RESEARCH ARTICLE

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Association of resting heart rate and arterial stiffness in healthy adults

Sağlıklı erişkinlerde istirahat kalp hızı ve arteriyel sertlik arasındaki ilişki

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ABSTRACT

Introduction: The arterial stiffness and resting heart rate (HR) are independent predictors of cardiovascular diseases. There are a few data about the association of HR with arterial stiffness in healthy men subjects. We aimed to evaluate this relationship in healthy male adults in the present study.

Materials and Methods: A total of 50 volunteer healthy-nonsmoking male individuals (mean age: 40 ± 12 years) enrolled in this observational study. According to the HR, the individuals were classified as group I, who have HR 50-70 beats/min (n= 25) and group II, who have HR 71-100 beats/min (n= 25). History of the enrolled adults was recorded and they were physically examined. Blood pressure, body mass index and waist/hip ratio were measured in accordance with standard protocol. Arterial age and aortic pulse wave velocity (aPWV) indicating direct measurement of arterial stiffness were calculated by TensioMed™ Arteriograph.

Results: There were no statistically significant differences between two groups with regard to age, body mass index, waist/hip ratio, systolic and diastolic blood pressure (for all p> 0.05). The arterial age and aPWV were significantly higher in group II than group I (both; p< 0.001). HR shows significant positive correlation with systolic blood pressure, body mass index, arterial age and aPWV (for all p< 0.001).

Conclusion: We conclude a relation between the HR and the increased arterial age and aortic pulse wave velocity levels in healthy male individuals. However, further studies are needed to clarify the pathophysiologic mechanisms responsible for the association between high HR and arterial stifness.

Keywords: *Resting heart rate, arterial age, aortic pulse wave velocity*

ÖZ

Giriş: Arteriyel sertlik ve istirahat kalp hızı, kardiyovasküler hastalıklar için bağımsız birer ön gördürücüdür. Sağlıklı erkek bireylerde arteriyel sertlikle istirahat kalp hızı arasında az sayıda çalışma mevcuttur. Mevcut çalışmada sağlıklı erkek bireylerde bu ilişkiyi araştırmayı amaçladık.

Materyal ve Metod: Sigara kullanmayan sağlıklı toplam 50 gönüllü erkek birey (ortalama yaş: 40 ± 12) bu gözlemsel çalışmaya dahil edildi. Katılımcılar kalp hızına göre iki gruba ayrıldı; grup I (n= 25) kalp hızı 50-70 atım/dakika olan bireyler ve grup II (n= 25) kalp hızı 71-100 atım/dakika olan bireyler. Katılımcıların tıbbi öyküleri kaydedildi ve fiziksel muayeneleri yapıldı. Kan basıncı, vücut kitle indeksi ve bel kalça oranları standart protokollere göre ölçüldü. Arteriyel yaş ve arteriyel sertliğin direkt bir göstergesi olan aortik nabız dalga hızları TensioMed™ Arteriyografi cihazıyla ölçüldü.

Bulgular: Yaş, vücut kitle indeksi, bel kalça oranı ve sistolik ve diyastolik kan basınçlarına göre gruplar arasında istatistiksel olarak anlamlı fark yoktu (tümü için p> 0.05). Arteriyel yaş ve aortik nabız dalga hızı grup II'de grup I'den anlamlı derecede fazlaydı (her ikisi için p< 0.001). İstirahat kalp hızı sistolik kan basıncı, vücut kitle indeksi, arteriyel yaş ve aortik nabız dalga hızı ile anlamlı derecede pozitif korelasyon göstermekteydi (tümü için p< 0.001).

Sonuçlar: Sağlıklı erkek bireylerde istirahat kalp hızının artmış arteriyel yaş ve artmış aortik nabız dalga hızı ile ilişkili olduğu sonucuna vardık. Ancak artmış kalp hızı ve arteriyel sertlik arasındaki ilişkiden sorumlu patofizyolojik mekanizmaları açıklamak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: *İstirahat kalp hızı, arteriyel yaş, aortic nabız dalga hızı*

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INTRODUCTION

Elevated resting heart rate (HR) is an independent risk factor for cardiovascular diseases such as congestive heart failure, hypertension and atherosclerosis. Both in patients with cardiovascular disease and in the general population, it has been shown that elevated resting HR is independently associated with atherosclerosis and high cardiovascular morbidity and mortality (1). There are several mechanisms between elevated HR and atherosclerosis. Generally, high resting HR leads to increased hemodynamic stress and subsequently increased mechanical load, tensile stress and low and oscillatory shear stress, all of which give rise to atherosclerosis and stiffness. Also, high resting HR causes increased mean blood pressure and cardiac work and finally increased O_2 consumption (2).

