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Assessment of the relationship between the central aortic pressure and ankylosing spondylitis

Ocena zależności między ciśnieniem centralnym w aorcie a zesztywniającym zapaleniem stawów kręgosłupa

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Abstract

Introduction. Ankylosing spondylitis (AS) is a chronic inflammatory disease with an unknown etiology that belongs to the group of spondyloarthropathies. Patients with AS have an increased cardiovascular mortality but the reason is controversial. Central aortic pressure (CAP) is defined as the blood pressure in the aortic root and can be measured non-invasively via arteriography. Inflammation in the aortic root, which also causes aortic regurgitation in late stages of AS, possibly causes increased levels of central aortic pressure and this may explain the increased mortality rates from cardiovascular events in patients with AS. We investigated the CAP levels in patients with AS compared to healthy age- and sex-matched control group in this novel study.

Material and methods. This is an observational case-control study composed of 30 patients with ankylosing spondylitis without conventional cardiovascular risk factors (such as known diabetes, hypertension, and smoking) or heart failure, peripheral or coronary artery disease. The peripheral blood pressures and CAP measurements were obtained with 'arteriograph' (TensioMed, Budapest, Hungary).Pulse wave velocity (PWV), peripheral and central augmentation index (pAIx and cAIx) and systolic central aortic pressure (sCAP) of both the AS and control group were compared.

Results. There was no statistically significant difference between the groups for pAIx, cAIx, PWV or PP. Patient with AS had higher sCAP values but there wasn't any statistically significant difference for sCAP.

Conclusion. Our objective was to investigate the relationship between the AS and sCAP. There was an increase in sCAP in AS group compared to controls. But this was not statistically significant. This result can be due to the small population size and should be verified in larger population.

Key words: central aortic pressure, ankylosing spondylitis, arterial stiffness

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Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease with an unknown etiology that belongs to the group of spondyloarthropathies (SpA). Patients with AS have an increased cardiovascular mortality [1]. The reason is controversial but it has been explained by increased cardiovascular risk factors in those patient group, inflammation, the non-steroid anti-inflammatory drugs (NSAIDs) or other drugs they have been taking that effect myocardium [2].

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Sclerosing inflammation (aortitis) in AS can effect aortic root and aortic valves and causes aortic regurgitation [3]. Aortic regurgitation is seen in 6–10% of all patients [4].

Central aortic pressure (CAP) is defined as the blood pressure in the aortic root. CAP is superior to peripheral arterial pressure for the prediction of cardiovascular events [5–7]. CAP can be measured by pressure sensors directly from the aorta or by catheters. Because this method is invasive and has the potential of complication, it is not used in daily practice. But CAP can be measured by the brachial cuff that can calculate pulse waves with software. These tools can provide measurements of CAP that are not different from those obtained with invasive methods [6].

According to our prespecified hypothesis this inflammation in the aortic root possibly causes increased levels of central aortic pressure and this may explain the increased mortality rates from cardiovascular events in patients with AS. The aim of this novel study is to investigate the CAP levels in patients with AS without conventional risk factors for atherosclerosis (hypertension, diabetes mellitus, smoking) or heart failure, peripheral/coronary artery disease, compared to healthy age and sex matched control group. This article is written according to the STROBE statement checklist for case-control studies.

Materials and methods

This study was approved by the ethical committee of Afyon Kocatepe University Hospital. Informed consent was taken from all patients and controls.

This was an observational case-control study composed of 30 patients with ankylosing spondylitis (mean age: 35.5 ± 12.1) without conventional cardiovascular risk factors (such as known diabetes, hypertension, and smoking) or heart failure, peripheral or coronary artery disease who were treated at the Afyon Kocatepe University Hospital, Department of Physical Therapy and Rehabilitation and Department of Cardiology compared with 30 healthy subjects (mean age: 34.9 ± 12.9) with similar age and sex.

The patients were recruited between May 2014 and November 2015. The patients had been previously diagnosed with AS in the physical therapy and rehabilitation clinic with modified New York Criteria [8]. The past medical history data of the patients were confirmed based on previous patient records and laboratory results. The previous laboratory data were also investigated to rule out diabetes/ /impaired fasting glucose or lipid profile disorders. Because CRP and/or erythrocyte sedimentation rate are accepted as risk factors, patients with elevated CRP and/or erythrocyte sedimentation rate were not accepted to the study [9]. Also, because TNF-alfa inhibitors can affect target organ damage [10], patients on TNF-alfa inhibitors were excluded from the study. Inclusion and exclusion criteria of patients are listed in Table 1.

Table 1. Inclusion and exclusion criteria

Inclusion criteria for the patient group
1. Patients with ankylosing spondylitis, diagnosed according to modified New York Criteria
2. Patients older than 18 years
Exclusion criteria for the patient group
1. Patients with chronic hypertension
2. Patients with known diabetes
3. Patients with known coronary artery disease
4. Patients with known peripheral artery disease
5. Patients with heart failure
6. Smokers
7. Patients with increased CRP/sedimentation rate
8. Patients on TNF-alfa inhibitors

The echocardiographic evaluation consisted of M-mode, 2-D and colored Doppler echocardiographic evaluation completed by one echocardiographer. Parasternal long axis, parasternal short axis and apical four chamber views were obtained. Philips HD 1 XE (Germany, 2008) echocardiography tool with 3.5 MHz transducer was used for the study.

