Original article

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DIAGNOSTIC IMPORTANCE OF THE THICKNESS OF THE INTIMA-MEDIA COMPLEX OF CAROTID ARTERIES IN PATIENTS SUFFERING FROM HYPERTENSION AS A RISK FACTOR FOR THE DEVELOPMENT OF CEREBROVASCULAR DISEASES

Snežana Zlatanović

Carotid diseases are very important for the increase of total morbidity and mortality of the population affected by cerebrovascular diseases. The primary pathologic factor responsible for the diseases of the cerebrovascular system is atherosclerosis, and the measurement of the thickness of the intima-media complex (IMC) in the carotid artery extracranial segment represents a measurable indication of atherosclerosis. The thickness of the IMC of the carotid arteries is influenced by many factors such as local hemo-dynamics, wall stress, arterial hypertension, and other.

The aim of our research was to confirm the influence of hypertension as a risk factor for the development of cerebrovascular diseases which influence the thickness of the intima-media complex of carotid arteries in asymptomatic and symptomatic observed patients concerning gender and age.

The research was conducted in 100 patients of both sexes who were treated at out-patient department or while hospitalized at the Neurology Ward, with hypertension as the main risk for the development of the cerebrovascular diseases. The measurement of the IMC of the carotid arteries was conducted by the ultrasound examination, and the value of IMC>0,9 mm was taken as a border line between normal and pathologic findings.

The research included 100 patients, out of which 36 were male, and 64 female patients. All patients had elevated values of blood pressure. In the male group, just 33.3% of the patients were affected by a hypertension disease only, while the remaining 66.7% had also suffered a cerebrovascular insult, and they had arterial hypertension as a risk factor in their anamnesis, as well. In the female group of 64 patients, 31.3% had a hypertension disease, 68.75% also suffered a cerebrovascular insult, as well as arterial hypertension.

The measurement of the thickness of the IMC of the carotid arteries by the ultrasound method is important for the detection of the subclinical structural damage of the arterial walls and is a part of the algorithm for the assessment of the cerebrovascular risk in patients who suffer from the elevated blood pressure. There is a significant corre-lation among the thickness of the carotid IMC, hypertension disease, and cerebrovascular diseases.

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Key words: *Carotid arteries, intima-media complex, hypertension, atherosclerosis, ultrasound diagnostics*

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Introduction

Cerebrovascular insult (CVI) in most of the countries of the world presents the third main cause of morbidity and mortality, next to cardiovascular diseases, and malignity. In this entity over 80% of the cases deal with diseases connected with brain ischemia, and in one third of the cases the syndrome of transitory ischemia attack appears (TIA) which represents an initial symptom for the presence of the carotid disease. Carotid disease, depending on the extent of the changes, can lead to hemodynamic dis-orders and can be the source of embolus, depending on the changes in the artery wall (that is, on the characteristics of surface, material and size of the arterial plaque and thickness of the intima-media complex) (1).

In most patients, atherosclerosis of the brain arteries, especially carotid arteries, is responsible for the occurrence of the cerebrovascular diseases.

Numerous epidemiology studies have proved the existence of risk factors such as artery hypertension, hyperlipidemia, diabetes mellitus, smoking, obesity, positive anamnesis of the cardiovascular diseases, consumption of alcohol, and others, for the occurrence of cerebral atherosclerosis (2). Most of the observed patients had two or more risk factors (3).

Primary pathological contributor for the occurrence of cerebrovascular diseases is atherosclerosis of the carotid arteries, and the measurement of IMC thickness of the extracranial part of the carotid arteries shows great sensitivity in the detection of the presence, regression, stagnation or progression of atherosclerosis (4). The thickness of the intima-media complex of the carotid arteries is influenced by many factors such as local haemodynamics, wall stress, blood pressure and others. Further, the thickness of the IMC wall of the extracranial segment of the carotid arteries, presents a measurable indicator of the progression of cerebral atherosclerosis, and it makes the assessment of the morphological characteristics of the neck blood vessels' wall possible (5).

