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ASSOCIATION OF INCREASED AORTIC PULSE PRESSURE AND AORTIC PULSATILITY WITH CORONARY ARTERY DISEASE AND METABOLIC SYNDROME

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ABSTRACT:

Purpose: Aortic pulse pressure and aortic pulsatility are reported to predict cardiovascular risk. Here, we aimed to investigate the association of coronary artery disease and metabolic syndrome with central blood pressure values, which are more reliable than peripheral pressure measurements.

Materials and Methods: Two hundred and four consecutive patients (129 men, mean age 56.3±11.1) who underwent cardiac catheterization for the first time were included in the study. All subjects also underwent biochemical investigations and hemodynamic measurements. Hemodynamic parameters like systolic and diastolic aortic pressures were measured during cardiac catheterization using a fluid-filled system in the ascending aorta. Parameters like aortic pulsatility and aortic pulse pressure were calculated and compared between four groups: I) control group, who did not have coronary artery disease or metabolic syndrome, II) patient group who had only metabolic syndrome, III) patient group who had only coronary artery disease, IV) patient group who had both coronary artery disease and metabolic syndrome.

Results: Hemodynamic parameters like aortic diastolic blood pressure did not differ between the groups. Aortic pulsatility was significantly higher in all 3 patient groups compared to the control group ($p< 0.001$). This difference was most significant in patient group IV ($p= 0.010$). Aortic pulse pressure was highest in group II, followed by group III and group IV, compared to the control group ($p=0.003$).

Conclusion: Our findings clearly show that high aortic pulsatility and aortic pulse pressure, which are evidence of atherosclerosis, are encountered as frequently or even more frequently in metabolic syndrome as they are in coronary artery disease. Secondly we demonstrated a close relationship between angiographically confirmed coronary artery disease and increased aortic pulse pressure, similar to previous reports.

Key Words: Aortic Pulsatility, Aortic Pulse Pressure, Coronary Artery Disease, Metabolic Syndrome

ARTMIS AORTİK NABIZ BASINCI VE AORTİK PULSATİLİTENİN KORONER ARTER HASTALIĞI VE METABOLİK SENDROM İLE OLAN İLİSKİSİ

ÖZ:

Amaç: Aortik nabız basıncı ve aortik pulsatilitenin kardiyovasküler riske dair bilgi verdiği bildirilmistir. Biz bu çalısmada periferik kan basıncı değerlerinden daha güvenilir olan santral kan basıncı değerlerinin, koroner arter hastalığı ve metabolik sendrom ile olan birlikteliğini ortaya koymayı amaçladık.

Gereç ve Yöntem: Çalısmaya ilk defa kardiyak kateterizasyon islemi uygulanan ardısık 204 hasta (129 erkek, 56.3± 11.1) dahil edildi. Çalısmaya alınan bütün hastalardan biyokimyasal parametreler çalısıldı, demografik verileri kaydedildi ve hemodinamik değerleri ölçüldü. Hastaların sistolik, diastolik ve ortalama aortik kan basıncı ölçümleri asendan aortadan sıvı dolu sistem kullanılarak ölçüldü. Aortik pulsatilite, santral aortik nabız basıncının, ortalama aortik kan basıncına oranı olarak hesaplanmıstır. Hastalar dört gruba ayrılmıstır. 1) koroner arter hastalığı ve metabolik sendromun olmadığı hastalar (kontrol grubu) 2) sadece metabolik sendromu olan hastalar 3) sadece koroner arter hastalığı olan hastalar 4) hem metabolik sendromun hem de koroner arter hastalığının olduğu hastalar.

Bulgular: Gruplar arasında aortik diyastolik kan basıncı değerleri yönünden fark izlenmedi. Aortik pulsatilite kontrol grubuna kıyasla diğer 3 grupta da belirgin sekilde yüksek saptandı ($p=0.003$).

Sonuç: Bulgularımız göstermistir ki aterosklerozun göstergesi olan aortik pulsatilite ve santral aortik nabız basıncı, metabolik sendromlu hastalarda, koroner arter hastaları kadar sık, hatta daha sıktır. Anjiografik koroner arter hastarıyla aortik nabız basıncı arasındaki göstermis olduğumuz bu iliski daha önceki çalısmalarda da vurgulanmıstır.