The peripheral blood pressures and CAP measurements were obtained with 'arteriograph' (TensioMed, Budapest, Hungary). This tool consists of a brachial cuff that measures the brachial peripheral arterial pressures automatically. It drops the pressure of the cuff to measure pulse waves and can define dicrotic notch and transmits the findings to the computer by infrared waves. We measured the true aortic length (estimated by the jugulum–symphysis distance) of the subjects by tape and enable the value to the software. Then, the software of the device calculated pulse wave velocity (PWV), peripheral and central augmentation index (pAIx and cAIx) and systolic central aortic pressure (sCAP). The patients were warned about not drinking coffee or tea before the measurement and they rested for 5 minutes in a quiet room. All measurements were completed while patients were lying in supine position.

The data obtained in the study were analyzed with SPSS (Statistical Package for Social Sciences for Windows) for statistical evaluation. Categorical variables are shown as percentage. Kolmogorov-Smirnov test was used to check whether those variables fit to normal distribution or not. The difference between the groups of variables with normal distribution was calculated with t-test and the difference between the groups of variables that did not fit to normal distribution was calculated with Mann-Whitney U test. The results are shown in 95% confidence interval and significance is accepted as $p < 0.05$.

Table 2. The demographic and clinical characteristics of the study groups

Variables	Patient (n = 30)	Control (n = 30)	p
Age [years]	35.5 ± 12.15	34.9 ± 12.91	0.06
Height [cm]	168.5 ± 7.71	171.9 ± 8.12	0.09
Weight [kg]	76.5 ± 12.59	74.6 ± 11.40	0.57
Body mass ındex [kg/m^2]	26.95 ± 4.81	25.15 ± 3.32	0.10
Systolic blood pressure [mm Hg]	132.1 (171–108)	122 (111–162)	0.60
Diastolic blood pressure [mm Hg]	81.2 ± 9.60	76.4 ± 9.0	0.052
Mean arterial blood pressure [mm Hg]	97.5 (83–122)	90.5 (75–121)	0.022
Heart rate [beat/min]	78.90 ± 11.70	70.10 ± 7.50	0.01

Table 3. The echocardiographic values in the patient and control groups

Variables	Patient (n = 30)	Control (n = 30)	p
Left ventricle diastolic diameter [mm]	44.4 ± 6.8	43.2 ± 6.7	0.069
Left ventricle systolic diameter [mm]	24.2 ± 4.2	24.1 ± 4.8	0.133
Ejection fraction [%]	61 ± 5.4	60.1 ± 6.2	0.070
Interventricular septum diameter [mm]	10.4 ± 1.7	10.1 ± 1.6	0.112
Posterior wall diameter [mm]	10.3 ± 1.8	10.2 ± 1.9	0.114
Left atrium length [mm]	38.7 ± 2.2	38.2 ± 2.1	0.151
Aortic root diameter [mm]	29.8 ± 3.5	30.1 ± 3.4	0.092

Table 4. Arterial stiffness parameters in the patient and control groups

Variables	Patient (n = 30)	Control (n = 30)	p
Pulse pressure [mm Hg]	50.5 (35-48)	46 (36–81)	0.52
Peripheral augmentation ındex	–53.7 (–80.9–25.1)	–61.75 (–84.1–25.2)	0.42
Central augmentation ındex	10.45 (–3.3–50.3)	6.35 (–5–50.4)	0.37
Pulse wave velocity [m/s]	7.5 ± 1.2	7.3 ± 1.4	0.64
Systolic central aortic pressure [mm Hg]	116.35 (97.3–166)	107.95 (90–161.7)	0.056

Results

Thirty patients with AS and 30 healthy subjects were recruited for the study. The demographic and clinical characteristics of the study groups are shown in Table 2. There was no statistical difference between the groups for age, sex, body mass index (BMI), systolic or diastolic pressures. But there was statistical difference for heart rate and mean arterial pressure (p = 0.01 and p = 0.022, respectively).

The M-mode, 2D echocardiographic parameters of the patient and control group were within normal limits. The echocardiographic values are shown in Table 3. Also 2 patients in the patient group had mild aortic regurgitation.

Arterial stiffness parameters were evaluated and there was no statistically significant difference between the groups for pAIx, cAIx, PWV or PP. Patients with AS had higher sCAP values but there wasn't any statistically significant difference for sCAP (Table 4).

Discussion

Coronary artery disease is the leading cause of death and unfortunately there is no effective single test to screen patients before the symptoms onset. So the risk factors for coronary artery disease are very important to diagnose patients. Patients with AS have an increased cardiovascular mortality rate. But the cause or the mechanism cannot be perfectly explained. It is also important because the cardiologists still cannot be sure whether to screen patients with AS for possible future cardiac events, except valvular heart disease. Should they screen asymptomatic AS patients for coronary artery disease?

