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# Comparison of the effect of aerobic and resistance training on fatigue, quality of life and biochemical factors in hemodialysis patients

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**Although hemodialysis has been able to increase the lifespan of dialysis patients, it has also brought many problems such as fatigue, low QOL, hypertension and physical weakness to them. Therefore, the aim of this study was to compare the effect of aerobic and resistance training on fatigue, quality of life (QOL), blood $Na^+$, hemoglobin, C-reactive protein (CRP) and urea-creatinine ratio in hemodialysis patients. This research was conducted on 51 patients in two dialysis centers in Kerman, Iran. Patients were randomly divided into resistance group (RG) (n = 17), aerobic group (AG) (n = 17) and control group (CG) (n = 17). The patients in RG and AG performed the training protocol for eight weeks. Research variables as fatigue, QOL, blood $Na^+$, hemoglobin, CRP, and urea-creatinine ratio were measured in pre-test and post-test. Data analysis was done using one-way ANOVA and Tukey's post hoc tests in SPSS25. ($p < 0.05$). The mean level of fatigue in RG and AG was significantly lower than the CG ($p = 0.001$). The mean levels of blood $Na^+$ in AG was significantly higher than RG and CG ($p = 0.01$). Also, the mean ratio of urea-creatinine in RG and AG were significantly lower than CG ($p = 0.001$). There was no significant difference in QOL, hemoglobin and CRP between the RG and AG compared to the CG ($p > 0.05$). Based on our evidence, resistance and aerobic training for 8 weeks, 3 times weekly, is likely to improve the conditions of hemodialysis patients, and might be an option to increase intradialytic exercise adherence. Future studies should determine whether the findings are generalizable and examine the long-term effects of intradialytic exercise training.**

**Keywords** Exercise training, QOL, CKD, Hemodialysis

Chronic kidney disease (CKD) is caused by progressive and irreversible destruction of nephrons, in which the body's ability is lost to maintain metabolism and balance of water and electrolytes. For treatment of CKD, renal replacement therapies including peritoneal dialysis, kidney transplant and hemodialysis are common, but hemodialysis is the most common treatment method in all countries[1]. Although hemodialysis has been able to increase lifespan in these patients, but it is associated with many physical and psychological problems[2].

Fatigue and lack of energy is one of the most common and painful symptoms in hemodialysis patients[3]. Fatigue leads to income loss and a reduced ability to afford healthcare[4], and increase mortality in these patients[5]. Despite advances in treatment of these patients, fatigue and restriction of liquids and food are still at the top of the health problems of theme[6]. Physiological factors include anemia, age and body size, malnutrition, uremia, high blood cholesterol level and other factors such as depression, behavioral factors, treatment and personal characteristics are the causes of fatigue in these patients[7]. In acute kidney failure, fatigue occurs suddenly, however in CKD, fatigue occurs slowly, quietly, and with sleepiness, which is very important for care[8].

There is a lot of evidence about significant reduction in quality of life (QOL) in patients with chronic diseases[9]. Hemodialysis complications also cause many changes in the QOL of hemodialysis patients. These complications include reduced ability to perform activities, fatigue, weakness, and multiple muscle contractions, which ultimately lead to hopelessness in the future, immobility, decreased self-confidence, and social isolation of these patients[10]. The results of various studies show that hemodialysis patients do not have a good QOL[11,12].

On the other hand, some biochemical factors in hemodialysis patients undergo changes that can lead to problems in these patients. CKD is usually associated with anemia. Low erythropoietin level is playing an important role; it is the main cause of normochromic anemia in CKD patients[13]. In addition, in CKD, chronic inflammation plays an important role in disease process. It seems that high levels of C-reactive protein (CRP)

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-a marker of inflammation and atherosclerosis- is associated with decreased kidney function[14]. In hemodialysis patients, early detection of peritonitis can be done by measuring CRP levels. Because the increase in CRP levels is dependent on the severity of the infection[15]. Another important biochemical factor in hemodialysis patients is the blood $Na^{+}$[16]. High concentration of the $Na^{+}$ during hemodialysis may lead to high blood pressure. Hemodialysis removes a hyponatremic ultrafilter from plasma water, and causes incomplete depletion of the $Na^{+}$ reservoir. The failure to achieve a neutral $Na^{+}$ balance during hemodialysis may lead to $Na^{+}$ accumulation throughout the body, excessive thirst, weight gain, and hypertension[17].

