Aortic strain and distensibility in patients with metabolic syndrome

Metabolik sendromlu hastalarda aort gerilimi ve esneyebilirliği

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Objectives: Metabolic syndrome (MetS) is associated with increased risk for cardiovascular disease. We evaluated aortic stiffness and factors affecting aortic stiffness by echocardiography in patients with MetS.

Study design: The study included 27 patients (18 men, 9 women; mean age 56±7.5 years) and 33 patients (20 men, 13 women; mean age 54.3±5.5 years) with and without MetS, respectively, according to the ATP-III criteria. Blood pressure, pulse pressure, waist circumference, and levels of total cholesterol, HDL and LDL cholesterol, triglyceride, and high-sensitivity C-reactive protein (hs-CRP) were measured. Systolic and diastolic diameters of the ascending aorta were measured by M-mode echocardiography from the parasternal long-axis views, and parameters of aortic stiffness (aortic strain and distensibility) were calculated.

Results: Compared to the control group, patients with MetS had significantly higher values of blood pressure, pulse pressure, waist circumference, and higher triglyceride, glucose, and hs-CRP levels and lower HDL cholesterol level ($p<0.05$). In the MetS group, aortic strain (9.0±3.5% vs. 6.3±3.8%; $p=0.007$) was significantly increased and aortic distensibility (2.7±1.9 cm2/dyn/103 vs. 4.8±1.9 cm2/dyn/103; $p=0.001$) was significantly decreased. Aortic distensibility was negatively correlated with age ($r=-0.269$, $p=0.03$), hs-CRP ($r=-0.287$, $p=0.002$), systolic blood pressure ($r=-0.533$, $p<0.001$), and diastolic blood pressure ($r=-0.275$, $p=0.03$). In age-adjusted multiple regression analysis, systolic blood pressure ($\beta=0.8$, $p<0.001$), waist circumference ($\beta=0.5$, $p=0.02$), and hs-CRP ($\beta=0.6$, $p=0.002$) were independent predictors of aortic distensibility.

Conclusion: Aortic stiffness is increased in patients with MetS. Using a noninvasive and readily available tool, transthoracic echocardiography, arterial stiffness can easily be assessed, so that the incidence of cardiovascular diseases and associated mortality can be decreased through appropriate treatment for risk factors.

Key words: Cardiovascular diseases; C-reactive protein; echocardiography; elasticity; metabolic syndrome X/complications; risk factors; vascular resistance.

Amaç: Metabolik sendrom (MetS) kardiyovasküler riski artıran bir durumdur. Bu çalışmada, MetS tanısı konan hastalarda ekokardiyografi ile aortik sertlik parametreleri ve bunları etkileyen faktörler araştırıldı.

Çalışma planı: Çalışmaya ATP-III ölçütlerine göre MetS tanısı konan ardışık 27 hasta (18 erkek, 9 kadın; ort. yaş 56±7.5) ve MetS bulunmayan 33 hasta (20 erkek, 13 kadın; ort. yaş 54.3±5.5) alındı. Hastaların kan basınçları, nabız basıncı, bel çevresi ve kan örneklerinde total kolesterol, HDL-kolesterol, LDL-kolesterol, trigliserit, glukoz ve yüksek duyarlıklı C-reaktif protein (hs-CRP) düzeyleri ölçüldü. M-mod ekokardiyografi ile parasternal uzun eksen görüntülerde çıkan aort sistolik ve diyastolik çapları ölçüldü ve aort sertliğinin göstergeleri olan aort gerilimi ve esneyebilirliği hesaplandı.

Bulgular: Kontrol grubu ile karşılaştırıldığında, MetS grubunda kan basıncı, nabız basıncı bel çevresi, trigliserit, glukoz ve hs-CRP değerleri daha yüksek, HDLkolesterol düzeyleri düşük bulundu ($p<0.05$). Aort gerilimi MetS grubunda (%9.0±3.5 ve %6.3±3.8; $p=0.007$) daha yüksek, esneyebilirlik (2.7±1.9 cm2/dyn/103 ve 4.8±1.9 cm2/dyn/103; $p=0.001$) ise daha düşük idi. Aort esneyebilirliğinin yaş ($r=-0.269$, $p=0.03$), hs-CRP ($r=-0.287$, $p=0.002$), sistolik kan basıncı ($r=-0.533$, $p<0.001$), diyastolik kan basıncı ($r=-0.275$, $p=0.03$) ile ilişkili olduğu görüldü. Yaşa göre düzeltilmiş regresyon analizinde, sistolik kan basıncı ($\beta=0.8$, $p<0.001$), bel çevresi ($\beta=0.5$, $p=0.02$) ve hs-CRP'nin ($\beta=0.6$, $p=0.002$) aortun esneyebilirliği için bağımsız öngördürücüler olduğu saptandı.

