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Effects of Moderate Intensity Aerobic Exercise on Blood Coagulation and Fibrinolysis in Post-Menopausal Hypertensive Women.

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Abstract:
Purpose: This study was conducted to determine how postmenopausal hypertensive women's blood coagulation and fibrinolysis parameters are affected by moderate-intensity aerobic exercise. **Methods:** Fifty hypertensive female cases aged 50 to 65 took part in the trial, with BMIs ranging from 25 to 34.9 kg/m2. (Overweight and class 1 obesity). The cases were randomly allocated into the control and research groups. The control group (group A), which was under medical supervision, obtained anticoagulation medication. While the research group (group B) which was under medical supervision, got anti-coagulation medication and moderately intense aerobic exercise in the form of three sessions each week for eight straight weeks of walking on an electronic treadmill for 40 to 50 minutes each sessions. Initial and two-month follow-up visits involve laboratory testing to measure clotting time, plasminogen activator inhibitor-1 (PAI-1), and to record systolic and diastolic blood pressure before and after the research. **Results:** Both groups' clotting times markedly increased in favor of the study group by 7.01%, and the study group noticeably decreased PAI-1 ($P < 0.05$) compared to the control group by 17.8%. In contrast to the control group, the study group's systolic and diastolic blood pressure were markedly lower ($p < .05$).

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Conclusion: In postmenopausal hypertensive women, moderate aerobic exercise markedly decreased arterial blood pressure and improved fibrinolysis by decreasing plasminogen activator inhibitor-1 (PAI-1) and lengthening the clotting time.

Key words: Aerobic exercises, Plasminogen activator inhibitor -1, Fibrinolysis, postmenopausal hypertensive women.

1.Introduction

Early postmenopausal women are most frequently affected by risk factors such as hypertension, cardiovascular disease, osteoporosis, abnormal lipid profiles, and obesity (1). Compared to both premenopausal women and men, postmenopausal women are more likely to have hypertension (2.3). After menopause, postmenopausal women's estrogen levels drop and blood lipid levels rise, causing atherosclerosis and raising their risk of cardiovascular disease (4.5). Additionally, cardiovascular disease is more common in women than in men, and it is more prevalent in postmenopausal women than in premenopausal women (6.7).

Lifestyle management is essential for postmenopausal women because they have specific physiological traits that enhance their risk of prehypertension and moderate hypertension (8). In comparison to males, premenopausal women exhibit a reduced prevalence of arterial hypertension and related illnesses; but, following menopause, it resembles that of men (9). Primary (essential) hypertension and secondary hypertension are two different types of elevated blood pressure; primary hypertension, which refers to high blood pressure without a clear medical explanation, accounts for around 90–95 percent of all instances. Secondary hypertension, which affects the remaining 5–10% of people, is brought on by various illnesses that affect the kidneys, arteries, heart, or endocrine system.

Hypertension greatly increases the risk of stroke, myocardial infarction (heart attacks), heart failure, aortic aneurysm, peripheral arterial disease, and chronic renal disease (10). Prothrombotic indicators like thrombin are seen in higher concentrations with aging, and the fibrinolysis system undergoes major alterations that reduce fibrin lytic activity (11).

Two physiological processes that are crucial for the establishment of hemostasis and thrombosis are coagulation and fibrinolysis. Due to alterations in blood coagulation, hemostatic system disturbances, disorders of fibrinogen, and partial thromboplastin time, (PTT) would increase the risk of cardiovascular disease (12). Numerous researches have been done to look into the connection between cardiovascular illnesses and physical activity, as well as the dysfunction of the coagulation system (13).

Regular exercise has been shown to substantially decrease all causes of mortality. An effective system is aided by exercise. Regular exercise enhances the activities of epithelial tissue by lowering avoirdupois, force per unit of space, the prevalence of hereditary disorders, and dyslipidemia (14). In overweight hypertensive postmenopausal women, aerobic activity, aquatic exercise, and relaxation are utilized as non-pharmacological approaches to reduce hypertension (15).

Numerous epidemiological and clinical academic works (16) have portrayed that regular exercise promotes a healthy cardiovascular system and is a crucial component of a healthy lifestyle. The benefits of consistent exercise, such as weight loss, lowering blood pressure, improved lipid profiles, and improved glucose metabolism, have been linked in studies to an increase in physical activity and a reduction in morbidity and mortality (17). Hence, the goal of the current academic work was to trace how aerobic exercise affected postmenopausal hypertensive women's blood coagulation and fibrinolysis.

