Review Article

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Intradialytic Exercise Programs for Hemodialysis Patients

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Although it is widely accepted that exercise is beneficial in patients with end-stage renal disease as in the general population, it is not easy to incorporate exercise programs into routine clinical practice. This review aimed to investigate the beneficial effects of exercise during hemodialysis and also to introduce various intradialytic exercise programs and their advantages as a first step in combining exercise programs into clinical practice. Aerobic and resistance exercise are beneficial not only in improving physical functioning, including maximal oxygen uptake and muscle strength, but also in improving anthropometrics, nutritional status, hematological indexes, inflammatory cytokines, depression, and health-related quality of life. However, it is not clear whether the beneficial effects of exercise are limited to only relatively healthy dialysis patients. Therefore, the effects of individualized exercise programs for elderly patients or patients with comorbid conditions need to be studied further.

Key Words: *End-stage renal disease; Dialysis; Exercise*

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INTRODUCTION

Chronic kidney disease (CKD) affects an increasing number of populations and 15% of adults in the United States are estimated to have CKD by the Modification of Diet in Renal Disease (MDRD) estimated glomerular filtration rate (eGFR) criteria.[1] In Korea, it is also a common disease and the prevalence of patients with end-stage renal disease (ESRD) ranks 12th in the world according to the data from the United States Renal Data System 2010.[1]

Muscle wasting, abnormalities in muscle function, and effects on exercise performance are common in patients with ESRD. Not only uremia *per se*, but also chronic inflammation, metabolic acidosis, oxidative stress, malnutrition, inactivity, androgen deficiency, insulin resistance, hemodialysis procedures, and concurrent illnesses are all related to muscle wasting. A specific form of muscle wasting in patients with ESRD is defined as the so called protein-energy wasting, or PEW. PEW is characterized by increased muscle protein catabolism relative to protein synthesis. It is also related to metabolic derangements, hormonal abnormalities, and consequent abnormalities in muscle structure in dialysis patients. In addition, muscle wasting is a strong risk factor for mortality in ESRD patients.[2] Therefore, prevention or treatment of PEW is important for the management of ESRD patients.

Exercise is one of the possible preventive maneuvers to reduce muscle protein loss and maintain muscle function. Recently, many studies have shown the importance of exercise or regular physical activity to prevent muscle wasting in ESRD patients. Therefore, this review aimed to investigate the beneficial effects of exercise during hemodialysis (intradialytic exercise) and also to introduce various intradialytic exercise programs and their advantages.

Generally, patients with ESRD have lower physical activities, muscle performance, and quality of life (QOL) than do healthy subjects. Numerous studies have suggested that exercise could improve many indicators of physical functioning, improve self-reported physical functioning, and also improve QOL in ESRD patients. In addition, considering that cardiovascular disease (CVD) is the major cause of death in patients with advanced CKD, exercise and regular physical activity have the potential to reduce cardiovascular mortality in ESRD patients. Some data are available to show the cardiovascular benefits of exercise in this population. Observational data have shown that sedentary behavior was associated with higher cardiovascular mortality in ESRD patients.[3] In addition, in a randomized

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controlled trial, exercise was shown to improve some indicators of risk of sudden cardiac death.[4]

Hemodialysis, as one of the main renal replacement therapies in patients with ESRD, is a time-consuming procedure that takes at least 3 to 5 hours a day, two or three times a week. Even though there are many debates about the beneficial effects of exercise during hemodialysis (intradialytic exercise),[5] many researchers expect advantages of both dialysis and exercise via intradialytic exercise. Therefore, various exercise programs, such as aerobic exercise, resistance exercise, combined aerobic and resistance exercise, and passive exercise including electrical stimulation have been developed for hemodialysis patients.[6-12]

AEROBIC EXERCISE

Intradialytic exercise programs are mostly composed of aerobic exercises. Cycle ergometer or bicycle training is used for aerobic exercise.

