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Relationship between Age and Thickness of Carotid Arteries in a Population without Risk Factors for Atherosclerosis

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ABSTRACT

The intima-media thickness (IMT) of carotid arteries is a marker of subclinical atherosclerosis associated with risk factors for atherosclerosis and a predictor of vascular disease. The aim of the research was to determine the correlation of IMT and age, and above normal IMT values in healthy adults in Slavonia (eastern Croatia). The study included 275 subjects of both sexes, aged between 20 and 79, who had no clinical manifestations of vascular disease or presence of major risk factors for atherosclerosis (hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking). Ultrasonic measurement of IMT in the B-mode was performed on far walls of the carotid arteries on both sides at three locations (common and internal carotid artery, carotid bifurcation). At all three sites of measurement a high correlation between the IMT values and age was found in both sexes, including the maximum for IMT of carotid bifurcation (men r=0.92, women 0.91). Upper normal values (75th percentile) IMT of common carotid arteries were determined for the ten-year age groups. It is the same for both men and women in age groups both 20-29 and 30-39 (0.41, 0.46 mm). On the other hand, in age groups 40-49, 50-59, 60-69 and 70-79 upper normal values for men are 0.57, 0.62, 0.77 and 0.96 mm, and for women 0.50, 0.57, 0.71 and 0.81 mm. Our study in healthy adults in Slavonia (eastern Croatia) established a clear connection between carotid IMT and age, which implies a need for taking the age as an essential factor into account when conducting researches that involve the IMT.

Key words: *atherosclerosis, carotid arteries, carotid intima media thickness, adult, age groups*

Introduction

The thickness of the arterial wall (intima-media thickness, IMT) is an accepted marker of early, subclinical atherosclerosis[1-4]. Earlier studies have shown links to increased carotid IMT with major risk factors for atherosclerosis[5-7]. Increased IMT of the carotid arteries is a predictor of stroke[8-11] and cardiovascular events[11-15]. Since the use of ultrasound for measuring IMT of carotid arteries is safe, reliable and inexpensive[16,17], it has established itself in epidemiological and clinical studies of primary and secondary prevention of cardiovascular disease[18-20].

The aims of our study are to determine the relationship between the IMT values of carotid arteries and age, and to define normal values in healthy adults without any major risk factors for atherosclerosis.

Subjects and Methods

The study was conducted from January 2007 to June 2008 at the Department of Neurology at University Hospital Centre in Osijek. All subjects lived in Slavonia, eastern Croatia, in a 40 km radius around the city Osijek, a region with the biggest proportion of cerebrovascular diseases in the total mortality rate in Croatia[21]. Subjects were recruited from a group of people who were referred for ultrasound examination of carotid arteries and after giving their consent underwent additional measurements of the arterial wall. Our group included patients diagnosed with tension-type headache, dizziness, benign paroxysmal positional vertigo, cervical and posttraumatic headache syndrome. Due to the insufficient number of subjects in the younger age groups, we included 28 volun-

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teers who were eligible for inclusion in the study. From 285 subjects aged between 20 and 79, 275 (52% women) who met the criteria were included in the study (10 of our subjects were excluded due to poor ultrasound images).

Excluding criteria were either a history of cured or currently existing cardiovascular disease (myocardial infarction, angina pectoris, ischemic cardiomyopathy), cerebrovascular disease (stroke, transient cerebral ischemic attack, amaurosis fugax), and peripheral arterial disease (symptoms of intermittent claudication or proven peripheral arterial occlusive disease), presence of other known severe illness, or previous therapeutic interventions due to atherosclerotic disease.

Further excluding criteria was the presence of major risk factors for atherosclerosis – hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking[22,23].

Arterial hypertension, diabetes mellitus and hypercholesterolemia were excluded by anamnestic data, details of any medication or diet therapy, blood pressure measurements on both upper arms (RR<140/90 mmHg), determination of fasting blood glucose (≤6.9 mmol/L), and total cholesterol (≤6 mmol/L) by standard laboratory procedures[24]. The cut-off values for risk factors were defined according to Chambless et al (ARIC Study) [25]. Smoking was defined as current or previous smoking >10 cigarettes a day throughout the year[13].