Sonuç: Metabolik sendromlu hastalarda aort sertliği artmaktadır. İnvaziv olmayan ve kolayca ulaşılabilen bir yöntem olan transtorasik ekokardiyografi ile MetS'li hastalarda arteryel sertlik kolayca değerlendirilebilir ve risk faktörlerine yönelik tedavi ile kardiyovasküler hastalıklar ve mortalitede azalma sağlanabilir.

Anahtar sözcükler: Kardiyovasküler hastalık; C-reaktif protein; ekokardiyografi; elastisite; metabolik sendrom X/komplikasyon; risk faktörü; vasküler direnç.

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Metabolic syndrome (MetS) which includes risk factors of atherosclerotic heart diseases such as hypertension, dyslipidemia and impaired glucose tolerance presents with increased prothrombic and proinflammatory conditions.[1] Each component of MetS is a risk factor for cardiovascular disease and the risk which arises from their combination is far more than the addition of every individual risk factor.[2]

Arterial stiffness is known to be increased under conditions such as coronary artery disease, diabetes mellitus, hypertension, and thyroid diseases.[3] The increased arterial stiffness further increases the risk of cardiovascular diseases by leading to hypertension, left ventricular hypertrophy and impaired coronary perfusion. Stiffness of the large artery is an independent risk factor for cardiovascular diseases.[3] Many methods are used in the evaluation of arterial stiffness including simple procedures such as the pulse pressure method and non-practical methods which may require costly equipments.[4] Transthoracic echocardio is a widely used, practical and non-invasive diagnostic tool. Although transthoracic echocardiography has been used in the evaluation of changes in aortic systolic and diastolic diameters, strain and distensibility in different patient groups,[5] stiffness of the aorta has so far not been evaluated with transthoracic echocardiography.

In this study we evaluated aortic stiffness in patients with MetS using echocardiography, a non-invasive method and investigated factors affecting the procedure.

PATIENTS AND METHOD

Choice of patients. Following hospitalization and scheduling for coronary angiography in our clinic due to a prediagnosis of coronary artery disease, a total of 27 consecutive patients who were diagnosed with MetS (18 men, 9 women; mean age 56±7.5) and 33 patients (20 men, 13 women; mean age 54.3±5.5) with no diagnosis of MetS according to the Adult Treatment Panel (ATP-III) of the National Cholesterol Education Program were included in the study. Blood pressures of the patients were obtained by sphygmomanometer immediately before echocardioraphy. The pulse pressure was calculated by subtracting the diastolic blood pressure from the systolic blood pressure. Waist circumference was measured at the midway between the lower ribs and the iliac crest, with the patients standing, having the inner wears on and during mild expiration. MetS was defined according to the criteria stipulated in the ATP-III guidelines.[6] The patient was diagnosed as having MetS when three or the stipulated criteria were present (waist circumference of ≥102 cm in men, and ≥88 cm in women; triglyceride of ≥150 mg/dl; HDL-cholesterol of ≤40 mg/dl in men, and ≤50 mg/dl in women; blood glucose of ≥100 mg/dl; blood pressure of ≥130/85 mmHg or patient receiving anti-hypertensive treatment). All patients were informed about the study and their consents were obtained. Approval for the study was obtained from the local Ethics Committee.

Patients with a history of acute coronary syndrome for the past 6 months, cardiac valve disease, congenital heart disease, left ventricular function disorder (left ventricular ejection fraction of >50%), and those with known inflammatory disease and severe renal and liver diseases were excluded from the study.

Biochemical parameters. Blood samples of the patients were obtained after 12 hours of fasting and levels of total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, glucose and high-sensitivity C-reactive protein (hs-CRP) were obtained.

Coronary angiography. The standard Judkins technique was applied by the femoral approach. Lesions were visually evaluated. Coronary artery disease was defined as a decrease in the coronary artery lumen diameter of at least >50%.

Echocardiography. All patients underwent transthoracic echocardiography (Aloka SSD-5500, Japan) in the left lateral lying position before coronary angiography. Aortic strain and distensibility was measured using M-mode echocardiography by calculating the systolic and diastolic diameter of the ascending aorta, approximately 3 cm above the aortic valve in the parasternal long axis view. The systolic diameter of the aorta was measured at the point of highest forward motion of the aorta, whereas the diastolic diameter was measured at the area equivalent to the peak of the QRS complex on electrocardiography. Measurements were repeated at three cardiac beats and the mean value was obtained (Figure 1).

