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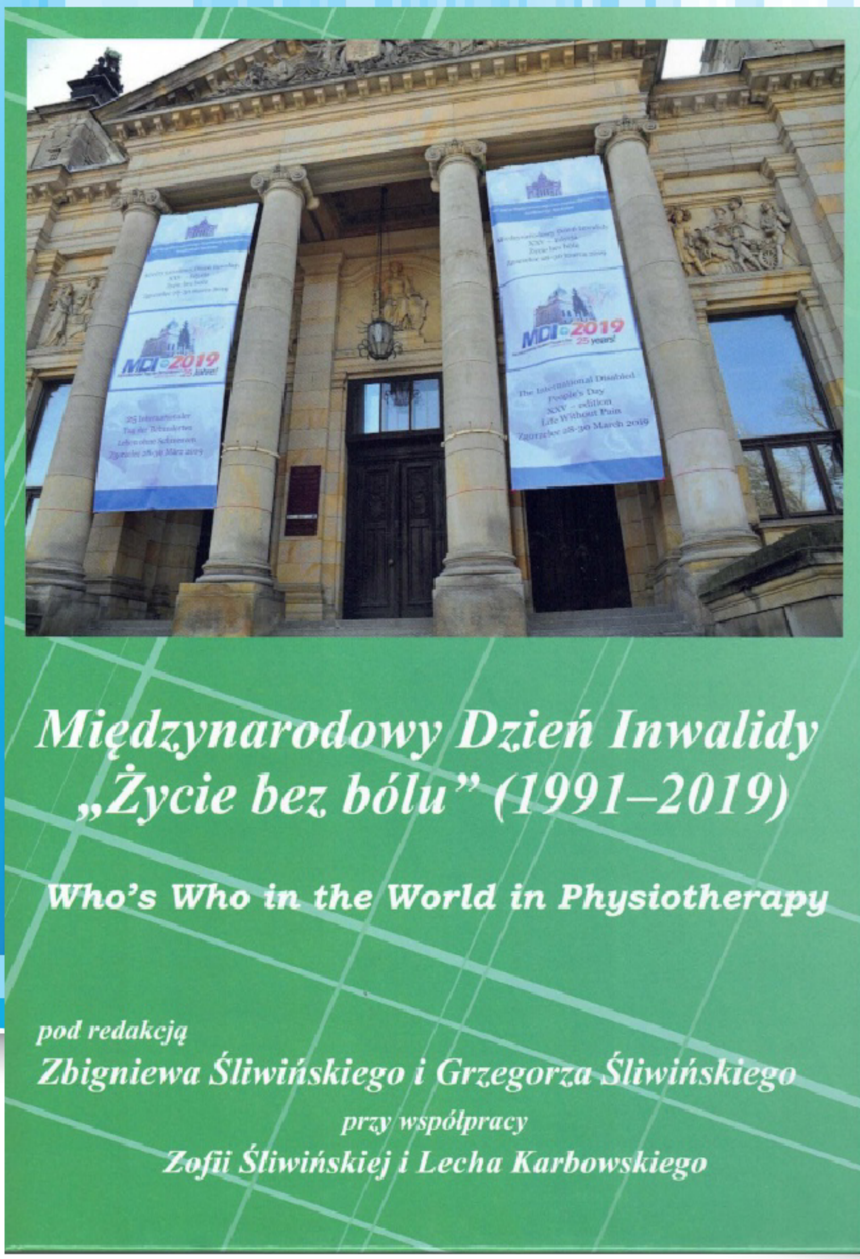

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Effect of aerobic versus resisted exercise on blood coagulation in chronic kidney disease patient

Wpływ ćwiczeń aerobowych lub ćwiczeń oporowych na krzepnięcie krwi u pacjentów z przewlekłą chorobą nerek