Some evidence suggests that physical activity and exercise training, may both offer benefits for hemodialysis patients and therefore prove cost-effective[18]. The benefits of exercise training for hemodialysis patients include cognitive benefits, improvement in QOL, reducing fatigue, reducing uremic nephropathy, reducing myopathy, improving cardiac function, increasing physical work capacity, increasing muscle blood flow, reducing blood pressure, reducing urea levels and reducing muscle cramp. Exercise training can help these patients to obtain physical fitness and thus become more active, which may help to improve their QOL[19,20]. Exercise training during hemodialysis by increasing muscle blood flow and increasing the surface of open capillaries can increase the removal of urea and other excess substances from the tissues into the vascular system and then eliminated through the hemodialysis[21]. Regular exercise training (aerobic and resistance training) can help hemodialysis patients to improve their physical performance[22]. In this regard, Salehi et al. (2020) showed that rehabilitation through exercise training on small bicycles has a significant effect in preventing fatigue of hemodialysis patients[23]. In another study, Hargrove et al. (2021) found that aerobic exercise improves several symptoms associated with hemodialysis, such as restless legs syndrome, depressive symptoms, muscle cramps, and fatigue[24]. The results of the study by Bastani et al. (2020) also showed that exercise training is a suitable and effective option for improving pain, fatigue and physical performance of elderly hemodialysis patients[25].

It has been reported that the anti-inflammatory effect of regular physical activity and exercise training may be mediated by a reducing visceral fat mass, decrease in the release of adipokines and/or by the induction of an anti-inflammatory environment[26]. Regular physical exercise also decreases resting heart rate, blood pressure, and atherogenic markers, and also improves myocardial perfusion and increases high-density lipoprotein (HDL) cholesterol levels. All of these factors and adaptations reduce stress on the heart and lead to improved cardiovascular function in healthy and diseased individuals[27].

Altogether, contrary to many scientific evidences that indicate the low level of physical activity and performance indicators in hemodialysis patients and despite many reports that show the benefits of regular exercise training in improving physical performance and QOL for these patients, however, the recommendation to do exercise training by the treatment staff is not a necessary process in hemodialysis units[25]. CDK and the frequency of hemodialysis sessions reduce and limit physical activity in hemodialysis patients[28]. Deteriorating health status, fatigue, and hemodialysis treatment make it difficult for patients to exercise and perform physical activity. The key and very important point in this regard is to encourage these patients to engage in exercise therapy and lifestyle modification by increasing the attractiveness of exercise, monitoring physical activity, and highlighting the benefits of regular exercise[29]. Regular exercise also releases feel-good hormones, which may reduce symptoms of depression and anxiety[30]. Considering that hemodialysis patients suffer from many complications and problems that affect the life of these people; therefore, it is necessary to take actions to reduce the problems of these patients in order to improve their lives. CDK is a major health problem worldwide. In addition to this disease, patients also have comorbidities that increase their mortality rate. Exercise training is an excellent tool that has beneficial effects on kidney patients. The main feature of this study is that over eight weeks, two exercise training programs were performed during hemodialysis on some fatigue, biochemical indicators and QOL of patients. Also, few studies have compared aerobic and resistance training during the first 2 h of dialysis. Most researchers have not yet concluded which type of exercise (aerobic or resistance) is best for hemodialysis patients. We hypothesized that performing exercise during hemodialysis sessions would be highly effective in improving physical condition, QOL, and biochemical indicators of hemodialysis patients. Hence, the aim of this study was to compare the effects of aerobic and resistance training on fatigue, QOL, blood Na +, Hemoglobin, CRP and Urea to creatinine ratio in hemodialysis patients.

## Results

Demographic data and baseline characteristics of patients were collected, including age, gender, body mass index (BMI), blood pressure, diabetes, medication use, underlying diseases, and duration of hemodialysis. This information is presented in the table of individual and demographic characteristics of patients. Initial statistical tests (Chi-square and ANOVA) showed that the groups were homogeneous in terms of baseline characteristics and no significant differences were observed between them. The normality of the data distribution was examined using the Shapiro–Wilk test. Based on the results, all variables had a normal distribution ($p > 0.05$). Also, homogeneity of variances was examined using the Leven test. Based on the results, the assumption of homogeneity of variances is valid for all variables ($p > 0.05$).

The mean and standard deviation of the individual characteristics of the subjects are shown in Table 1.

The demographic and background information of the patients are shown in Table 2.

According to Table 2, the groups were homogeneous at the beginning of the study and there was no difference between the groups.

In our study, the effects of resistance and aerobic training on fatigue levels, QOL, and certain biochemical factors in hemodialysis patients were examined. Statistical analysis of the results indicated significant changes in some of the investigated variables following the eight-week intervention. In this study, all 51 patients remained in the study until the end of the intervention period and no sample dropout was reported. Therefore, all statistical analyses were performed on 51 participants and there was no missing data. The results presented in the tables

| Variable | Group | Mean | Std | F | P value | Partial eta squared |
|---|---|---|---|---|---|---|
| Weight (kg) | Resistance training | 69.7 | 10.96 | 0.615 | 0.545 | 0.025 |
| | Aerobic training | 73.82 | 4.01 | | | |
| | Control | 69.76 | 12.04 | | | |
| Height (meter) | Resistance training | 1.69 | 0.05 | 1.614 | 0.210 | 0.63 |
| | Aerobic training | 1.7 | 0.08 | | | |
| | Control | 1.73 | 0.04 | | | |
| BMI ($Kg/m^2$) | Resistance training | 24.45 | 3.26 | 0.964 | 0.389 | 0.039 |
| | Aerobic training | 24.68 | 1.96 | | | |
| | Control | 23.34 | 3.66 | | | |

