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Does Physical Activity Level Affect Homocysteine and Obesity Variables in Women with Cardiovascular Disease?

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ABSTRACT

Background and objectives: Physical activity has long been considered as the cornerstone of interventions for reducing the burden of cardiovascular diseases (CVDs). Homocysteine and obesity indices are important indicators of CVD risk. The present research aimed to evaluate homocysteine and obesity variables in female CVD patients and healthy counterparts with different physical activity levels.

Methods: This study was carried out on 85 CVD patients (40-55 yr, n=41, 60-75 yr, n=44) and 80 healthy women (40-50 yr, n=40, 60-75 yr, n=40). Subjects were divided into three groups based on their physical activity level: sedentary, moderately active and active. Serum homocysteine, body roundness index (BRI), a body shape index (ABSI), body mass index (BMI) and waist circumference (WC) were measured. Data were analyzed using the independent t-test and one-way ANOVA.

Results: Physically active middle-aged CVD patients had significantly lower BRI ($p=0.022$) and homocysteine ($p=0.008$) levels compared with the sedentary counterparts. In addition, physically-active old CVD patients had significantly lower BRI ($p=0.041$), ABSI ($p=0.011$) and homocysteine ($p=0.001$) compared with the sedentary counterparts. Physically-active healthy middle-aged individuals had significantly lower BRI ($p=0.013$) and BMI ($p=0.008$) levels compared with sedentary counterparts. Active elderly subjects also had significantly lower BRI ($p=0.001$) and WC ($p=0.008$) compared with the sedentary counterparts.

Conclusion: Physical activity can reduce the risk of CVD and improve health status of women by reducing homocysteine, BRI and ABSI.

Keywords: Exercise, Cardiovascular Diseases, Homocysteine, Obesity.

INTRODUCTION

Cardiovascular diseases (CVDs) are serious disorders affecting the heart and blood vessels that are also the main cause of mortality worldwide (1). According to the World Health Organization (WHO), lack of physical activity is a major risk factor for the development of CVD. This group of disorders is known as the fourth leading cause of mortality and morbidity in the world. Regular physical activity in adults decreases risk of hypertension, coronary artery diseases (CAD) and stroke (2). Unlike some CVD risk factors that have a genetic basis and are not modifiable (e.g. hypertension and hyperlipidemia), low physical activity could be resolved by proper planning as well as change in attitude and behavior (2).

It is established that adults characterized by excessive adipose tissue and ectopic fat stores have a higher risk of CVDs (3). Evidence indicates an association between obesity and increased risk of hypertension, type-2 diabetes mellitus and dyslipidemia, which are major risk factors for CVD (4). Body mass index (BMI) is generally recognized as an anthropometric index of obesity that might also predict the risk of CVD (5). Nevertheless, the neglect of body fat distribution is considered as a typical limitation of BMI. Waist circumference (WC) is recommended as an effective index for measuring visceral fat distribution (6). However, none of these indices alone is able to distinguish subcutaneous fat from visceral fat, which is more strongly associated with metabolic abnormalities. Some studies still suggest that these indices provide limited information on fat distribution (7).

Recently, a body shape index (ABSI) was proposed by Krakauer and Krakauer (8) as a new body index that is more significantly associated with abdominal adipose tissue and premature death than WC and BMI (9,10). However, some studies reported that ABSI seemed to be a weaker index for identifying risk of hypertension, diabetes, CVD and metabolic syndrome compared with BMI (11,12). Body roundness index (BRI) is another index recently proposed by Thomas et al. and based on WC and height. This index is a good predictor of body fat percentage and visceral adipose tissue compared with the traditional indices such as BMI, WC or hip circumference (13). Several studies have shown that BRI could be used as an indicator of adipose distribution and the presence of eccentric left ventricular hypertrophy, hyperuricemia, CVD and diabetes (11,14).

Homocysteine (Hcy) is a sulfhydryl-containing amino acid produced via methionine demethylation, which is essential for intravascular metabolism (15). Hyperhomocysteinemia has been considered as a risk factor for systemic atherosclerosis, CVD and stroke (16). However, results of studies on the relationship of physical activity with Hcy concentration are contradictory (17-19). Given the importance of physical activity and its role in the prevention of chronic diseases, the aim of the present study was to evaluate Hyc, BRI and ABSI levels in CVD women with different physical activity levels.

