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The Effects of Aerobic and Resistance Training on Physical Performance, Sleep Quality, and Pain in Hemodialysis Patients

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Abstract

Introduction: Hemodialysis may impair physical performance, disrupt sleep, and exacerbate pain. The present research sought to investigate and compare the impacts of aerobic and resistance training on muscular endurance, muscle strength, static balance, physical performance, sleep quality, and pain in patients undergoing hemodialysis.

Methods: Fifty-one patients undergoing hemodialysis were randomly assigned to a control (CO), resistance training (RT), or aerobic training (AT) group (n = 17 per group). Resistance training was conducted three times per week for eight weeks using 0.5–2 kg sand weights. Aerobic training was performed in three 20-minute sessions per week for eight weeks. Study variables were assessed at both the baseline and after the intervention. Statistical analyses were carried out in SPSS version 25 using a one-way ANOVA followed by Tukey's post-hoc test, with the significance level set at $P < 0.05$.

Results: Both RT ($P = 0.001$) and AT ($P = 0.008$) groups showed significantly greater improvements in muscular endurance than the CO group. The RT group demonstrated greater improvements in muscular endurance than the AT group ($P = 0.005$). Both RT and AT groups showed significant improvements in muscle strength compared with the CO ($P = 0.001$). The AT group demonstrated greater improvements in muscle strength than the RT group ($P = 0.04$). Both RT and AT groups showed significant improvements in static balance ($P = 0.001$ and $P = 0.01$, respectively) and physical performance ($P = 0.001$ and $P = 0.004$, respectively). Significant improvements in sleep quality were observed in the RT ($P = 0.001$) and AT ($P = 0.004$) groups compared to the CO.

Conclusion: Both RT and AT programs effectively improved physical performance and sleep quality in patients undergoing hemodialysis.

Keywords: Exercise therapy, Hemodialysis, Physical fitness, Sleep, Pain

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Introduction

Chronic kidney disease (CKD) is a progressive, irreversible loss of nephron function that results in fluid and electrolyte imbalances and uremic toxin buildup (1,2). Although peritoneal dialysis and kidney transplantation are viable alternatives, hemodialysis remains the most widely used treatment worldwide, prolonging survival but often associated with reduced QOL, increased hospitalizations, and higher overall costs (3,4).

Recumbent, prolonged inactivity during hemodialysis contributes to muscle weakness and atrophy, reduced endurance, and functional disability, resulting in poorer physical functioning compared with healthy individuals (5–6). Although such weakness may arise from muscle atrophy, impaired motor unit activation, malnutrition, and carnitine deficiency, interval aerobic training has markedly enhanced physical performance in individuals receiving hemodialysis treatment (7–8).

In addition to reduced muscle strength and endurance, patients undergoing hemodialysis often experience sleep disturbances, which further compromise their overall health (9). Globally, the prevalence of sleep disorders in this population is estimated to range from 50%-80%, with rates in Iran reported at 70%–80% (10). These disturbances are often linked to elevated blood urea nitrogen, creatinine, and parathyroid hormone levels, abnormal blood pressure, comorbidities, and lifestyle factors (11).

Alongside poor sleep quality, chronic pain is another major challenge for individuals undergoing hemodialysis, adding to both physical and psychological burdens. Hemodialysis patients frequently experience muscle cramps, headaches, and bone and joint pain related to osteodystrophy, as well as roughly 300 arteriovenous-fistula needle punctures each year, which further contribute to stress and discomfort (5,12). The severity and frequency of this chronic pain are linked to increased mortality and are further associated with heightened depression, insomnia, anxiety, and stress, underscoring the urgent need for effective pain management to improve treatment adherence and overall well-being (13).

Regular physical exercise is a key nonpharmacological intervention for preventing chronic disease, as it enhances antioxidant capacity, reduces oxidative stress and inflammation, and improves energy metabolism. Exercise-induced reactive oxygen species function as signaling molecules that modulate pro-inflammatory pathways and promote neuromuscular and neuroendocrine adaptations. Concurrently, the upregulation of antioxidant defenses and favorable shifts in cytokine profiles work together to support improved muscle function and overall homeostasis (14,15).