Arterial hypertension is most prevalent among the grown-up population. According to the data published by the World Health Organization, about a billion people suffer from elevated blood pressure, which makes about 20-25% of the total population. It is connected with elevated incidence of clinical manifestations of atherosclerosis, such as myocardial infarction, and especially with cerebrovascular diseases. About two thirds of those who experienced apoplexia cerebri, have the record of hypertension as the risk factor in their anamnesis, and, at the moment the elevated blood pressure values were established, more than 60% of the observed patients already had atherosclerotic changes in the walls of the carotid arteries.

As an effect of the arterial hypertension, blood vessels become less elastic, the arterial walls thicken, and the arterial plaque is formed. Arterial hypertension can significantly influence the thickness of the IMC carotid arteries through the remodeling of the blood vessel or by their hypertrophy. Variations in the IMC thickness on various parts of the arterial blood vessel show the differences in local hemodynamic forces inside the blood vessel (6).

By the consensus of the American Echocardiography Society reached in 2007, carotid arteries are defined as a place of choice for the measurement of IMC, and the thickness of 0.9 mm is defined as an indicator of atherosclerosis and a significant risk for cerebrovascular diseases (7).

Asymptomatic carotid disease means the presence of stenosis lesions and the changes in the walls of carotid arteries in patients who did not experience neurological symptoms of cerebral insufficiency. The screening of the asymptomatic carotid disease is mainly done by the ultrasound examination and is recommended for grown-up persons with a high level of risk factors. The other asymptomatic period of the elevated blood pressure and multi-year presence of other atherogenic factors in persons with a predisposition for cerebrovascular diseases significantly enlarges the risk of ischemic lesions in the brain tissue (8).

Aim

The aim of this research was to confirm the influence of hypertension, as a risk factor for the development of cerebrovascular diseases, on the thickness of the intima-media complex of carotid arteries in asymptomatic patients, regarding gender and age.

Material and methods

The research was conducted in 100 patients treated at the General Hospital in Prokuplje at out patient department and in patients hospitalized at the Neurology Ward, all with arterial hypertension in their anamnesis. A certain number of observed patients suffering from arterial hypertension (62) experienced a cerebrovascular insult, and a certain number of patients (38) showed the signs and symptoms of hypertension disease only, but the symptoms of carotid disease were found during the diagnostic procedure as well.

The examination of the observed patients was done by ultrasonography apparatus, type Vivid 3, Syne Master 796 MB, with the linear probe of 10 MHz in B-mode. In B-mode echo sonography, the artery was presented longitudinally as a double line. The double line is hyperechogenicity and one of them was bordered by the lumen of the blood vessel, and the other by the hypoechogenic layer of adventitia (9,10).

The thickness of the hyperechogenic layer, immediately bordered by the lumen of the blood vessel, was measured by the ultrasound. The measurement was conducted on the back wall of the common carotid artery (CCA), in the segment directly behind the bifurcation point of the common carotid artery, at about 1cm before the actual bifurcation. The measurements were performed mutually, on the back wall of both CCA, the value of the IMC thickness was taken for each side separately, obtained results were processed as independent samples and the average value was calculated and established.

The values below 0.9 mm were considered normal, while all the measured values above 0.9 mm were considered as wall thickening of the blood vessel. For each patient the data about the family anamnesis of cerebrovascular diseases and hypertension as a significant risk factor for the incidence of vascular brain diseases were gathered.

The blood pressure was measured during the examination of the patients (the average value of the both upper-arm parts). According to the National Guide arterial hypertension is defined as a disease characterized by the elevated values of systolic (SP) and diastolic (DP) blood pressure ≥ 140/90 mmHg (11), and these border values for hypertension are identically recommended in Europe and USA.

Statistical analyses of the obtained data were conducted by the use of the following statistical tests: Student's t-test, Hi square test, and Anova. Recording of data, tabular and graphical presentation of data were performed using the MS Office Excel program. Results of the statistical analyses were pressented as tabular and graphic presentations. The program SPSS, version 20, was used for the statistical calculations.