MATERIALS AND METHODS

The study was carried out on 85 patients with symptoms of CVD (middle-aged: 40-55 yr, n=41 and elderly: 60-75 yr, n=44) who had been referred to the heart unit of hospitals in Mashhad (Iran) in 2019. The study received approval from the ethics committee of Islamic Azad University, Aliabad Katool branch, Iran (ethics code: IR.IAU.AK.REC.1398.013). A written informed consent was obtained from all subjects before participating in the study. Participants were categorized into two groups: CVD (myocardial infarction, stroke and heart failure) and CVD risk factors (hypertension and hypercholesterolemia).

For middle-aged and elderly groups, an age-matched control group comprising of healthy individuals was also included. Individuals with history of smoking and kidney disorders were excluded. Patients and healthy subjects were divided into three groups based on their physical activity level: sedentary, moderately active and active. A questionnaire was also used to record the participants' dietary habits over the past year.

Physical activity assessment

The International Physical Activity Questionnaire (IPAQ) was used for determining the physical activity. Weekly physical activity was computed by multiplying time (minutes of given activity in the reported week) by intensity (MET) corresponding to that activity. The total weekly activity was obtained by calculating the sum of the activities and expressed in MET·min/week.

Based on the results, the subjects were classified as sedentary (score of less than 600 MET·min/week), moderately active (score of at least 600 but less than 1600 MET·min/week) and active (score of more the 1600 MET·min/week) (20).

Obesity variables

Weight, height, WC and BMI were measured according to standard procedures. The ABSI was calculated using the following formula (8): ABSI=$\left(\frac{WC}{BMI^{2/3}\times height^{1/2}}\right)$.

The BRI was based on height (m) and waist circumference (m). First, the eccentricity of the body was determined using the formula below. Eccentricity (non-dimensional value) quantifies the degree of circularity of an ellipse, and it ranges between zero (perfect circle) to one (a vertical line) (14).

$$\varepsilon = \sqrt{1-\left(\frac{(WC/(2\pi))^2}{(0.5\times height)^2}\right)}$$

Subsequently, BRI was calculated using the formula below. As described by Thomas et al., values closer to 1 are related to leaner individuals, whereas larger values are associated with rounder individuals (13).

$$BRI = 364.2-(365.5\times\varepsilon)$$

Blood sample collection

Blood samples (5 ml) were taken from subjects' forearms in a comfortable sitting position after at least eight hours of overnight fasting. The samples were centrifuged at 2000 rpm for 10 min to separate serum. Serum samples were then stored at 70 °C until use. The level of serum Hcy was measured using a commercial ELISA kit (Axis-shield diagonist, Germany) according to the manufacturer's instructions.

Statistical analysis

The Shapiro-Wilk was used to assess normal distribution of data. The independent t-test and one-way analysis of variance (ANOVA) with Tukey post-hoc test were used for analysis of data. All statistical analyses were performed in SPSS24 and at significance of ≤0.05.

RESULTS

The basic characteristics and mean of variables in different groups for middle-aged subjects are shown in table 1.

Compared with healthy subjects, CVD patients had higher WC, BMI, Hcy, BRI and ABSI levels. Physically-active CVD patients had significantly lower BRI (p=0.022) and Hcy (p=0.008) levels compared with sedentary subjects. There was no significant difference in ABSI, BMI and WC between CVD patients with different activity levels.

Active healthy subjects had significantly lower BRI (p=0.013) and BMI (p=0.008) compared with sedentary individuals. There was no significant difference in ABSI, Hcy and WC between healthy subjects with different activity levels.

Results of the t-test indicated a significant difference between sedentary CVD patients and sedentary healthy subjects for ABSI (p=0.008), BRI (p=0.021) and Hcy (p=0.001). Moreover, Hcy level differed significantly between moderately-active CVD patients and moderately-active healthy individuals (p=0.039). In addition, there were significant differences between active CVD patients and active healthy individuals in terms of BRI (p=0.008) and Hcy (p=0.016) levels.