Aerobic and resistance training stimulate molecular pathways that regulate muscle function. Aerobic exercise increases mitochondrial capacity and fatty acid oxidation by activating AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) (16). In contrast, resistance training relies on mechanical overload to stimulate muscle growth and strength. This overload activates the mammalian target of rapamycin (mTOR) signaling pathway, thereby promoting muscle hypertrophy and stimulating the release of myokines, cytokines, and other endocrine mediators. These factors not only facilitate muscle repair and neuromuscular adaptations but also contribute to systemic metabolic improvements (17). The rising prevalence of CKD patients undergoing hemodialysis necessitates care that extends beyond physical management alone. Although exercise improves physical function and QOL in largely inactive hemodialysis patients, it is rarely recommended for them, thereby creating a significant care gap (5). Frequent dialysis sessions, declining health, and fatigue limit patients' ability to exercise; therefore, strategies should aim to make exercise appealing, monitor activity, and highlight its benefits (18). In hemodialysis patients, combining standard medications with a low-cost, low-risk exercise training program that boosts endorphin release can enhance QOL by reducing depression and anxiety (19). In addition, in hemodialysis patients with comorbidities and elevated mortality risk, exercise training provides an accessible, cost-effective, and low-risk nonpharmacological intervention that improves clinical outcomes and QOL. However, few comparative clinical trials have directly compared the effects of aerobic versus resistance exercise on pain, balance, and sleep quality in dialysis patients. The present study was designed to compare the impact of aerobic and resistance exercise programs on key performance indicators, sleep quality, and pain levels in patients undergoing hemodialysis. It was hypothesized that performing exercise while undergoing hemodialysis would significantly improve patients' physical function, sleep quality, and pain levels.

Methods

Population and procedure

This quasi-experimental study, conducted in 2023, employed a pre-test–post-test design involving patients undergoing hemodialysis at Shafa Hospital and Javadolaemeh Clinic in Kerman, Iran. Ethical approval was obtained from the Research Ethics Committee of Birjand University (Ethical code: IR.BIRJAND.REC.1402.011), and the research was registered with the Iranian Registry of Clinical Trials (IRCT20240806062675N1). A total of 278 patients who met the inclusion criteria were recruited using convenience sampling. Participants were then randomly assigned to one of three groups: An aerobic training (AT) group, a resistance training (RT) group, or a control (CO) group (that received routine care). Randomization was carried out using block randomization software. The sample size for each group was determined using the free trial version of PASS 2021 software. The calculation targeted a power of 0.80, an alpha value of 0.05, a standard deviation of 17, and an effect size of 0.42, yielding a total sample size of 51 subjects. To account for potential dropouts, 17 participants were allocated to each group. The inclusion criteria were: A history of hemodialysis for at least six months with a minimum of three dialysis sessions per week; an age between of 30 to 55 years; the capability to move independently without needing help from others; the capability to engage in physical exercise (evaluated through a questionnaire designed to assess physical activity); without any history of operations over the previous three months; and maintaining stable blood pressure throughout hemodialysis sessions. The exclusion criteria were: having experienced ischemic heart disease, a heart attack, or angina in the last six months; the presence of pulmonary disease requiring supplemental oxygen; having experienced a stroke or transient ischemic episode in the last three months; musculoskeletal disorders of the legs prevent exercise participation; symptomatic cardiovascular events within the past three months; the use of beta-blockers; participation in two or fewer training sessions; and unfavorable physical condition during exercises, including changes in blood pressure, shortness of breath, reduced alertness, or dizziness.

Measuring variables

After explaining the study's objectives and methods to all participants, written informed consent was obtained. Demographic and background information (age, sex, marital status, educational attainment, number of offspring, residential location, and occupation) were collected using a structured form. Additionally, disease-related information including the cause of kidney failure, underlying conditions, duration of illness, duration and frequency of hemodialysis, and medication regimen was recorded. Before the intervention, participants attended a separate session to receive detailed information on the research methodology and the training program (resistance and aerobic exercises). Baseline measurements, including muscular endurance, muscle strength, static balance, physical performance, sleep quality, pain levels, height, weight, and body mass index (BMI), were then obtained.

Each patient's weight was measured using a Seca scale (Germany) with a precision of < 100 g. Participants wore minimal clothing and had their height measured without shoes, recorded to the nearest 0.5 cm. BMI was calculated as weight (kg) divided by height (m)².

Lower limb muscular endurance was assessed using the sit-to-stand-to-sit test. On the examiner's signal, the participant rises from a chair to a standing position without using their arms, then sits back down. The test result is the number of completed cycles performed in one minute. The participant performed the test at their own pace; if they experienced marked fatigue, they were allowed to pause briefly without extending the overall duration. They were encouraged to perform the task at the maximum possible rate (20).

Total work was calculated as the sum of the weight lifted during a single exercise session. This value was calculated by multiplying the weight lifted by the total number of movements, repetitions, and sets performed.

Static balance was assessed using the Stork test. Participants stood on one leg with their hands placed on their waists. The other foot was placed against the inner knee. They attempted to maintain this position for up to 50 seconds on a balance mat. The test ended if the standing leg shifted, the hands were removed from the waist, or the opposite leg was lifted. Participants chose which leg to stand on. The test was performed three times using the same leg, and the mean duration sustained across the three trials was recorded as the result (21).

Physical performance was assessed using the two-minute walk test. This test is a widely recognized tool for evaluating physical performance, especially in individuals with chronic health conditions. A 20 × 20 m square was clearly marked to serve as the walking course. Participants were allotted two minutes to walk as far as possible within the designated area. The distance covered during the two minutes was recorded. Participants were instructed to walk at a normal, comfortable pace within the marked area (22).