There are various exercise programs using different exercise frequencies, intensities, and duration. However, the exercise program mostly consists of two or three times a week (during hemodialysis), with moderate or vigorous intensity for 30 minutes or more, and lasting from 8 weeks to 12 months.[13-18] When aerobic exercise is planned, heart rate reserve (HRR) or rating of perceived exertion (RPE) should be considered to tailor exercise intensity in individual patients. HRR can be calculated by a modification of the Karvonen method: $(HR_{max} - HR_{rest}) \times (40\text{-}80\%) + HR_{rest}$.[19] In addition, to measure exercise intensity, Borg's 15-point scale for RPE[20] can be used as shown in Table 1. A proposed summary of exercise intensity, frequency, and duration is presented in Table 2.

TABLE 1. Borg's 15-point scale for rating of perceive exertion (RPE)[20]

6-20% effort
7-30% effort - Very, very light (Rest)
8-40% effort
9-50% effort - Very light - gentle walking
10-55% effort
11-60% effort - Fairly light
12-65% effort
13-70% effort - Somewhat hard - steady pace
14-75% effort
15-80% effort - Hard
16-85% effort
17-90% effort - Very hard
18-95% effort
19-100% effort - Very, very hard
20- Exhaustion

It is reported that aerobic exercises improves peak oxygen consumption (VO_{2peak}) in ESRD patients. Johansen et al showed that there was about 17% improvement in VO_{2peak} through aerobic exercise lasting from 8 weeks to 6 months in patients with ESRD.[21] In addition, Storer et al reported that 9 weeks of leg-cycling during hemodialysis improves not only cardiopulmonary fitness and endurance but also muscle strength, power, fatigability, and physical function.[14] Moreover, many studies have reported that aerobic exercise improves anemia, hyperlipidemia, chronic inflammation, blood pressure, insulin resistance, arterial stiffness, and removal of urea or phosphate.[24-32] It was also beneficial to improve the Beck depression score, reduce anxiety, and improve QOL in dialysis patients.[31,32]

However, these data must be interpreted cautiously. First of all, it is not clear whether improvement in VO_{2peak} is directly linked to improvement in physical performance or QOL in ESRD patients. In addition, the subjects studied in the previous reports were usually the healthiest dialysis patients and, therefore, it is difficult to extrapolate these data to whole dialysis populations.

RESISTANCE EXERCISE

It is well known that muscle strength is one of the most important determinants of physical function and an essential point to maintain the activities of daily living in pa-

TABLE 2. Proposed exercise programs for hemodialysis patients

Mode	Methods	Measures	Intensity/frequency/duration	Time to goal
Aerobic[21]	Cycling	HR RPE	40% HRR at start 60% HRR in first 1 month 80% HRR in next 1 month RPE 13-14 3 days/week 60 min/day	At least 2 months
Resistance[6]	Free-weight dumbbell Weighted ankle cuff Theraband	HR RPE 10 RM	2 sets of 10 RM RPE 15-17 3 days/week $<$60 min/day	At least 2 months 1 RM is not recommended

HR: heart rate, RPE: rating of perceive exertion, HRR: heart rate reserve, RM: repetition maximum.

tients with ESRD.[21,33] In addition, muscle strength in ESRD patients on hemodialysis is weaker than that in normal populations with a sedentary lifestyle.[34] A previous study showed that isokinetic muscle strength was an important determinant of VO_{2peak} in patients on dialysis.[35] Therefore, an intradialytic exercise program including resistance exercise could be beneficial in ESRD patients on hemodialysis.

Various resistance exercise programs are available for ESRD patients during hemodialysis: upper extremity strengthening with progressive resistance training (PRT) with free-weight dumbbells, lower extremity strengthening with weighted ankle cuffs, or use of the Thera-band stretch strap (The Hygenic Corp, Akron, OH, USA) in a sitting position. Furthermore, many specific exercises can be used, as follows: shoulder press, side shoulder raise, triceps extension, biceps curl, and external shoulder rotation for upper extremity strengthening; seated knee extension, supine hip flexion, supine hip abduction, supine straight-legged raise, and seated leg curl for lower extremity strengthening; and bilateral straight-leg raises in a supine position or bilateral leg lifts in a seated position for abdominal strengthening.[9]