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Abstract

Purpose. To compare the effects of aerobic and resistive activity on blood coagulation in chronic kidney disease (CKD). Methods. Randomized controlled trial. Sixty male patients with CKD (stages 2 & 3) participated in study; their age ranged from 40 to 50 years old. They were randomly assigned into equal two groups (A & B). Group A received aerobic exercise for 16 weeks (n = 30), while group B received resisted exercise for 16 weeks (n = 30). Pre- and post-treatment measurements included body weight, blood coagulation parameters (platelet count and fibrinogen concentration) and 6- minute walk test (6 MWT). Results. There were significant improvements in weight, blood coagulation parameters and 6 MWT within both groups ($p < 0.05$), while there were no significant differences ($p > 0.05$) between the two groups after treatment. Conclusion. Aerobic and resisted conditioning exercises both increase blood coagulation parameters and efficiency in CKD patients. Following therapy, there was little disparity between the two classes.

Key words:

chronic kidney disease, aerobic exercise, resisted exercise, blood coagulation

Streszczenie

Cel. Porównanie wpływu aktywności aerobowej i oporowej na krzepnięcie krwi w przewlekłej chorobie nerek (PChN). Metody. Randomizowana próba kontrolowana. W badaniu wzięło udział 60 mężczyzn z PChN (stadium 2 i 3); ich wiek wahał się od 40 do 50 lat. Zostali losowo przydzieleni do równych dwóch grup (A i B). Grupa A wykonywała ćwiczenia aerobowe przez 16 tygodni (n = 30), podczas gdy grupa B wykonywała ćwiczenia oporowe przez 16 tygodni (n = 30). Pomiary przed i po leczeniu obejmowały masę ciała, parametry krzepnięcia krwi (liczba płytek krwi i stężenie fibrynogenu) oraz test 6-minutowego marszu (6MWT). Wyniki. Wystąpiła znaczna poprawa wagi, parametrów krzepnięcia krwi i wyników testu 6MWT w obu grupach ($p < 0,05$), podczas gdy nie było znaczących różnic ($p > 0,05$) między dwiema grupami po leczeniu. Wniosek. Ćwiczenia kondycyjne aerobowe i oporowe zwiększają zarówno parametry krzepnięcia krwi, jak i wydajność u pacjentów z PChN. Po terapii różnice między obiema grupami były niewielkie.

Słowa kluczowe

przewlekła choroba nerek, ćwiczenia aerobowe, ćwiczenia oporowe, krzepnięcie krwi

Introduction

Chronic kidney disease (CKD) affects 14.8 percent of the adult population of the United States, accounts for $64 billion in Medicare spending, and is associated with high rates of injury, morbidity, and mortality. Despite the pressure that CKD poses on patients and the US healthcare system, fewer than 10% of patients with laboratory markers of CKD are aware of their diagnosis. Few people understand skills they need to manage CKD and its associated co-morbidities like diabetes and hypertension [1].

Patients with CKD also have elevated levels of typical thromboembolic risk factors, such as hypertension, diabetes, obesity, and dyslipidemia; these factors often impair the coagulation mechanism [2]. Coagulation problems are a common and possibly fatal complication of acute renal failure. In the one side, patients with severe kidney failure are more likely to experience bleeding (with symptoms varying from moderate skin/mucosal to overt gastrointestinal hemorrhage). Studies in this same group, on the other hand, revealed an elevated rate of arterial and venous thrombosis. Enhanced bleeding susceptibility has been linked to thrombocytopenia, platelet dysfunction, anemia, and the use of anticoagulants can also be attributed to the patient's symptoms or the medical treatments that those conditions necessitate. A related strategy can be taken to understand thrombosis in this context: uremia, other essential illnesses, and the use of hemodialysis can both cause inflammation, endothelial dysfunction, and coagulation activation [3].