Ultrasound scanning was performed by a single expert sonographer using a 7 MHz linear transducer (Aloka Pro Sound 5000, Tokyo, Japan). By longitudinal position of the probe IMT measurement[20] was done on the far walls of extracranial carotid arteries on both sides. The measurement was done in three segments: the distal segment of common carotid artery 10 mm proximally to the carotid bifurcation (IMT-CCA), in carotid artery bulb (IMT-BIF), and 10 mm distally from the beginning of the internal carotid artery (flow divider) (IMT-ICA). In these segments, measurements of the far walls were done from 4 different angles (180, 150, 120 and 90 degrees to the right and 180, 210, 240 and 270 degrees on the left)[26], and thus provided us with 24 measurement results for each subject.

Statistical methods

For the initial analysis of the measurement results classical methods of descriptive statistics were used. This means that frequency tables, means, standard deviations, medians and quartiles were calculated and shown with appropriate graphics. Differences in distributions were tested by the exact Mann-Whitney test in case of continuous variables with a small dimension of the sample. In case of continuous variables with a large dimension of the sample, differences in distributions were confirmed by the classical asymptotic t(z)-test for differences in expected values and by the asymptotic variant of the Mann-Whitney test. Differences were considered significant at p=0.05. Statistica software (StatSoft, Tulsa, USA) was used for statistical analysis.

Results

The subjects did not differ significantly in age and sex distribution (Pearson's χ^2=1.944003, p=0.857, Table 1).

By comparing the results, we found that the values of IMT-CCA in both men and women were significantly higher on the left side (t=-2.998; p=0.003 and t=-2.361; p=0.019), whereas there were no significant differences in the IMT-ICA results regarding the side of the measurements (male t=-1.777; p=0.078, female t=-0.443; p=0.659). Furthermore, the results for IMT-BIF are different between gender groups, i.e. there is no difference in male (t=-1.975; p=0.050), whereas in female higher values appeared on the left side (t=-2.188; p=0.030).

At all measurement sites higher average IMT values were registered in male in comparison with female respondents (IMT-CCA t=2.456; p=0.011, IMT-ICA t=3.812; p<0.001, IMT-BIF t=3.391; p=0.001). Gender differences of intima-media thickness carotid bifurcations are shown in Figure 1.

In all age groups, the highest are IMT-BIF values, and the lowest IMT-ICA values. With increasing age in both sexes also the IMT value increases at all three sites of measurement (Figure 2).

The average values and 75th percentile IMT-CCA for male and female by age groups are shown in Tables 2 and 3. In the youngest age groups (20-29, 30-39) no significant differences in the values of 75th percentile IMT between male and female exist at any of the three sites of measurement (p>0.05). In the age groups above the age of 40 higher IMT values of 75th percentile were found in males at all

TABLE 1
AGE AND GENDER DISTRIBUTION OF SUBJECTS

Gender	Age groups (years)						Total	$\overline{X}$ (years)	t-value	p
	20–29	30–39	40–49	50–59	60–69	70–79				
Male (N)	20	21	23	22	22	23	131	49.98	0.963	0.336
Female (N)	24	26	29	21	26	18	144	48.04		
Total	44	47	52	43	48	41	275			

N – Number of subjects, $\overline{X}$ – mean age, p – level of statistical significance

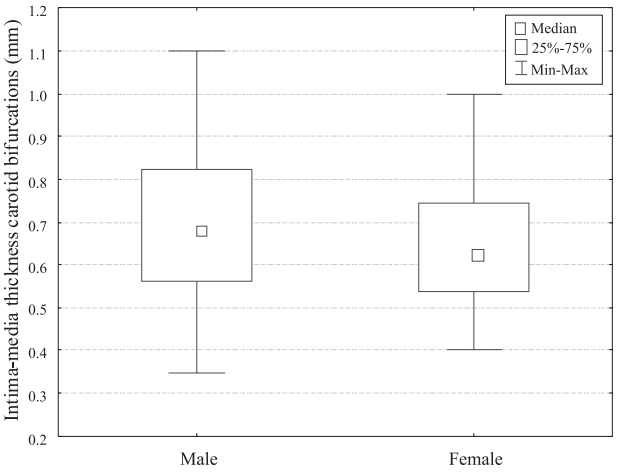

Fig. 1. Diference of intima-media thickness carotid bifurcations between male and female subjects.

