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# Elastic Characteristics of The Aorta in Patients with A New Diagnosis of Metabolic Syndrome

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**ABSTRACT**

Metabolic syndrome (MS) is a known risk factor of cardiovascular disease. However, it is not identified whether MS made alterations in the elasticity of the aorta in the early period before significant atherosclerosis occurred. The purpose of the study was to evaluate aortic elastic properties of patients who were newly diagnosed with MS.

The research was performed among 100 patients of newly diagnosed MS (49 males; mean age 46 ± 9 years) with normal sinus rhythm, and 55 cases without MS (29 males; mean age 45 ± 9 years), matched by age . All participants underwent comprehensive physical and cardiological examination, biochemical examination, anthropological measurement and echocardiography.

Aortic diameter change was significantly lower in MS group compared to control group (0.014 ± 0.04 vs 0.25 ± 0.1, p <0.01), aortic stiffness was significantly higher in the MS group (10.65 ± 4.52 vs 5.7 ± 2.42, p<0.01) compared to the age-matched control group. Multiple regression analysis shows that there is an independent relationship with each of the age, body mass index, HDL cholesterol and systolic blood pressure.

Aortic stiffness index was higher in newly diagnosed MS patients compared to the control group. The vascular system can be affected even without diabetes, hypertension, hyperlipidemia, and coronary artery disease, which is excluded by history and noninvasive evaluation.

**Keywords:** Metabolic syndrome, aorta, vascular stiffness, compliance

## Introduction

Metabolic syndrome (MS) is a combination of atherosclerotic risk factors that increase the incidence of cardiovascular risk, including hypertension, impaired glucose tolerance, hyperlipidemia, and abdominal obesity (1-3). The effect of cardiovascular risk factors on vessels has been the subject of many studies. Stiffness of the wall was observed as a result of structural changes made by these risk factors in large vessels. Especially in stiffness studies in large vessels, this process has been found to directly affect cardiovascular morbidity and mortality (4).

Aortic stiffness is arterial rigidity which is loss of widening capacity of the aorta caused by elastic tissue loss. In most studies examining stiffness in the aorta, the pulse wave velocity (PWV) measured by noninvasive or invasive methods was used as the stiffness index (5). Even if the pulse wave recording in PWV measurement is done with Doppler, the measurement of the distance travelled by this wave is a big problem. The need for invasive and angiographic methods for the exact measurement of this distance makes it challenging to use PWV practically. In this regard, aortic strain and stiffness values, which are calculated based on echocardiographic aortic diameter and sphygmomanometric blood pressure measurements, have been proposed (6). These non-invasively obtained parameters have been shown to be similar to those obtained invasively (7). Different indexes are used for an accurate evaluation of arterial stiffness in terms of stretchability, aortic tension, compliance and stiffness index (8).

In this study, we investigated whether there was a change in the aortic elastic properties of patients who

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were newly diagnosed with MS without a history of coronary artery disease, diabetes mellitus, dyslipidemia and hypertension.

## Material and methods

**Patients:** The study was conducted with 100 patients with a new diagnosis of MS, with normal sinus rhythm (49 males; mean age 46 ± 9 years), and age-matched 55 patients in a control group without MS (29 males; mean age 45 ± 9 years). Patients with coronary artery disease, diabetes mellitus, left ventricular dysfunction, heart valve disease, uncontrolled hypertension, or those treated for hypertension, those treated for hyperlipidemia, and patients with acute myocardial infarction in their history were excluded from the study. An exercise stress test was applied to exclude coronary artery disease in all contributors and the control group, and patients with normal results were included. The study was approved by the institutional ethical board and informed written consent was acquired from all contributors.

**Diagnostic Criteria in Metabolic Syndrome:** The diagnosis of MS was made with the International Diabetes Federation (IDF) diagnostic criteria (9). Accordingly, two or more of the subsequent criteria must be found together with abdominal obesity (waist perimeter >94 cm in men, >80 cm in women): i. High Triglyceride level (150mg / dl), ii. Low high-density lipoprotein cholesterol (HDL-C) level (<40 mg/dl in male), iii. High blood pressure (presence of systolic pressure >130 mmHg or diastolic pressure >85 mmHg or any antihypertensive agent). iv. Increased fasting blood sugar level (100mg / dl).