Arterial stiffness/age (AS) is the result of functional and structural disorders of the vascular wall which are caused by several factors (3). The AS reflects the end organ damage and increased risk of cardiovascular events (4). Therefore, it is considered that AS is a considerable parameter for the cardiovascular risk estimation. Moreover, aortic pulse wave velocity (aPWV) is an important indicator of AS. The aPWV is the time of the travel of the pulse wave between two points. The accelerated times indicate anatomical and/or functional disorders of arteries (3,5).

Several studies investigating relationship between HR and AS were conducted in various populations such as healthy individuals, patients with atrial fibrillation and paced patients with a low degree of atherosclerosis (6-10). These studies demonstrated positive correlation between HR and AS. However, only a few of these studies were performed in a healthy population (6,7).

The aim of this observational study was to investigate the relationship between HR and arterial stiffness in healthy nonsmoking male adults.

MATERIALS and METHODS

Study Population

A total of 50 volunteer healthy-nonsmoking male individuals (mean age: 40 ± 12 years) enrolled in this observational study. The mean resting HR was 70.3 in all subjects, and thus the individuals were classified as group I, who have HR 50-70 beats/min (n= 25) and group II, who have HR 71-100 beats/min (n= 25). Medical history of the enrolled adults was recorded and they were physically examined. Blood pressure (BP), body mass index and waist/hip ratio were measured in accordance with standard protocol.

The study was conducted according to the recommendations set forth by the Declaration of Helsinki on Biomedical Research Involving Human Subjects and the Institutional Ethics Committee approved the study protocol; each participant provided written, informed consent.

The subjects who have any following exclusion criteria were not included in the study; female sex, smoking, known atherosclerotic vascular disease (coronary or peripheral), left heart rate, arrhythmia, ventricular hypertrophy, diabetes mellitus, hypertension, systemic inflammatory diseases, renal or hepatic dysfunctions, lung diseases including obstructive and interstitial disorders, thyroid dysfunctions, anemia, and other systemic disorders.

Echocardiographic Assessment and Measurement of Resting Heart Rate, Arterial Age, and Pulse Wave Velocity

Echocardiographic assessment was performed in all subjects, and measurements were obtained based on recommendations of the American Society of Echocardiography guidelines (11,12). Resting HR was measured according to recommendations of European Society of Hypertension (13). After at least 5 minutes resting in a quiet room at a comfortable temperature, resting HR was measured by the TensioMedTM Arteriograph.

Arterial age (years) and aPWV (m/sn) indicating direct measurement of arterial stiffness were calculated noninvasively by the commercially available TensioMedTM Arteriograph, based upon oscillometric principle in detection of the brachial artery pulsations through cuff which is determined automatically by the TensioMedTM Arteriograph. The device assigned cuff-size according to person's height, weight, arm circumference and the jugulum-symphysis size (which is equal to the interval between the aortic root and the aortic bifurcation). After at least 15 minutes resting, measurements were obtained with appropriate cuff on the right brachial area. The aPWV and arterial age were calculated by analysis of the shape of brachial artery pulse wave. The aPWV was measured by the calculation of travel time of the pulse wave between two points. This device defines the global aortic stiffness (arterial age) and also makes possible the estimation of the central systolic BP of the individual (14).

Statistical Analysis

Continuous variables were expressed as mean ± SD and categorical variables were expressed as percentages. A one-sample Kolmogorov-Smirnov test was used to test the normalization of data distribution. All variables had

a normal distribution. Therefore, statistical analysis was performed using unpaired t test, Pearson correlation and multiple regression analysis tests. p< 0.05 was considered to be statistically significant. All analyses were conducted using SPSS version 11.5 (IBM Corporation, USA).

RESULTS

There were no statistically significant differences between two groups with regard to age, body mass index, waist/hip ratio, systolic and diastolic blood pressure (for all p> 0.05) (Table 1). Additionally, basal laboratory characteristics and echocardiographic measurements were similar in both groups (Table 2).

The aPWV (m/sec) was considerably higher in group II than group I (respectively, 9.84 ± 1.19 m/sec and 8.42 ± 1.19, p< 0.001). Similarly, the mean arterial age (years) was also significantly higher in group II than group I (respectively, 57 ± 4 years and 47 ± 10 years, p< 0.001) (Table 1).

