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Original Article

Augmentation index and aortic pulse wave velocity in patients with abdominal aortic aneurysms

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Abstract: Background: Abdominal aortic aneurysm (AAA) is a severe disease that can prove fatal. Factors such as advanced age, male gender, family history and cigarette use increase the risk of AAA. These factors associated with AAA development also increase arterial stiffness. Aortic pulse-wave velocity (PWV) was measured as an index of aortic stiffness. The heart rate-corrected augmentation index (AIx@75) was estimated as a composite marker of wave reflections and arterial stiffness. Elevated arterial stiffness increases the risk of development of cardiovascular events and impairs cardiovascular functions. In this study we investigated whether arterial stiffness rises in patients with AAA by measuring aortic PWV and AIx@75 parameters. Methods: Eighteen patients with AAA (age 69 ± 4 years) and 20 patients with no aneurysm (age 66 ± 6) were included. AAA was diagnosed using computerized tomography. Arterial stiffness was measured non-invasively in all patients using a SphygmoCor device. Aortic PWV and AIx@75 were used as arterial stiffness parameters. Results: There was no significant difference between the two groups in terms of demographic characteristics. AIx@75 (33.2 ± 8.9 vs 25.1 ± 7.8, p=0.008) and aortic PWV (14.8 ± 4.9 vs 10.0 ± 1.7, p=0.002) were significantly elevated in the AAA group compared to the control group. Conclusion: Elevated AIx@75 and aortic PWV shows that arterial stiffness increases in patients with AAA.

Keywords: Aortic aneurysm, augmentation index, pulse wave velocity

Introduction

Abdominal aortic aneurysm (AAA) is defined as an aortic diameter greater than 3 mm and is generally seen in the infrarenal region [1]. It is seen in 4%-9% of patients aged 60 and above [2, 3]. Although AAA generally follows an asymptomatic course, it can lead to serious complications, such as aneurysm rupture [4]. Advanced age, male gender, a family history of AAA, cigarette use and hyperlipidemia are the best known risk factors for AAA [5, 6]. Atherosclerosis and weakening of the aortic wall as a result of a change in arterial wall structural components are responsible for the pathogenesis of AAA.

Arterial stiffness, an important mechanical property of the arterial system, is evaluated by using the heart rate-corrected augmentation index (AIx@75) and aortic pulse wave velocity (PWV) [7]. Elevated stiffness increases the development of cardiovascular events in hypertensive patients and normal individuals [7, 8]. Damage in the structural elements of the arterial wall, a change in vascular smooth muscle tonus, chronic low-grade inflammation and endothelial dysfunction are among the factors leading to increased stiffness [7, 8]. A change in arterial wall components is involved in the pathogenesis of AAA and arterial stiffness. This study investigated whether the arterial stiffness parameters AIx@75 and aortic PWV rise in patients with AAA.

Materials and methods

Study population

Eighteen patients with AAA, determined using computerized tomography (CT) applying to the Karadeniz Technical University Faculty of Medicine Cardiology Department and Coronary-Vascular Surgery Department clinic between 01.11.2009 and 30.09.2010 were enrolled

after routine evaluation. Twenty age and gender-matched patients who underwent CT due to possible non-cardiovascular disease and were found normal used for control group. Study and control group patients' clinical and laboratory findings were recorded. Arterial stiffness parameters were then measured non-invasively.

Patients with non-sinus rhythm, malign hypertension (>180/110), connective tissue disease, valvular and congenital heart disease, peripheral artery disease, coronary artery disease, chronic obstructive pulmonary disease, a history of aortic or heart surgery, known aortic wall disease (Marfan, etc.), active infectious or inflammatory disease or known malignity were excluded. Approval was obtained from the Karadeniz Technical University Faculty of Medicine ethical committee and written consent was obtained from the entire study group.

Computerized tomography

CT was performed using a 16-slice CT scanner (Somatom Sensation, Siemens Medical Systems, Erlangen Germany). 130 mL intravenous contrast (Ultravist (Iopromide), 300 mg I/mL, Bayer Schering Pharma AG, Berlin, Germany) was injected at a rate of 3 mL/s. Images were obtained at the portal venous phase with a 60 s delay after the start of injection. The scan protocol was as follows; slice collimation, 16 x 1.5 mm; rotation time, 0.5 s; table feed/rotation, 18.0 mm; Kv 120; mAs 160. Images were reconstructed with a slice thickness of 2 mm. Examinations were performed from the level of the diaphragm to the iliac crest for the upper abdomen and to the symphysis pubis for the whole abdomen. Patients with an abdominal aorta diameter greater than 3 mm were defined as AAA [1].