In this study, sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), developed by Buysse et al. (1989). The PSQI is a self-reported questionnaire consisting of 19 items, 10 of which evaluate specific domains of sleep quality. It evaluates seven sleep domains: Subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. Each PSQI item is scored on a 0-3 scale, with higher scores indicating greater sleep disturbances. The total PSQI score ranges from 0 to 21 and is calculated as the sum of all component scores (23).

Pain intensity was assessed using the Visual Analog Scale (VAS). Participants rated their pain level on a 10-cm line, with 0 representing no pain and 10 representing the most severe imaginable pain. The distance marked by each participant was measured and expressed as a percentage score. The validity and reliability of the VAS have been well-established in numerous studies (24).

Training program

After two familiarization sessions with the training program, the resistance and aerobic training programs were implemented for the respective groups as follows:

Resistance training program

The resistance program consisted of three sessions per week for eight weeks, synchronized with hemodialysis treatments. Each session lasted approximately 50 minutes and was supervised by a physician and an exercise physiologist. The program focused on lower-limb exercise and utilized sandbag ankle weights ranging from 0.5 to 2 kg. Overload was achieved by progressively adjusting the weight load according to each patient's tolerance and performance during previous sessions. Additionally, the number of repetitions and sets was increased gradually over the 8-week intervention as participants demonstrated reduced perceived effort or fatigue.

All exercises were performed either seated on or lying down in the hemodialysis chair (25). Each session included a 10-minute warm-up, 30 minutes of resistance exercise, and a 10-minute cool-down (Table 1).

Aerobic training program

The exercise program was conducted throughout the hemodialysis treatment sessions. Each session began with a 5-minute warm-up consisting of active stretching of the upper and lower limbs. The main component of the session consisted of 20 minutes of stationary cycling exercise at 60–70% of heart rate reserve (Table 2) (26). Exercise intensity was monitored by measuring heart rate. The target was set at 60 – 70% of the heart rate reserve, which was determined using the Karvonen formula from predicted peak HR (HR_{peak}) and resting HR (HR_{rest}) as follows:

THR = (HRpeak − HRrest) × k + HRrestpredicted HRpeak = 220 − agewhere *k* is the constant number of exercise intensity (8).

The session concluded with a 5-minute cool-down consisting of passive stretching of the upper and lower limbs.

Both the resistance and aerobic training programs were conducted during hemodialysis sessions supervised by a physician and an exercise specialist, and within the first two hours of hemodialysis sessions. Participants

Table 1. Resistance training program

Movements	Free weight	Frequency per week	Set No.	Repetition No.	Rest between sets (min)
Foot abduction	0.5-2	3	3	8	2
Flexion of a straight leg for one foot	0.5-2	3	3	8	2
Flexion of a straight leg for both feet	0.5-2	3	3	8	2
Flexing one knee to 90 degrees	0.5-2	3	3	8	2
Flexing two knees to 90 degrees	0.5-2	3	3	8	2
Single-leg knee extension (Keeping the foot flat on the ground with a slightly bent knee, and then actively straightening the knee by raising the leg upwards)	0.5-2	3	3	8	2

were instructed to stop exercising immediately if they experienced any adverse symptoms, such as dizziness, headache, palpitations, nausea, anxiety, fatigue, or forms of discomfort. During exercise, vital signs were recorded at 15-minute intervals. Following the eight-week intervention, data were collected for all participants across multiple domains, including muscular endurance, muscular strength, static balance, physical function, sleep quality, pain intensity, height, weight, and BMI. These post-intervention measurements were identical to those collected during the pre-test phase. An overview of the research methodology is presented in Figure 1.

Table 2. Aerobic training program

Week Variable	1	2	3	4	5	6	7	8
Duration (min)	20	20	20	20	20	20	20	20
Intensity (from maximum heart rate reserve)	60-70%	60-70%	60-70%	60-70%	60-70%	60-70%	60-70%	60-70%

Statistical analysis

Data were analysed using SPSS version 25. Descriptive statistics (frequencies, percentages, means, and standard deviations) were used to summarize the participants' demographic characteristics and to describe disease-related information and research variables. The Chi-squared test was used to compare the baseline characteristics among the three groups. The Shapiro-Wilk test was applied to assess data normality, and the Levene test was used to evaluate the homogeneity of variances. Given that the assumptions of normality and homogeneity of variance were satisfied, analysis of variance (ANOVA) followed by Tukey's post-hoc test was conducted to compare mean differences in