Anahtar Kelimeler: Aortik Pulsatilite, Aortik Nabız Basıncı, Koroner Arter Hastalığı, Metabolik Sendrom

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INTRODUCTION

Increased brachial pulse pressure (PP) is known to be associated with increased atherosclerosis as well as higher cardiovascular and coronary mortality. Recently, use of intraaortic measurement techniques has led to the development of new terminology such as aortic pulse pressure (APP) and aortic pulsatility (AP) and as a result central blood pressure is suggested to be more important than peripheral blood pressure in predicting cardiovascular risk.

Components of metabolic syndrome (MS) have been previously shown to be related to higher coronary artery disease (CAD), cardiovascular mortality, and atherosclerosis. However, the association of intraaortic measurements and MS has been targeted in very few studies.

In the present study, we investigated the association of angiographically confirmed CAD and MS with central blood pressure values, which are more reliable than peripheral pressure measurements.

Subjects and methods

Subjects. Two hundred and four consecutive patients (129 men [63.2%], mean age 56.3±11.1) who underwent cardiac catheterization for the first time between January 2008 and May 2008 were included in the study. The inclusion criteria were I) admission with typical angina pectoris and angiographically confirmed CAD or II) silent myocardial ischemia diagnosed with noninvasive investigations (myocardial perfusion scintigraphy or cardiovascular exercise test) and angiographically confirmed CAD. For comparisons, four groups were formed: I) control group, composed of subjects who underwent coronary angiography in the same time window and did not have MS or CAD, II) patient group who had only MS, III) patient group who had only CAD, IV) patient group who had both MS and CAD. For all groups, the exclusion criteria were the presence of peripheral arterial disease, valvular heart disease, congenital heart disease, atrial fibrillation, creatinine value >1.4 mg/dl, unregulated hypertension, chronic obstructive pulmonary disease, and liver disease.

MATERIALS AND METHODS

Coronary angiography. Coronary angiography using the Judkins technique and left ventriculography investigations were performed on digitalized coronary angiography equipment. All angiographical images were assessed by[2]

experienced cardiologists, and vascular stenosis >50% in at least one of left main, left anterior descending, the left circumflex, and the right coronary arteries were accepted as CAD. Degree of stenosis was calculated using images in 2 planes.

Measurement of hemodynamic parameters. Hemodynamic parameters were measured during cardiac catheterization while the patients were in the supine position. Aortic blood pressure was obtained using a fluid-filled system (pigtail catheter) in the ascending aorta. Systolic and diastolic aortic pressures were written from pressure tracings at a paper speed of 25 mm/s (Figure 1). For analytical purposes, in each patient an average of 10-12 blood pressure curves were used. Mean aortic pressure was calculated using the following formula:

$$\frac{\text{Aortic systolic blood pressure}}{3} + \frac{2\ \text{Aortic diastolic blood pressure}}{3}$$

APP was calculated as follows:

Aortic systolic blood pressure – aortic diastolic blood pressure

Aortic pulsatility (fractional PP) was defined as follows 6:

$$\frac{\text{Aortic PP}}{\text{Mean aortic blood pressure}}$$

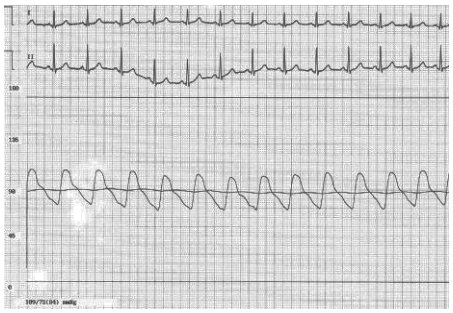

Figure 1. Aortic blood pressure tracing showing ECG and systolic (109 mmHg), diastolic (72 mmHg), and mean arterial (84 mmHg) pressures of one patient.

Definition of metabolic syndrome

Criteria in the diagnosis of MS were adopted from the guidelines of the International Diabetes Federation, published in 2005. According to this definition, the presence of at least two of the below mentioned criteria along with abdominal obesity, which is measured by waist circumference (for men >94 cm, for women >80 cm), was required:

1- Triglycerides level ≥150 mg/dL

2- HDL level <40 mg/dL in men, <50 mg/dL in women

3- Blood pressure ≥130/85 mmHg or treatment with antihypertensive therapy

4- Fasting blood glucose ≥100 mg/dL

Biochemical investigations. All biochemical investigations were performed after 12 hours of fasting. Blood glucose level was measured by the glucose oxidase technique, whereas in measuring serum total cholesterol and triglycerides levels the complete enzymatic technique was used. Moreover, LDL level was calculated using the formula suggested by Friedewald and colleagues.[7]

Measurement of waist circumference. Waist circumference measurements were made by passing through the narrowest point in the plane of the anterior superior iliac spine and 12th ribs while the patients were standing during expiration of tidal volume.