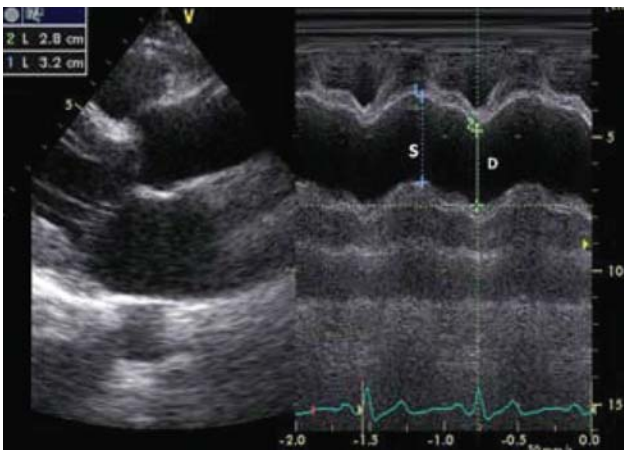

Figure 1. Systolic and diastolic diameter of the ascending aorta measured using M-mode echocardiography approximately 3 cm above the aortic valve in the parasternal long axis view.

Table 1. Characteristic of the metabolic syndrome and control groups

	Metabolic syndrome (n=27)			Controls (n=33)			
	Number	%	Mean±SD	Number	%	Mean±SD	*p*
Age			56.0±7.5			54.3±5.5	0.3
Gender							0.6
Male	18	66.7		20	60.6		
Female	9	33.3		13	39.4		
Coronary artery disease	12	44.4		10	30.3		0.2
Cigarette smoking	13	48.2		14	42.4		0.8
Systolic blood pressure (mmHg)			134.1±18.5			119.2±14.3	**0.001**
Diastolic blood pressure (mmHg)			86.2±15.0			80.0±14.0	**0.002**
Pulse pressure (mmHg)			49.9±12.4			39.2±10.7	**0.001**
Waist circumference (cm)			101.5±7.5			95.7±10.0	**0.014**
Glucose (mg/dl)			107.9±18.0			95.7±8.0	**0.009**
Cholesterol (mg/dl)			201.7±34.5			200.3±41.9	0.8
LDL-C (mg/dl)			126±38.8			120.9±27.8	0.4
HDL-C (mg/dl)			43.5±8.3			49.7±12.7	**0.02**
Triglyceride (mg/dl)			176.7±78.0			112.0±26.7	**0.001**
hs-CRP (mg/dl)			0.8±0.5			0.5±0.3	**0.013**
Aortic strain (%)			9.0±3.5			6.3±3.8	**0.007**
Aortic distensibility ($cm^2/dyn/10^3$)			2.7±1.9			4.8±1.9	**0.001**

The following formula was used for strain and distensibility measurements:[5]

Aortic strain (%) = (Systolic – Diastolic diameter) x 100/Diastolic diameter.

Distensibility ($cm^2/dyn/10^3$) = (2 x Aortic strain)/Pulse pressure.

Statistical analysis. Continuous variables were expressed as mean±standard deviation, whereas categorical variables were expressed as frequency and percentages. Comparison of the groups was performed for continuous variables using the T-test and for categorical variable using the Chi-square test. The multivariable regression analysis was used to identify variable related to distensibility of the aorta of all groups. A *p* value of P<0.05 was considered as statistically significant.

RESULTS

There was no significant difference between the MetS group and the control group in terms of age, gender, presence of coronary artery disease, total cholesterol, and LDL cholesterol. On the other hand, and as anticipated, patients with MetS were found to have significantly higher values of systolic and diastolic blood pressure, waist circumference, higher triglyceride, and glucose levels and lower HDL cholesterol levels, compared to the control group (Table 1). The hs-CRP levels were found to be higher in the MetS group (0.8±0.5 mg/dl and 0.5±0.3 mg/dl; p=0.013). Pulse pressure was also found to be higher in the MetS group of patients (49.9±12.4 mmHg and 39.2±10.7 mmHg; p=0.001). The aortic strain, an indicator of aortic stiffness in patients with MetS, was found to be higher (9.0±3.5% and 6.3±3.8%; p=0.007), whereas the aortic distensibility was found to be lower (2.7±1.9 $cm^2/dyn/10^3$ and 4.8±1.9 $cm^2/dyn/103$; p=0.001) in the MetS group of patients. On the other hand, aortic distensibility was associated with age (r=-0.269, p=0.03), hs-CRP (r=-0.287, p=0.002), systolic blood pressure (r=-0.533, p<0.001), and diastolic blood pressure (r=-0.275, p=0.03) in both groups.

In the regression analysis where aortic distensibility was selected as an independent variable and adjusted according to patient age, systolic blood pressure (,=0.8, p<0.001), waist circumference (,=0.5, p=0.02) and hs-CRP (,=0.6, p=0.002) were found to show an independent correlation with aortic distensibility. No significant relationship was found between the other MetS components and lipid parameters.

