Original Article / *Klinik Çalışma - Araştırma*

The relationship between the inflammatory markers and arterial distensibility in patients with sarcoidosis

Sarkoidozlu Hastalarda İnflamasyon Belirteçleri ile Arteriyel Genişleyebilirlik Arasındaki İlişki

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Objectives: Sarcoidosis is a multisystem disorder of unknown etiology and is characterized by noncaseating granulomas in organs. The purpose of this study was to test the hypothesis that chronic inflammation may impair arterial function and lead to an increase in arterial pulse wave velocity (PWV) in patients with sarcoidosis.

Patients and Methods: We recruited 19 patients (12 women, 7 men) with sarcoidosis, and 19 sex-matched healthy controls. Aortic PWV was determined by using an automatic device, the Complior Colson (France), which allowed on-line pulse wave recording and automatic calculation of PWV.

Results: The PWV, glucose, LDL cholesterol, uric acid, high-sensitivity C-reactive protein and erythrocyte sedimentation rate were higher in patients with sarcoidosis than in control subjects (p=0.04, p=0.03, p=0.02, p=0.008, p=0.04, p=0.005, respectively). We found significant correlation between PWV and age (p=0.001, r=0.52), body mass index (p=0.01, r=0.40), systolic blood pressure (p<0.001, r=0.71), diastolic blood pressure (p<0.001, r=0.63), mean blood pressure (p<0.001, r=0.68), pulse pressure (p<0.001, r=0.63), pulse transit time (p<0.001, r=-0.90), total cholesterol (p=0.002, r=0.47) and LDL cholesterol (p=0.001, r=0.51).

Conclusion: The carotid-femoral (aortic) PWV was higher in patients with sarcoidosis than in control subjects. PWV is influenced by total cholesterol, LDL cholesterol, age, body-mass index and blood pressure level.

Key words: Pulse wave velocity; arterial stiffness; sarcoidosis; blood pressure; inflammation.

Amaç: Sarkoidoz, etyolojisi bilinmeyen, organlarda nonkazeöz granulomlarla karakterize bir multisistem hastalıktır. Bu çalışmanın amacı, kronik inflamasyon arteriyel fonksiyonları bozabilir ve sarkoidozlu hastalarda arteriyel nabız dalga hızında (NDH) artışa yol açabilir hipotezini araştırmaktır.

Hastalar ve Yöntemler: Çalışmaya toplam 19 sarkoidozlu hasta (12 kadın, 7 erkek) ve benzer cinsiyette 19 sağlıklı kişiden oluşan kontrol grubu dahil edildi. Aortik NDH, otomatik online nabız dalga kaydına ve nabız dalga hızının otomatik hesaplanmasına imkan veren Complior cihazı (Fransa) kullanılarak hesaplandı.

Bulgular: NDH, glükoz, LDL kolesterol, ürik asit, yüksek duyarlıklı C-reaktif protein ve eritrosit sedimentasyon hızı sarkoidozlu hasta grubunda kontrol grubuna göre daha yüksekti (sırası ile p=0.04, p=0.03, p=0.02, p=0.008, p=0.04, p=0.005). NDH ile yaş (p=0.001, r=0.52), vücut kitle indeksi (p=0.01, r=0.40), sistolik kan basıncı (p<0.001, r=0.71), diastolik kan basıncı (p<0.001, r=0.63), ortalama kan basıncı (p<0.001, r=0.68), nabız basıncı (p<0.001, r=0.63), nabız dalgası ilerleme zamanı (p<0.001, r=-0.90), total kolesterol (p=0.002, r=0.47) ve LDL kolesterol (p=0.001, r=0.51) arasında anlamlı korelasyon saptandı.

Sonuç: Karotis-femoral (aortik) NDH sarkoidozlu hastalarda kontrollere göre daha yüksekti. NDH total kolesterol, LDL kolesterol, yaş, vücut kitle indeksi ve kan basıncı seviyelerinden etkilenmektedir.

Anahtar sözcükler: Nabız dalga hızı; arteriyel sertlik; sarkoidoz; kan basıncı; inflamasyon.