**Table 1**. Individual characteristics of subjects.

| Group | Resistance training | | Aerobic training | | Control | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | Frequency | Percentage | Frequency | Percentage | Frequency | Percentage | Chi-square test | P value | Effect size (Phi) |
| Gender | | | | | | | | | |
| Male | 11 | 64.7 | 12 | 70.6 | 13 | 76.5 | 0.56 | 0.75 | 0.10 |
| Female | 6 | 35.3 | 5 | 29.4 | 4 | 23.5 | | | |
| High blood pressure | | | | | | | | | |
| Yes | 12 | 70.6 | 8 | 47.1 | 6 | 35.3 | 4.39 | 0.11 | 0.29 |
| No | 5 | 29.4 | 9 | 52.9 | 11 | 64.7 | | | |
| Diabetes | | | | | | | | | |
| Yes | 4 | 23.5 | 6 | 35.3 | 6 | 35.3 | 0.72 | 0.69 | 0.12 |
| No | 13 | 76.5 | 11 | 64.7 | 11 | 64.7 | | | |
| Drug consumption | | | | | | | | | |
| Yes | 1 | 5.9 | 0 | 0 | 0 | 0 | 2.04 | 0.36 | 0.2 |
| No | 16 | 94.1 | 17 | 100 | 17 | 100 | | | |
| Congenital diseases | | | | | | | | | |
| Yes | 1 | 5.9 | 0 | 0 | 1 | 5.9 | 1.04 | 0.59 | 0.143 |
| No | 16 | 94.1 | 17 | 100 | 16 | 94.1 | | | |
| Urological disease | | | | | | | | | |
| Yes | 1 | 5.9 | 0 | 0 | 1 | 5.9 | 0 | 1 | 0.00 |
| No | 16 | 94.1 | 17 | 100 | 16 | 94.1 | | | |
| Protein excretion | | | | | | | | | |
| Yes | 0 | 0 | 2 | 11.8 | 3 | 17.6 | 3.1 | 0.21 | 0.274 |
| No | 14 | 100 | 15 | 88.2 | 14 | 82.4 | | | |

**Table 2**. Demographic and background information of patients in intervention and control groups.

and statistical analyses show the mean and standard deviation of the main variables for each group. The mean and standard deviation of the subjects' biochemical indices are shown in Table 3.

According to Table 3, the blood $Na^+$ level after the intervention in the aerobic training group was significantly higher than the resistance training and the control groups ($p = 0.01$). This finding suggests that aerobic exercise may play a role in regulating $Na^+$ balance and improving fluid homeostasis in hemodialysis patients. These results align with previous findings by Penne et al. (2011), which emphasized the role of exercise in electrolyte regulation[16].

No significant differences in hemoglobin or CRP levels were observed between the intervention and control groups ($p > 0.05$). This result contrasts with studies such as da Silva et al. (2021), which reported increased hemoglobin levels following six months of resistance training[31]. A possible explanation for this discrepancy is the shorter intervention duration in the present study.

A significant reduction in the urea-creatinine ratio was observed in both the resistance and aerobic training groups compared to the control group ($p = 0.001$) (Table 3). This suggests that exercise training may enhance kidney function by improving waste removal efficiency. These findings align with previous research by Lin et al. (2011), which reported reductions in blood urea levels following regular physical activity[32].

The mean and standard deviation of the QOL index in research groups are shown in Table 4.

According to Table 4, the mean QOL after the intervention in resistance and aerobic training groups was higher than in control group, but this difference was not statistically significant ($p = 0.87$). This finding contrasts with previous studies, such as Lin et al. (2021), which reported improvements in QOL[33]. The lack of

| Group Variable | | Resistance training | | Aerobic training | | Control | | F | P value | Partial eta squared |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std | Mean | Std | Mean | Std | | | |
| **$Na^+$ (meq/l)** | **Pre test** | **137.17** | **4.47** | **138.23** | **3.73** | **137.94** | **3.92** | **0.48** | **0.7** | **0.12** |
| | Post test | 133.29 | 4.41 | 138.05 | 6.06 | 137.41 | 3.77 | 4.82 | 0.01* | 0.16 |
| Hemoglobin (g/dl) | Pre test | 16.47 | 5.61 | 10.74 | 1.28 | 1.42 | 1.97 | 0.92 | 0.4 | 0.37 |
| | Post test | 11.95 | 1.23 | 11.87 | 1.72 | 11 | 1.94 | 1.69 | 0.19 | 0.66 |
| CRP mg/l | Pre test | 1 | 0.61 | 1.12 | 0.35 | 1.37 | 0.51 | 1.03 | 0.37 | 0.10 |
| | Post test | 1.43 | 0.82 | 1.9 | 0.87 | 1.63 | 0.67 | 0.78 | 0.46 | 0.05 |
| Urea to creatinine ratio (meq/L) | Pre test | 10.53 | 3.35 | 9.92 | 2.1 | 11.06 | 3.59 | 0.58 | 0.56 | 0.09 |
| | Post test | 5.53 | 1.95 | 5.09 | 1.95 | 9.04 | 4.51 | 8.33 | 0.001* | 0.56 |

