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BETA STIFFNESS – SETTING AGE STANDARDS

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SUMMARY – Beta stiffness index is one of the most commonly used measures of depicting mechanical arterial properties and development of preclinical atherosclerosis. Main influences on its value hold age and blood pressure levels. The goal of this study was to determine age standards of beta stiffness index on common carotid artery in our population using a formula modified by Kawasaki. The study was conducted in 150 healthy volunteers aged 25-75 on an Aloka 5500-SSD Prosound ultrasound platform using B and M modes. The data obtained were analyzed by appropriate statistical methods. Study results confirmed linear relationship of beta index and age. Calculation of beta index is applicable for assessment and monitoring of vascular physiology changes because it is simple for use, prompt in analysis and suitable for bed-side evaluation.

Key words: *Arteries – physiopathology; Atherosclerosis – diagnosis; Carotid arteries – physiology; Elasticity; Aging*

Introduction

Life expectancy has significantly increased in the last century and therefore the elderly are strongly represented in the population. Most diseases in the elderly are chronic and usually of atherosclerotic origin, and most named among them are cerebrovascular diseases in women and cardiovascular diseases in men[1]. Therefore, timely prevention, primary and secondary, will play key role in the near future.

Physiologic changes in vascular system are a normal process of aging. Still, we all are aware that some people can enjoy good health and high quality of life even in the old age. Data from the BLSA study[2] imply that vascular aging *per se* does not necessarily imply the beginning of vascular disease or the loss of homeostasis of physiologic processes, and that vascular disease is sequestered from those that managed to age 'unsuccessfully'[3]. Some of the changes observed in aging are the loss of arterial elasticity, and when noted at an earlier age than expected as in hypertensives, it is considered to be a trait of preclinical disease initiation[4]. For this reason it is important to develop strategies for proper evaluation and further monitoring, and thus retardation of the possible proatherogenic mechanisms[5].

Subclinical atherosclerosis on carotid arteries can be detected by measurement of the intima-media thickness (IMT), number of present plaques and arterial stiffness assessment[6]. Beta stiffness index (BSI) is one of the most common clinically used markers[7], its advantage being its derivation from regional diameter and blood pressure change, systolic blood pressure alone also being identified as an independent risk factor for future vascular events[2].

The aim of this study was to set age standards for BSI in our population, so that in future studies we can determine whether the noted values are due to

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successful or unsuccessful vascular aging, i.e. pinpoint disease onset.

Methods

The study was performed in 150 volunteers of both sexes, age range 25-75, divided into five age groups by 10-year ranges. All subjects were fully informed and they signed an informed consent approved by the Hospital Ethics Committee and all procedures were performed in accordance with institutional guidelines. Inclusion criteria were: age 25-75, normotension or controlled hypertension (blood pressure levels <140/90 mm Hg), and normolipoproteinemia or controlled hyperlipoproteinemia (blood lipid values within laboratory limits). Exclusion criteria were: established heart disease, diabetes mellitus, carotid artery stenosis, evident early atherosclerotic changes (IMT in distal wall of common carotid artery (CCA) ≥0.8 mm), prior stroke or transient ischemic attack (TIA), and alcoholism. Upon taking history data, blood pressure measurements were repeated three times. Body-mass index (BMI) was calculated and subjects were categorized accordingly (overweight, BMI >30 kg/m^2), and subjects were asked if they were current (assessment of pack-years), occasional, former or non-smokers.

The subjects underwent ultrasound examination on an Aloka ProSound SSD-5500 platform (Aloka Co., Ltd.) using high-resolution 13-MHz linear probe. All measurements were performed in supine position with head elevation of up to 45° and side tilt of 30° to the right and then to the left. B mode IMT measurements on the distant wall in diastole were performed. M mode examinations were performed subsequently 1.5 cm proximally to the flow divider on the distal wall of CCA bilaterally on the best obtained image. Measurements were performed over three cardiac cycles by a single investigator and the results were expressed as arithmetic means. Systolic and diastolic inter-adventitial excursions were noted and BSI was calculated according to the formula modified by Kawasaki[8].