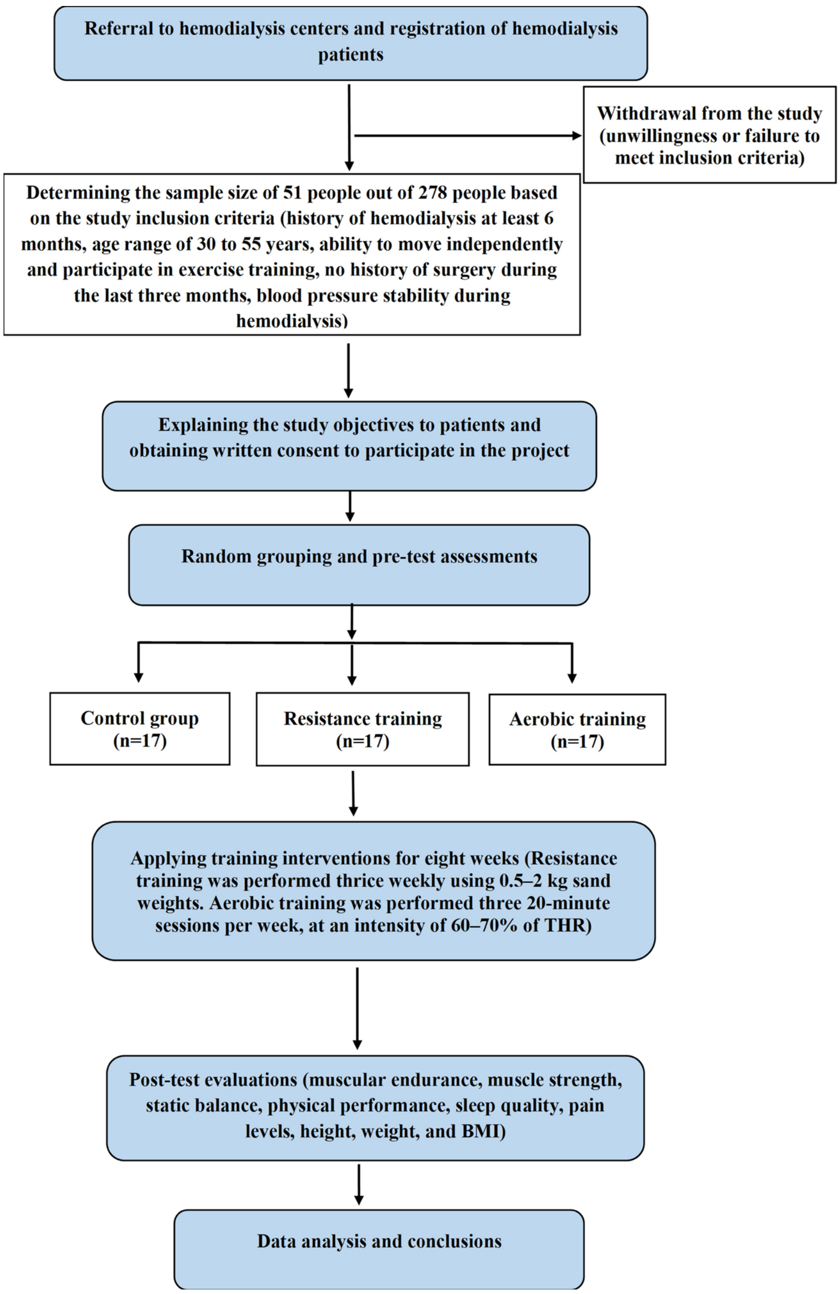

Figure 1. Summary of the research method

the research variables across groups before and after the intervention. Statistical significance was set at $P < 0.05$.

Results

Individual and demographic characteristics

Demographic information and initial patient characteristics were gathered, such as age, sex, BMI, blood pressure, diabetes status, drug utilization, comorbidities, and duration of hemodialysis. The data are presented in Table 3. Preliminary statistical analyses (Chi-squared and ANOVA) showed that the groups were similar in their baseline characteristics, and no significant differences were detected between them. Data normality was assessed using the Shapiro–Wilk test, and all variables were found to be normally distributed ($P > 0.05$). Levene's test was performed to evaluate the equality of variances, confirming that the homogeneity assumption was met for all variables ($P > 0.05$). Table 3 summarizes the descriptive statistics, including mean and standard deviation (SD), for the personal characteristics of the study subjects, while Table 4 summarizes their demographic and background information.

Table 4, along with the results of the Chi-squared test, indicated that the three groups were homogeneous at baseline with respect to demographic and clinical characteristics, and no differences were detected among them.

Table 3. Individual characteristics of the subjects

Variable	Group	Mean	SD	F	*P* value	Partial eta squared	95% Confidence Interval	
							Lower	Upper
Weight (Kg)	RT	69.70	10.96					
	AT	73.82	4.01	0.615	0.545	0.025	0.000	0.132
	CO	69.76	12.04					
Height (m)	RT	1.69	0.05					
	AT	1.70	0.08	1.614	0.210	0.63	0.000	0.201
	CO	1.73	0.04					
BMI (Kg/m^2)	RT	24.45	3.26					
	AT	24.68	1.96	0.964	0.389	0.039	0.000	0.160
	CO	23.34	3.66					

Comparison of the effect of resistance and aerobic training on research variables