**Table 3**. Mean and standard deviation of biochemical indices. * Significant difference between the groups after the intervention.

| Group variable | | Resistance training | | Aerobic training | | Control | | F | P value | Partial eta squared |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std | Mean | Std | Mean | Std | | | |
| **QOL** | **Pre test** | **88.05** | **4.95** | **88.35** | **3.87** | **87** | **3.88** | **0.47** | **0.62** | **0.009** |
| | Post test | 88.35 | 3.99 | 88.82 | 3.82 | 88.11 | 4.25 | 0.13 | 0.87 | 0.004 |

**Table 4**. Mean and standard deviation of QOL.

| Group Variable | | Resistance training | | Aerobic training | | Control | | F | P value | Partial eta squared |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std | Mean | Std | Mean | Std | | | |
| **Fatigue index** | **Pre test** | **37.29** | **9.96** | **38.94** | **10.67** | **39.58** | **11.51** | **0.2** | **0.81** | **0.009** |
| | Post test | 27.17 | 6.93 | 29 | 8.81 | 39.76 | 11.27 | 9.33 | 0.001* | 0.280 |

**Table 5**. Mean and standard deviation of fatigue index. * Significant difference between the groups after the intervention.

significant change in this study may be attributed to the short intervention duration, low baseline QOL levels, and psychological variations among participants.

The mean and standard deviation of the fatigue index in the research groups are shown in Table 5.

According to Table 5, the mean fatigue index after the intervention in resistance and aerobic training groups was significantly lower than the control group ($p = 0.001$). These findings suggest that exercise training can be an effective non-pharmacological strategy for reducing fatigue in hemodialysis patients. This is consistent with previous studies by Bastani et al. (2020) and Salehi et al. (2020), which highlighted the positive impact of exercise on muscle blood flow and energy levels and fatigue in this patient population[23,25].

## Discussion

The present study was conducted with the aim of comparing the effect of aerobic and resistance training on fatigue index, QOL and some biochemical factors in hemodialysis patients. The present study showed that there is a significant decrease in the level of fatigue index of the resistance and aerobic training groups compared to the control group. In line with the current study, Bastani et al. (2017) showed that the selected core stability exercises were an effective and suitable option for elderly hemodialysis in reducing the pain, fatigue and improving physical function. Therefore, this type of exercise training can be used as a non-pharmacological strategy by therapists and care staff[25]. Afaqi et al. (2024) found that the otago exercise program in home for eight weeks prevented the increase in fatigue index of hemodialysis patients[34]. Grigoriou et al. (2021) showed that a combined exercise training program (aerobic + resistance training) for nine months in hemodialysis patients improved post dialysis fatigue symptoms and overall fatigue perception[35]. Therefore, combined exercise training is a safe and effective non-pharmacological approach to improve fatigue symptoms in hemodialysis patients. Salehi et al. (2020) showed that rehabilitation through exercise using small bicycles has a significant effect in preventing more fatigue in hemodialysis patients[23]. Astri Zeini Wahida et al. (2023) in a systematic literature review and meta-analysis showed that the characteristics of intradialytic exercise programs that are considered effective in ameliorating fatigue are aerobic exercise lasting > 20 min and performed in the first 2 h of hemodialysis, with a frequency of < 12 sessions[36]. Ying Li et al. (2024) in a network meta-analysis investigated the influence of different exercise methods (resistance training, baduanjin exercise, bicycle exercise and combined movement) on sarcopenia patients receiving maintenance hemodialysis. They showed that resistance training has a positive effect on improving handgrip strength in these patients. Combined movement also showed good results in enhancing skeletal muscle mass index in these individuals. They also stated that more randomized controlled trials are required to better understand the effectiveness of these exercise training programs and the potential underlying mechanisms[37].

Researchers believe that exercise training dilates muscle arteries, improves perfusion, and reduces diseases that affect blood circulation in muscles[38]. Therefore, exercise training reduces fatigue index by improving perfusion, increasing blood circulation, better elimination of excess substances and increasing muscle strength[23]. Also exercise training helps the body to oxygen delivery to the muscles more efficiently, improves overall circulation, lowers blood pressure, and inhibits lactic acid production. These mechanisms ultimately lead to improve the fatigue index[39].