Table 1- Mean values of research variables in middle-aged CVD patients and healthy individuals based on the level of physical

Variables	CVD patients				Healthy individuals			
	Sedentary	Moderately active	Active	P-value	Sedentary	Moderately active	Active	P-value
Age (years)	49.4 ± 4.7	44.2 ± 3.4	46.4 ± 5.4	0.047	51.2 ± 5.7	47.4 ± 4.4	49.2 ± 5.3	0.347
Weight (kg)	74.24±9.5	71.17±9.3	70.43±7.2	0.269	72.78±6.3	74.41±7.6	71.16±7.4	0.248
Height (cm)	162.2±5.1	161.67±6.2	164.14±5.1	0.147	163.1±4.5	165.3±7.4	162.87±6.2	0.311
ABSI	0.087±0.4	0.085±00.5	0.086±00.5	0.076	0.083±0.5	0.084±00.3	0.084±00.5	0.102
BRI	7.26 ± 1.7	6.85±1.4	6.08±2.1	0.031	6.14 ± 1.9	6.21±1.5	5.01±1.7	0.031
WC (cm)	99.39±8.5	96.36±9.7	95.14±8.3	0.147	100.2±9.3	95.11±8.7	94.25±7.9	0.034
BMI (kg/m^2)	28.42±3.8	27.68±4.1	26.25±3.1	0.089	27.53±4.2	27.34±3.8	26.85±5.3	0.167
Hcy (µmol/L)	18.87±2.1	19.25±1.7	16.26±2.3	0.008	14.51±2.4	13.14±2.9	13.42±2.1	0.089

Results are presented as mean ± standard deviation.

The basic characteristics and mean of variables of elderly subjects are shown in table 2. Active CVD patients had significantly lower BRI (p=0.041), ABSI (p=0.011) and Hcy (p=0.001) levels compared with the sedentary counterparts. There was no significant difference in BMI and WC between the mentioned groups. Active healthy individuals had significantly lower BRI (p=0.001) and WC (p=0.008) levels compared with the sedentary counterparts. There was no significant difference in ABSI, WC and Hcy between the mentioned groups.

Results of the t-test showed that there were significant differences between sedentary CVD patients and sedentary healthy subjects in terms of ABSI (p=0.001) and Hcy (p=0.008) levels. In addition, there were significant differences between moderately-active CVD patients and moderately-active healthy individuals in terms of Hcy (p=0.001) and WC (p=0.049). Moreover, WC differed significantly between active CVD patients and active healthy individuals (p=0.001).

Table 2- Mean values of research variables in old CVD patients and healthy individuals based on the level of physical activity

Variables	CVD patients				Healthy individuals			
	Sedentary	Moderately active	Active	P-value	Sedentary	Moderately active	Active	P-value
Age (years)	66.3 ± 5.7	68.1 ± 4.4	65.2 ± 5.1	0.0126	68.2 ± 6.1	64.1 ± 4.7	65.7 ± 5.6	0.214
Weight (kg)	72.31±6.4	72.1±7.2	71.48±7.1	0.347	74.5±7.1	71.82±5.2	73.23±6.1	0.187
Height (cm)	160.4±4.7	159.27±4.2	161.14±6.1	0.347	161.5±5.3	163.5±6.2	162.46±5.1	0.389
ABSI	0.089±0.4	0.087±00.5	0.086±00.5	0.008	0.086±0.5	0.085±0.5	0.085±0.4	0.214
BRI	7.84 ± 1.5	7.53±1.8	6.49±1.7	0.021	7.51 ± 1.7	7.11±1.6	5.77±1.6	0.011
WC (cm)	97.14±6.3	98.47±8.2	96.47±8.3	0.211	102.1±9.2	97.11±8.7	93.17±6.4	0.001
BMI (kg/m^2)	28.31±4.2	28.53±5.2	27.61±4.3	0.113	28.13±5.7	27.01±4.5	27.99±4.8	0.129
Hcy (µmol/L)	20.11±3.7	20.24±2.8	15.11±2.7	0.001	17.24±2.1	16.67±2.4	15.94±2.5	0.056