Measurement of pulse wave velocity

Aortic PWV was determined using the foot-to-foot method using the SphygmoCor system (AtCor Medical, Sydney, Australia) [7]. Consecutive registrations of the carotid and femoral artery pulse waves are electrocardiogram gated and the time shift between the appearance of wave at the first and the second sites can thus be calculated. The distance between the two sites was measured on the body surface to determine aortic PWV in meters/second (m/s). We used the total distance between the carotid and femoral sites of measurement. The average of measurements over a period of 8 s (9-10 cardiac cycles) was calculated after the exclusion of extreme values.

Pressure waveform analysis

Assessment of arterial wall properties and wave reflection characteristics was performed non-invasively using the SphygmoCor system. Radial artery pressure waveforms were recorded at the wrist, using applanation tonometry with a high-fidelity micromanometer (Millar Instruments, Houston, TX). After 20 sequential waveforms had been acquired and averaged, a validated generalized mathematical transfer function was used to synthesize the corresponding central aortic pressure waveform [9]. Augmentation index (AIx) and augmentation pressure (AP) were derived from this using pressure waveform analysis [7]. The merging point of the incident and the reflected wave (the inflection point) was identified on the generated aortic pressure waveform. AP was the maximum systolic blood pressure minus pressure at the inflection point. AIx was defined as the AP divided by pulse pressure and expressed as a percentage. Greater AIx values indicate increased wave reflection from the periphery or earlier return of the reflected wave as a result of increased PWV (attributable to increased arterial stiffness). AIx is dependent upon the elastic properties of the entire arterial tree (elastic and muscular arteries). In addition, because AIx is influenced by heart rate, an index normalized for a heart rate of 75 bpm was used in accordance with Wilkinson et al. [10]. Only high-quality recordings, defined as an in-device quality index of >80% (derived from an algorithm including average pulse height, pulse height variation, diastolic variation, and the maximum rate of rise of the peripheral waveform), and acceptable curves on visual inspection, were included in the analysis. All measurements were performed by the same person with the patient in the supine position in a quiet temperature-controlled room after a brief rest period of at least 5 min.

Statistical analyses

Continuous data are expressed as the mean ± SD. Comparison between two groups was performed using the unpaired t test or nonparametric means test (Mann-Whitney U test) for

Table 1. Baseline characteristics and arterial stiffness indices of study population

	AAA (n:18)	Control (n:20)	p
Age (years)	69 ± 4	66 ± 6	NS
Female Sex (%)	38.9	35	NS
Hypertension (%)	66.7	60	NS
Diabetes Mellitus (%)	11.1	15	NS
Cigarettes (%)	22.2	30	NS
Body Mass Index (kg/m^2)	26.7 ± 4.4	29.5 ± 4.4	NS
Heart rate (bpm)	62.1 ± 10.8	65.3 ± 9.1	NS
Systolic BP (mmHg)	127± 12	125 ± 16	NS
DiastolicBP (mmHg)	78 ± 7	75 ± 12	NS
LDL Cholesterol (mg/dl)	132 ± 41	131 ± 34	NS
HDL Cholesterol (mg/dl)	42 ± 8	46 ± 9	NS
Total Cholesterol (mg/dl)	202 ± 58	200 ± 41	NS
Triglyceride (mg/dl)	153 ± 53	150 ± 85	NS
Aspirin (%)	22.2	0	NS
Beta-blocker (%)	61.1	5	0.001
ACE inhibitors (%)	0	25	0.04
ARB (%)	55.6	25	NS
Statin (%)	11.1	0	NS
Calcium channel blocker (%)	11.1	0	NS

AAA: Abdominal aortic aneurysms, BP: Blood Pressure, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, ACE: Angiotensin converting enzym, ARB: Angiotesin receptor blocker, NS: Non significant.

Table 2. Arterial stiffness indices of study population

	AAA (n:18)	Control (n:20)	p
Central Aortic Pressure			
Systolic Pressure (mmHg)	114 ± 29	110 ± 28	NS
Diastolic Pressure (mmHg)	79 ± 7	76 ± 12	NS
Aortic PWV (m/s)	14.8 ± 4.9	10.0 ± 1.7	0.002
AIx@75 (%)	33.2 ± 8.9	25.1 ± 7.8	0.008

AAA: Abdominal aortic aneurysms, PWV: Pulse wave velocity, AIx@75: Heart rate corrected augmentation index, NS: Non significant.

continuous variables, and using the Fisher exact test for categoric variables. A *p* value of $p<0.05$ was considered statistically significant. Statistical analyses were performed using SPSS software (Version 16.0, SPSS Inc., Chicago, IL).