The present study showed that there was no significant difference in QOL between resistance and aerobic training groups compared to the control group. In line with the current study, Greenwood et al. (2021) showed that six months of intradialysis aerobic training does not improve the QOL in hemodialysis patients[40]. Also, Ortega-Pérez de Villar et al. (2021) showed that the implementation of a 16-weeks exercise program during dialysis and at home has no effect on the QOL of hemodialysis patients[41]. On the other hand, Nasirzadeh et al. (1401)[42], Hosseinpour Setobadi et al. (1402)[43] and Lin et al. (2021)[33] showed that exercise training during hemodialysis has a significant effect on improving the QOL of hemodialysis patients. Anyway, these findings are not in line with the current study. One of the reasons for this disparity can be pointed to the difference in the duration and intensity of the exercise training used in the present study compared to other studies. Also, the fatigue and malaise from exercise, mental and psychological conditions of the subjects have a significant impact in this regard. The lack of statistical improvement in QOL can be explained in part by the participants having poor compliance and very poor adherence to the exercise intervention. Nevertheless, perhaps including such patients prevented benefits of the exercise training being realized in the relatively short 8-weeks intervention, and it is possible that some of these patients may require a slower rate of overload progression and adaptation/adjustment periods to an intradialytic exercise training program. Future research should explore the effects of long-time exercise programs combined with psychological support.

The improvement in the QOL caused by exercise training may be explained because the implementation of exercise training can be reduce the symptoms of fatigue, sleep disorders and shortness of breath associated with kidney disease and increase the self-management ability of patients in life. Also, the practical benefit of exercise training for hemodialysis patients are to reduce the risk factors such as intra-dialysis blood pressure drop, improve the inflammatory condition and reduce the risk of cardiovascular diseases[44]. For hemodialysis patients, the implementation of moderate-intensity aerobic exercises can effectively improve the physical role, general health, and pain management, increase their social interactions and enhance their self-attitude[45]; alleviate their disease-related conditions and complications; and improve their physical functioning and prognosis[46]. Regular physical activity can improve the physical performance, muscle tension and strength, physical and mental component score of hemodialysis patients[47]. Exercise can also stabilize their cognitive function, reduce their risk of developing health conditions, and improve QOL in hemodialysis patients[48].

The results of the present study showed that after eight weeks of the training program, a significant decrease in blood $Na^+$ was observed in the resistance training group compared to the aerobic training and control groups. $Na^+$ balance depends primarily on dietary salt intake and $Na^+$ removal during hemodialysis[49]. High $Na^+$ concentration during hemodialysis may lead to positive $Na^+$ balance and caused fluid overload and increased blood pressure. Generally, the serum $Na^+$ increases after hemodialysis by 2 to 4 milliequivalents compare to pre-hemodialysis values. This process increases plasma $Na^+$ activity and may lead to accumulation of total body $Na^+$, excessive thirst, weight gain, and intensification of blood pressure in susceptible individuals[17]. Exercise training is considered as a non-pharmacological strategy to control blood pressure by regulating $Na^+$ retention and water homeostasis[50]. This feature can be explained by neurohormonal mechanisms relative to structural changes (such as vascular remodeling or angiogenesis) which is largely stimulated by exercise training[51]. Another explanation in this regard may lie in the characteristic of resistance training, that using more muscle mass during the training session leads to an increase in heart rate and blood pressure and subsequent adaptation to training. This adaptations may be associated with reduced stimulation of muscle metaboreceptors and mechanoreceptors and a net reduction in muscle sympathetic nerve activity[52].

In the present study, there was no significant difference in blood hemoglobin values in resistance and aerobic training groups compared to the control group. There is a possibility that the duration and intensity of the exercise training program in the present study were not enough to change the hemoglobin level of the patients. On the other hand, da Silva et al. (2021) stated that six months of resistance training in hemodialysis patients improved clinical parameters such as hemoglobin, iron, body composition and redox balance[31]. Also, De Mora et al. (2010) showed that the serum level of hemoglobin in hemodyalisise paeitents increased significantly after 12 weeks of training[53]. André Bonadias Gadelha et al., (2021) investigated the effects of pre-dialysis resistance training on sarcopenia, inflammatory profile, and anemia biomarkers in older patients with CKD. They showed that the 24-week resistance training program elicited a better sarcopenia status, better inflammatory profile, and improved anemia biomarkers (subjects submitted to pre-dialysis resistance training positively increased iron status, while reducing ferritin, hepcidin,

TNFα, and IL-6.)[54]. Liu, Haiying et al. (2023) investigated the effect of exercise on cardiopulmonary function and the life quality of maintenance hemodialysis patients. Their results showed that, following intervention the experimental group had better force vital capacity and peak expiratory flow, anaerobic threshold, 6-min walk test, physical functioning, social functioning, general health, and vitality scores, depression score compared to the control group. Also, after the intervention, hemoglobin improved significantly in the experimental group. So, 24 weeks intradialytic exercise training can improve hemoglobin, albumin, pulmonary function, aerobic capacity, and exercise endurance in maintenance hemodialysis patients[55]. These results are not consistent with the present study. The reasons for this inconsistency is the existence of differences in the type, duration and intensity of training programs.

