympathetic activity (19). Autonomic neuropathy, mainly increased sympathetic activation, is a common complication of chronic uremia which contributes to abnormal hemodynamic responses during dialysis (20). Moreover, depressed cardiac vagal activity is associated with decreased heart rate variability (HRV) and enhanced cardiac arrhythmias (19,20). It is also well known that reduced HRV could be used as a reliable independent prognostic marker of malignant arrhythmias, especially in cardiac patients. A recent study supported that exercise training enhances cardiac parasympathetic tone in hemodialysis patients, as illustrated by a significant increase in HRV, and suppresses the incidence of arrhythmias (19). This increase in HRV was closely correlated with increased VO_{2peak} , suggesting an association between the improvement of exercise capacity and reduction of autonomic imbalance. However, long-term follow-up studies are needed to find out whether physical training decreases vulnerability to malignant arrhythmias in the dialysis population.

Previous studies have shown marked changes in skeletal muscle histology, metabolism, and perfusion in dialysis patients (21,22). Muscular weakness, fatigue, myoclonus, and cramps limit daily physical activities dramatically (14). The reasons for muscle atrophy and impaired strength in these patients seem to be multifactorial. Malnutrition, uremic myopathy and neuropathy, neurohormonal activation, uremic toxin accumulation, underperfusion, and inactivity are known contributing factors (14,21,22). Atrophy of both Type I and II muscle fibers was noted to be associated with an increased percentage of Type IIB fibers and other histological abnormalities (14). It is likely that there is a defect of oxidative metabolism in the skeletal muscles of dialysis patients, which is consistent with a reduction of number, volume, and enzyme activity of mitochondrial cristae (14).

Exercise training is found to improve skeletal muscle endurance and strength and, thus, peak exercise performance in hemodialysis patients (7,14,15). Biopsy studies have demonstrated an in-

crease in both Type I and Type II muscle fiber cross-sectional areas after both endurance and strengthening training in chronic uremic patients (14,16). In addition, regeneration of degenerated fibers, increase in capillary density, and favorable changes in the structure and number of mitochondria were also described (14). Exercise training also improved maximal isometric strength of the lower limbs, as well as peripheral nerve electrophysiological properties (14–16). These results are in contrast with an earlier study by Moore et al., who have not found any significant morphological change in skeletal muscle, however, after only 12 weeks of cycling (22). It is likely that benefits of training on muscle function predominantly occur through partial correction of muscle metabolic abnormalities, in addition to the improvement of skeletal muscle blood flow. Moreover, training may reduce the exaggerated muscle ergoreflex activity, thereby improving the responses to exercise, as has been shown in patients with chronic heart failure (23).

At present, there is no evidence to provide a conclusive answer regarding the influence of exercise training on the prognosis of dialysis patients. However, training-induced benefits in cardiovascular and autonomic function and reduction of known risks for coronary heart disease, including changes in lipid profile, suggest a favorable effect on prognosis (7,24). Furthermore, it is difficult to isolate the effects of exercise alone, because these patients are usually exposed to multiple interventions, and compliance cannot be assessed accurately. More clinical research is needed to identify the dialysis population most likely to respond favorably to permit efficient resource use.

WHEN TO TRAIN DIALYSIS PATIENTS?

Exercise rehabilitation aims first to restore the ability to perform usual daily activities and then to increase functional capacity in such a way that these daily activities are performed without early fatigue. It is recommended that patients with end-stage renal disease participate in an exercise rehabilitation program while they are in the predialytic state because it helps them to attain the greatest and longest lasting benefits. It is reported that exercise training in predialysis patients improves their functional and aerobic capacity, muscle strength, and blood pressure without compromising renal function (25,26). It is recently supported that resistance training is effective against the catabolism of a low-protein diet and uremia in predialysis patients by improving muscle mass and strength, protein use, and nutritional status (16,27). In addition, training provides them with the

psychological adjustment needed for working and participating in social activities. Thus, exercised predialysis patients are able to resist decline into frailty, continue to take care for themselves more accurately, and achieve a better quality of life (25).

While on dialysis, both CAPD and hemodialysis patients can participate either in a supervised center-based or in a nonsupervised home-based exercise training program (3,4,12). Both interventions seem to be effective and safe because there are no differences in the distribution of adverse events relative to the location of training (12). Supervised outpatient training programs on the nondialysis days are preferred, because they increase the likelihood to engage in more *aggressive* and, thus, more effective, rehabilitation. It is likely that in dialysis patients, extra weight can decrease their exercise capacity. In patients on CAPD, the dialysis solution retained in the peritoneal cavity does not change VO_{2peak} or maximum heart rate but shortens exercise time, which is prolonged after the drainage of dialysis solution (28,29).

Despite benefits, compliance in outpatient programs on the nondialysis days is found to be limited (12). Factors affecting adherence are transportation difficulties, lack of time, dependency, lack of outcome, changes in medical status, depression, etc. (12,30). Coexisting medical problems are also an important reason for dropout (7,12). The physician's support and the strength of his or her recommendation as perceived by the patient are predictive of participation in exercise rehabilitation programs. In addition, limited, inconvenient, or unfavorable program hours are perceived as barriers by program participants and may discourage program adherence (12,30).