Table 5 presents the mean, standard deviation (SD), F-values, and significance levels for each key variable (functional indices, sleep quality, and pain intensity) measured in each group before and after the intervention. Table 5 shows that there were no significant differences in the mean values of the research variables among the three groups at baseline. After the intervention, analysis of variance (ANOVA) revealed significant differences among the groups in muscle strength ($F = 21.85$, $P = 0.001$), muscular endurance ($F = 28.56$, $P = 0.001$), static balance ($F = 8.63$, $P = 0.001$), physical performance ($F = 24.00$, $P = 0.001$), and sleep quality ($F = 2.07$, $P = 0.001$). However, no significant differences in pain intensity were observed among the groups ($F = 1.38$, $P = 0.25$). According to Tukey's post-hoc test, both the RT and AT groups exhibited significantly greater improvements in muscular endurance compared to the CO group ($P = 0.001$, $P = 0.008$, respectively). Furthermore, the AT group demonstrated significantly greater improvements than the RT group ($P = 0.005$).

While both the RT and AT groups demonstrated significantly greater improvements in muscle strength compared to the CO group ($P = 0.001$), the AT group exhibited significantly greater muscle strength than the RT group ($P < 0.04$). Additionally, both the RT and AT groups showed significantly greater improvements in static balance compared to the CO group ($P = 0.001$, $P = 0.01$, respectively). According to Tukey's post-hoc test,

Table 4. Baseline demographic data of subjects belonging to the RT, AT, and CO groups

Group Variable	RT		AT		CO		Chi-squared test	*P*-value	Effect size (Phi)
	Frequency	Percent	Frequency	Percent	Frequency	Percent			
Sex Male Female	11 6	64.7 35.3	12 5	70.6 29.4	13 4	76.5 23.5	0.56	0.75	0.10
Hypertension Yes No	12 5	70.6 29.4	8 9	47.1 52.9	6 11	35.3 64.7	4.39	0.11	0.29
Diabetes Yes No	4 13	23.5 76.5	6 11	35.3 64.7	6 11	35.3 64.7	0.72	0.69	0.12
Medication use Yes No	1 16	5.9 94.1	0 17	0 100	0 17	0 100	2.04	0.36	0.2
Congenital disease Yes No	1 16	5.9 94.1	0 17	0 100	1 16	5.9 94.1	1.04	0.59	0.143
Urological disease Yes No	1 16	5.9 94.1	0 17	0 100	1 16	5.9 94.1	0	1	0.00
Protein excretion Yes No	0 17	0 100	2 15	11.8 88.2	3 14	17.6 82.4	3.1	0.21	0.274

Table 5. Comparison of the mean and SD values for functional indices, sleep quality and pain intensity in the intervention and CO groups

Group Variable		RT		AT		CO		F	*P*-value	Partial eta squared	95% Confidence Interval	
		Mean	SD	Mean	SD	Mean	SD				Lower	Upper
Muscle strength	Before	66.58	8.82	68.47	7.05	65.88	11.49	0.35	0.7	0.477	0.000	0.103
	After	200.47	56.24	145.88	45.30	96.70	32.71	21.85	0.001*	0.014	0.250	0.608
Muscular endurance	Before	19.76	5.5	20.35	5.7	15.7	5.4	3.54	0.3	0.129	0.000	0.288
	After	24.88	5.06	29.41	5.46	16	5.25	28.56	0.001*	0.543	0.327	0.660
Static balance	Before	16.52	3.58	12.17	7.83	11.05	6.51	1.32	0.27	0.052	0.000	0.184
	After	24.82	14.27	20.94	8.67	10.47	6.82	8.63	0.001*	0.265	0.061	0.427
Physical performance	Before	6.73	0.95	6.38	0.69	6	0.7	1.63	0.3	0.132	0.000	0.291
	After	7.58	0.98	7.70	0.77	5.94	0.7	24	0.001*	0.500	0.276	0.626
Sleep quality	Before	5.84	1.08	5.79	0.88	5.82	0.82	2.82	0.1	0.167	0.009	0.331
	After	4.23	0.66	4.76	0.83	5.82	0.72	2.07	0.001*	0.455	0.227	0.591
Pain level	Before	2.7	0.91	2.41	1.17	2.82	1.18	0.63	0.53	0.026	0.000	0.133
	After	2.47	0.79	2.11	1.05	2.70	1.21	1.38	0.25	0.055	0.000	0.188

* A significant difference between the groups after the intervention.

both the RT and AT groups demonstrated significantly greater improvements in physical performance and sleep quality compared with the CO group ($P=0.001$, $P=0.004$, respectively).