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Sarcoidosis is a multisystem disorder of unknown etiology and is characterized by noncaseating granulomas in organs.[1-4] The reported prevalence of sarcoidosis varies from 9 to 64 per 100.000 population (in Sweden and in Italy, respectively).[5] Although sarcoidosis is known to be a systemic inflammatory disease which can affect virtually any organ system, it unusually complicates vascular involvement. However in fact, several authors have suggested that vasculitis may be a feature of sarcoidosis; but, such reports are usually related to cutaneous vasculitis.[6,7] In one study, granulomatous angiitis and microangiopathy were reported in 30.8% of sarcoidosis patients with cutaneous involvement.[6] On the other hand, reports on the coexistence of sarcoidosis and vasculitis had led us to think the possibility that sarcoidosis and vasculitis may be etiopathogenetically related. In this regard we may suggest that an immunological link exists between vasculitis and sarcoidosis whether it is due to an autoimmune reaction or not. But until now, it has not been confirmed, however, whether vasculitis is a true manifestation of the disease or an occasional, incidentally concurring abnormality. On the other hand, systemic inflammation is an important factor in the initiation or the progression of atherosclerosis.[8] Damage to the arterial wall due to inflammation causes decreased arterial distensibility and compliance.[9] Noninvasive ultrasound techniques are used to evaluate vascular system and cardiovascular condition. One such technique, pulse wave velocity (PWV), which is defined as arterial pulse's velocity of moving along the vessel wall, as an indicator of arterial elasticity, correlates inflammation markers.[10,11] Pulse wave velocity is inversely correlated with arterial distensibility and relative arterial compliance.[11,13] Inflammation may impair arterial function and lead to an increase in arterial PWV. None of the studies carried out so far investigated the relationship between sarcoidosis and arterial inflammation by using an indicator of arterial elasticity, which, in fact, is an actual, reliable and easily implemented method in the assessment of arterial distensibility. Therefore, this study aims to investigate arterial stiffness using carotid-femoral (aortic) PWV measurements in patients with sarcoidosis.

PATIENTS AND METHODS

Study Population

We recruited 19 patients (12 women, 7 men; sarcoidosis duration: 124.8±85.9 years) with sarcoidosis, and 19 sex-matched controls. All subjects gave their consent for inclusion in the study. The investigation conforms with the principles outlined in the Decleration of Helsinki. The study was approved by the ethics committee of Cerrahpaşa Medical Faculty of the University of Istanbul. The database contained full records of patients with sarcoidosis which include demographic features, presenting clinical features, initial diagnosis methods and the age at the initial diagnosis for each patient. The diagnosis of sarcoidosis was established when clinicoradiological findings were supported by histological evidence of non-caseating epithelioid cell granulomas in one or more organ system and exclusion of other disorders known to cause granulomatous disease. Mycobacteria and fungus were excluded by tissue stainings and cultures.[2] It is clearly reported that clinical activity is assessed on the basis of onset, worsening, or persistence of sarcoidosis of symptoms or signs directly related to sarcoidosis.[2] Thereby, clinical activity was assessed in each patient according to this published criteria of WASOG (World Association of Sarcoidosis and Other Granulomatous Diseases) / ATS (American Thoracic Society) / ERS (European Respiratory Society) mentioned above.

Chest radiographs were classified as Scadding described: stage 0, normal chest radiographic findings; stage 1, bilateral hilar lymphadenopathy (BHL) alone; stage 2, BHL with pulmonary infiltrates; stage 3, pulmonary infiltrates only; stage 4, pulmonary fibrosis/fibrocystic parenchymal changes.[1] Löfgren's syndrome was defined as the association of erythema nodosum with BHL and/or right paratracheal lymphadenopathy with or without pulmonary infiltrates.

Exclusion criteria were a previous myocardial infarction, constrictive, restrictrive or dilated cardiomyopathy, heart failure, valvular heart disease, diabetes mellitus, peripheral arterial disease, cerebrovascular disease, renal failure, liver failure, anemia (Hct < 30%), electrocardiogram (ECG) conduction and rhythm disorders, systolic blood pressure > 140 mmHg, diastolic blood pressure > 90 mmHg, body mass index (≥ 35 kg/m^2) and waist/hip ratio ≥ 1 cm. None of our patients was treated at the time of examination with antihypertensive drugs, statins or immunosupressive drugs. None of them were smoking or had alcohol.

Body mass index and waist - hip ratio measurements

Body mass index (kg/m^2) were calculated dividing body weight in kilograms by square of body height in metres. The circumference of waist divided by circumference of hipgave the waist - hip ratios.

Blood pressure and carotid-femoral (aortic) pulse wave velocity measurements

Clinic blood pressure was measured using a mercury sphygmomanometer with a cuff appropriate to the arm circumference in patients at rest for 20 min (Korotkoff phase I for systolic blood pressure and V for diastolic blood pressure).