2.Patients and Methods

2.1. Subjects:

In the months of December 2022 to March 2023, 50 post-menopause hypertensive cases between the ages of 50 and 65 were randomly chosen from Deraya University's outpatient clinic. The cases have been sub-categorized in an interventional, randomized investigation into two equal groups. There were twenty-five patients in each group. Both the study group (B) and the control group (A)

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were given antihypertensive medications along with an aerobic exercise program. The patients also signed a formal informed consent form to take part in our study. Ethics Committee No. P.T. REC/012/004296 approved this study before its start. Cairo University's physical therapy department is in Egypt.

Inclusion criteria:

BMI ranged from 25 to 34.9 kg/cm2, blood pressure ranged from 140/90 mmHg to <160/100 mmHg and age ranged from 50 to 65 years old. At least two years had passed since menopause for each case.

Exclusion Criteria:

Cases with illnesses like musculoskeletal ailments, hepatic, renal, cardiac, chest, or endocrine issues that potentially affect the study's conclusion were excluded.

2.2. Study Design:

Cases of this trial were allocated at random to one of two groups: the control group (A) obtained anticoagulant and hypertensive medicine, whereas the study group (B) got both medications together with aerobic exercise. At the first visit and eight weeks later, we compared the groups. Each member of group B had three sessions each week for an intervention that lasted eight consecutive weeks.

2.3. Methods:

- **Measurement methods:**

Before the trial began for both groups, the Model MC. A health scale (RTZ-120A, made in China) was adopted to measure body mass index. Additionally, each woman's systolic and diastolic blood pressure was gauged before and after the study using mercury sphygmomanometers (Models Riester, Germany, and Littman, USA).

- **Therapeutic methods:**

A Kettler Treadmill, made in the UK with a good maximum user weight of 120-150kg, was adopted in the current academic work.

2.4. Evaluation procedures:

The following measurements were made on each case in each of the two study domains by a doctor and a physical therapist. Before and after the 8-week period, their parameters were gauged and documented.

- **Physiological measurements:**

a) Before initiating the study, each case's left arm was utilized to assess their systolic and diastolic blood pressure using a Littmann stethoscope (made in the U.S.A.) and sphygmomanometer. (Riester, made in Germany). The brachial artery in the left arm was utilized to gauge the arterial blood pressure. To ensure precision and dependability, the patient was strapped into the cuff of a mercury-type sphygmomanometer for five minutes. The measurement was then taken three more times, with the average value being recorded.

b) Heart Rate: Both the treadmill sensor and the pulse oximeter were adopted to gauge the case's resting heart rate (HR).

c) Measurement and calculating maximum heart rate (HR): The first phase involved using a pulse oximeter to measure each case's resting heart rate. Next, using the Karvonen method, each patient's maximal heart rate and goal heart rate were determined. Target HR is equal to 60% to 75% of the maximum HR plus resting HR (18). Age and maximum heart rate are the same (19).

- **Anthropometric measurements:**

Weight and height must be measured in order to calculate a case's BMI (defined as weight in kilograms divided by height in meters squared). Chinese-made Health Scale (RTZ-120A Model: MC). An assessment was carried out in accordance with the accepted anthropometric technique using the formula below: The BMI is determined as follows: (2.20) Weight (kg) / Height (m).

- **Laboratory investigation:**

Cairo University's Faculty of Medicine's Department of Biochemistry carried out the chemical analysis. laboratory testing was done on cases in both groups before and after the study's eight-week period of time. After an eight-hour overnight fast, a 5ml antiseptic syringe was used to collect a fasting venous blood sample. Using a Stat fax2100 Micro Plate Reader to measure each patient's plasminogen activator inhibitor-1 (PAI-1) and clotting time before and after the entire trial period (8 weeks).

2.5. Theraputic procedures:

- **Methodology of exercises program:**

1. Each case has obtained a detailed depiction of the training protocol.
2. The study's cases (group B) all engaged in an eight-week program of treadmill walking under the following conditions:

-**Mode of exercise**: aerobic exercise.

-Intensity: according to heart rate (60-75% of maximum heart rate) MHR=220-age.
-Duration: 40 to 50 minutes each. Each session began with a 5–10-minute stretch on the treadmill to warm up, followed by a similar stretch to cool down. There were 30 minutes of conditioning exercises, which included accelerating the treadmill until the maximum heart rate was reached (60-75%).
- Frequency: 3 times/week for 8 weeks.