A nonsupervised home-based exercise-training program seems to be an alternative, because this gives a solution to most of the preceding problems, saving time (12). However, it is difficult to ensure compliance with exercise which is certainly a disadvantage. It depends on the willingness and the mood of the patients, whether they will exercise or not. Encouragement of family support throughout the home-based rehabilitation process is necessary. Therefore, the resumption of unsupervised home physical training should take place after education of the patient and the family in a rehabilitation center. Dialysis patients have to become accustomed to exercise training intensities and workloads. For these reasons, it is recommended to motivate active and independent patients (7,12).

Hemodialysis patients have another possibility. They can be exercised during their hemodialysis ses-

sions which seems to be a more convenient and time-efficient way of training in patients on hemodialysis (12,31). An advantage of this method is that it does not create a need for extra time because patients are in the hospital 3 times per week anyway. Therefore, this mode of training is more applicable and preferable from the patient's point of view, because the reported compliance with exercise training during hemodialysis is high (12).

Comparing all modes of training, the outcome is more pronounced in patients who participate in an outpatient supervised program, because a greater dose and variety of exercises are applied (12). However, each patient should be encouraged to participate in any exercise-training program according to his or her needs and time schedules. Initial improvements in functional capacity in traditional programs occur at 4 weeks, and peak adaptations are seen at 16–26 weeks of training (7). Patients should be motivated and incited to include physical activity in their lifestyle, because all exercise benefits are lost within a few weeks of nontraining, and those who receive no exercise seem to deteriorate over time (7).

HOW TO TRAIN DIALYSIS PATIENTS?

Despite the reported beneficial effects, exercise training may pose a risk to patients who are predisposed to cardiovascular complications or to those with specific medical conditions. Physicians should follow the relative and absolute contraindications for entry into inpatient/outpatient exercise programs (32). That means that properly screening the patients for participation in training programs is recommended. Therefore, patients undergo a baseline evaluation of risk factors and exercise capacity, along with an assessment of physical and psychological disability (7,18). In particular, baseline exercise testing is important to determine whether a patient has exertional ischemia or arrhythmias and serves as a basis for prescribing an exercise regimen.

After proper screening tests, exercise training should be initiated according to the patient's clinical status and functional capacity. Components of a systematic individualized exercise prescription include the appropriate mode, duration, intensity, frequency, and progression of exercise. It is important to begin each exercise session with a slow, prolonged warm-up phase, which usually involves low-intensity aerobic exercises, stretching, and calisthenics (2,7,12). The main training session initially lasts for 10 min and is progressively extended to 60 min, applying intensities of 60–80% of the predetermined peak heart rate (12–14). Training is gradually in-



FIG. 1. Exercise training during dialysis is shown.

creased in duration and intensity according to symptoms and clinical status (7). At least three training sessions per week are recommended. In addition, each exercise session should finish with a cool-down period (12–14).

Mainly aerobic-type steady-state or interval exercises, which involve large muscle groups, such as walking and use of the bicycle ergometer, have been the preferred form of exercise training (2,7,12). These activities are characterized predominantly by isotonic muscle work. Interval training (e.g., work phases of 30–60 s and recovery phases of 60 s) is recommended for patients with very low exercise capacity and/or cardiac diseases. It allows more intense exercise stimuli on peripheral muscles without inducing greater cardiac stress compared with steady-state exercise. The exercise-training program during hemodialysis sessions traditionally contains a combination of exercises, consisting of up to 30 min cycling with a bed bicycle ergometer and up to 20 min exercises for flexibility, coordination, and muscle strength (12,31). This training program is usually performed within 2 h after the start of each dialysis session (Fig. 1).

Resistive exercise training has recently gained popularity in renal rehabilitation programs because most daily activities involve arm exercise and lower body muscular work (12,13,16,27). It should be considered as supplemental for the aerobic part of the exercise session and should be preferably performed after it or on a separate day. This form of training has beneficial effect on muscle wasting, minimizing loss of muscle mass and improving muscle strength and endurance (16,27). Circuit weight training with

resting intervals between stations and rhythmic strength exercises is recommended. Muscular endurance is best developed by lifting lighter weights with a greater number of repetitions whereas muscle strength is enhanced by using heavier weights with fewer repetitions. The amount of workload performed depends on the method chosen, the intensity of muscle contraction, and the muscle group chosen. Free weights, therabands, isotonic/isokinetic machines, and other resistive modalities may be used for exercise for major muscle groups (7,12). Once patients have achieved desired loads, the rate of progression should be initiated by increasing the number of sets. Stretching exercises should be performed before and after resistive training to enhance joint mobility.

Physicians responsible for the care of dialysis patients have the opportunity to include exercise training as an integral part of the long-term management. Moreover, participation in collaborative, clinical research trials appropriately designed to define the role of this potentially efficacious intervention on outcomes such as functional capacity of elderly dialysis patients, quality-adjusted life expectancy, morbidity, and health care and transportation costs, is the next step.

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