Pulse pressure = systolic blood pressure – diastolic blood pressure

Mean blood pressure = (systolic blood pressure + 2 x diastolic blood pressure) / 3

Arterial stiffness was assessed by automatic carotid-femoral PWV measurement using the Complior Colson device whose technical characteristics have been described.[13] Pulse wave velocity along the aorta can be measured by using two ultrasound or strain-gauge transducers [noninvasively using a TY-306 Fukuda pressure sensitive transducer (Fukuda, Tokyo, Japan)] fixed transcutaneously over the course of a pair of arteries separated by a known distance: the femoral and right common carotid arteries. During preprocessing analysis the gain of each waveform was adjusted to obtain an equal signal for the two wave forms. During PWV measurements, after pulse waveforms of sufficient quality were recorded, the digitization process was initiated by the operator and automatic calculation of the time delay between two upstrokes was started. Measurement was repeated over 10 different cardiac cycles, and the mean value was used for the final analysis. Pulse wave velocity is calculated from measurements of pulse transit time and the distance (the distance between two recording sites is measured on the surface of body in meters) travelled by the pulse between two recording sites, according to the following formula:

PWV (m/s) = distance (m) / transit time (s)

Laboratory measurements

Overnight-fasting blood samples were taken in the morning from the antecubital vein. All samples were centrifuged at 2000 rpm for 15 min and stored at −20°C until further analysis (approximately 30 days). Biochemical parameters (serum fasting blood glucose, albumin, uric acid, urea, creatinine, triglyceride, total cholesterol, HDL, LDL and VLDL cholesterol) were measured using an Abbott C8000 (Abbott, Japan) automatic analyzer. Glucose was analyzed using the hexokinase method. The methods were Bromocresol pruple for albumin and uricase method for uric acid. Total cholesterol, HDL, LDL, VLDL cholesterol and triglycerides were measured by enzymatic methods in all samples. Creatinine and urea levels were measured by the Jaffé reaction and urease methods. Thyroid-stimulating hormone and insulin were measured with Immulite 2000 (DPC; LosAngeles, USA) by Chemiluminescent immunometric assay. Plasma level of homocysteine was determined by high performance liquid chromatography (HPLC) (by Agilent 1100 Series), coupled with fluorescence detector. Blood cell were counted on the HMX analyzer (Beckman Coulter, USA). Serum concentrations of high-sensitivity C-reactive protein (hs-CRP) were measured by the Behring BN II Nephelometer (Dade Behring, Malburg, Germany). Hs-CRP was expressed as milligram per liter. Serum oxidized LDL (oxLDL) concentrations were determined by a commercial enzyme-linked immunosorbent assay (ELISA) (Mercodia AB, Uppsala, Sweden). The ESR is measured using the Westergren method.

Table 1. Stage of the chest X-ray, duration and delayed diagnosis and Lofgren's Syndrome in patient with sarcoidosis

Pat.	Age	Chest X-ray	DD (months)	De-Di (months)	Löfgren's synd.
A.S	67	Stg1	312	0	
A.G	39	Stg1	144	0	+
N.B	57	Stg1	156	0	
H.B	44	Stg3	180	17	
M.E	35	Stg1	29	9	
S.K	43	Stg0	168	0	
H.D	63	Stg4	156	0	
O.P	48	Stg2	156	2	+
S.Ç	65	Stg2	168	2	
E.Ç	36	Stg1	25	0	+
N.D	53	Stg2	156	0	+
N.T	56	Stg1	60	4	
H.T	43	Stg2	288	1	
İ.S	34	Stg3	96	8	
H.C	43	Stg0	26	2	
Ç.G	37	Stg1	72	0	+
S.A	18	Stg1	1	0	
G.A	43	Stg1	144	1	+
A.P	29	Stg2	36	1	

Pat: Patient, DD: Duration of disease, De-Di: Delayed diagnosis, Syn: Syndrome, Stg: Stage.

Statistical analysis

Statistics were obtained using SPSS version 11.0. All the values were expressed as mean ± standard deviation. The obtained results were assessed by independent samples test. Correlations were calculated with the Pearson test. $P<0.05$ was considered significant.