Table 1. Clinical and laboratory values in two groups

Variables	Group I (HR= 50-70) (n= 25)	Group II (HR= 71-100) (n= 25)	*p*
Age (years)	40 ± 13	39 ± 10	0.422
Body mass index (kg/m^2)	27 ± 4	28 ± 4	0.502
Waist/hip ratio	0.97 ± 0.12	0.99 ± 0.12	0.836
Systolic blood pressure (mmHg)	115 ± 13	116 ± 12	0.946
Diastolic blood pressure (mmHg)	72 ± 8	70 ± 8	0.201
Arterial age (years)	47 ± 10	57 ± 4	< 0.001
Pulse wave velocity (m/sec)	8.42 ± 1.19	9.84 ± 1.19	< 0.001

All variables are expressed as mean ± standard deviation. HR: Heart rate.

Table 2. Laboratory and echocardiographic characteristics in both groups

Characteristics	Group I (HR= 50-70) (n= 25)	Group II (HR= 71-100) (n= 25)	*p*
Laboratory			
Glucose (mg/dL)	84 ± 6	86 ± 7	0.245
Creatinine (mg/dL)	0.75 ± 0.07	0.77 ± 0.08	0.283
Alanine aminotransferase (U/L)	26 ± 5	27 ± 4	0.347
Total cholesterol (mg/dL)	186 ± 6	188 ± 7	0.210
LDL cholesterol (mg/dL)	111 ± 6	114 ± 8	0.151
HDL cholesterol (mg/dL)	40 ± 2	39 ± 3	0.349
Triglyceride (mg/dL)	175 ± 13	178 ± 12	0.366
White blood cells (10^3/μL)	8.6 ± 0.6	8.5 ± 0.6	0.573
Hematocrit (%)	42 ± 2	41 ± 3	0.378
Echocardiography			
Left ventricle diastolic diameter (mm)	47 ± 3	49 ± 3	0.065
Left ventricle systolic diameter (mm)	32 ± 2	31 ± 2	0.490
Left ventricle ejection fraction (%)	62 ± 3	63 ± 3	0.487
Interventricular septum thickness (mm)	8.3 ± 1.1	8.6 ± 1.0	0.222
Left ventricle posterior wall thickness (mm)	7.9 ± 1.2	8.0 ± 1.1	0.801
Mitral E/A ratio	1.27 ± 0.15	1.24 ± 0.12	0.502
Deceleration time of mitral E wave (msec)	186 ± 15	190 ± 16	0.379

All variables are expressed as mean ± standard deviation. HDL: High density lipoprotein, HR: Heart rate, LDL: Low density lipoprotein.

HR shows significant positive correlation with systolic BP, body mass index, arterial age and pulse wave velocity in bivariate correlation analysis in all individuals (for all p< 0.05) (Table 3). The positive correlation between HR and aPWV has been shown in figure 1. However, in regression analysis, we found out that HR was not an independent predictor of aPWV in all participants.

DISCUSSION

We found that the arterial age and the aPWV have been increased with HR in a small healthy non-smoking male population, and that HR has significant positive correlation with aPWV, but not an independent predictor.

It is known that both AS and HR are implications of atherosclerosis. There are several measurements of AS such as augmentation index, pulse pressure amplification, central pulse pressure/stroke volume index, and total arterial compliance as well as aPWV (3,15). The aPWV was confirmed to be a gold standard arterial stiffness index in previously studies like 2013 ESH/ESC guidelines for the management of hypertension (16,17). The guideline proposed 12 m/s as a normal threshold value (18). Values of aPWV in the present study were within normal limits, but the values varied significantly according to HR (lower in group I than group II). A large-scale study published in 2010 showed that reference values for arterial stiffness may be affected by mean blood pressure and age (5). However, the study did not take account of HR. Our study suggests that normal or reference values of aPWV might be varied with HR, and perhaps that corrected values according to HR would be required.