The basic descriptive statistical parameters used were, in fact, the standard statistical methods for qualitative and quantitative evaluation of the obtained results: absolute numbers, relative numbers, percentage (%), arithmetical mean value , standard deviation (SD), minimal and maximal values. The normal distribution was examined by the use of Kolomogorov-Smirnov test. The comparison of arithmetic mean values of the two samples was conducted by the use of Student's t-test, while, in the case of three results, the ANOVA was used.

For the testing of the statistical significances the absolute frequencies among samples, Hi square test was used. The causality among the variables was examined by the Pirson's coefficient of simple linear correlation.

Statistical hypothesis was tested at the level of significance for the risk of $\alpha = 0.05$, that is, the difference among the samples was significant if $p < 0.05$.

Results

The research was conducted in 100 patients, out of which 36 (36%) were males, and 64 (64%) were female patients. All the patients suffered from the elevated blood pressure. The average age of the whole group of patients was 64.28 ± 10.02 years, among which, the youngest patient was 38, and the oldest 78 years old.

Age structure, according to the sex of the patients, didn't show statistically significant difference ($p = 0.666$) (Figure 1).

In the tested group, 68 (68%) of patients suffered a cerebrovascular insult, while 36 (36%) showed signs of hypertension disease. In the tested male group of 36 patients, 12 (33.3%), showed the signs of hypertension disease and 24 (66.7%) suffered a cerebrovascular insult and had arterial hypertension as a risk factor in their anamnesis as well. Out of 64 women, 20 showed the signs of hypertension disease (31.3 %) and 44 (68.75%) suffered a cerebrovascular insult and had arterial hypertension as well.