RESULTS

Stage of the chest X-ray, duration and delayed diagnosis and Löfgren's syndrome in patients with sarcoidosis were shown in Table 1. Initial demographic features, initial symptoms and signs and diagnostic procedures in patients with sarcoidosis were shown in Table 2. The PWV, glucose, LDL cholesterol, uric acide, hs-CRP and erythrocyte sedimentation rate were higher in patients with sarcoidosis than in control subjects ($p=0.04$, $p=0.03$, $p=0.02$, $p=0.008$, $p=0.04$, $p=0.005$, respectively) (Table 3). We found significant correlation between PWV and age ($p=0.001$, $r=0.52$), body mass index ($p=0.01$, $r=0.40$), systolic blood pressure ($p<0.001$, $r=0.71$), diastolic blood pressure ($p<0.001$, $r=0.63$), mean blood pressure ($p<0.001$, $r=0.68$), pulse pressure ($p<0.001$, $r=0.63$), pulse transit time (it is inversely related to the arterial PWV to the classical formula in figure 1) ($p<0.001$, $r=-0.90$), total cholesterol ($p=0.002$, $r=0.47$) and LDL cholesterol ($p=0.001$, $r=0.51$) (Table 4).

Table 2. Initial demographic features, initial symptoms and signs and diagnostic procedures in patients with sarcoidosis

	A.Ş	A.G	N.B	H.B	M.E	S.K	H.D	O.P	SÇ	E.Ç	N.D	N.T	H.T	İ.S	H.C	Ç.G	S.A	G.A	A.P
SK	+	+				+		+				+			+	+			
RS		+	+	+	+		+	+		+		+	+	+		+	+	+	+
SLNE				+		+									+			+	
EN			+			+			+		+	+					+		+
CS				+	+					+	+		+			+	+	+	+
A/A			+		+	+				+	+	+					+		+
OI										+	+		+						
HM								+											
P/LGI																			
P																			
S																			
M											+	+		+					
HI																			
MCF																			
LS																			
CD																			
PPDA	+	+	+	+	–	–	+	+	+	+	+	+	+	–	+	–	–	+	+
HBI										+									
Hca	+																		
LP						+													
L/P																			
N	+																		
SI												+							
HCuria													+						
TB			+		+		+	+	+		+		+				+		+
MC		+			+				+	+				+		+			
SLNB						+			+										
PLNB				+											+			+	
SB	+	+				+		+				+			+	+			
SSB																			
SNB																			
Kveim B	+																		
LB								+											

SK: Skin lesions, RS: Respiratory symptoms, SLNE: Superficial lymph node enlargement, EN: Erythema nodosum, CS: Constitutional symptoms, A/A: Arthralgia/artritis, OI: Ocular involvemenT, HM: Hepatomegaly, P/LGI: Parotis/lacrimal gland involvement, P: Poliüria, S: Splenomegaly, M: Myalgia, HI: Heart involvement, MCF: Macroscopic changes on the fingers, LG: Löfgren's syndrome (without biopsy), CD: Cancer development, PPDA: PPD anergy, HBI: Hand bone involvement, HCa:Hypercalcemia, LP: Lupus pernio, L/P: Lactation/pregnancy, N: Nephrolithiasis, SI: Scar involvement, HCüria: Hypercalcüri, TB: Transbronchial biopsy, MC: Mediastinoscopy, SLNB: Scalen lymph node biopsy, PLNB: Peripheral lymph node biopsy, SB: Skin biopsy, SSB: Scar-skin biopsy, SNB: Subcutan nodul biopsy, Kweim B: Kveim biopsy, LB: Liver biopsy.

DISCUSSION

Inflammation may play a role in the process of arterial stiffening.[13] Since sarcoidosis is a systemic inflammatory disease, we were interested whether the carotid-femoral (aortic) PWV is increased in patients with sarcoidosis or not. We found that the carotid-femoral PWV was higher in patients with sarcoidosis than in control subjects. Pulse wave velocity is a technique in which large artery distensibility is evaluated from analysis of the peripheral arterial waveform.[14] It is calculated from measurements of pulse transit time and the distance travelled by the pulse between two recording sites. It is an index of arterial stiffness and a surrogate marker for coronary atherosclerosis. A close relation between increased PWV and atherosclerosis development has been reported.[15] Sarcoidosis is a systemic inflammatory multiorgan disease of unknown etiology, characterized in the affected organs by T-lymphocyte-mononuclear phagocyte infiltration, granuloma formation, and distortion of normal microarchitecture. Histology of granulomas shows a central zone with macrophages, epithelioid cells, and multinucleated giant cells in addition to activated CD4 lymphocytes, and a peripheral zone with macrophages, fibroblasts, CD4 and CD8 lymphocytes.[5,6,16] T-helper-1