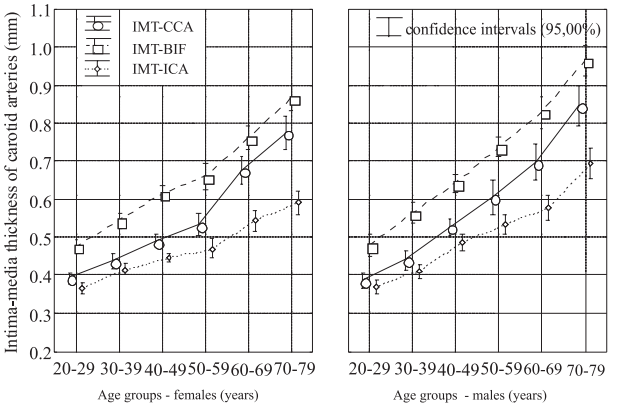

Fig. 2. Age and site dependent intima-media thickness of carotid arteries in both sexes (IMT-CCA – intima-media thickness common carotid arteries, IMT-BIF – intima-media thickness carotid bifurcations, IMT-ICA – intima-media thickness internal carotid arteries).

measurement sites ($p<0.05$), except in the age group 60-69 in IMT-CCA and IMT-ICA ($p>0.05$).

The high correlation between IMT and age is present for all localization measurements in both sexes (Table 4), the highest being for IMT-BIF (Figures 3 and 4).

The growth of the average IMT value ((IMT-CCA+IMT-BIF+IMT-ICA)/3) in male is equable between 0.06 and 0.08 mm during the 10-year-long periods, with exception in the oldest age group where higher value (0.13 mm) in comparison with the previous decade is registered. In female, the increase of average IMT (0.04 to 0.06 mm) per decade is lower than in male up to the 60-69 age group, when the increase is pronounced with respect to the previous decade (0.11 mm).

Discussion

In order to display the association of age and IMT carotid arteries as an indicator of subclinical atherosclerosis more accurately, the research has been conducted on vascularly healthy subjects of a wide age range (20-79 years old), divided into ten-year age groups. In other similar studies[27-29] the age range of subjects is different, and they are not regularly distributed into ten-year intervals.

The research is limited by the selection of subjects from a population of people referred for an ultrasound diagnostic procedure. When the choice was being made, the subjects with possibly present other (less important) risk factors for atherosclerosis were not excluded.

For a clearer ultrasound image and a more accurate measurement of IMT, the measurement was performed on far arterial walls[20,27,28]. The measurement was conducted from several different angles[26] in order to obtain more results for each location of measurement, i.e. for each subject. In our study only 3.6% of subjects were not included due to poor ultrasound images, or the impossibility of reliable measurement of IMT-ICA or IMT-BIF.

In previous studies the link between age and IMT in both sexes[13,18,22] was confirmed. Our results suggest a high

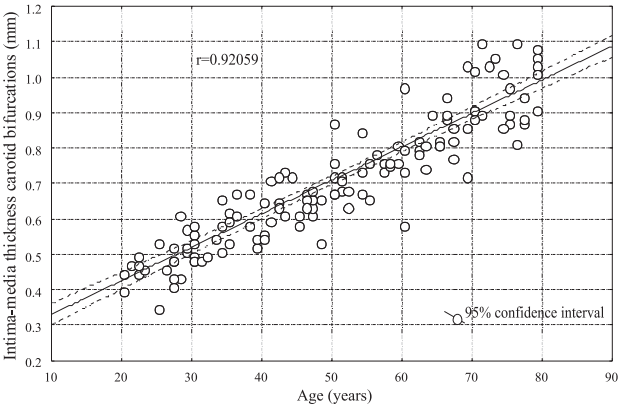

Fig. 3. Correlation of intima-media thickness of both carotid bifurcations and age in male subjects (r – correlation coefficient).