Results are presented as mean ± standard deviation

DISCUSSION

Based on the results, CVD patients had higher WC, BMI, Hcy, BRI and ABSI levels compared with healthy subjects. Both CVD patients and healthy individuals with a higher physical activity level had lower values of WC, BMI, Hcy, BRI and ABSI. These findings are consistent with results of a study by Vincent et al. that indicated a decrease in Hcy level following resistance training among inactive elderly people (21). Two other studies also showed that Hcy decreased after exercise training in male CVD patients and obese/overweight women (22, 23). On the other hand, Di Santolo et al. found no relationship between recreational sports and Hcy level among young women (24). Another study also showed that Hcy concentration is not significantly affected by submaximal exercise (25). Furthermore, Bambaeichi et al. reported that aerobic exercise did not change Hcy level in young (26). Various factors such as intensity, type and duration of exercise as well as gender and age of the participants may have contributed to the discrepancy between results of the mentioned studies.

Elevated level of Hcy has been associated with an increased risk of CVD. Plausible mechanisms of this association include vascular endothelial activation, promotion of oxidation of low-density lipoprotein cholesterol, vascular smooth cell proliferation, generation of superoxide anion and coagulation abnormalities (27). The effect of exercise on Hcy can be explored from different aspects. This amino acid is a critical biochemical juncture between methionine metabolism and the biosynthesis of the amino acids' cysteine and taurine; therefore, decreased methionine level leads to Hcy reduction (27,28). Increased demand for energy during exercise training might lead to the conversion of Hcy back to methionine, which can be used in the Krebs cycle for energy production. The relationship of Hcy with vitamin B12 has also been reported confirming the importance of these vitamins for regulating Hcy levels. In addition, reduction of oxidative stress indices following regular exercise can also reduce Hcy levels (28).

The present study showed that BRI and ABSI were significant lower in physically-active subjects than in sedentary subjects. Some studies have found that BRI has a good discriminative power for diabetes (13) and CVD and its risk factors (29) compared to BMI, WC and other indices. Chang et al. showed that the adjusted odds ratio (OR) for predicting diabetes increased with increasing quintiles of BRI, after adjustment for age, smoking, alcohol consumption and other confounding variables (11). Despite the favorable discriminative capabilities of BRI, a study reported that the adjusted OR of BRI for health outcomes was not superior to that of BMI or WC in men and women, except for hyperuricemia in women (29). Consistent with results of some previous studies (29,30), the present study emphasized a coincident predictive ability between BRI and weight-to-height ratio with respect to area under the receiver operating characteristic and partial correlation coefficients for cardiometabolic abnormalities. The advantage of BRI over the weight-to-height ratio could be related to the ability of accurate estimation of body fat percentage and visceral adipose tissue (11).

Several studies have delineated ABSI as an inferior indicator of the CVD risk when compared to indices such as waist-to-height ratio and WC. In line with these findings, an earlier study concluded that waist to-height ratio and WC are better predictors of CVD risk compared to ABSI, despite ABSI being directly proportional to WC (31). Savva et al. have specified that the risk factors of CVD in children can be better predicted by WC and waist- to-height ratio (32). Adegbija et al. indicated that the risk of CVD is directly proportional to WC (33). Similarly, Haghighatdoost et al. have concluded that ABSI is a weaker predictor of CVD risk in an Iranian population than BMI and waist to-height ratio (12). In contrast, Bozorgmanesh et al. has reported ABSI as a better indicator of CVD risk than BMI, WC and waist-to-hip ratio (34). Findings also suggest that ABSI is more significantly associated with circulating total cholesterol and insulin than BMI in young sedentary men.

Regular physical activity is considered a cornerstone in the prevention and management of hypertension and CVD (35). It has been well-demonstrated that physical activity can reduce the risk of CVD-related morbidity and mortality (36). However, the effect of physical activity might partly be mediated by adiposity (37), implying that the adjustment for WC is overly conservative. Physical activity of at least moderate intensity affects a range of biological processes that may influence cardiometabolic risk factors without affecting adiposity.

CONCLUSION

Our findings indicate that major CVD risk factors were favorably affected by physical activity. Active individuals generally had lower CVD risk factors. It is suggested to offer behavioral interventions to sedentary individual to promote the effectiveness of physical activity as a supportive mean for a healthier lifestyle.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding publication of this article.

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