SPSS version 8.0 for Windows was used for statistical analysis (alpha <0.05).

Results

There were 104 (69.3%) women and 46 (30.7%) men. The majority of subjects (80%) were normotensive (n=120) and 20% were controlled hypertensives (n=30). There were 16 (10.7%) overweight subjects; according to smoking habit, there were 85 (25.3%) non-smokers, 24 (16%) former smokers, 21 (14%) occasional smokers and 20 (13.3%) active smokers with pack-years ranging from 1.3 to 50.

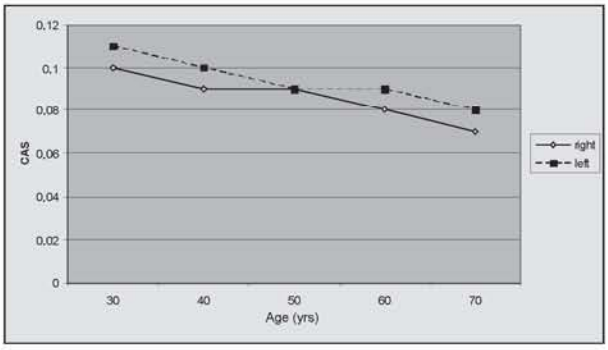

Fig. 1. Relationship between circumferential arterial strain (CAS) and age showing potential plateau values between 40 and 50 years in the right common carotid artery and between 50 and 60 years in the left common carotid artery.

Characteristics of CCA morphology using B mode and M mode ultrasound were: IMT was found at 0.39-0.56 mm in the right CCA and at 0.40-0.58 mm in the left CCA; inter-adventitial diameter ranged from 5.79 to 8.12 mm in the right CCA and from 5.53 to 8.02 mm in the left CCA; CAS values varied from 5.14% to 11.84% in the right CCA and from 5.29% to 13.25% in the left CCA .

The mean BSI values in five age groups (each consisting of 30 subjects) are shown in Table 1. The

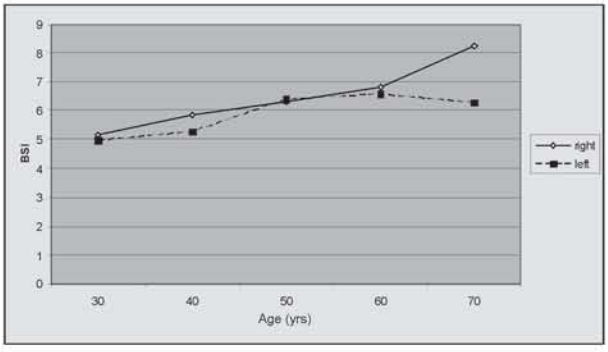

Fig. 2. Relationship between beta stiffness index (BSI) and age showing a linear increase differing between the right and left common carotid artery after age 60.

Table 1. IMT measurement, beta indexes measured by conventional ultrasound and three-dimensional ultrasound, descriptive statistics