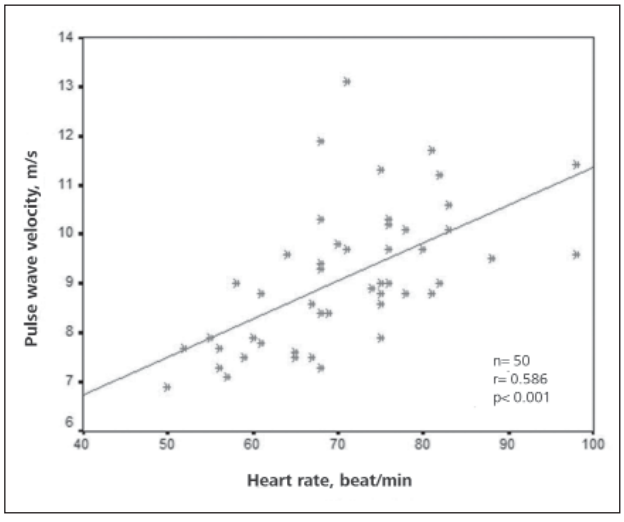

Figure 1. *The correlation between heart rate and aortic pulse wave velocity in all cases.*

There are a few data about relationship HR and AS in healthy subjects (6,7). Koskela et al. reported that HR was considerably correlated with aPWV in individuals without any disease or medication effecting on BP and HR. In her study with 522 subjects, aPWV was notably higher in individuals with high HR (who have HR> 59 beats/min) than lower HR (who have HR< 59 beats/min) (6). Salvi et al. found that HR was related to aPWV in untreated subjects of different age and aPWV was more closely related to left ventricular systolic function than to heart period (the reciprocal of heart rate) (7). In the present study, we also found a considerably relationship between HR and AS (aPWV and arterial age) in healthy male individuals. Thus, our results were agreed with the previous studies (6,7).

On the other hand, several investigators reported that HR was related to aPWV and arterial stiffness in different populations (8-10). Chu et al. demonstrated that HR was positively correlated with arterial stiffness evaluated by brachial-ankle PWV in atrial fibrillation patients (8). Haesler et al. reported that carotid-femoral PWV had an important connection with HR in post pacemaker implantation due to sick sinus or carotid hypersensitivity syndromes and with a low degree of atherosclerosis. In his study, by increasing HR, carotid-femoral PWV was significantly raised at 80, 90 and 100 beats/min (9).

Even though the mechanisms of it cannot be explained, it is known that HR is higher in females than males (19,20). Yang et al. displayed that both premenopausal and postmenopausal women had higher HR than men. His study also showed that postmenopausal women treated by conjugated estrogen had lower HR compared with premenopausal women, and estrogen led to this reduction by affecting the autonomic nervous system (20). It was demonstrated that carotid-femoral pulse wave velocity

Table 3. The heart rate and associated parameters

	Pearson correlation coefficient	*p* values	Multivariate ß regression coefficient	%95 confidence interval	*p* values
SBP	0.436	0.002	0.127	-0.148-0.395	0.364
BMI	0.338	0.016	0.065	-0.526-0.864	0.627
Arterial age	0.630	< 0.001	0.407	-0.013-0.922	0.056
PWV	0.586	< 0.001	0.165	-1.926-4.443	0.430

BMI: Body mass index, PWV: Pulse wave velocity, SBP: Systolic blood pressure.

had considerably lower in women than men (21,22). For all these reasons; we did not include female individuals in the present study, and we thought that the arterial stiffness should be assessed gender-specific.

It is known also that increased resting HR is an independent risk factor for atherosclerosis (1). A high resting HR leads to progression of atherosclerosis via a variety of mechanisms. These mechanisms include increased hemodynamic stress, mechanical load, tensile stress, endothelial dysfunction, vascular oxidative stress, and low oscillatory shear stress as well as increased mean blood pressure and cardiac work (2,19,23). Likewise, the changes may contribute to the risk of plaque disruption which is the leading cause of acute coronary events. A previous study analyzing patients who underwent two coronary angiograms within 6 months showed that the high HR (> 80 bpm) was an independent predictor of plaque disruption (24). Although the exact pathophysiological mechanism remains to be elucidated, the present study suggests that increased resting HR may result in increased arterial age and aPWV by similar mechanisms. Additionally, our results showed also that resting HR has an independent relationship with systolic blood pressure just as previous studies (25-27).

LIMITATIONS

The study has some limitations. Small number of patient is mainly limitation. Other limitation is not taken into account of exercise capacity and depression-anxiety-stress scales of individuals.

CONCLUSION

We conclude that although it is not fully explained, there is a relation between the HR and the increased arterial age and aPWV levels in healthy individuals. However, HR was not an independent predictor of aPWV. Further studies are needed to clarify the pathophysiologic mechanisms responsible for arterial stiffness induced by high HR.

CONFLICT of INTEREST

None declared.

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