**Biochemical Analysis:** Patients were asked to starve 12 hours before taking blood samples. Complete enzymatic technique was performed to measure serum total cholesterol and triglyceride levels. Triglycerides (TG), total cholesterol and HDL-C levels were measured for all patients by using an automated chemistry analyzer (Siemens Advia 2400 Chemistry System, Siemens Diagnostic, Tarrytown, NY, USA). The low-density-lipoprotein cholesterol (LDL-C) estimation was calculated using the Friedewald equation: LDL-C = Total Cholesterol - HDL-C - (TG/5). Plasma glucose level was measured by the glucose oxidase technique.

**Anthropometric Measurements:** The weight of each contributor was measured by a SECA 861 self-calibrating digital scale (Saint Paul, MI, USA) with an exactness of up to 100 g. All contributors were requested to take off their clothes and shoes previously. Height readings were performed using a SECA anthropometer. In an upright position, contributors height were measured without shoes on. Then, the flat headpiece was located on top. The contributors' weight and height were measured twice. Two measurements average was taken into consideration. On the flat plane at utmost buttocks protuberance the waist circumference was surveyed, which in the front came across with the symphysis pubis. SECA measuring tape was used to measure the waist circumference which was flexible, inextensible with an accuracy of 0,5 mm. Body mass index was obtained by dividing the weight by the square of the height (kg / m2). Blood pressures were recorded with a sphygmomanometer using a standard sleeve (wrapping 80% of forearm at least). Before the measurements were taken, contributors were rested 15 min in the supine position at a temperature of 21–22 °C in a quiet room. The average of two systolic and diastolic blood pressure readings was recorded for analysis.

**Echocardiography:** All echocardiographic analyzes were performed on the day the patient was included in the study using a two-dimensional, M-mode, PW Doppler and tissue Doppler equipped Vivid 5 echocardiography device and a 2.5 MHz phase transducer. Echocardiographic examination was applied to all contributors by the same cardiologist. Measurements were performed from the long axis of the parasternal window and 4. and 5. cavities from the apical window, when the patients were lie down to the left lateral decubitus position. The readings were acquired by calculating 3 consecutive measurements' average at 25 cm/sec, accompanied by simultaneous electrocardiographic recording in expiration.

In apical 4 cavity imaging, by placing the pulsed wave Doppler sample volume to the endpoints of the mitral valve the transmitral flow sample was recorded. Early diastolic (E) and late diastolic (A) peak flows were measured. E/A ratios and E wave deceleration time (EDT) were calculated.

Echocardiographic analyzes were evaluated for three consecutive cycles and their averages were recorded digitally. M-mode measurements were made in accordance with the recent American Echocardiography Association recommendations (10). In the parasternal long axis, proximal aortic image is obtained clearly in the position where the right coronary and non-coronary valve movements are monitored together.

M-mode bar was placed to aortic region 3 cm above the coaptation line of the aortic valve in the parasternal long-axis image. End diastolic and systolic diameters of the aortic tract were measured. Systolic and diastolic diameters were made from the section where the aortic trace had the maximum forward movement, and from the region matching the R peak

**Table 1.** Basic Clinical, Biochemical and Anthropometric Findings of Patients

| | Metabolic Syndrome Group (n = 100) | Control Group (n = 55) | P value |
|---|---|---|---|
| Age (mean ± years) | 46.29 ± 9.07 | 45.54 ± 9.08 | 0.62 |
| Male (%) | 49 (49) | 29 (52) | 0.65 |
| Height (cm) | 165 ± 11 | 164 ± 9 | 0.83 |
| Weight (kg) | 86.32 ± 11.23 | 75.82 ± 14.68 | <0.001 |
| Body mass index (kg / m2) | 31.78 ± 4.44 | 27.81 ± 4.60 | <0.001 |
| Waist circumference (cm) | 102.61 ± 8.51 | 92.43 ± 13.37 | <0.001 |
| Glucose (mg / dl) | 103.88 ± 15.71 | 92.61 ± 6.57 | <0.001 |
| High density lipoprotein (mg / dl) | 43.01 ± 11.61 | 54.32 ± 10.26 | <0.001 |
| Triglyceride (mg / dl) | 200.58 ± 87.26 | 128.01 ± 36.65 | <0.001 |
| Systolic blood Pressure (mmhg) | 139.16 ± 12.91 | 127.20 ± 11.57 | <0.001 |
| Diastolic blood Pressure (mmhg) | 83.51 ± 9.22 | 78.41 ± 8.61 | <0.001 |

of the ECG.