Results

Study group basal, clinical and demographic characteristics are shown in **Table 1**. The groups were similar in terms of age, gender, hypertension, diabetes mellitus, body mass index, heart rate, systolic and diastolic blood pressure, lipid levels and cigarette use. Aneurysm diameter in the AAA group was 5.5 ± 1.18 cm. Infrarenal abdominal aortic dimater of the control group was 2.2 ± 0.3 cm. B blocker use was higher in the AAA group and angiotensin converting enzyme (ACE) inhibitors use in the control group. Arterial stiffness parameters are shown in **Table 2**. AIx@75 (33.2 ± 8.9 vs 25.1 ± 7.8 p=0.008) and aortic PWV (14.8 ± 4.9 vs 10.0 ± 1.7 p=0.002) values were significantly higher in the AAA group compared to the control group (**Table 2**).

Discussion

AIx@75 and aortic PWV values were significantly elevated in the AAA group compared to the control group in this study. These results show that arterial stiffness rises in AAA patients.

There have to date been various studies investigating the mechanical features of the arterial system in AAA patients. In one newly published study, PWV in the abdominal aneurysm region was determined using in-vivo pulse wave imaging to be significantly higher in two AAA patients than in the control group [11]. Xiong et al. found that local stiffness increased and distensibility decreased in the aneurysmal segment [12]. Ruegg et al. investigated 114 AAA patients and determined similar AIx in patients with rapid progression and slow progression [13]. However, AIx values were not compared with the control group in that study. Shingu et al. reported that AIx values in 21 patients with thoracic aortic aneurysm determined using ultrasound from the carotid artery were significantly high compared to the control group [14].

Local measurement of aortic distensibility using ultrasonography and magnetic resonance imaging, regional measurement of PWV by tonometer and Doppler probes, and the systemic measurement of arterial stiffness by central waveform shape analysis are the main methods of assessing arterial stiffness [7]. We did not evaluate local elastic properties in the aneurysmal segment in this study. We employed the regional and systemic method. Local arte-

rial stiffness can be measured directly at various sites along the arterial tree and can provide information about local mechanics [7]. Problems in characterizing arterial stiffness arise from the complexity of the arterial system, because the physical and chemical wall properties may be different at different points. Therefore, we used regional and systemic methods. The measurement of aortic PWV and AIx@75 is generally regarded as the most simple, non-invasive, reproducible model method for determining arterial stiffness [7]. Aortic PWV and AIx@75 have also been used in epidemiological studies demonstrating the predictive value of aortic stiffness for CV events [7].

Various risk factors for AAA have been reported. The best known of these are advanced age, male gender, a family history of AAA, cigarette use and hyperlipidemia [5, 15]. These factors lay the foundations for atherosclerosis or aneurysm by causing structural changes in the aortic wall. Most of these factors also increase stiffness. A rise in arterial stiffness also increases systolic blood pressure (afterload) by accelerating wave reflection [16]. This rise may lead to structural changes in both the myocardium and the arterial system. Increased arterial stiffness may therefore play a role in the development or progression of AAA.

Hertzer determined an annual coronary event mortality of 1.9% in a patient group with no coronary artery disease before AAA resection over 6-11 years' monitoring [17]. On the basis of that study, the third report of the National Cholesterol Education Program regarded the risk of AAA and coronary artery disease as comparable [18]. Arterial stiffness is well known to increase the risk of coronary event [19]. Elevated arterial stiffness in AAA patients may be responsible for this increase in coronary events.

Limitations of study

The main limitation of this study is the low patient number. These data need to be confirmed with studies involving larger patient numbers. In addition, drug use was not equal between the groups. Vasodilating drugs such as nitrates, ACE inhibitors, decrease wave reflections and AIx [20]. ACE inhibitors were used much more commonly in control group. On the other hand use of B blockers was higher in the AAA group. B blockers have little or no effect on PWV or wave reflections, but they enhance AIx by reductions in heart rate [21]. We therefore used AIx@75, an index normalized for a heart rate of 75 bpm.

In conclusion, increased AIx@75 and aortic PWV in AAA patients shows that arterial stiffness is elevated in these patients. Increased arterial stiffness may be responsible for the pathogenesis of AAA or the increased coronary events seen in these patients.

Disclosure of conflict of interest

None.

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