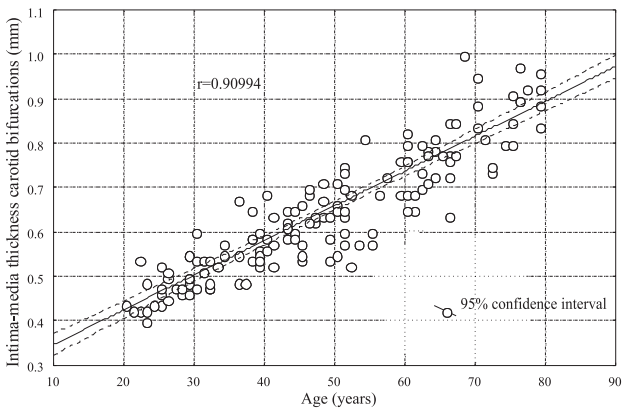

Fig. 4. Correlation of intima-media thickness of both carotid bifurcations and age in female subjects (r – correlation coefficient)

TABLE 2
INTIMA-MEDIA THICKNESS OF COMMON CAROTID ARTERIES IN MALE SUBJECTS ACCORDING TO AGE GROUPS

Age groups (years)	N	IMT-CCA means (mm)	95% CI (mm)	75th percentile (mm)
20–29	20	0.386	0.365–0.407	0.400
30–39	21	0.441	0.415–0.467	0.450
40–49	23	0.527	0.504–0.549	0.575
50–59	22	0.606	0.562–0.650	0.625
60–69	22	0.697	0.649–0.745	0.775
70–79	23	0.846	0.794–0.898	0.962

N – number of subjects, IMT-CCA – intima-media thickness of common carotid arteries (mm), CI – confidence interval

TABLE 3
INTIMA-MEDIA THICKNESS OF COMMON CAROTID ARTERIES IN FEMALE SUBJECTS ACCORDING TO AGE GROUPS

Age groups (years)	N	IMT-CCA means (mm)	95% CI (mm)	75th percentile (mm)
20–29	24	0.393	0.376–0.409	0.412
30–39	26	0.438	0.417–0.459	0.462
40–49	29	0.491	0.475–0.507	0.500
50–59	21	0.534	0.503–0.566	0.575
60–69	26	0.676	0.639–0.713	0.712
70–79	18	0.776	0.733–0.818	0.812

N – number of subjects, IMT-CCA – intima-media thickness of common carotid arteries (mm), CI – confidence interval

TABLE 4
CORRELATION COEFFICIENT BETWEEN INTIMA-MEDIA THICKNESS OF CAROTID ARTERIES AND AGE ACCORDING TO MEASUREMENT SITE

Correlation coefficient	Measurement site					
	IMT-CCA		IMT-BIF		IMT-ICA	
	R	L	R	L	R	L
Male (N=131)	0.86	0.84	0.91	0.90	0.85	0.85
Female (N=144)	0.88	0.87	0.88	0.90	0.81	0.81

MT-CCA – intima-media thickness of common carotid arteries, IMT-BIF – intima-media thickness of carotid bifurcations, IMT-ICA – intima-media thickness of internal carotid arteries, R – right, L – left, N – number of subjects

degree of correlation between age and IMT values for all three sites of measurement. The study of Junyent et al.[30] found a 0.57 correlation of IMT and age for men and 0.61 for women. In our study an even more prominent association of age and IMT was proven – depending on the location of measurement the correlation coefficient is between 0.84 and 0.91 for male and between 0.81 and 0.9 for female. In both sexes the highest correlation exists for carotid bifurcation.