The following formulas were used for aortic stiffness measurements according to the literature (11):

- Aortic compliance (cm/mmHg) = (Systolic diameter - Diastolic diameter) / (Systolic pressure - Diastolic pressure);
- Aortic strain% = 100 X (Systolic diameter - Diastolic diameter) / Diastolic diameter;
- Aortic stiffness index = Logarithm [100 x (Systolic pressure / Diastolic pressure) / Aortic strain]

Statistical Analysis: IBM SPSS Statistics version 12.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Numerical data are expressed as mean ± standard deviation and categorical variables as percentages. In numerical data, unpaired t test was performed, and categorical data were analyzed with chi-square test. Univariate and multivariable lineer regression analysis was used to determine the more extensive relationship between aortic stiffness and MS subcomponents. Results are presented as beta coefficients and their corresponding 95% confidence intervals (CI). P value <0.05 was considered statistically significant.

## Results

Clinical biochemical and anthropometric information of both groups are shown in Table 1. There was no statistically difference between the groups in terms of age and gender. As expected in the MS group, BMI and waist circumference were higher, triglyceride levels, high fasting blood sugars and HDL-cholesterol values are lower than expected. MS group had significantly higher mean diastolic and systolic blood pressures than the control group.

When the groups are compared in terms of conventional echocardiography parameters; while no significant difference was detected in left ventricular diameters between the groups, the septum thickness was lower in the control group (p <0.001). In terms of posterior wall thickness, no statistical difference was found between the groups. As expected, lower left ventricular mass was observed in the control group than the MS group (Table 2).

When aortic strain (5.32 ± 1.56 vs 9.34 ± 2.34, p <0.001), aortic compliance (0.0028 ± 0.001, vs 0.0055 ± 0.0014, p <0.001) and aortic stiffness (10.65 ± 4.52 vs 5.7 ± 2.42, p<0,001) are examined between two groups, all parameters in the MS group was significantly higher compared to the age-matched control group (Table 3).

**Table 2.** Comparison of Conventional Echocardiographic Parameters of Groups

| | Metabolic Syndrome Group (n = 100) | Control Group (n = 55) | P value |
|---|---|---|---|
| LVEDD (cm) | 4.52 ± 0.23 | 4.43 ± 0.25 | 0.71 |
| LVESD (cm) | 2.68 ± 0.18 | 2.66 ± 0.21 | 0.80 |
| IVS (cm) | 0.93 ± 0.13 | 0.76 ± 0.06 | <0.001 |
| PW (cm) | 0.90 ± 0.11 | 0.86 ± 0.04 | 0.67 |
| E wave (cm/sn) | 63.66 ± 5.35 | 76.88 ± 4.54 | <0.001 |
| A wave (cm/sn) | 78.81 ± 9.32 | 56.34 ± 4.6 | <0.001 |
| E/A<1 (%) | 85 (85) | 3 (1,5) | <0.001 |

LVEDD: Left ventricular end-diastolic dimension, LVESD: Left ventricular end-systolic diamention, IVS: interventricular septum thickness, PW: left ventricular (LV) posterior wall thickness

**Table 3.** Aortic Strain, Compliance and Stiffness Values of The Study Group

| | Metabolic Syndrome Group (n = 100) | Control Group (n = 55) | P value |
|---|---|---|---|
| Aortic Diameter Change (cm) | 0.14 ± 0.04 | 0.25 ± 0.1 | <0.001 |
| Aortic Strain (%) | 5.32 ± 1.56 | 9.34 ± 2.34 | <0.001 |
| Aortic Compliance, (cm/mmHg) | 0.0028 ± 0.001 | 0.0055 ± 0.0014 | <0.001 |
| Aortic Stiffness index | 10.65 ± 4.52 | 5.7 ± 2.42 | <0.001 |

In univariate analysis, outcome variable ascending aortic stiffness was used to determine whether there was any relationship between physiological and clinical plausible variables. Covariates related to ascending aortic stiffness further examined by multivariate analysis. Multivariable lineer regression test (Table 4) showed that there was a separate independent relationship with aortic stiffness and age (0.199; CI 0.155, 0.243; p=0.002) , waist circumference (0.315; CI 0.260, 0.370; p<0.01), HDL (-0.203; CI -0.236, -0.170; p=0.001) and systolic blood pressure (0.581; CI 0.503, 0.654; p<0.001). There was a negative beta value between HDL and aortic stiffness showing that stiffness decreases as HDL values increase.