All resistance exercises can be applied to the patients in a supine or a sitting position. The exercises can take place three times a week during hemodialysis as for aerobic exercises. PRT programs usually consist of 2 sets of supervised training of 8-10 repetitions with an RPE of 15-17. The effects of resistance exercise have been evaluated by using outcome measurements of PRT such as thigh muscle cross-sectional area, physical tests (e.g., muscle strength, 6-min walk), anthropometrics, nutritional status, hematological indexes, inflammatory cytokines, and questionnaires to evaluate depression and health-related QOL.[36-40]

As in aerobic exercises, the heart rate or RPE should be monitored during resistance exercise. In addition, repetition maximum (RM) is also used to guide the intensity of exercise. RM is defined as the most weight one can lift for a defined number of exercise movements. Generally, 1 RM is the basic unit used for the normal population, but in ESRD patients, 10 RM is adequately proposed as shown in Table 2.

Johansen et al[37] have shown an increase in quadriceps muscle cross-sectional area and an improvement in self-reported physical functioning by lower extremity resistance exercise training for 12 weeks during hemodialysis sessions three times per week with the use of ankle weights. In addition, Cheema et al[36] suggested that patients with ESRD could improve skeletal muscle quality and derive other health-related adaptations solely by engaging in a 12-week high-intensity PRT regimen during routine hemodialysis treatment sessions.

COMBINED AEROBIC AND RESISTANCE EXERCISE

As mentioned before, both intradialytic aerobic exercise and resistance exercise have many advantages. Therefore, additional positive effects are expected by combining aerobic and resistance exercise. The forms of combination of each aerobic and resistance exercise differ according to different programs. Some programs use the combination of intradialytic aerobic and resistance exercise; others use intradialytic aerobic exercise and resistance exercise before or after hemodialysis (interdialytic exercise).[12,41-43]

Mostly, cycling is used as the aerobic exercise and knee flexor and/or extensor strengthening is used as the resistance exercise. Resistance exercise is usually taken earlier than aerobic exercise because some patients cannot advance to resistance exercise owing to fatigue after a relatively long time of aerobic exercise during hemodialysis.[44] The overall time for a combined exercise program is longer than that for a single exercise. As for aerobic exercise alone, a combined program is also properly applied during the first 2 hours of hemodialysis, because cardiac decompensation may preclude exercise after 2 hours of hemodialysis.[45]

Van Vilsteren et al[42] showed the beneficial effects of cycling during dialysis together with a pre-dialysis strength training program on behavioral changes, physical fitness, physiological conditions, and health-related QOL. In addition, the combined exercise program improved the physical function subscale of the Short Form-36 (SF-36), the submaximal exercise test, and muscle strength by progressive resistance isotonic quadriceps and hamstring exercise and training on a cycle ergometer.

Although there are clear advantages of intradialytic exercise for hemodialysis patients, there are always some risks, especially in patients with CVD. In addition, these studies of intradialytic exercise programs were undertaken in relatively healthy dialysis patients: that is, young and active patients who did not have serious combined diseases. Therefore, these beneficial effects of intradialytic exercise could not be extrapolated to all ESRD patients on dialysis. Therefore, other new individualized programs for patients with co-morbidities need to be developed. Farese et al[10] reported the short-term effect of intradialytic transcutaneous muscle stimulation (TEMS) and passive cycling movements (PCMs) on blood pressure and clearance of urea and phosphate. Interestingly, even passive treatment during hemodialysis in patients with at least two co-morbid conditions is beneficial to increase urea and phosphate removal. The effect on blood pressure needs to be further studied.

In summary, exercise can be performed either as 'intradialytic' or 'interdialytic,' and both exercise programs have pros and cons. Although debate still exists, intradialytic exercise programs are superior to interdialytic exercise programs in terms of a lower dropout rate.[21,41,45-49] In addition, intradialytic exercise can be safely done in the first 2 hours of dialysis without cardiac decompensation.

In conclusion, exercise or regular physical activities should be mandatory, not optional, in patients with ESRD. However, despite the many beneficial effects of exercise in

ESRD patients, exercise programs are still not a part of routine clinical practice in many centers. Moreover, it is undeniable that there are still many practical burdens to the clinical staff if intradialytic exercise programs are incorporated into routine clinical practice. Further studies of intradialytic and interdialytic exercise will be needed. Also, individualized exercise programs for elderly patients or patients with comorbid conditions need to be developed.

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