Blood coagulation abnormalities are typical in patients with CKD. The associated thrombotic symptoms have been the leading cause of death and one of the most complex aspects of renal replacement therapy in CKD patients [4, 5]. In the general population, fibrinogen is an additional risk factor for cardiovascular (CV) accidents and mortality [6, 7]. However, uremia has been shown to have a detrimental effect on hemostasis, a condition known as uremic coagulopathy. Uremic coagulopathy induces an increase in the synthesis and/or clearance of procoagulant proteins, resulting in an increase in fibrinogen levels [8-10]. Low fibrinogen levels can increase the risk of bleeding, as well as the morbidity and mortality associated with CV events. Moreover, the relationships between some nontraditional CV risk factors, such as albumin and hemoglobin, and mortality are nonlinear [11]. End-stage renal disease patients are at a high risk of CV incident morbidity and mortality [12]. People with a high fibrinogen level in their blood are more likely to have cardiovascular disease (2-3 times more likely) than people with a low fibrinogen level [13].

Chronic kidney disease patients have poor levels of physical activity and function. Their aerobic ability is typically half that of an average person, their stamina is limited, and they are likely to struggle with endurance and simple everyday activities. Diabetes mellitus, anemia, peripheral vascular disorder, hypertension, coronary heart disease, and stroke are all more common among them. Because of electrolyte imbalance and other factors, individuals usually complain of pain, fatigue, and muscle weakness in the spine, hips, knees, and lower extremities [14].

Physical activity improves functional ability, quality of life, cardiovascular risk factors, anemia, and serum lipid levels, endothelial function, inflammation, type 2 diabetes mellitus, and psychosocial issues in patients with CKD [15]. A variety of experiments have also been performed to elucidate the biological relationship between physical activity and hemostatic function, as well as the impact of aerobic exercise on hemostatic function and the fibrinolytic system [16]. Exercise is one of the potential prevention measures to minimize blood coagulation abnormalities in people with CKD. Many recent findings have shown the significance of exercise or daily physical activity in preventing or reducing blood coagulation abnormalities in CKD patients. As a result, the current research was carried out to compare the effects of aerobic exercise versus resistive exercise on blood coagulation in CKD.

Subjects and methods

Design

The study was designed as randomized, pre and post, 2 groups, experimental design. The study was approved by the Institutional Ethical Committee of Faculty of Physical Therapy, Cairo University with code number [No. P.T.REC/012/002334]. The study followed the Guidelines of Declaration of Helsinki on the conduct of human research.

Participants

Sixty adult male patients were selected from EL Tall EL Kebir Hospital, EL Esmalia, Egypt. Their age ranged from 40-50 years. They had CKD (stages 2 & 3), diabetes, hypertension and no restrictions to perform exercises with sufficient cognition and education to understand the requirements of the study. The exclusion criteria were kidney transplant or dialysis, New York Heart Association class 3-4 heart failure, unstable angina or coronary revascularization within the last 3 months, uncontrolled arrhythmia, severe chronic lung disease, Orthopaedic, neurologic or other condition that would preclude resistance exercise training, uncontrolled hypertension and body mass index (BMI) of more than 35 Kg/m^2.

Randomization

Informed consent was obtained from all participants following the detailed explanation of the study. The privacy of all received data and the right to refuse or leave at any moment were also provided to all participants. They were randomly divided into two equal group's numbers using computerized random sequence generator method [17]. There was no dropping out of subjects after randomization, Figure 1.

Interventions

Group A included 30 participants who received aerobic exercise for 16 weeks, whereas group B included 20 participants who received resisted exercise for 16 weeks.

Aerobic exercise

Each participant in group A received aerobic exercise, using treadmill, for 40 minutes per session, three sessions per week, for 16 weeks. The exercise session included warming up phase, training phase and cooling phase. The participant started the exercise session with warming up exercise at a speed at 0.5 mph for 5 minutes to allow for conditioning of the body for the