Table 3. Basic data, hemodynamic values and laboratory data in patients with sarcoidosis and control subjects

	Sarcoidosis	Controls	*p*
Age (years)	44.8±12.8	41.5±10.1	0.38
Body mass index (kg/m²)	26.93±4.01	26.59±4.08	0.79
Waist / hip ratio (cm)	0.79±0.10	0.80±0.06	0.75
Systolic blood pressure (mmHg)	119.21± 16.43	112.10±9.17	0.10
Diastolic blood pressure (mmHg)	76.57±11.18	71.57±8.34	0.12
Mean blood pressure (mmHg)	90.96±13.05	85.08±8.41	0.10
Pulse pressure (mmHg)	43.15±7.49	40.52±4.04	0.18
Heart rate (beat/min)	74.00±8.35	70.73±4.61	0.14
Pulse wave velocity (m/s)	10.04±1.73	9.05±1.18	0.04
Pulse transit time (ms)	64.47±11.97	69.84±10.97	0.15
Glucose (mg/dl)	92.31±19.05	81.68±9.59	0.03
Urea (mg/dl)	29.94±9.00	29.52±7.36	0.87
Creatinine (mg/dl)	0.90±0.10	0.89±0.15	0.88
Albumin (g/dl)	4.04±0.26	4.19±0.26	0.09
Total cholesterol (mg/dl)	195.21±35.99	177.15±23.26	0.07
HDL cholesterol (mg/dl)	46.57±17.93	53.52±9.41	0.14
LDL cholesterol (mg/dl)	123.57±34.21	100.42±24.30	0.02
VLDL cholesterol (mg/dl)	24.84±13.64	19.26±8.21	0.13
Triglyceride (mg/dl)	124.15±68.63	96.31±40.93	0.13
Uric acide (mg/dl)	5.26±1.61	4.07±0.91	0.008
Leukocytes (/mm3)	6752.63±1841.30	6689.47±1633.97	0.91
Hemoglobin (g/dl)	13.52±1.17	13.94±1.43	0.32
Hematocrit (%)	40.06±3.54	41.78±4.27	0.18
Platelets (/cu mm)	256.52± 54.91	241.94±50.05	0.39
Hs-CRP (mg/dl)	6.76±9.53	2.1±1.8	0.04
TSH (mIU/ml)	1.53± 0.8	1.21±0.73	0.20
Homocysteine (μmol/l)	11.29±2.59	12.85±4.19	0.17
Oxide LDL (U/l)	55.39±14.07	59.28±5.66	0.35
ESR (mm/hr)	21.63±15.35	10.42±1.63	0.005

HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very-low-density lipoprotein, Hs-CRP: High sensitive C-reactive protein, TSH: Thyroid stimulating hormone, ESR: Erythrocyte sedimentation rate.

(Th1) mediated cytokines, especially IFN-γ (interferon gamma) have major roles in the pathogenesis of the disease but IL-1, TNF-α and IL-2 are also contributory cytokines in inducing and maintaining of granuloma formation. This exaggerated Th-1 immune response is thought to be secondary to stimulation by either exogenous antigens (infectious or environmental), or by autoantigens.[3]

The atherosclerotic process is initiated when cholesterol-containing LDL accumulate in the endothelium. Leukocyte adhesion molecules and chemokines promote recruitment of T cells and monocytes. T cells in lesions recognize local antigens and mount Th-1 responses with secretion of pro-inflammatory cytokines that contribute to local inflammation.[17] This inflammation of sarcoidosis may act to impair endothelial function, arterial compliance and arterial elasticity and as a contributing factor in the initation or the progression of atherosclerosis.[13]

In this study, we showed that serum glucose, LDL cholesterol, uric acid, hs-CRP and erythrocyte sedimentation rate were higher in patients with sarcoidosis than in control subjects. Although some inflammatory proteins such as hs-CRP and fibrinogen are high in inflammatory diseases and general population, we didn't find an association between PWV and inflammatory proteins.[18-21] We did observe relationship between PWV and total cholesterol and LDL cholesterol similarly with the literature.[22,23] Wilkinson et al.[23] showed that patients with hypercholesterolemia have a higher central pulse pressure and stiffer blood vessels than matched controls.