Discussion

Hemodialysis patients often experience prolonged periods of inactivity and endure the physically demanding nature of the treatment, which may result in multiple complications, including physical deconditioning and psychological distress. This study aimed to evaluate and compare the effects of aerobic and resistance exercise programs on performance indicators, sleep quality, and pain intensity in patients undergoing hemodialysis. According to our findings, both the RT and AT groups demonstrated a significant increase in muscular endurance, as assessed by the ability to sit and stand from a chair, compared with the CO group. Notably, the RT group experienced significantly greater improvements in muscular endurance than the AT group. These findings are consistent with those of Karimi et al. (2018), who reported that an intermittent aerobic exercise program reduced homocysteine and enhanced physical function in patients undergoing hemodialysis (8). Esther Torres et al. (2020) reported that a three-month resistance training program administered during hemodialysis significantly improved physical performance- evidenced by enhanced ability to sit and stand from a chair- and had positive effects on body composition and lipid profile in hemodialysis patients (27). Jonathan Myers et al. (2021) demonstrated that a 12-week home-based exercise program, combining resistance and aerobic training, enhanced physical performance- particularly sit-to-stand ability- and improved several QOL indicators in hemodialysis patients (28). These results align with the findings of the present study, suggesting that structured exercise programs can significantly enhance muscular endurance in patients undergoing hemodialysis. Moreover, exercise interventions in this population are generally well tolerated, produce minimal adverse effects, and do not significantly disrupt routine hemodialysis care. As hemodialysis sessions typically require a substantial time commitment- 4 to 5 hours per session, three times per week- patients frequently exhibit markedly reduced physical activity. Furthermore, co-existing medical conditions can further restrict physical activity. Impaired renal function is associated with various pathophysiological changes- particularly microangiopathy- that result from a complex interplay of abnormal angiogenesis, reduced vascular density, and endothelial dysfunction (29). CKD adversely affects protein metabolism, diminishes mitochondrial content, and impairs satellite cell activation, thereby accelerating muscle atrophy. Engaging in a workout routine incorporating both aerobic and resistance exercises has been shown to enhance skeletal and vascular muscle function, with benefits evident even at the molecular level (30). A 12-week sit-to-stand exercise program has been shown to significantly improve quadriceps strength, joint range of motion, and mobility in patients undergoing hemodialysis. This exercise regimen not only increases the size and strength of the quadriceps muscles but also improves mobility and facilitates better performance of daily activities in this population (31).

This study revealed that while both the RT and AT groups significantly increased muscle strength compared to the CO group, the magnitude of improvement varied between the two exercise modalities. Notably, the AT group demonstrated a greater increase in muscle strength than the RT group following the exercise program. Yue Lu et al. (2019) demonstrated that regular resistance exercise performed at moderate to high intensity significantly increased muscle mass and strength in patients undergoing hemodialysis. They also suggested that combining aerobic and resistance training could provide additional improvements in patients undergoing hemodialysis (32). Yoshifumi Moriyama et al. (2019) found that a six-month resistance training program was associated with significant improvements in muscle strength and physical performance among hemodialysis patients (33). These findings, consistent with the findings of the present study, suggest that exercise training is a safe and effective strategy for enhancing physical fitness and increasing muscle strength in patients undergoing hemodialysis. Esther Torres et al. (2020) observed significant increases in muscle mass and intracellular water, while interstitial fluid remained unchanged (27). Previous studies have demonstrated that muscle wasting among patients with CKD is strongly associated with an increased mortality risk. Given the association of muscle wasting and overhydration with adverse outcomes- such as loss of independence, disability, increased cardiovascular risk, and mortality- exercise interventions may offer substantial clinical benefits (34).

Another important result of the present research was the considerable improvement in static balance in both the RT and AT groups relative to the CO group. Previous research strongly supports incorporating increased physical activity into rehabilitation programs for hemodialysis patients as an effective strategy to improve postural balance (35). Consistent with the findings of the present study, Bastani et al. (2017) reported significant improvements in static balance, dynamic balance, and muscular endurance. These results suggest that a structured program of core stability exercises may lead to substantial improvements in these variables. Therefore, healthcare professionals-such as physical therapists- may recommend core stability exercises as a safe and practical strategy to improve balance and muscular endurance in hemodialysis patients, potentially enhancing independence and reducing fall risk (36). Similarly, Hosseinpour Setobadi et al. (2023) reported that an eight-week combined resistance and aerobic exercise program significantly improved static and dynamic balance, QOL, and overall satisfaction among individuals undergoing hemodialysis (37). Bechir Frih et al. (2018) demonstrated that patients undergoing hemodialysis who participated in specific balance training, integrated into a conventional endurance-resistance training program, experienced significantly greater improvements in both static and dynamic balance (38). Similarly, Abduelaal and Abdulaziz (2019) investigated the effects of exercise therapy on physical performance and functional balance in patients undergoing hemodialysis. Their findings indicated that aerobic as well as resistance exercise produced positive outcomes; however, participation in aerobic exercise was related to more favorable short- and long-term improvements in physical performance and functional balance compared with resistance exercise training (39). These findings suggest that various exercise training modalities can effectively support the maintenance and enhancement of balance in patients undergoing hemodialysis. Erdoğanoğlu et al. (2019) proposed that aerobic-resistance training enhances balance by positively influencing the sensory systems involved in movement perception. By enhancing muscle strength, endurance, and neuromuscular coordination, this type of training likely facilitates improvements in both static and dynamic balance (40). Given these findings and the demonstrated benefits of exercise training on neuromuscular and sensory systems, combined aerobic-resistance training may enhance both static and dynamic balance in older hemodialysis patients. This can be achieved by activating the core muscles, which function synergistically with other muscle groups to maintain postural control and facilitate movement. Improvements in balance resulting from resistance and aerobic training can be attributed to several factors, including activation of proprioceptive receptors, priming of motor neurons, enhanced coordination of motor units, co-contraction of synergistic muscles, and greater inhibition of antagonistic muscles. In particular, strength training promotes neuromuscular adaptations that strengthen coordination among motor units, thereby improving overall neuromuscular efficiency and control (41).