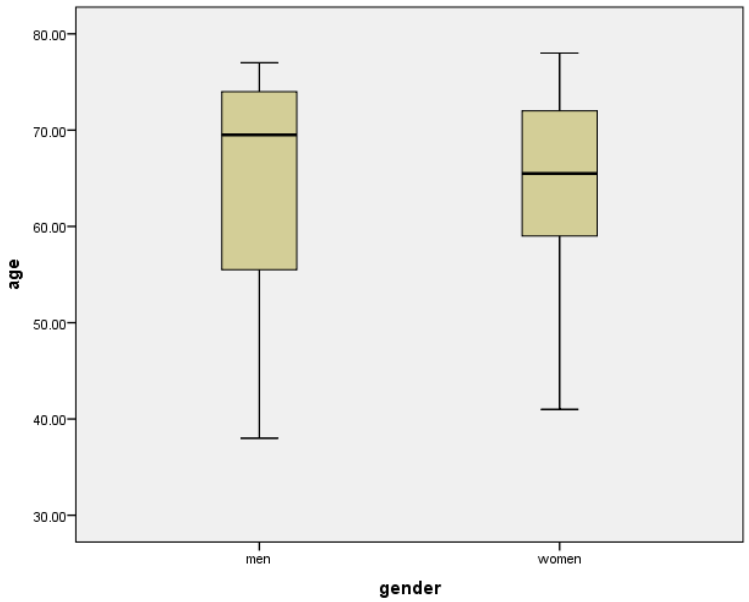


Figure 1. Age structure according to sex

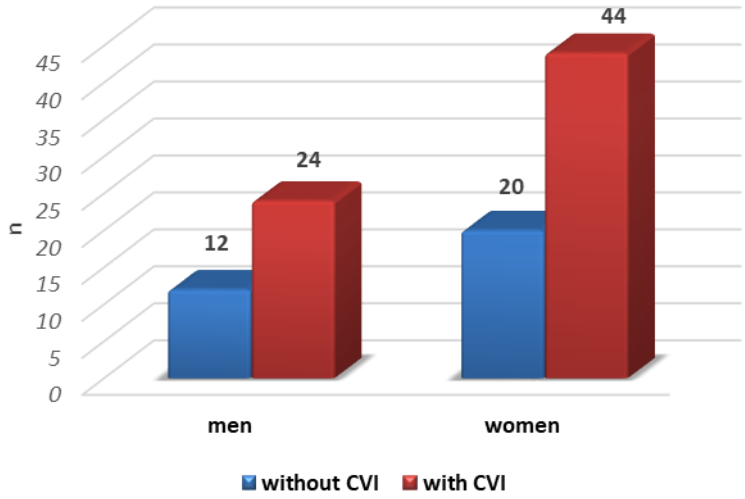


Figure 2. The distribution of CVI patients according to sex

There was no statistically significant difference in the presence of CVI with respect to the sex of the patients ($\chi 2$ =0.046; p= 0.830) (Table 1). The ageing of hypertensive patients contributes to the thickening of the intima-media complex of carotid arteries in both sexes (F=83.382; p<0.001) (Table 2). The presence of hypertension as a risk factor contributes to the thickness of carotid IMC. The ageing of hypertensive patients of both sexes who suffered cerebrovascular disease contributes significantly and shows statistically significant thickening of the intima-media complex of the extra cranial segment of carotid arteries (F=222.006; p<0.001), as showed in Table 3.

Table 1. The distribution of the cerebrovascular disease according to sex

	Elevated TA	CVI	χ^2	p
Men	12 (33.3%)	24 (66.7%)		
Women	20 (31.3%)	44 (68.8%)	0.046	0.830

Table 2. The distribution of patients with arterial hypertension without cerebrovascular diseases

age	men	women	Average thickness IMC/mm	F	p
30 – 49	1(8.3%)	0 (0.0%)	0.50 ± 0.00		
50 – 69	4(33.3%)	13(65.0%)	0.76 ± 0.05		
70 – 80	7(58.3%)	7(35.0%)	0.90 ± 0.00	**83.382**	**< 0.001**
total	**12(100.0%)**	**100(100.0%)**			

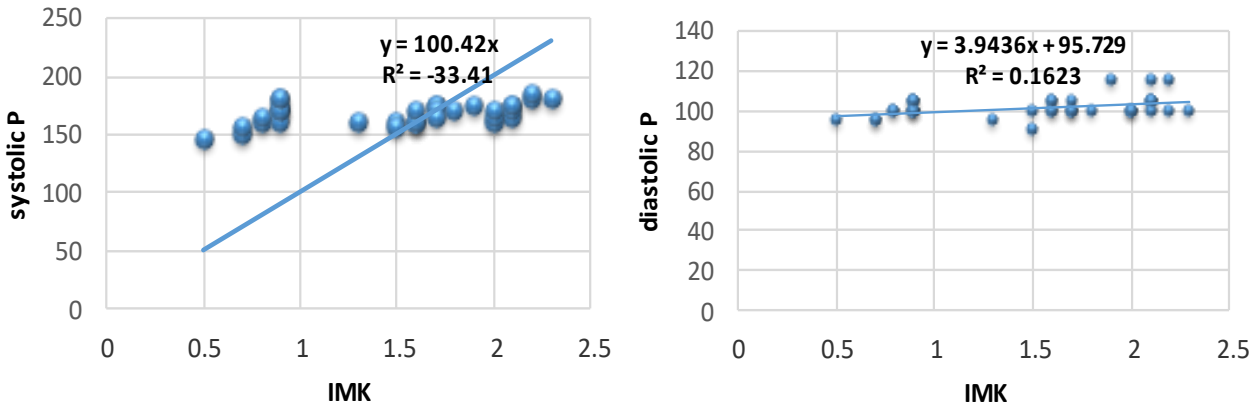
Table 3. The distribution of patients with both arterial hypertension and cerebrovascular diseases

age	men	women	Average thickness IMC/mm	F	p
30 – 49	3(12.5%)	8(18.2%)	1.40 ± 0.09		
50 – 69	10(41.7%)	20(45.5%)	1.70 ± 0.11		
70 – 80	11(45.8%)	16(36.40%)	2.12 ± 0.11	**222.006**	**< 0.001**
total	**24(100.0%)**	**44(100.0%)**			