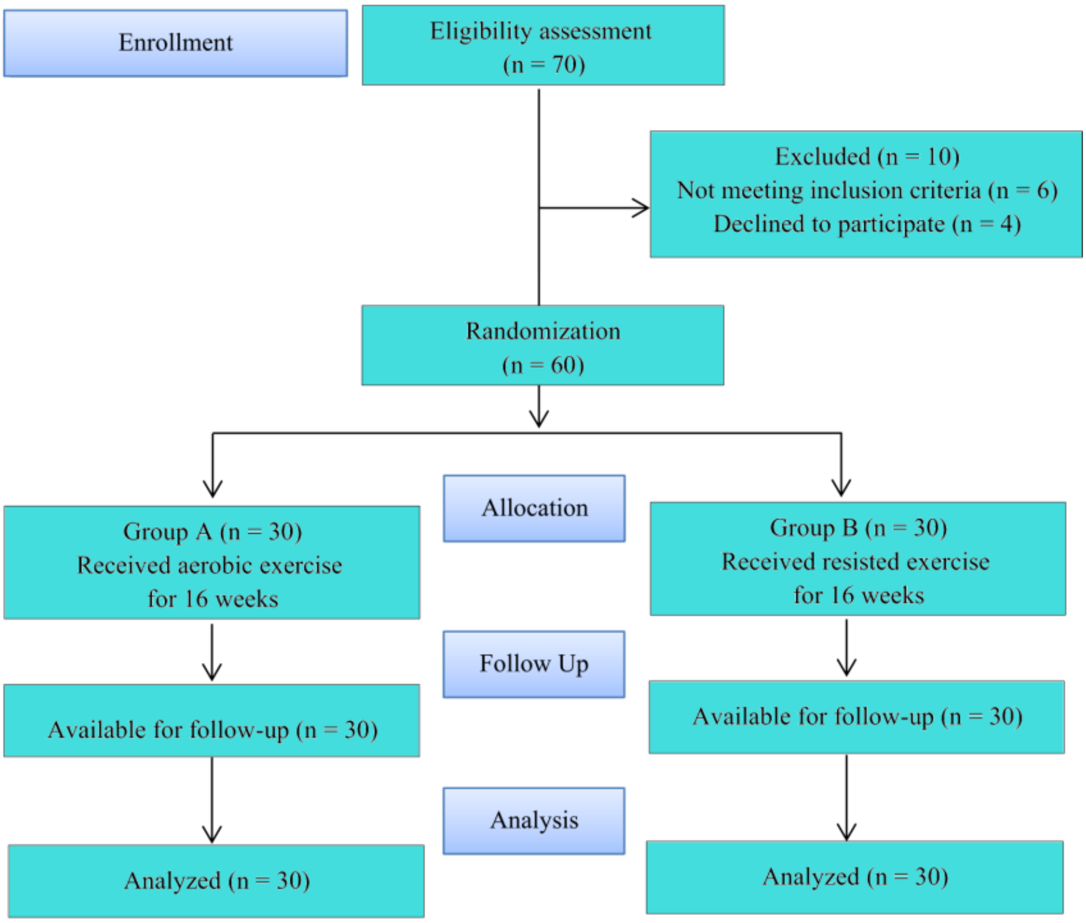

Figure 1. Flow chart of the study

exercise. Then, the speed was increased to 2 mph for 3 minutes, after that the speed had increased in increments of 1.0 mph every 2 minutes until the subject reached level of 60-75% effort of maximal heart rate (HRmax). During the training phase, the participant walked at the level of speed obtained at this level for 25-30 minutes. The training program was performed at 60-75% of the individual age predicted HRmax, which was calculated by subtracting the age from 220 [18]. The heart rate determined by sensor of treadmill the correspondent intensity, determined for each patient. Finally, the speed is decreased to 0.5 mph and the session was terminated with cooling down for 5 minutes.