- **Exercises prescription for the study group:**

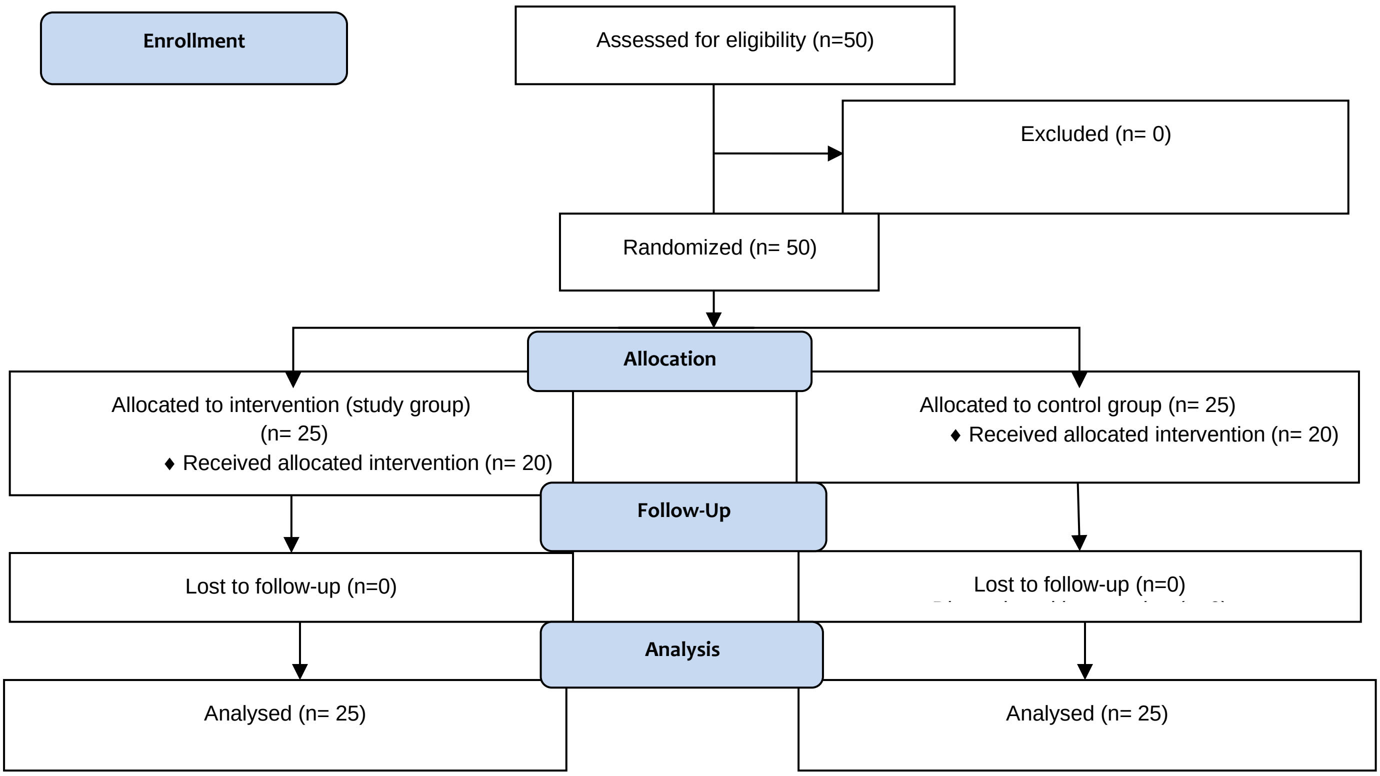
For eight weeks, the study group's cases engaged in three sessions per week of aerobic activity on a treadmill for 40 to 50 minutes each. Each session consisted of three phases: a warm-up, an exercise, and a cool-down. On the treadmill, a low-intensity warm-up phase lasting 5–10 minutes was performed to start the session. In the first and second weeks, the training phase lasted 30 minutes

at 60% of the maximal heart rate (HR max), and in the next six weeks, it increased to 40 minutes at 75% of HR max. Age was subtracted from 220 to obtain the HR maximum (21). The workout concluded with a 5- to 10-minute cooling-off period on a treadmill that had little to no resistance.