All patients included in the study gave informed consent and the study was approved by the local ethics committee.

Statistical analysis. For comparisons four groups were formed: I) control group, who did not have MS or CAD, II) patient group who had only MS, III) patient group who had only CAD, IV) patient group who had both MS and CAD.

The data were analyzed using SPSS 11.5 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, United States). Continuous variables were presented as mean values ± SD or median (in ranges), whereas nominal variables were in numbers and percentages. Distribution of continuous variables was assessed by the Shapiro Wilk test.

To evaluate differences in age and waist circumference between the four groups we used analysis of variance for repeated measures. Differences in serum lipid levels and hemodynamic parameters were analyzed by the Kruskal Wallis test. When a significant difference was found we used post hoc Tukey or Kruskal Wallis multiple comparison tests to determine group/groups leading to significance. Comparisons were performed using Pearson's chi-square test for qualitative data. $p<0.05$ was considered the level of significance.

RESULTS

There were 37, 18, 84, and 65 patients in groups I, II, III, and IV, respectively. Mean age of the subjects in the control group was significantly lower than that in all other three groups ($p<0.001$). The predominance of female patients was significant in the MS group (group II) and male patients were predominant in groups who had CAD (groups III and IV) ($p<0.001$). Incidence of diabetes mellitus and hypertension was higher in groups with MS, as expected ($p<0.001$). Mean waist circumference and mean lipid values were also significantly higher in the groups with MS ($p<0.001$). Medications, except for the statin and fibrate group, did not differ significantly between the groups. Demographic, clinical, and biochemical features of all 4 groups are presented in Table 1.

Table 1. Demographic, clinical, and biochemical features of the four groups.

Variables	**CAD (-) MS (-) (n=37)**	**CAD (-) MS (+) (n=18)**	**CAD (+) MS (-) (n=84)**	**CAD (+) MS (+) (n=65)**	**p**
Age (y, mean±SD)	48.0±10.93	56.7±10.19d	57.1±11.24d	59.8±8.80d	<0.001a
Sex (%)					<0.001b
Women	10 (27.0)	16 (88.9)	18 (21.4)e	31 (47.7)d,e,f	
Men	27 (73.0)	2 (11.1)	66 (78.6)	34 (52.3)	
DM (%)	5 (13.5)	13 (72.3)d	14 (16.7)e	52 (80.0)d,f	<0.001b
HT (%)	8 (21.6)	14 (77.8)d	20 (23.8)e	49 (75.4)d,f	<0.001b
Smoking (%)	20 (54.1)	3 (16.7)d	52 (61.9)e	25 (38.5)f	0,987b
WC (cm, mean±SD)	90.6±13.04	106.9±9.68d	91.1±10.24e	100.9±9.92d	<0.001a
Lipid parameters (mg/dL, mean, min-max)					
Triglycerides	117 (57-314)	181 (104-302)d	118.5 (50-303)e	158 (42-293)d,f	<0.001c
HDL	40 (23-60)	42 (22-67)	41 (23-67)	40 (23-78)	0.915c
LDL	114 (78-205)	101 (60-191)	120 (52-221)	123 (64-190)	0.265c
Medications (%)	34 (91.8)	17 (94.4)	78 (92.8)	63 (96.9)	0.682b
Antiplatelets	24 (64.8)	12 (66.6)	70 (83.3)	44 (67.7)	0.067b
B-blockers	19 (51.4)	12 (66.7)	59 (70.2)	46 (70.8)	0.181b
ACE Inh	8 (21.6)	9 (50.0)d	65 (77.4)d,e	41 (63.1)d	<0.001b
Statins/fibrates					
Calcium antagonists	4 (10.8)	3 (16.6)	11 (13.0)	10 (15.3)	0.902b

CAD, coronary artery disease; MS, metabolic syndrome; DM, diabetes mellitus; HT, hypertension; WC, waist circumference; HDL, high density lipoprotein; LDL, low density lipoprotein; ACE inh, angiotensin converting enzyme inhibitors.
Data are given as mean±SD, minimum-maximum or n, %.
a One-way ANOVA. b Pearson's chi-square test. c Kruskal Wallis test.
d Statistically significant difference between CAD (-) and MS (-) groups ($p<0.05$).
e Statistically significant difference between CAD (-) and MS (+) groups ($p<0.05$).
f Statistically significant difference between CAD (+) and MS (-) groups ($p<0.05$).