## Discussion

As a result of this research, we determined that aortic stiffness may increase even in newly diagnosed MS patients who applied to the clinic for the first time and did not receive medication for any of the MS components.

MS is a set of atherosclerotic risk factors and has a close relationship with an increased incidence of cardiovascular events (3). There is a linear correlation between the number of criteria forming MS and mortality (12). The close relationship of MS with vascular stiffness in large arteries suggests that this may be the mechanism to explain the negative effect of this condition on the cardiovascular system. In fact, there is a correlation between some MS components such as hypertension, hyperglycemia, visceral adipose tissue and aortic vascular stiffness (13,14,15).

Today, it is obvious that there may be a link between loss of elasticity in major arteries and cardiovascular adverse events (16). In the Framingham Cardiology study, over 20 years of monitoring, increased pulse pressure, which is an indication of large vessel wall stiffness, and has been shown to increase coronary artery disease risk in the middle and older age group, who had no clinical coronary artery disease (17).

To date, there are papers investigating the relationship between the entire MS and arterial wall stiffness. It has been shown that there is a relationship between carotid artery distensibility and some of the MS

**Table 4.** Evaluation of Independent Variables Related To Ascending Aortic Stiffness Using Univariate and Multivariable Lineer Regression Models

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Beta Coefficient | Confidence İnterval | P | Beta Coefficient | Confidence İnterval | P |
| Age | 0.205 | 0.141, 0.268 | 0.008 | 0.199 | 0.155, 0.243 | 0.002 |
| Waist circumference | 0.324 | 0.243, 0.406 | <0.001 | 0.315 | 0.260, 0.370 | <0.001 |
| High density lipoprotein | -0.227 | -0.268, -0.186 | <0.001 | -0.203 | -0.236, -0.170 | 0.001 |
| Systolic blood pressure | 0.643 | 0.545, 0.741 | <0.001 | 0.581 | 0.503, 0.654 | <0.001 |

components and some of its subgroups on the group of 180 healthy middle-aged women without diabetes mellitus complaints (16). The relationship between MS and aortic pulse wave has been shown in the study conducted on Japanese middle-aged men, and also its relationship with the stiffness of carotid artery has been shown by long-term Baltimore study on aging (17,18). In these studies, aortic stiffness was not measured echocardiographically, and the use of these methods in routine practice is limited, but in our study, aortic stiffness could be calculated using noninvasive methods. It has been previously shown that these parameters obtained noninvasively are similar to those obtained invasively (7).

A number of mechanisms can be considered for the relationship between aortic vessel stiffness and MS. The mechanisms of the effects of hypertension and diabetes increasing aortic stiffness are not fully known. While the stress caused by high pressure in the vascular wall in hypertension causes structural changes in the vascular wall causing atherosclerosis; impaired glucose metabolism may lead to vascular matrix proteins glycation and the accumulation of these substances on the elastin fibers and collagen and in the vascular wall (18,19). In our study, 43% of the patient group had a blood pressure of stage I or above and only 4% of the patient groups fasting blood sugar was above 126 mg/dl, suggesting that the aortic wall stress and accumulated glycosylated substances alone cannot be responsible for increased stiffness.

In the multiple regression analysis, the absence of an independent relationship between fasting blood sugar and aortic stiffness is probably due to the low fasting blood sugar values of the patient group. In the same analysis, an independent relationship was found between systolic blood pressure and stiffness.

In addition, visceral adipose tissue may cause the release of leptin and similar peptides, causing changes in arterial wall motion (20,21). In our study, a serious independent relationship was found between visceral fattening determined by waist circumference measurement and aortic stiffness. This shows us that visceral fat is important rather than total body fat on aortic vessel stiffness, compatible with Schillaci et al. study (22).

The most important limitation in our study is that the aortic elasticity belongs to the aorta, that this region is also affected by coronary blood flow and only the history and exercise stress test is used to exclude coronary artery disease. The low number of study population is another limitation to be noted.

In conclusion, even in patients with newly diagnosed MS without coronary artery disease diagnosis, aortic stiffness can be seen. In patients with MS, the vascular system may be affected even before evident coronary artery disease, diabetes mellitus, hypertension or dyslipidemia develops.

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