In addition, no significant difference was observed in blood CRP level of resistance and aerobic training groups compared to the control group. This finding was consistent with the research of Ammar et al. (2020)[56]. Also, in line with the current study, Ghoraba et al. (2022) showed that aerobic exercise training has no effect on inflammatory factors such as CRP[57]. On the other hand, Melendez-Oliva et al. (2022) showed that four months of combined strength and endurance training improved the inflammatory status of hemodialysis patients in those who performed intra-dialysis exercises (decrease in IL-6) and in those who performed exercises at home (decrease in CRP)[58]. It has also been shown that higher levels of physical activity and fitness are associated with lower levels of CRP in hemodialysis patients[59]. In addition, Sovatzidis et al. (2020) showed that participating in cardiovascular exercises during dialysis, changes the redox status, decreases in CRP, and improves performance in patients with end-stage renal disease[60]. Also, Shaukti Basir and Mirzaei (2022) showed that combined aerobic and resistance exercise training can be considered as a strong stimulus to make adaptation in aerobic capacity, reduce the risk factors of cardiovascular diseases and decrease in CRP levels in patients with CKD[61]. However, these findings are not consistent with the present study. Probably, the duration and intensity of the exercise training program in the present study were not enough to affect the CRP level. For CRP, it was demonstrated that several types of exercise training did not stimulate CRP level in hemodialysis patients. Moraes et al. discovered reductions in CRP after resistance exercise, while Dong et al. found the same results after high-intensity resistance exercise[62,63]. When resistance exercise was carried out with high intensity, the effects on CRP were more apparent. It is also discovered a reduced CRP in medium-intensity aerobic exercise program. However, it has been found that no difference between aerobic exercise and usual care/sham exercise[64]. This inconsistency indicated that there is probably an association between CRP reduction and exercise intensity. A published study consistently reported this view, they supposed better results of CRP in patients who perform aerobic exercise with medium-intensity training or resistance exercise with high-intensity procedures. Therefore, adjusting training intensity is key factor in reducing CRP in hemodialysis patients[65].

Among other findings of the current study, it can be mentioned that a significant decrease in the urea-creatinine ratio was observed in resistance and aerobic training groups compared to the control group. Bijeh and Farahti (2013) showed that the ratio of urea-nitrogen to creatinine decreased after a period of aerobic exercise, but it was not significant[66], which is not consistent with the present study. On the other hand, in line with the current study, Lin et al. (2011) showed that regular physical activity leads to decrease in the level of urea nitrogen and serum creatinine and improves kidney disorders[32]. Also, Sylow et al. (2016) showed that a period of resistance training during dialysis lead to a significant decrease in blood urea nitrogen[67]. In addition, it has been shown that regular aerobic exercise has a significant effect on glomerular filtration rate, serum creatinine, 24-h urine protein and blood urea nitrogen in kidney patients[68]. Also, Nataraj et al. (2023) reported in a systematic review and meta-analysis that regular aerobic exercise training reduce urinary albumin-to-creatinine ratio, urinary protein-to-creatinine ratio, serum urea nitrogen, creatinine clearance, and urinary protein excretion[69].

The present study had some limitations such as the mental and psychological conditions, motivation to participate in exercises, nutrition, sleep, daily activity and circadian rhythm of the patients, that are suggested to be considered in future studies. Also, during this study, the fatigue and lack of patience of the patients due to the nature of the disease, was a limitation for the researchers and led to the less desire of the patients to participate in exercise training. In addition, the present study used a convenience sampling method and small sample, which may cause selection bias. Therefore, caution should be exercised in interpreting and generalizing the results of this study. However, the small sample may limit the ability of the study to detect small differences. In future studies, it is recommended to increase the number of participants to provide higher statistical power and allow for better generalizability of the results.

Anyway, there was more specific limitations (e.g. medication use and dietary habits) in oure study. In this study, erythropoietin was injected after the dialysis session to prevent anemia in patients (depending on the patients' hemoglobin level, every session or just once a week). You should also limit your fluid intake when you are on hemodialysis. Apart from water, some fruits and vegetables also contain a lot of water. These include melons, grapes, apples, oranges, etc. Fluids can accumulate between dialysis sessions, causing swelling and weight gain. Nutrition is an important factor in treatment of patients with chronic kidney disease, and an inadequate diet can reduce the QOL and increase complications, morbidity, and mortality in these patients. In the present study, dietary recommendations (foods high in sodium, potassium, and phosphorus) for patients were made by dialysis center nurses.