Hemodynamic parameters like heart rate and aortic diastolic blood pressure did not differ significantly between the four groups (Table 2).

Table 2. Heart rate and diastolic aortic blood pressure in the four groups.

Variables Mean, min-max	**CAD (-) MS (-)**	**CAD (-) MS (+)**	**CAD (+) MS (-)**	**CAD (+) MS (+)**	**p[a]**
Heart rate	66 (49-110)	74.5 (55-104)	70.5 (52-113)	74 (53-110)	0.145
DAP	64 (38-99)	71.5 (35-106)	61 (18-106)	63 (28-123)	0.142

DAP, diastolic aortic pressure, CAD, coronary artery disease; MS, metabolic syndrome
a Kruskal Wallis test.

AP was significantly higher in all 3 patient groups compared to the control group ($p< 0.001$) (Table 3) (Figure 3). This difference was most significant in patient group IV, who had both CAD and MS ($p= 0.010$). APP was highest in the MS only group, followed by the CAD only group and the both CAD and MS group, and this was significantly higher when compared to the control group ($p=0.003$) (Figure 2). Findings regarding hemodynamic parameters are given in Table 3.

Table 3. Association of aortic PP and AP with CAD and MS.

	Groups	**CAD (-)**	**CAD (+)**	**All**	**p[a]**	**p[b]**	**p[c]**	**p[d]**
APP	MS (-)	46 (25-93)	54.5 (24-98)	49 (24-98)	0.013			
	MS (+)	65.5(33-99)	53 (14-135)	58 (14-135)	0.177	<0.001	0.472	0.016
	All	49 (25-99)	54 (14-135)		0.233			
AP	MS (-)	0.60 (0.28-0.98)	0.65 (0.33-1.36)	0.63(0.28-1.36)	0.007			
	MS (+)	0.73 (0.38-1.17)	0.75(0.50-1.25)	0.75 (0.38-1.25)	0.744	0.008	0.010	<0.001
	All	0.61 (0.28-1.17)	0.69(0.33-1.36)		0.007			

APP, aortic pulse pressure; AP, Aortic pulsatility; CAD, coronary artery disease; MS, metabolic syndrome.
Data are given as mean±SD, minimum-maximum or n, %.
a Comparisons between CAD (-) and CAD (+)
b Comparisons between MS (-) and MS (+) groups in CAD (-) group
c Comparisons between MS (-) and MS (+) groups in CAD (+) group
d Comparisons between MS (-) and MS (+) groups in all group

Figures 2 and 3 show the distribution of APP and AP in CAD and MS.

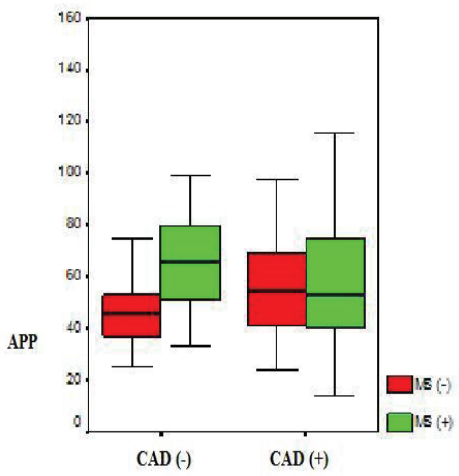

Figure 2. Association of CAD and MS with APP.

CAD, coronary artery disease; MS, metabolic syndrome; APP, aortic pulse pressure

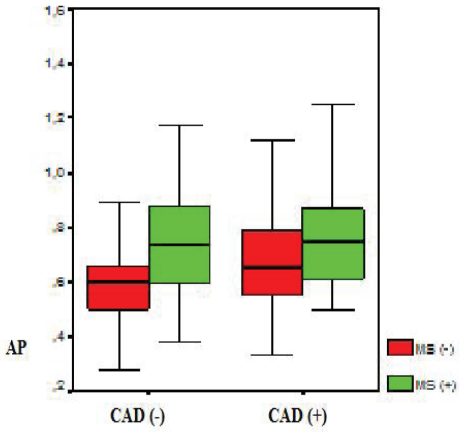

Figure 3. Association of CAD and MS with AP.