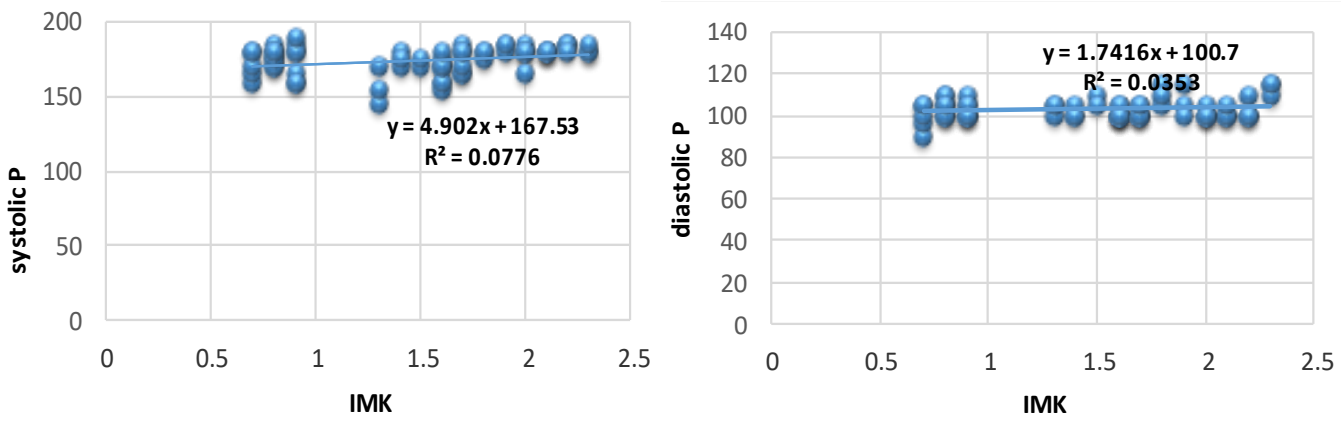
Table 4 shows the values of Pirson's coefficient of linear correlation of systolic and diastolic blood pressure with the values of the intima-media complex: in patients without CVI, a positive correlation was established with the systolic (r = 0.447; p = 0.010), as well as with the diastolic blood pressure (r = 0.413; p = 0.019); positive, statisticaly significant correlation was also noticed in patients suffering from CVI:
systolic P (r= 0.596; p = < 0.001),
diastolic P (r = 0.596; p = 0.008).

Table 4. Correlation between the systolic and diastolic blood pressure with IMC

	Patients without CVI		Patients with CVI	
	r	p	r	p
Systolic P	0.447	0.010	0.596	< 0.001
Diastolic P	0.413	0.019	0.318	0.008



Graph 1. The correlation between systolic and diastolic blood pressure and IMC in patients without CVI



Graph 2. The correlation between systolic and diastolic blood pressure and IMC in patients with CVI

A significant correlation was established between elevated values of systolic blood pressure and the IMC thickening in patients suffering from arterial hypertension but without the signs of neurological diseases ($\chi 2 = 35.034$; $p < 0.001$).

Table 5. The distribution of patients with elevated systolic blood pressure (SP) without cerebrovascular disease with respect to the thickness of the wall

	The values of the systolic blood pressure in mmHg						χ^2	p
The thickness IMC/mm	**140-149**	**150-159**	**160-169**	**170-179**	**180-189**	**190-200**		
0.5 – 0.6	1(100.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)		
0.7 – 0.8	0(0.0)	2(11.8)	4(23.5)	5(29.4)	6(35.3)	0(0.0)		
0.9	0(0.0)	0(0.0)	4(28.6)	4(28.6)	5(35.7)	1(7.1)	**35.034**	**< 0.001**

There was no statistically significant difference in the values of diastolic blood pressure and the IMC thickening in patients suffering from arterial hypertension, but without a sign of neurologic diseases ($\chi2=9.281$; $p=0.054$).

Table 6. The distribution of patients with elevated diastolic blood pressure (DP) who didn't suffer from cerebrovascular diseases with respect to the wall thickness

	The values of the diastolic blood pressure in mmHg			χ^2	p
The thickness IMC/ mm	**90 – 99**	**100 – 109**	**110 – 120**		
0.5 – 0.6	1(100.0)	0(0.0)	0(0.0)		
0.7 – 0.8	4(23.5)	11(64.7)	2(11.8)		
0.9	0(0.0)	13(92.9)	1(7.1)	**9.281**	**0.054**

The existence of a significant correlation was established between the elevated values of systolic blood pressure and the IMC thickening with the patients suffering from arterial hypertension with signs of neurological diseases ($\chi2 = 22.830$;$p = 0.004$). Statistically significant difference was establi-shed in the values of diastolic blood pressure and IMC thickening in patients suffering from arterial hypertension with signs of neurological diseases ($\chi2 = 11.712$; $p = 0.020$).