In determining the upper limit of normal values of IMT in healthy people, most researchers agree that it should be the 75th percentile[17,18,20] while others claim the 97.5th percentile[28] to be the highest normal IMT value. In the display of our results, we have determined the 75th percentile as the normal upper limit for the ten-year age groups. Furthermore, we have selected IMT–CCA due to the simplest measurement and higher frequency of appearance in scientific literature[31]. Our results indicate lower values of the upper normal limit than in other studies[32]. The median values of IMT-CCA in younger age groups (up to 50 years of age) are lower in comparison with other studies on similar sample[27]. On the other hand, for older subjects comparison is impossible due to the different distribution into age groups.

In order to compare results for progression of carotid artery IMT we matched a selected age range of our pa-

tients (40 to 70 years) to the age range of subjects of Howard et al.[33]. We found a different pattern of progression of IMT in our population without major vascular risk and/or vascular disease (approximately 0.007 mm/y for females and 0.009 mm/y for males at the bifurcation, and 0.005 mm/y in both sexes at the internal carotid artery) than in general population described by Howard et al.[33] (0.015 mm/y for females and 0.018 mm/y for males at the bifurcation, and 0.01 mm/y in both sexes at the internal carotid artery).

In our results we have not found a significant difference between sexes of IMT in age groups below 40 years of age. On the other hand, a steady accelerated growth of IMT values in males and a more pronounced increase in females aged 60-69 has been registered, which is in accordance with generally accepted knowledge that most clinical manifestations of atherosclerosis occur after the age of 40, prevalently among males. On the other hand, in females a substantial increase in clinical manifestations of atherosclerosis occurs approximately 10 years later than in males[34].

Conclusion

In conclusion, our results suggest a high correlation of carotid IMT and age in healthy adults, and therefore the need for research involving the determination of carotid IMT as an indispensable factor together with the age of the respondents.

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POVEZANOST IZMEĐU DOBI I DEBLJINE STIJENKE KAROTIDNIH ARTERIJA KOD OSOBA BEZ RIZIČNIH ČIMBENIKA ZA ATEROSKLEROZU

S A Ž E T A K

Debljina arterijske stijenke (IMT) karotidnih arterija je marker subkliničke ateroskleroze, povezan s rizičnim čimbenicima za aterosklerozu i prediktor vaskularnih bolesti. Cilj istraživanja je određivanje povezanosti IMT-a i dobi, te gornjih normalnih vrijednosti IMT-a kod zdravih odraslih ljudi u Slavoniji (istočna Hrvatska). U istraživanje je uključeno 275 ispitanika oba spola, u dobi od 20-79 godina, koji nisu imali kliničkih manifestacija vaskularnih bolesti niti prisutnih glavnih čimbenika rizika za aterosklerozu (arterijska hipertenzija, hiperkolesterolemija, šećerna bolest, pušenje cigareta). Ultrazvučno mjerenje IMT-a u B-modu je provedeno na daljim stijenkama karotidnih arterija obiju strana na tri lokacije (zajednička i unutarnja karotidna arterija, karotidna bifurkacija). Na sve tri lokacije mjerenja u oba spola je utvrđena visoka povezanost vrijednosti IMT-a i dobi, najveća za IMT karotidne bifurkacije (kod muškaraca r=0,92, kod žena 0,91). Gornje normalne vrijednosti (75. centil) IMT zajedničkih karotidnih arterija su određene za desetgodišnje dobne skupine. Za muškarce i žene u dobnim skupinama 20-29 i 30-39 godina su jednake (0,41, 0,46 mm). U dobnim skupinama 40-49, 50-59, 60-69 i 70-79 godina gornje normalne vrijednosti za muškarce su 0,57, 0,62, 0,77 i 0,96 mm, a za žene 0,50, 0,57, 0,71 i 0,81 mm. Našim istraživanjem kod zdravih odraslih ljudi u Slavoniji (istočna Hrvatska) utvrđena je jasna povezanost karotidnog IMT-a i dobi iz čega proizlazi potreba da se kod istraživanja koje uključuje IMT treba uzeti u obzir dob ispitanika kao neizostavan čimbenik.