The present study identified significant differences in physical performance, as measured by the two-minute walk test, among the RT, AT, and CO groups. Both RT and AT groups exhibited significant improvements in physical performance compared with the CO group. Similarly, Kalani and Riahi (2015) reported that a five-month aerobic training program significantly improved physical performance - as measured by the two-minute walk test - while also increasing muscle strength and reducing muscle atrophy in hemodialysis patients (42). Bastani et al. (2020) reported that a six-week core stability exercise program resulted in significant improvements in physical performance, reductions in pain levels, and alleviation of fatigue among patients undergoing hemodialysis (5). Similarly, Esther Torres et al. (2020) demonstrated that implementing exercise programs during hemodialysis improved physical performance - as measured by the six-minute walk test - as well as body composition, lipid profile, and anemia indicators (27). Exel et al. (2021) demonstrated that individuals undergoing hemodialysis exhibited significantly lower functional capacity compared with healthy, sedentary individuals. This decline in functional capacity has been associated with decreased survival rates and impaired ability to perform daily activities, underscoring its clinical significance in the hemodialysis population. Resistance training administered during hemodialysis sessions has gained recognition as an effective therapeutic strategy, demonstrating improvements in physical performance and lower-limb muscle strength (43). These findings, which align with the results of the present study, highlight the positive impact of exercise training on the physical performance of individuals undergoing hemodialysis.

Exercise training may exert beneficial effects in individuals with CKD by modulating immune cell function and reducing systemic inflammation. Clinical evidence suggests that regular physical training attenuates the expression of the early activation marker CD69 on $CD4^+$ and $CD8^+$ T cells following stimulation with the superantigen staphylococcal enterotoxin B (SEB) (44). Experimental data also support that exercise is associated with a shift toward an anti-inflammatory circulating immune cell profile in individuals undergoing hemodialysis (45). Evidence indicates that an intradialytic resistance exercise program increases the expression of peripheral blood mononuclear cell (PBMC) and nuclear factor erythroid 2-related factor 2 (Nrf2) mRNA compared with pre-intervention levels in patients undergoing hemodialysis (46).

Aerobic exercise may reduce pulse wave velocity in both healthy individuals and patients with CKD (47). This potential improvement in arterial stiffness due to exercise training has been attributed to enhanced endothelial function, leading to increased nitric oxide (NO) release and improved vasodilation. Enhanced NO may also improve arterial compliance in patients with CKD. Together, these factors lead to reductions in systolic and diastolic blood pressure following exercise training (48). In CKD, exercise training activates AMPK, which leads to upregulation of PGC-1α. As a transcriptional coactivator, PGC-1α promotes mitochondrial biogenesis and enhances oxidative metabolism. According to Razie Ghoraba et al. (2022), aerobic exercise training reduces oxidative stress in hemodialysis patients (49). These adaptations may enhance muscle function and mitigate metabolic dysregulation in patients with CKD (50).

Notably, both the RT and AT groups showed significant improvement in sleep quality compared with the CO group. This result agrees with the findings of Ali Mohammadi et al. (2021), who reported that an eight-week resistance-aerobic exercise program significantly improved sleep quality of older patients undergoing hemodialysis (51). Nasirzadeh et al. (2022) reported that in patients undergoing hemodialysis, aerobic exercise led to significant reductions in ankle-brachial index, improvements in dialysis adequacy, and enhancements in both QOL and sleep quality (52). Corrêa et al. (2021) reported that a three-month resistance training program improved the clinical profile of hemodialysis patients by enhancing sleep quality and reducing oxidative stress and inflammatory markers (53). These results are in agreement with the findings of the current study. Oxidative stress and inflammation are well established as being associated with reduced NO levels and elevated asymmetric dimethylarginine (ADMA) levels, potentially explaining the relationship between CKD and sleep disturbances (54). It has been reported that, in hemodialysis patients, elevated levels of pro-inflammatory oxidant factors and asymmetric ADMA concentrations are associated with poorer sleep quality. Conversely, evidence indicates that exercise training enhances NO bioavailability, reducing inflammation, oxidative stress, and ADMA levels, thereby improving sleep quality in this patient population. Redox balance, inflammation, and NO are thought to form a common mechanistic pathway linking ADMA, CKD, and sleep disorders. Reduced NO bioavailability is associated with impaired sleep quality in both humans and animals, reflecting its essential function in circadian rhythm regulation and modulation of neural centers governing sleep (55). In patients undergoing hemodialysis, exercise training has been shown to decrease body fat, improve glycemic control, and promote better sleep quality (56). The physiological mechanisms underlying sleep quality remain unclear and debated. Nevertheless, current evidence indicates that melatonin, secreted by the pineal gland, promotes hypnotic effects by modulating central body temperature, and its secretion is influenced by exercise and physical activity. Notably, melatonin secretion is influenced by multiple factors, including gender, age, and the type, duration, and intensity of exercise. Moreover, physical activity may beneficially modulate the diurnal rhythm and increase adenosine concentrations, thereby facilitating mechanisms that enhance sleep quality (57).