Our objective was to investigate the relationship between the AS and sCAP. There was an increase in sCAP in AS group compared to controls. But this was not statistically significant. This result can be due to the small population size and should be verified in larger population.

Also our prespecified hypothesis was the inflammation in aortic root in patients with AS can cause an increased CAP. And the increased CAP may explain the increased cardiovascular mortality in patients with AS. The aortic regurgitation is usually a late sign in patients with AS and it is due to the inflammation/aortitis [3]. But our population consisted of AS patients without moderate or severe aortic regurgitation. So it is possible to conclude that the inflammation in aorta of our AS population wasn't severe. It might be possible to find a significant increase in CAP in patients with AS compared to controls, if this study was designed with a larger population. It will also be vise to divide the AS group at least at 2 as with moderate/severe aortic regurgitation and normal/mild aortic regurgitation.

Similar studies also showed increased arterial stiffness parameters. We investigated PWV, AIx and PP. But there wasn't any increase in arterial stiffness. This can be explained in two different ways. One of the hypothesis to explain the increased cardiovascular mortality was the increased risk factors in patients with AS. Our study population consisted of patients without known cardiovascular risk factors. The first possible explanation for not finding a significant difference for arterial stiffness parameters in this study is the fact that the AS group population was chosen from patients without known cardiovascular risk factors. The second explanation for not finding a significant difference for arterial stiffness parameters in this study is limited sample size.

On the other hand, the study group was relatively young for AS, which is mostly seen in the third decade of life. So it can be stated that the study group consisted of patients with short disease duration and eventually short time to cause target organ damage. Considering the results of the arterial stiffness, parameters were not significantly different in both groups and the short disease duration may not be enough to cause target organ damage. So, a long term follow-up study design will be needed to show which arterial stiffness parameter is changing first. If the CAP is worsening first, it can be stated that the aortic inflammation is the beginning of the cardiovascular problems.

Overall, our study did not show a relationship between AS and increased sCAP. But this idea was never evaluated before and insignificant increase in CAP in patients with AS is still important for future studies. We believe it could explain a very important mechanism for increased cardiovascular mortality in patients with AS but the study should be designed with larger population.

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Disclosures

The authors declare that there is no conflict of interest.

Streszczenie

Wstęp. Zesztywniające zapalenie stawów kręgosłupa (AS) to przewlekła choroba zapalna o nieznanej etiologii należąca do spondyloartropatii. U chorych z AS obserwuje się zwiększoną śmiertelność sercowo-naczyniową, jednak przyczyny tego zjawiska nie są znane. Ciśnienie centralne w aorcie (CAP) jest definiowane jako ciśnienie krwi w korzeniu aorty. Możliwy jest nieinwazyjny pomiar CAP metodą arteriografii. Zapalenie w obrębie korzenia aorty, będące również przyczyną niedomykalności w późnym stadium AS, może powodować wzrost ciśnienia centralnego w aorcie, co może tłumaczyć zwiększoną śmiertelność z powodu zdarzeń sercowo-naczyniowych w grupie chorych z AS. Autorzy zbadali wartości CAP u chorych z AS w porównaniu z wartościami uzyskanymi w grupie kontrolnej złożonej ze zdrowych osób dobranych pod względem wieku i płci.

Materiał i metody. Tym obserwacyjnym badaniem kliniczno-kontrolnym objęto 30 chorych z AS, u których nie występowały tradycyjne czynniki ryzyka sercowo-naczyniowego (rozpoznana cukrzyca, nadciśnienie tętnicze, palenie tytoniu), niewydolność serca, choroba tętnic obwodowych ani choroba wieńcowa. Wartości obwodowego ciśnienia tętniczego i pomiary CAP uzyskano metodą arteriografii (TensioMed, Budapeszt, Węgry). Porównano wartości następujących parametrów w grupie AS i grupie kontrolnej: szybkość fali tętna (PWV), wskaźnik wzmocnienia ciśnienia obwodowego i centralnego (pAIx, cAIx) i skurczowe ciśnienie centralne w aorcie (sCAP).

Wyniki. Nie stwierdzono statystycznie istotnych różnic między grupami pod względem wartości pAIx, cAIx, PWV ani PP. U chorych z AS zaobserwowano wyższe wartości sCAP, jednak różnice nie osiągnęły poziomu istotności statystycznej.

Wnioski. Badanie przeprowadzono w celu zbadania zależności między AS a sCAP. W grupie chorych na AS wartości sCAP były wyższe niż w grupie kontrolnej. Jednak różnice nie były istotne statystycznie. Wyniki te mogą być spowodowane niewielką liczebnością badanej populacji i powinny zostać zweryfikowane w badaniu z większą liczbą uczestników.

Słowa kluczowe: ciśnienie centralne w aorcie, zesztywniające zapalenie stawów kręgosłupa, sztywność tętnic

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