Table 7. The distribution of patients with elevated systolic blood pressure (SP) who suffered from cerebrovascular diseases with respect to the wall thickness

	The values of the systolic blood pressure in mmHg					χ^2	p
The thickness IMC/mm	**140-149**	**150-159**	**160-169**	**170-179**	**180-189**		
1.3 – 1.5	1(100.0)	2(18.2)	2(18.2)	5(45.5)	1(9.1)		
1.6 – 1.9	0(0.0)	1(3.3)	8(26.7)	12(40.0)	9(30.0)		
2.0 – 2.3	0(0.0)	0(0.0)	4(14.8)	5(18.5)	18(66.7)	**22.830**	**0.004**

Table 8. The distribution of patients with elevated diastolic blood pressure (DP) who didn't experience cerebrovascular diseases with respect to the wall thickness

	Values of the diastolic blood pressure in mmHg			χ^2	p
Thickness IMC/ mm	**90 – 99**	**100 – 109**	**110 – 120**		
0.5 – 0.6	2(18.2)	8(72.7)	1(9.1)		
0.7 – 0.8	0(0.0)	26(86.7)	4(13.3)		
0.9	0(0.0)	21(77.8)	6(22.2)	**11.712**	**0.020**

Discussion

Carotid disease is one of the main causes for the development of cerebrovascular diseases; atherosclerosis is the most common disease of the carotid arteries. Atherosclerosis of carotid arteries is the cause of almost one fifth of ischemic brain apoplexy incidences (12) and it starts most often in the distal part, more precisely at the bifurcation point of common carotid artery (CCA) and spreads in the first few centimeters of the proximal part of the internal carotid artery (ICA) and the external carotid artery (ECA), making the ICA much narrower. The initial examination for establishing the diagnosis of carotid arteries diseases is Color Doppler ultrasound examination (CDU) because of its noninvasiveness, portability and relatively low price (13).

The first morphological changes which signify the beginning of the atherosclerotic process are thickenings of the blood vessel walls. The arterial blood vessel wall consists of three layers. The interior layer, or intima is formed from a single layer of endothelial cells, and this layer is the most important in the structural and functional sense. The medial layer, or media, consists of muscular and elastic fibers. The outer layer, or adventitia, consists of connective tissues. The interior and medial levels form intima-media complex (IMC), the thickness of which is established by the ultrasound examination. IMC thickening normally begins with ageing, and these changes in the wall structure of carotid arteries are important for the blood flow in the brain, and serve for the assessment of already diagnosed atherosclerotic disease. In this way, the patients with elevated risk levels for the occurrence of cerebrovascular diseases can be detected early, and their status could be influenced by the application of certain preventive measures and therapy, with a much greater effect than the later treatment of cerebral apoplexy, accompanied with rehabilitation (14).

Structural alterations in the arterial wall, the intima-media thickenings, can be detected by the ultrasound examination of the carotid arteries in patients suffering from cerebrovascular diseases as well as in patients who developed risk factors. The evaluation of the risk for the development of cerebrovascular diseases in patients suffering from arterial hypertension depends on the severity of hypertension level (mild, moderate, severe), the present damage of the organs in question, the existence of previously combined clinical conditions and the presence of other risk factors (15).

The connection of risk factors for the development of cerebrovascular diseases and IMC thickness of carotid arteries are the subject of many conducted researches. The literature data show the existence of a correlation between the risk factors for CVI and the thickness of the carotid IMC (16).