Resisted exercise

Each participant in group B received resisted exercise, using free weights, for 40 minutes per session, three sessions per week, for 16 weeks. The program consisted of three parts; the first part was warming up (approximately 5 minutes) in the form of free passive stretching for lower limb. The second part involved 30 minutes of resisted training by free weights for muscle groups: (1) quadriceps (leg extension), (2) hamstrings (seated leg curl), and (3) gluteal (hip abduction). Training intensity was gradually increased during the first four weeks. The intensity of the training stimulus was initially set at 40-60% of one-repetition maximum (1RM) with a work range of two sets of 10 to 15 repetitions. 1RM tests were performed every two weeks for the first month and then every four weeks until the end of the program. Between these tests, the load was increased for those participants who were able to easily complete 12 or more repetitions for both sets; with two to three minutes of rest between sets to allow recovery. The exercise sessions were supervised by one of the investigators and the determined intensity of exercise was monitored and registered for each participant. The third part was cooling down (approximately 5 minutes) that involved passive exercise and stretching of lower limb as well as breathing exercise. The participants were taught to stop the exercise and notify if they felt any dizziness, headache, palpitations, nausea, anxiety, exhaustion or any other adverse effects.

Outcome measures

Body weight

A weight and height scale was used to evaluate the weight and height of each participant in both groups (A & B) before and after 16 weeks of treatment. During measurement, the participants wore light clothes with bare feet.

Blood coagulation parameters

After an overnight fast, a venous blood sample (6ml) was drawn from the antecubital vein from all participants in both groups (A & B) to be assayed later for measurement of platelet count and serum fibrinogen concentration before the initiation of the training program and after 72 hours of the last day of the exercise (i.e. after 16 weeks). The blood coagulation parameters were analyzed by spectrophotometer (Stanbio Glycohemoglobin Procedure, No.0350 made in China) using colorimetric method.

The 6-minute walk test (6 MWT)

The functional performance, using 6 MWT, were evaluated for all participants in both groups (A & B) before and after 16 weeks of treatment. The test performed indoors, along a long, flat, straight, enclosed corridor with a hard surface that was seldom traveled. The length of the corridor marked at starting line and end line marked on the floor using brightly colored tape. The participant was asked to walk as far as possible without jogging or running; the participant performed the test at his own rate [19].

Statistical analysis

Descriptive statistics and unpaired t-test were conducted for comparison of subject characteristics between both groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to ensure the homogeneity between groups. Mixed MANOVA was conducted to compare the effect of time (pre versus post) and the effect of treatment (between groups), as well as the interaction between time and treatment on mean values of body weight, platelet count, fibrinogen concentration and 6 MWT. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparison. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

Results

At baseline, there were no significant differences between both groups in age, BMI and all outcome measures ($p > 0.05$) (Tables 1-2).

The body weight showed statistically significant reductions ($p < 0.05$) within both groups (A & B). The post-treatment comparison of both groups showed a statistically non-significant difference ($p > 0.05$). However, there was a greater improvement percentage in group A (4.46%) than in group B (3.08%) (Table 2).

The platelet count showed statistically significant increases ($p < 0.05$) within both groups (A & B). The post-treatment comparison of both groups showed a statistically non-significant difference ($p > 0.05$). However, there was a greater improvement percentage in group A (8.91%) than in group B (5.01%) (Table 2).

The fibrinogen concentration showed statistically significant reductions ($p < 0.05$) within both groups (A & B). The post-treatment comparison of both groups showed a statistically non-significant difference ($p > 0.05$). However, there was a greater improvement percentage in group A (8.27%) than in group B (5.35%) (Table 2).

The 6 MWT showed statistically significant increases ($p < 0.05$) within both groups (A & B). The post-treatment comparison of both groups showed a statistically non-significant difference ($p > 0.05$). However, there was a greater improvement percentage in group A (6.87%) than in group B (6.29%) (Table 2).

Table 1. Baseline characteristics of participants in both groups

	Group A Mean ± SD	Group B Mean ± SD	MD	t-value	p value
Age [years]	47.4 ± 2.59	47.16 ± 2.73	0.24	0.08	0.92^{NS}
BMI [kg/m^2]	31.06 ± 3.62	30.22 ± 2.79	0.84	0.92	0.36^{NS}

SD: Standard deviation; MD: Mean difference; p value: Probability value; NS: p > 0.05, non-significant

Table 2. Body weight, platelet count, fibrinogen concentration and 6MWT for both groups