We found significant correlation between PWV and age and blood pressure. Aging and genetic factors are responsible for structural (involve the composition of the arterial wall, hypertrophy of smooth muscle cell and decrease in contents of extracellular matrix) and functional changes of the arterial wall, leading to decreased

Table 4. Correlation between PWV and basic data, hemodynamic values and laboratory data

	p	r
PWV- Sex	0.11	–0.26
PWV- Disease's duration (months)	0.30	0.19
PWV- Age (years)	0.001	0.52
PWV- Body mass index (kg/m^2)	0.01	0.40
PWV- Waist / hip ratio (cm)	0.50	0.11
PWV- Systolic blood pressure (mmHg)	<0.001	0.71
PWV- Diastolic blood pressure (mmHg)	<0.001	0.63
PWV- Mean blood pressure (mmHg)	<0.001	0.68
PWV- Pulse pressure (mmHg)	<0.001	0.63
PWV- Heart rate (beat/min)	0.83	0.03
PWV- Pulse transit time (ms)	<0.001	–0.90
PWV- Glucose (mg/dl)	0.07	0.29
PWV- Urea (mg/dl)	0.44	0.12
PWV- Creatinine (mg/dl)	0.13	–0.24
PWV- Uric acide (mg/dl)	0.99	–0.001
PWV- Albumin (g/dl)	0.84	0.03
PWV- Total cholesterol (mg/dl)	0.002	0.47
PWV- HDL cholesterol (mg/dl)	0.88	–0.25
PWV- LDL cholesterol (mg/dl)	0.001	0.51
PWV- VLDL cholesterol (mg/dl)	0.90	0.02
PWV- Triglyceride (mg/dl)	0.89	0.02
PWV- Leukocytes (/mm3)	0.09	0.27
PWV- Hemoglobin (g/dl)	0.60	–0.08
PWV- Hematocrit (%)	0.65	–0.07
PWV- Platelets (/cu mm)	0.14	0.24
PWV- hs-CRP (mg/dl)	0.59	–0.90
PWV- TSH (mIU/ml)	0.44	–0.12
PWV- Homocysteine (μmol/l)	0.95	0.009
PWV- Oxide LDL (U/l)	0.36	–0.15
PWV- ESR (mm/hr)	0.51	0.10

PWV: Pulse wave velocity, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very-low-density lipoprotein, hs-CRP: High sensitive C-reactive protein, TSH: Thyroid stimulating hormone, ESR: Erythrocyte sedimentation rate.

distensibility and increased stiffness as a consequence of the reduction in arterial elastin and increase in collagen content.[24-26] Increased arterial stiffness is associated with an inadequate increase in systolic blood pressure and a relative decrease in diastolic blood pressure, hence increasing pulse pressure at any given value of mean blood pressure.[27] Stiffness becomes higher at high blood pressure and lower at low blood pressure, through mechanical change in arterial wall streching and resulting change in contrubition of elastin and collagen fibers to the elastic modulus.[28]

Increased body mass index might adversely affect cardiovascular health through association with hyperlipidemia, hypertension and inflammation. Obesity which is a traditional cardiovascular risk factor, could be a marker of inactivity and it could represent insulin resistance, and it might also exert adverse affects on the vascular system by decreasing arterial elasticity.[11,29] In this study, we found a significant correlation between carotid-femoral PVW and body mass index. These findings showed that arteries become less elastic with body mass index and arterial stiffening is observed with increasing body mass index.

In conclusion, the carotid-femoral PWV was higher in patients with sarcoidosis than in control subjects. Pulse wave velocity is influenced by total cholesterol, LDL cholesterol, age, body-mass index and blood pressure level.

Limitations

Despite the method measures the stiffness of the aorta indirectly, it is the best described method (The pressure wave forms are easily recorded in both areas, the distance between two areas is long enough, and elasticity of arterial wall could have been reflected on a large scale as in aorta, measurement of carotid-femoral pulse wave velocity was preferred).[14] We took great care to exclude subjects with known cardiovascular disease or risk factors, such as a previous myocardial infarction, constrictive, restrictrive or dilated cardiomyopathy, heart failure, valvular heart disease, diabetes mellitus, peripheral arterial disease, cerebrovascular disease, renal failure, anemia (Hct < 30%), electrocardiogram (ECG) conduction and rhythm disorders, systolic blood pressure > 140 mmHg, diastolic blood pressure > 90 mmHg, body mass index (≥ 35 kg/m^2) and waist/hip ratio ≥ 1 cm; antihypertensive drug, statins or immunosupressive drug use. Therefore, these conclusions may not be extended to a greater population, therefore; the results of this study will need confirmation in larger studies.

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