Age (yrs)		IMT right (mm)	IMT left (mm)	CAS right	CAS left	BSI right	BSI left
25-35	Mean	0.39±0.07	0.40±0.07	0.10±0.04	0.11±0.06	5.18±2.13	4.94±2.18
	V%	18.26	17.37	38.98	51.36	41.09	43.96
	CI	0.36<x<0.42	0.38<x<0.42	0.09<x<0.11	0.09<x<0.13	4.42<x<5.94	4.18<x<5.74
35-45	Mean	0.43±0.07	0.46±0.09	0.09±0.03	0.10±0.04	5.82±2.12	5.27±2.03
	V%	15.15	18.59	38.35	37.18	36.34	38.45
	CI	0.41<x<0.45	0.43<x<0.49	0.08<x<0.10	0.08<x<0.11	5.06<x<6.58	4.55<x<6.00
45-55	Mean	0.47±0.08	0.50±0.11	0.09±0.03	0.09±0.03	6.28±2.96	6.38±3.30
	V%	17.49	21.18	37.11	37.11	47.17	51.79
	CI	0.44<x<0.50	0.47<x<0.54	0.08<x<0.10	5.22<x<7.34	0.08<x<0.10	5.20<x<7.56
55-65	Mean	0.52±0.11	0.54±0.11	0.08±0.03	0.09±0.04	6.82±3.75	6.58±4.63
	V%	21.01	20.89	38.96	46.00	54.92	70.36
	CI	0.48<x<0.56	0.50<x<0.58	0.07<x<0.09	5.48<x<8.16	0.08<x<0.10	4.93<x<8.24
65-75	Mean	0.55±0.09	0.57±0.09	0.07±0.02	0.08±0.02	8.22±5.21	6.25±1.76
	V%	16.65	14.60	35.12	28.17	63.34	28.23
	CI	0.53<x<0.59	0.55<x<0.61	0.06<x<0.08	6.36<x<10.08	0.07<x<0.09	5.62<x<6.88

IMT = intima-media thickness; CAS = circumferential arterial strain; BSI = beta stiffness index; V% = variance; CI = confidence interval

relationship between CAS and age was found to be negatively linear in both CCA with a possible plateau at age 40-50 in the right CCA and at age 50-60 in the left CCA (Fig. 1). The relationship between BSI and age was also linear, but slowly increasing with age in both CCA, on average by 7.6% in the right CCA and by 4% in the left CCA (Fig. 2). ANOVA analysis showed age dependence for IMT (strong correlation, r^2=0.97 right CCA and r^2=0.97 left CCA), CAS (strong correlation, r^2=0.94 right CCA and r^2=0.97 left CCA) and BSI (strong correlation, r^2=0.94 right CCA and r^2=0.93 left CCA). F parameter (test statis-

Table 2. Comparison of circumferential arterial strain (CAS) according to sex, body mass index (BMI) and smoking habit

	CAS right CCA (%)	CAS left CCA (%)	BSI right CCA (%)	BSI left CCA (%)
Sex				
Women	8.75±3.61	9.53±4.60	6.51±4.02	6.36±3.25
Men	7.85±2.57*	8.23±3.25	5.89±2.13	5.90±2.40
BMI				
Normal	8.52±3.44	8.34±3.11	6.55±3.67	5.79±3.00
Overweight	9.54±3.98*	8.74±3.95	5.77±3.00	6.74±3.06
Smoking				
Non-smokers	8.13±3.15	9.30±3.27	6.64±3.87	5.53±2.97
Active	9.57±3.43*	9.24±5.27	6.91±3.40	6.91±3.40*

CCA = common carotid artery; *statistically significant value

tics) proved that there was little chance for these results to be accidental. No statistically significant difference was found in BSI between normotensive and controlled hypertensive individuals.

CAS was higher in women, overweight subjects and active smokers when measured in the right CCA, whereas BSI was only higher in active smokers when measured in the left CCA (Table 2).

Discussion

Population characteristics showed the subject model investigated to be representative of a predominantly healthy population. The study included a significantly greater number of women, probably because women are more observant to their bodies, report more symptoms when facing an illness and would prefer to take preventive action[9].

BSI analysis performed in this study showed a slow yearly increase, linear in appearance, and a separation point after 60 years of age found between the right and the left CCA. It was the first study of this type performed in Croatian population, and only a few others were done worldwide. Niki *et al.* found similar values in their study, somewhat higher even after age 26 and even more so around age 60[10]. In their studies, Kawasaki *et al.*[8], Liao *et al.*[11], Hirai *et al.*[12] and Niki *et al.*[10] included normotensive healthy volunteers, the first reporting on BSI with similar findings to ours, whereas the other three groups of researchers found slightly elevated mean BSI values. Hirai *et al.*[12] also performed an additional substudy in cardiovascular patients with three-vessel disease and found increased BSI, whereas Liao *et al.*[11] report on a subgroup of hypertensive individuals also showing BSI increase. This is important since these authors conclude that the increase in beta stiffness may precede hypertension for those in the highest quartile[11]. It is still not clear what comes first: hypertension or stiffness increase. However, increased arterial stiffness is often accompanied by generalized atherosclerosis, left ventricular hypertrophy, and consequently some form of vascular event[3].