3.DATA ANALYSIS:

An unpaired t-test was adopted successfully to compare subject characteristics between groups. To evaluate if the data had a normal distribution, the Shapiro-Wilk test was utilized. Levene's test for homogeneity of variances was adopted to trace the homogeneity between groups. Using a mixed-design MANOVA, the effects on blood pressure, clotting time, and PAI-1 were assessed both within and across groups. Post hoc testing using the Bonferroni correction was done for further multiple comparisons. The significance level for each statistical test was set at p 0.05. For all statistical analyses, the statistical program for social studies (SPSS) version 25 for Windows was adopted. (IBM SPSS, Chicago, IL, USA).

Figure (1): Study flow chart.



4. Results

- **Subject characteristics:**

The research and control groups' subject characteristics are highlighted in Table 1 for

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comparison. Age, weight, height, and BMI did not markedly differ across groups (p > 0.05).

- **Blood pressure**

Descriptive statistics and t-test for the means of arterial blood pressure of study and control groups (table 2):

• Systolic and diastolic blood pressure pre-treatment did not markedly differ across groups (p > 0.05). Systolic and diastolic blood pressure significantly decreased after treatment compared to before (p <0.05).

• Systolic and diastolic blood pressure in the study group post-treatment compared to that pre-treatment noticeably decreased (p< 0.05), while the control group saw no significant changes in blood pressure (p > 0.05). Systolic and diastolic blood pressure variation in the study group was 6.31% and 8.83% respectively, compared to 0.03% and 0.09% in the control group. (Table 2).

- **Clotting time**:

Descriptive statistics and t-test for the mean clotting time of study and control groups (table 3)

• The clotting time pre-treatment did not differ substantially across the groups (p > 0.05), however the post-treatment clotting time differed significantly (p< 0.05).

• The clotting time within the groups clearly increased in both groups post-treatment compared to pre-treatment (p< 0.05). Following treatment, the study group's clotting time changed by 7.01%, compared to the control group's clotting time which changed by 2.52%. (Table 3).

- **Plasminogen activator inhibitor-1(PAI-1):**

Descriptive statistics and t-test for the mean PAI-1 of study and control groups (table 3)

• Between the groups, there was no marked disparity in the PAI-1 pre-treatment (p > 0.05). while there was a noticeable decrease in the PAI-1 post-treatment (p < 0.05).

• The PAI-1 in both groups clearly decreased after treatment as compared to before treatment within the groups (p <0.05). In the study group, the percent of variance of PAI-1 was 17.8%, whereas, in the control group, it was 4.23%. (Table3).

Table 1. Basic characteristics of participants.

	Study group	Control group	MD	t- value	p-value	Sig
	Mean ± SD	Mean ± SD				
Age (years)	59.96 ± 3.85	59.04 ± 3.99	0.92	0.82	0.41	NS
Weight (kg)	77.43 ± 3.7	78.91 ± 4.54	-1.48	-1.26	0.21	NS
Height (cm)	162.44 ± 2.75	163.04 ± 3.25	-0.6	-0.7	0.48	NS
BMI (kg/m²)	29.36 ± 1.61	29.69 ± 1.68	-0.33	-0.71	0.47	NS

SD, standard deviation; MD, mean difference; p-value, level of significance, NS: Non-significant

Table 2. Mean systolic and diastolic blood pressure pre-and post-treatment of the study and control groups:

	Study group	Control group		
	Mean ±SD	Mean ±SD	MD (95% CI)	P value
Blood pressure (mmHg)				
Systolic				

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Pre-treatment	128 ± 4.11	128.04 ± 3.99	-0.04 (-2.34: 2.26)	0.97*
Post-treatment	121.2 ± 3.97	128 ± 3.96	-6.8 (-9.06: -4.54)	0.001**
MD (95% CI)	6.8 (6.56: 7.04)	0.04 (-0.19: 0.27)		
% of change	6.31	0.03		
	p = 0.001*	***p = 0.73****		
Diastolic				
Pre-treatment	87.8 ± 3.8	86.92 ± 3.71	0.88 (-1.25: 3.01)	0.41*
Post-treatment	84.44 ± 3.72	86.84 ± 3.76	-2.4 (-4.52: -0.27)	0.02**
MD (95% CI)	3.36 (3.2: 3.52)	0.08 (-0.08: 0.24)		
% of change	8.83	0.09		
	p = 0.001*	***p = 0.32****		

SD, Standard deviation; MD, Mean difference; CI, Confidence interval; p-value, Level of significance, * non-significant; **significant.