In the present study, no meaningful changes in pain levels were detected among the RT, AT, and CO groups. Potential contributing factors may include participants' psychological conditions and variations in duration and intensity of exercise. Pain is frequently reported as a primary barrier to participation in physical activity among individuals with CKD. Eghtedar et al. (2024) demonstrated that an eight-week walking program, consisting of 30-minute sessions three times per week, effectively reduced pain and muscle cramps in patients undergoing hemodialysis (58). According to Király et al. (2024), a 12-week combined aerobic and core stability training program significantly reduced pain intensity in patients undergoing hemodialysis (59). Exercise training has been shown to produce beneficial effects on cardiovascular, cardiorespiratory, and neuromuscular function across diverse patient populations (60). These adaptations may increase tolerance to dialysis sessions and improve both physical and mental functioning after dialysis, which in turn may encourage long-term adherence to physical activity. Notably, participation in exercise programs has been linked to enhanced pain perception and tolerance (61). Nevertheless, these results do not align with the findings of the present study. Analgesic regimens, dialysis prescription parameters (e.g., ultrafiltration rate, session length), and intra-session hemodynamic fluctuations may obscure subtle changes. Hemodialysis-related pain may arise from multiple mechanisms, including musculoskeletal (e.g., cramps, joint stiffness), neuropathic (e.g., uremic toxins, nerve entrapment), and vascular access–related or procedural sources. Given these considerations, the impact of our educational protocols on hemodialysis-related pain may have been diminished. In addition, we employed a unidimensional VAS, which does not capture pain quality, distribution, or temporal patterns.

Aerobic and resistance training activate distinct neuroendocrine mechanisms that contribute to exercise-induced hypoalgesia. Aerobic training robustly activates the hypothalamic–pituitary- adrenal (HPA) axis, eliciting acute increases in β-endorphin and enkephalin–endogenous opioids that bind to spinal and supraspinal receptors to attenuate nociceptive transmission (62, 63). Moreover, aerobic training enhances endocannabinoid signaling (64), thereby increasing the pain threshold and reducing pain perception. On the other hand, resistance training evokes a complex cascade of neuroendocrine responses that converge to produce significant hypoalgesia. In addition to classic stress hormones, resistance training enhances endocannabinoid signaling. Plasma concentrations of anandamide and 2-arachidonoylglycerol increase after a set of multi-joint strength exercise training, engaging CB_1 receptors in pain pathways and potentiating opioid-mediated analgesia. This "runner's high" phenomenon emerges after resistance training, suggesting an integrated endocannabinoid-opioid synergy in exercise-induced analgesia (65). Neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), increase in response to mechanical overload. Elevated peripheral BDNF can cross the blood–brain barrier, promoting plasticity within descending pain-inhibitory pathways. By enhancing synaptic strength in the periaqueductal gray and rostral ventromedial medulla, resistance training–induced BDNF promotes more efficient endogenous pain modulation, a mechanism that may contribute to alleviation of chronic pain syndromes during structured strength-training programs (66, 67).

Despite the valuable insights provided by the present study, several limitations should be considered in future research. These include variability in participants' psychological states, motivation, nutritional habits, sleep patterns, daily activity levels, and circadian rhythms. Additionally, CKD-related fatigue may have diminished participants' motivation and adherence to the training programs. Follow-up studies with longitudinal designs are warranted to evaluate the persistence of the benefits observed here.

Conclusion

The findings of the present study indicate that both resistance and aerobic training improve muscular endurance, increase muscle strength, enhance static balance and overall physical performance, improve sleep quality, and reduce fatigue. Given their demonstrated effectiveness, affordability, safety, and ease of implementation of resistance and aerobic training, these modalities should be integrated into the routine care of hemodialysis patients in dialysis centers to promote overall health and well-being.

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Competing Interests

The authors declare no conflict of interest.

Data Availability Statement

All necessary data will be available from the corresponding author upon reasonable request.

Ethical Approval

All ethical principles were strictly observed in this study. Informed consent was obtained from all participants, personal data confidentiality was maintained, and participants had the right to withdraw at any time. Furthermore, the study was approved by the Research Ethics Committee of Birjand University (Ethical code: IR.BIRJAND.REC.1402.011) and registered in the Iranian Registry of Clinical Trials (IRCT20240806062675N1).

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