		Pre-treatment Mean ± SD	Post-treatment Mean ± SD	MD	t-value	p value
Body weight [kg]	Group A	92.76 ± 9.85	88.3 ± 8.43	4.46	4.81	0.0001^{S}
	Group B	93.2 ± 8.23	90.33 ± 7.55	2.87	3.08	0.0001^{S}
	p-value	p = 0.85 NS	p = 0.33 ^{NS}			
Platelet count [× 109/L]	Group A	245.7 ± 50.88	267.6 ± 42.51	−21.9	8.91	0.0001^{S}
	Group B	243.93 ± 52.05	256.16 ± 46.68	−12.23	5.01	0.0001^{S}
	p-value	p = 0.89 NS	p = 0.32^{NS}			
Fibrinogen concentration [mg/dL]	Group A	253.8 ± 22.91	232.8 ± 26.1	21	8.27	0.0001^{S}
	Group B	251.83 ± 28.03	238.36 ± 25.62	13.47	5.35	0.0001^{S}
	p-value	p = 0.76^{NS}	p = 0.4^{NS}			
6 MWT [m]	Group A	480.66 ± 39.34	513.66 ± 34.48	-33	6.87	0.0001^{S}
	Group B	479.56 ± 38.45	509.73 ± 36.82	−30.17	6.29	0.0001^{S}
	p-value	p = 0.91^{NS}	p = 0.67^{NS}			

SD: Standard deviation; MD: mean difference; p value: Probability value; NS: p > 0.05, non-significant; S: p < 0.05, significant

Discussion

The aim of this research was to compare the effects of aerobic exercise versus resisted exercise on weight, platelet count, fibrinogen level, and 6 MWT. The study found statistically meaningful improvements in fibrinogen and weight loss, platelet count boost, and 6 MWT in both groups post-treatment (Group A) that obtained aerobic exercise and (Group B) that received resisted exercise, while there were no statistical significant difference in body weight, platelets count, fibrinogen concentration and 6 MWT between both group post treatment.

The current study's findings revealed a reduction in body weight pre and post-treatment, but there was no substantial gap post-treatment between Group A and Group B.

The current study found that fibrinogen levels decreased pre and post-treatment, but there was no substantial gap post-treatment between Group A and Group B.

The current study found that platelets count increased pre and post treatment in both groups, but there was no substantial difference post-treatment between Group A and Group B.

The current study's findings revealed a substantial change in the 6 MWT pre and post-treatment in both study classes, with a non-significant gap post treatment in both groups of the study while there was a non-significant difference post treatment between Group A and Group B.

Zoccali et al. [20] found a link between high plasma fibrinogen levels and mortality in hemodialysis patients, but this has been refuted by other research on hemodialysis patients [21, 22].

Kumar et al. [23] and Wosornu et al. [24] hypothesized that aerobic activity after a coronary bypass that induces a reduction in fibrinogen concentration improves graft success and decreases the risk of myocardial infarction.

Weight lifting exercise not only contributes to muscle strengthening and toning and bone restructure, but also to the increase in metabolic rate [25-27].

Given the essence of high-intensity interval exercise, the most plausible cause of a reduction in fibrinogen levels is a rise in plasma volume and enhancement in the cardiovascular system, with other potential causes being an increase in the nervous system involved and a shift in lipid profile [28,29].

Three months of running exercise can increase blood cells in general (leucocytes, erythrocytes and platelets) function that may lead to reduction of cardiovascular events risk in middle-aged men [30].

In CKD, one significant treatment consideration is the use of "exercise as medication." Exercise prescriptions are a common treatment for many chronic conditions, but they were only recently considered for CKD patients. Exercise treatments can help to avoid CKD's negative effects, such as coronary complications; they can also help to delay the disease's development and increase longevity and quality of life [31].

Mustata et al. [32] discovered that people who were sedentary at early stages of dialysis had a 62% greater chance of dying as compared to nonsedentary patients at the start of dialysis.