It should be noted that BSI measurement showed great variation, which might be explained by the small sample size or the potential variations caused by diurnal distensibility variations[13], or maybe some other variations that were not taken into account, such as recent caffeine or nicotine intake[14], although investigators tried to annihilate as many interferences as possible. Additional possibility may be that the measurements are better evaluated individually than in groups.

In this study, IMT measurement on distal CCA wall was performed as recommended for atherosclerosis risk watching[15] and all subjects were categorized as having normal IMT. This is supported by the need to utilize the measurement of IMT, already proven as an atherosclerotic marker and possible predictor of cerebral vessel involvement[16].

However, IMT measurement alone does not determine subclinical atherosclerosis and additional evaluation of arterial mechanics through assessment of other parameters including arterial diameter, axial strain and transmural pressure consequential to some physical conditions need to be noted, as was recently once again confirmed in a model study[17]. Our data showed slow CAS decrease with age and possible plateau formation in the middle adulthood age. CAS was found to decrease yearly by 7.2% in the right CCA and by 4.7% in the left CCA. The side-to-side difference may be a coincidence due to the small sample size, or it may point to a mechanical property difference not yet recognized. CAS was also smaller in women, in overweight subjects and in active smokers, pointing to some provocation by the aforementioned factors and potentially discovering those individuals that may age 'unsuccessfully' and ultimately develop cerebrovascular disease.

Setting the BSI standard values for a specific population is crucial in risk factor assessment and monitoring of a healthy or risk factor compromised population. Still, further studies in a greater number of subjects are needed to appraise BSI in group *versus* individual evaluation and in respect to specific risk factors. Most of the subjects included in the study were normotensive and only 30 (20%) of them were using antihypertensive medication lowering their blood pressure levels to normal. There was no statistical difference between the two groups -most likely due to the small sample size and lack of age and risk factor adjustment - since chronic exposure of arterial wall to stretching will lead to vascular remodeling, increase in arterial stiffness indicators and calcification of arterial wall and, lastly, cause target organ damage as previously noted in literature[18].

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Sažetak

BETA KRUTOST – UTVRĐIVANJE DOBNIH STANDARDA

M-J. Jurašić, S. Josef-Golubić, R. Šarac, A. Lovrenčić-Huzjan i *V. Demarin*

Beta indeks krutosti (engl. *beta stiffness index*) je jedna od klinički najčešće upotrebljavanih mjera za opisivanje mehaničkih svojstava arterija i pojave pretkliničke ateroskleroze. Glavni utjecaj na njegovu vrijednost imaju životna dob i vrijednost krvnoga tlaka. Cilj ovoga rada bio je utvrditi dobne standarde beta indeksa krutosti na zajedničkoj karotidnoj arteriji u našoj populaciji prema formuli koju je modificirao Kawasaki. Ovo istraživanje provedeno je na 150 zdravih dobrovoljaca u dobi od 25 do 75 godina na ultrazvučnom aparatu Aloka 5500-SSD Prosound uporabom B i M prikaza. Na prikupljenim podacima izvršila se prikladna statistička obrada. Rezultati su pokazali da beta indeks raste linearno u ovisnosti s dobi. Računanje beta indeksa primjenjivo je za procjenu i praćenje nastanka rane promjene vaskularne fiziologije, jer je jednostavno, brzo i primjenjivo uz krevet bolesnika.

Ključne riječi: *Arterije – patofiziologija; Ateroskleroza – dijagnostika; Karotidne arterije – fiziologija; Elatičnost; Starenje*