The measurement of the IMC thickness is important for the establishing the subclinical damages to the carotid arteries and is a part of the algorithm for the assessment of cerebral risk in persons who suffer from the elevated blood pressure. Ultrasound measurement of the IMC thickness presents a noninvasive screening test for the identification of morphological changes in the structure and function of arteries in patients suffering from arterial hypertension (17). A great causality has been proved between the hypertension as a risk factor in the development of cerebrovascular diseases and the structural and functional changes in the walls of carotid arteries (IMC thickenings, the formation of atherosclerotic plaque).

Vascular aging, induced by atherosclerosis, can be tracked by the measurement of the IMC of the carotid arteries, thereby enabling the identification of patients with elevated risks, and application of preventive and therapeutic measures and procedures (18). The importance of the measurements of the IMC of the carotid arteries is confirmed by the fact that different national and international guidelines classify IMC as an additional factor in the assessment of the total risk for the occurrence of vascular diseases.

Our research showed that the older the age of patients of both sexes affected by arterial hypertension, the greater the thickness of the carotid IMC. There is a statistically significant correlation between the thickening of the carotid IMC and the elevated values of the blood pressure in patients who suffered a cerebrovascular insult (19).

Subclinical phase of atherosclerosis in the carotid arteries is the damage of the endothelium and gradual diffuse thickening of the IMC, further detailed researches of the altered IMC values of the carotid arteries will offer a better definition of this parameter as a predictable factor for cerebrovascular diseases (20).

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DIJAGNOSTIČKI ZNAČAJ DEBLJINE INTIMOMEDIJALNOG KOMPLEKSA KAROTIDNIH ARTERIJA KOD BOLESNIKA SA HIPERTENZIJOM KAO FAKTOROM RIZIKA ZA NASTANAK CEREBROVASKULARNIH BOLESTI

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Karotidna bolest doprinosi povećanju ukupnog morbiditeta i mortaliteta populacije obolele od cerebrovaskularnih bolesti. Primarni patološki činilac odgovoran za bolesti u ekstrakranijalnom delu cerebrovaskularnog sistema je ateroskleroza, a merenje debljine intimomedijalnog kompleksa (IMK) ekstrakranijalnog dela karotidnih arterija predstavlja merljiv pokazatelj ateroskleroze. Na debljinu IMK karotidnih arterija utiču brojni faktori, kao što su lokalna hemodinamika, zidni stres, hipertenzija arterialis i drugi.

Cilj našeg istraživanja bio je utvrđivanje uticaja hipertenzije kao faktora rizika za nastanak cerebrovaskularnih oboljenja na debljinu intimomedijalnog kompleksa karotidnih arterija kod asimptomatskih i simptomatskih ispitanika u odnosu na pol i starost.

Istraživanje je sprovedeno na 100 ispitanika oba pola koji su lečeni u ambulantnim uslovima ili hospitalizovani na Odeljenju neurologije, a u anamnezi bolesti su imali hipertenziju kao faktor rizika za nastanak cerebrovaskularnih oboljenja. Merenje IMK karotidnih arterija vršeno je ultrazvučnim pregledom, a kao granična vrednost normalnog i patološkog nalaza uzeta je vrednost debljine IMK > 0,9 mm.

Od ukupnog broja ispitanika bilo je 36 muškaraca i 64 žene. Svi ispitanici su imali povišene vrednosti krvnog pritiska. U ispitivanoj grupi bolesnika muškaraca sa znacima samo hipertenzivne bolesti bilo je 33,3%, a 66,7% je doživelo cerebrovaskularni insult i arterijsku hipertenziju kao faktor rizika. Od 64 žene sa znacima samo hipertenzivne bolesti bilo je 31,3%, a 68,75% je doživelo cerebrovaskularni insult, pri tom boluju od arterijske hiperenzije. Merenje debljine IMK karotidnih arterija ultrazvučnom metodom ima značaja u otkrivanju subkliničkog oštećenja strukture zida arterija i predstavlja deo algoritma za procenu cerebrovaskularnog rizika osoba sa povišenim krvnim pritiskom. Postoji značajna korelacija između debljine karotidnog IMK, hipertenzivne bolesti i cerebrovaskularnih oboljenja.

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Ključne reči: *karotidne arterije, intimomedijalni kompleks, hipertenzija, ateroskleroza, ultrazvučna dijagnostika*