## Conclusion

Based on our evidence, resistance and aerobic training for eight weeks, three times weekly, is likely to improve the conditions of hemodialysis patients (by affecting the level of fatigue, blood $Na^+$, and the ratio of urea-creatinine), and might be a suitable option to increase intradialytic exercise adherence. However, in the present study, no significant difference was observed in the QOL, CRP and hemoglobin levels of the patients. Considering the effectiveness of resistance and aerobic exercise training, as well as the low cost and high safety, it is suggested that these types of exercise training can be used in dialysis centers to improve the conditions of hemodialysis patients. Future studies should determine whether the findings are generalizable and examine the long-term effects of intradialytic exercise training in larger populations.

# Methods
## Study design
This research is a semi-experimental study (pre-test and post-test design), which was conducted on 51 hemodialysis patients in Shafa Hospital and Javad Al-Aeme Clinic in Kerman. This study was a parallel single-blind randomized control trial (Clinical registration No: IRCT20240806062675N1-19–10-2024) and was conducted under the supervision of university of Birjand's ethics committee (No: IR.BIRJAND.REC.1402.011). The aim of our study was to compare the effects of aerobic and resistance training on fatigue, QOL, $Na^+$, CRP, hemoglobin and urea-creatinine ratio in hemodialysis patients. All procedures were performed in accordance with the guidelines and regulations for human studies (Declaration of Helsinki). Only participants with complete data at baseline and 8-week follow-up were included in the final analysis.

For single-blinding, all patients were blinded to their group assignment, which was accomplished by not disclosing there was more than one group in this study. Specifically, participants were told that the main focus of the study was to determine the benefits of exercise during hemodialysis. The study participants received their assigned tasks and detailed information about their specific regimen after they were grouped, with the information tailored to their respective groups. However, the exact nature of the intervention was only revealed to the participants after the study concluded. In addition, to further maintain the integrity of the blinding process, all individuals providing patient care were also kept unaware of group assignments.

## Study population
Hemodialysis patients (n = 278) who had the inclusion criteria were selected by convenience sampling method. To determine the sample size in research groups, the free trial version of Power Analysis & Sample Size 2021 (PASS2021) software was used (test power 0.80, alpha value 0.05, standard deviation 17, effect size 0.42). The total number of samples was 51 patients and 17 patients were equally placed in each group. Then subjects were randomly divided into two intervention groups (aerobic training (n = 17) and resistance training (n = 17)) and one control group (n = 17). Randomization was performed using Random Permutation Block software to maintain balance between groups.

Inclusion criteria include: age 30 to 55 years, having at least six months history of hemodialysis and at least three times per week, ability to move without assistance, physical ability to participate in training program (by using International Physical Activity Questionnaire)[70], no history of surgery in the last three months and blood pressure was stable during hemodialysis. Exclusion criteria include: history of ischemic disease, history of myocardial infarction and angina in the last six months, lung disease that requires artificial oxygen, history of stroke or transient ischemic attacks in the last three months, abnormalities in the musculoskeletal system of the legs, symptomatic cardiovascular disease in the last three months, of more than two sessions absence in training program and improper physical condition during training (changes in blood pressure, dyspnea, decreased level of consciousness and dizziness). We confirm that in this study, the objectives and methods of the study were explained to the patients. All patients also signed an informed consent form to participate in the study. Then, demographic information (age, gender, marital status, education level, number of children, place of residence, occupation), disease-related information (cause of kidney failure, underlying diseases, number of years of disease, duration of hemodialysis, number of hemodialysis sessions per week and drug regimen) were recorded in a special form. Before the beginning of the exercise training program and in order to familiarize the subjects to the training program, the patients participated in a familiarization session separately. Also, the data related to the study variables ($Na^+$, CRP, hemoglobin, urea-creatinine ratio, QOL and fatigue index) as well as height, weight and BMI were measured and recorded in the pre-test stage.

## Individual characteristics and research variables measuring
The weight of the patients without shoes and with minimal clothing was measured in kilograms using a Seka scale (manufactured by Seka, Germany, sensitivity of 100 g). Their height was also measured without shoes and in centimeters with an accuracy of 0.5 cm. The BMI was measured as the body mass divided by the square of the body height, and was expressed in units of kg/m2, resulting from mass in kilograms (kg) and height in meter (m).

At pretest, $Na^+$ measurement was done through blood sampling. In order to evaluate the amount of CRP, the Anisan kit was used qualitatively and on the slide. Hemoglobin level was measured by cell counter. The urea-creatinine ratio was measured using an autoanalyzer. These Measurements was performed at three times: 7:00 AM, 13:00 PM, and 19:00 PM (before hemodialysis). Also, hemodialysis sessions were performed at three times: 7:00 AM—11:30 AM, 13:00 PM—16:30 PM, and 19:00 PM—23:30 PM.