AP, Aortic pulsatility; CAD, coronary artery disease; MS, metabolic syndrome

DISCUSSION

In our study, the main finding was increased AP and APP in CAD and MS patients since we showed that AP and APP was higher in the MS only group, the CAD only group, and the both CAD and MS group in comparison to the control group, and for AP this difference was more prominent in group IV (patients with both CAD and MS).

PP is the difference between systolic and diastolic pressures, and in atherosclerosis it generally seems more valuable than increased mean blood pressure.[8] Measurement of PP either through a sphingomanometric procedure using the brachial artery (peripheral PP) or by an invasive catheter procedure in the ascending aorta (APP) is possible. Increased peripheral PP was previously reported to predict cardiovascular mortality independently by Benetos and colleagues in 1998. In the Framingham Heart study increased PP was found to be a predictor of large vessel atherosclerosis and to coexist with CAD in middle and old age. It is widely accepted that PP measured by central procedures is physiologically lower than that measured by peripheral procedures. Although measurement of peripheral PP is noninvasive, it is not as sensitive as an invasive catheter procedure. Any structural or functional change in any peripheral artery may lead to false measurement of blood pressure. In the CAFE study published in 2006, all antihypertensive medications were shown to decrease peripheral PP by similar degrees but APP by different degrees, suggesting the presence of different clinical effects. AP of the ascending aorta, which is fractional PP, is parallel to APP and seems a reliable way, as reported, to predict restenosis in CAD after percutaneous coronary intervention (PCI). However, it is not replicated in studies using brachial PP. Therefore, the invasive method is a reliable but indirect technique to predict atherosclerosis. Although in the case of high atherosclerosis load PP increases, probably, high AP and increased PP are also responsible for vascular endothelial dysfunction and the tendency of thrombosis to develop.

Given those previous reports, we suggest that we showed the load of atherosclerosis reliably in our patients. In CAD, increased APP and AP is an expected and well-known result. However, an important finding of our study is the demonstration of an independent relationship of APP and AP in the ascending aorta with MS, suggesting a possible underlying mechanism of cardiovascular events in MS. MS, which is a cluster of atherosclerotic risk factors, is highly related to a higher incidence of cardiovascular events. The substantial correlation of clinically matched criteria of MS with mortality as well as the close relationship between MS and large vessel atherosclerosis indirectly show a negative effect on the cardiovascular system. Components of MS like hypertension,4 hyperglycemia, and visceral adipose tissue are also related to aortic atherosclerosis. As far as we know, to date, there have been few studies investigating MS and findings of atherosclerosis manifested by invasive methods. Distensibility of the carotid artery was shown to be associated with components of MS in 180 non-diabetic middle age women. MS is known to be associated with aortic PP and carotid artery atherosclerosis.Our study also suggests that indirect evidence of atherosclerosis is as high as or even higher than in CAD. Increased PP is also one of the possible casual factors of atherosclerosis in MS since increased blood pressure may increase vascular shear stress and lead to vascular endothelial dysfunction. However, impaired glucose metabolism was shown to cause glycation of matrix proteins and loss of vascular elasticity. In addition, visceral fat deposition lead to secretion of leptins and similar peptides inducing change in arterial wall motion. Therefore, increased APP may be an indirect predictor of atherosclerosis in MS in those cases.

Although we obtained important results, our study has some major drawbacks. Firstly, since we included only symptomatic patients or patients with positive noninvasive tests, we cannot generalize for all types of CAD patients. The heterogeneous distribution of basal demographic features may have affected hemodynamic parameters and may have caused bias. Lack of investigation of insulin resistance is another weakness of our study. Although a reliable method, central blood pressure changes are an indirect way to predict atherosclerosis. Therefore, further studies using direct methods like intravascular ultrasonographic evaluation of vascular lipid load may be more valuable. However, our findings clearly show that high AP as well as APP, which are evidence of atherosclerosis, are encountered as frequently as or even more frequently in MS compared to in CAD and secondly we also demonstrated a close relationship between angiographically confirmed CAD and increased APP, similar to previous reports.

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