DISCUSSION

In this study we demonstrated that distensibility as an indicator of aortic stiffness decreased aortic stiffness increased in patients with MetS, as observed on the non-invasive echocardiography. We also demonstrated that decrease in aortic distensibility had a negative age, hs-CRP, and blood pressure.

Stiffness of the aorta is an independent indicator of cardiovascular and all-cause mortality, independent from previous cardiovascular events, age and diabetes mellitus.[3] Many methods have been described in the

evaluation of stiffness of the aorta. These techniques include simple methods such as measurement of brachial pulse pressure by sphygmomanometer and also detailed and complex techniques for the determination of pulse wave velocity, aortic impedance and aortic elastic properties. Measurement of the pulsatile changes in aortic diameter using ultrasonographic catheter gives information about the elasticity of the aorta.[7] Echocardiography can also be used to evaluate pulsatile changes in aortic diameter.[5]

The risk of cardiovascular disease is three-fold higher in patients with MetS, compared to non-MetS patients. In addition, MetS patients have a 2.3-fold higher risk for developing stroke and 2.6-fold higher risk for myocardial infarction, compared to non-MetS patients.[8] Several studies have demonstrated that MetS and its components increase arterial stiffness in all age groups.[9-11] Endothelial dysfunction, inflammatory response (cytokines), sympathetic nervous system, rennin-angiotensin system, and the hyperdynamic circulation play an important pathophysiologic role in MetS.[12-14] Changes in the vascular tonus as a result of this abnormalities lead to increased arterial stiffness due to hypertrophy and hyperplasia of smooth muscles and also to increased collagenous synthesis.[15] On the other hand, insulin resistance which plays an important role in the physiopathology of MetS has been shown to have a relationship with indicators of arterial stiffness both in diabetics and non-diabetics.[16] Interestingly, insulin decreases the augmentation index, an important indicator of arterial stiffness of large arteries in healthy individuals; however, under conditions of insulin resistance higher levels of insulin are required to have this effect.[17] In addition to patient age, blood pressure and hs-CRP, our study also demonstrates that increased insulin resistance and the close association of central obesity are independently related to aortic distensibility.

Studies investigating the relationship of MetS with arterial stiffness have demonstrated that there is an increased arterial stiffness in patients with MetS.[10,18-24] Increase in arterial stiffness is, indeed, an important indicator of vascular ageing;[25] however, these arterial changes are usually observed at a younger age in patients with MetS.[9,20,26-28] Prospective studies have demonstrated that impairment of arterial stiffness which increases with age is more rapid in patients with MetS compared to those without MetS.[11,18] Interestingly, precautions associated with this syndrome and the increased rate of arterial stiffness have been shown to be decreased.[29] As a result, the development of cardiovascular diseases may be prevented through the evaluation of arterial stiffness with easily accessible methods such as echocardiography and the implementation of necessary precautions in high risk patients.

Central obesity and blood pressure are not the only factors affecting arterial stiffness in patients with MetS. Impaired fibrinolysis and endothelial dysfunction have also been reported to play an important role on vascular structure and function.[30] The level of hs-CRP and fibrinogen have been shown to be increased in patients with MetS.[31] These inflammatory markers have been reported to independently affect arterial stiffness in hypertensive patients.[32-34] On the other hand, hs-CRP associated with MetS has been reported to further increase arterial stiffness.[35] In our study, hs-CRP was also shown to have a significant relationship with parameters of aortic stiffness.

The most important limitation of our study was the small number of patient in both groups. However, this was the first study which investigated the evaluation of arterial stiffness with echocardiography in patients with MetS. Another limitation was the inability of compare measurement of large artery stiffness by non-invasive methods, with methods such as analysis of pulse wave velocity which is considered as a golden standard. Changes in the elasticity of central arteries are known to be more important indicators for cardiovascular events compared to peripheral arteries. There are also reports in literature which state that diabetes mellitus and MetS mostly affect peripheral artery stiffness compared to central arteries.[25] These differences are mostly related with the investigated patient groups and the methods used for investigation. Large elastic arteries are suggested to be primarily affected taking into consideration the high cardiovascular morbidity and mortality observed in both cases. Although stiffness of large arteries alone were evaluated in our study, the higher peripheral pulse pressure in patients with MetS suggested that the peripheral arteries were also affected by a similar process.

In conclusion, patients with MetS have increased aortic stiffness evaluated by echocardiography. On the other hand, aortic stiffness has been shown to be associated with cardiovascular risk factors such as high systolic blood pressure, waist circumference, and hs-CRP. Arterial stiffness, which is an indicator of early vascular ageing, can easily be evaluated by transthoracic echocardiography, a non-invasive and easily accessible method and thereby cardiovascular diseases and mortality can be decreased through intensive treatment of risk factors.

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