Platelet activation, adhesion, and aggregation, in addition to the production of thrombin and fibrin, are essential in hemostasis, and both submaximal and maximal exercise of either short or long duration tends to enhance platelet adhesiveness and aggregability [33-35].

Naguib and Ashem [36] discovered a substantial decrease in the levels of C-reactive protein (CRP) (mg/L) and creatinine (mg/dL), an increase in albumin (g/dL), and a significant change of the outcomes of the Sit-to-stand-to-sit test and 6 MWT respectively pre-treatment and post-treatment in both study classes (p 0.05). Finally, there were no variations in the results of resisted and aerobic movements in patients with chronic kidney disease.

Painter et al. [37] The distance walked on the 6 MWT increased by 8% in 44 patients who enrolled in an 8 week home program and an 8 week intradialytic exercise program relative to their baseline distance of 517 190m. Reboredo et al. [38] confirmed that 12 weeks of aerobic exercise training during hemodialysis sessions improved bodily functioning, decreased blood pressure levels.

Afshar et al. [39] Aerobic and resisted workouts performed on hemodialysis patients were shown to be substantially associated with a reduction in serum creatinine and CRP levels, with aerobic exercise causing a greater reduction; nevertheless, the exercise has little effect on weight, Kt/V values, serum urea, albumin, hemoglobin, or lipid levels.Leehey et al. [40] investigated the impact of 24 weeks of exercise on medical treatment in patients with CKD. These patients performed exercise 3 times a week. The exercise training resulted in an increase in physical and functional capacity of the patients, accompaniment by a slight but insignificant decrease in systolic blood pressure at rest, and increased muscle strength as assessed by static and dynamic resistance.

After 8 weeks of concurrent training, fibrinogen levels in the concurrent population were substantially lower. Physical exercise decreased the occurrence of CVD. Fibrinogen and high-sensitivity C-reactive protein (hsCRP) are two new risk factors that closely predict CVD risk [41]. Resistance exercise at a high level for six weeks was associated with a substantial decrease in fibrinogen [42, 43].

Kilic-Toprak et al. [44] after three weeks of progressive strength training, fibrinogen levels decreased, but after twelve weeks of training, plasma fibrinogen levels rose before exercise.

Sharma and colleagues [45] in their research, treadmill training for 12 weeks (three days a week) resulted in an increase in platelet in stable young females. There was no research that looked at the long-term consequences of exercise on platelet in middle-aged men. Release of platelets from organs, such as liver, bone marrow, spleen and lungs, is a possible mechanism related to platelet elevation after exercise.

Young et al. [46] found that eleven of the sixteen patients with chronic hemodialysis reported a substantial increase in arterial stiffness after doing one hour of exercise per day for 12 weeks. This was translated as a result of increased mechanical tension in the broad arteries and a greater supply/demand myocardial equilibrium.

According to Diehl et al. [47] habitual activity is an important lifestyle intervention strategy for improving endothelial fibrinolytic capacity (with increase tissue-type plasminogen activator (t-PA)) in pathological infected adults.

Lisa et al. [48] used one of the most recent reviews to affirm our findings. In mice, voluntary aerobic exercise reverses arterial inflammation associated with ageing. This may be accomplished in part by inhibiting macrophage penetration of perivascular tissue and arterial adventitia. These anti-inflammatory effects may be significant in the positive effects of voluntary aerobic exercise on vasculature function observed in middle-aged and older adults.

Laswati et al. [49] reported that CRP and fibrinogen levels did not improve after five weeks of low-intensity resistance exercise.

Furthermore, no substantial difference in fibrinogen was observed following the performance of a circuit resistance exercise session. In line with this finding, a study found that the Bruce Protocol had no substantial impact on fibrinogen levels in young female athletes. In the current study, circuit resistance exercise was unable to provide the required conditions for the synthesis and release of liver fibrinogen; therefore, increases in blood volume were not important enough to influence fibrinogen levels [50].

Conclusion

Both aerobic and resisted training exercises are effective in improving blood coagulation in chronic kidney disease patients.

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