Kidney disease quality of life questionnaire- short form (KDQOL-SF) was used to evaluate the QOL of patients. This questionnaire which measures the quality of general life (36 items) and specific life (43 items) of patients. Scoring in this questionnaire is done by using a three-point scale (with scores 0, 50, 100), a five-point scale (with scores 0, 25, 50, 75, 100) and a six-point scale (with scores 0, 20, 40, 60, 80 and 100). The maximum and minimum effect was determined by calculating the percentage of people who had a score of 100 and zero, respectively. This index should be less than 20% to include all criteria and show changes over time. A high score indicates a better QOL. The validity and reliability of the Persian version of this questionnaire was confirmed by Montazeri et al. (2014) and Cronbach's alpha was reported as 0.65[71].

Fatigue Severity Scale (FSS) was used to measure patients' fatigue index. The level of fatigue was obtained from the total points obtained by the patient in answering the nine questions of this scale, which were graded according to 7-point Likert scale (1 = absence of fatigue, 2–4 = moderate fatigue, and above 4 = extreme fatigue). This index is one of the best-known scales of fatigue, which is useful for the effect of therapeutic interventions on the severity of patients' fatigue. The reliability of this index has been confirmed with Cronbach's alpha coefficient of 0.83[72]. Its content and face validity have also been confirmed[73].

| Exercises | Weight (kg) | Number of weeks | Number of sets | Number of repetitions | Rest between sets (minutes) |
|---|---|---|---|---|---|
| Leg abduction | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |
| Thigh flexion with straight leg for one leg | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |
| Thigh flexion with straight leg for both legs | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |
| Thigh flexion with the knee bent at 90 degrees with one leg | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |
| Thigh flexion with the knee bent at 90 degrees with both legs | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |
| Knee extension with one leg | 0.5, 1, 1.5, 2 | 8 | 3 | 8 | 2 |

**Table 6**. Resistance training protocol.

| Week<br>Variable | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 | Week 7 | Week 8 |
|---|---|---|---|---|---|---|---|---|
| Exercise duration (minutes) | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Exercise intensity (% of heart rate reserve) | 60–70 | 60–70 | 60–70 | 60–70 | 60–70 | 60–70 | 60–70 | 60–70 |

**Table 7**. Aerobic training protocol.

### Resistance training protocol

The patients in resistance training group performed eight weeks of resistance training during hemodialysis and under the supervision of a doctor and exercise physiologist. The training program was three days a week and about 50 min per day. Resistance exercises were designed for the lower body by using sand weights (0.5, 1, 1.5, and 2 kg) tied to the ankles. Subjects performed resistance training exercises while sitting or lying on the back on the hemodialysis chair[74]. Training session consisted of 10 min of warm-up, 30 min of resistance training exercises, and 10 min of cooling down (Table 6).

### Aerobic training protocol

During hemodialysis, the patients in aerobic training group performed three sessions of aerobic exercise (20 min) per week by using an electric bicycle (made in Switzerland) for eight weeks. Before starting the exercise training, active stretching movements in the lower and upper limbs were done for warming up (five minutes). Then, the patients performed aerobic exercise training on a Stationary Bike Keep Fit 6572- China[75]. This device was capable of monitoring heart rate during aerobic training. Exercise intensity (60–70% of reserve heart rate) was controlled by measuring maximum heart rate and based on Karvonen's formula[76]. The training session ended with five minutes cool-down using passive stretching of the lower and upper limbs (Table 7).

It should be noted that patients in the control group received the usual care of the hemodialysis center. Also, resistance and aerobic exercise training were performed in the first two hours of hemodialysis. In addition, the patients were told to stop the exercise training immediately if they feel dizzy, headache, heart palpitations, nausea, anxiety and worry, excessive fatigue and any other unpleasant feelings. Vital signs of patients were also monitored every 15 min. 48 h after the end of the training protocols, the data related to the study variables ($Na^+$, CRP, hemoglobin, urea-creatinine ratio, QOL and fatigue index) as well as the height, weight and BMI of the subjects in the post-test as in the pre-test were measured and recorded.

Statistical Package for the Social Sciences (SPSS) version 25 software was used to analyze the data. Descriptive statistics were used to describe the demographic characteristics of the patients and the information related to the disease and research variables. Chi-square test was used to check the homogeneity of the contextual variables in research groups. Shapiro–Wilk test was used to check the normality of data distribution. Also, homogeneity of variances was checked using Levene's test. Considering the establishment of parametric conditions, analysis of variance and Tukey's post hoc test were used to compare the mean of variables before and after the intervention. A significance level of less than 0.05 was considered.

## Data availability

All data can be made available upon request by contacting the corresponding author.

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## Author contributions
N. N. collected and compiled subject's data. S. I. developed the study idea and methodology. M. M-A. and A. S. wrote the whole paper as a team.

## Declarations

### Competing interests
The authors declare no competing interests.

### Additional information
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