Table 3. Mean clotting time and PAI-1 pre-and post-treatment of the study and control groups:

	Study group	**Control group**		
	Mean ±SD	**Mean ±SD**	**MD (95% CI)**	**P value**
Clotting time (min)				
Pre-treatment	5.71 ± 0.53	5.75 ± 0.86	-0.04 (-0.45: 0.36)	0.81*
Post-treatment	6.11 ± 0.96	5.78 ± 0.87	0.33 (-0.2: 0.84)	0.02**
MD (95% CI)	-0.4 (-0.64: -0.15)	-0.03 (-0.27: 0.22)		
% of change	7.01	2.52		
	p = 0.0001*	***p = 0.0001****		
PAI-1				
Pre-treatment	52.59 ± 18.06	51.12 ± 16.57	1.47 (-8.38: 11.33)	0.76*
Post-treatment	43.23 ± 15.59	51 ± 16.48	-7.77 (-16.88: 1.36)	0.03**
MD (95% CI)	9.36 (8.36: 10.36)	0.12 (-0.87: 1.12)		
% of change	17.8	4.23		
	p = 0.0001*	***p = 0.0001****		

SD, Standard deviation; MD, Mean difference; CI, Confidence interval; p-value, Level of significance, * non-significant; ** significant.

5. Discussion

This academic work attempted to determine how postmenopausal hypertensive women's blood coagulation and fibrinolysis factors were affected by moderate-intensity aerobic exercise. Fifty healthy female's hypertensive cases who had mildly managed hypertension for five years participated in this work. After menopause, a drop in estrogen is linked to rising blood pressure. After menopause, this hormone levels drop, which causes the arteries to not fully expand, causing the blood vessels to constrict and raising blood pressure. Menopausal women must therefore control their blood pressure (22).

The elements were assessed and discussed in a way to provide an explanation for the findings of the recent scholarly work. The variables in concern were clotting time, systolic blood pressure,

diastolic blood pressure, and plasminogen activator inhibitor-1 (PAI-1). The final results of the study showed that PAI-1 markedly dropped in both study domains, with the study domain having a higher drop. Both domains' clotting times markedly increased, although the research domain's increase was larger. Although there was no visible difference between them in the control group, both systolic and diastolic blood
pressure dramatically dropped in the study group.

These outcomes are consistent with earlier research by Hisham et al. (2019) (23), Abdullah MR et al. (2016) (24), Lamina and Okoye (2012) (19), and Guimaraes et al. (2010) (25) who examined the effects of continuous exercise training on people with essential hypertension. They came to a conclusion and agreed with the advice to use a continuous, moderate-intensity exercise program to lower blood pressure. Furthermore, according to El-Sayed MS. et al. (2004) (26), moderate exercise intensity results in blood fibrinolysis activation without concurrent hypercoagulability.

The current academic research supports Camarillo-Romero et al.'s (2012) (27) assertion that people with metabolic syndrome can effectively reduce PAI-1 with moderate-intens continuous exercise. This is in line with Borhar (2013) (28) investigation of how aerobic exerc affected individuals with ischemic heart dise who were also taking an oral anticoagulant. Thi male cases were sub-categorized into two grou the first domain got oral anticoagulant medicat along with moderate-intensity aerobic activities an electronic treadmill. the group under control t solely got oral anticoagulants. A considerable sl in the fibrinolysis coagulation profile was found be caused by moderate-intensity aerobic exercise

In addition to making the point that sho term aerobic exercise may stop the decline fibrinolytic function in postmenopausal wom who are inactive, Jahangard T. et al. (2009) (asserts that a 3-week routine of submaxir exercise will increase the fibrinolytic activity postmenopausal women. According to Esmat et (2010) (30), moderate-intensity exercise low lipid profile and PAI-1 levels as well, which m lower the risk of cardiovascular diseases a improve metabolic syndrome.

J. E. Smith (2003) (31) also noted that samples taken before and after exercise had faster whole blood coagulation times. Strenuous activity stimulates both the coagulation and fibrinolytic cascades, although it is still unclear how the two cascades are related in time and what this means clinically. At the highest levels of exercise intensity, unfavorable hemostatic alterations may increase the risk of intravascular thrombus development and cause sudden cardiac death.

Conclusion

Exercises of moderate aerobic intensity markedly improved the fibrinolysis process by lowering the plasminogen activator inhibitor-1 (PAI-1) and lengthening the clotting time. Moderate aerobic exercise apparently reduced

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