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CLINICAL TRIAL

Nature and structure of atherosclerotic lesion of common carotid arteries depending on cardiac remodelling in patients with arterial hypertension

Hajiyev A.B.[1], Kandilova V.N.[2], Jahangirov Tofig[1]

[1]*Scientific Research Institute of Cardiology named after J. Abdullayev. J. Abdullayev*
[2]*Central Military Polyclinic of the Ministry of Defense of the Azerbaijan Republic*

Abstract

As arterial hypertension (AH) progresses, deformations, sclerosis and remodelling of both myocardium and vessels develop, which usually leads to various complications (myocardial infarctions, strokes, etc.). Modern ultrasound methods of research (echocardiography, Doppler vascular dopplerography), have provided an opportunity to differentiate structural and functional changes both in the heart and in the arteries, as well as in the ultrasound structure of formed intravascular atherosclerotic plaques (AP). At present, as a result of analysis and comparison of the accumulated clinical and instrumental data, it has become clear that APs of different echo structure have different prognostic value in terms of the possibility of complications, their rupture, emboli, etc. In connection with the above-mentioned the aim of the presented study was a comparative evaluation of the heart condition and wall structure of common carotid arteries (CCA) in patients with AH with absence and different variants of myocardial remodelling.

124 patients (86 men and 38 women) aged 27 to 81 years (mean age 55.66+1.01 years) were examined. 17 (11 men and 6 women) of them had stage I AH, 88 (66 men and 22 women) had stage II AH, and 19 (9 men and 10 women) had stage III AH. The diagnosis of ischemic heart disease (IHD) and AH was verified according to the existing modern clinical recommendations. Clinical-anamnestic and instrumental examination of patients with verification of diagnoses was performed with assessment of the variant of myocardial remodelling they had. Using echocardiographic examination (EchoCG) in one-dimensional (M) and two-dimensional (B) scanning modes, a number of parameters reflecting the state of intracardiac haemodynamics and myocardial remodelling were investigated. Ultrasound scanning was used to investigate both sides of CCA with determination of intima-media complex thickness (IMCT), detection of intravascular atherosclerotic plaques (AP), assessment of their echo structure (hypo-, hyper- and heterogeneous), haemodynamic significance (% stenosis of the vessel lumen), surface (smooth or fissured edges). The data were analyzed using Statistica 12.6 application software package.

The results of the study confirm the presence of cardiac and vascular remodelling in patients with AH, and the degree of vascular remodelling and formation of prognostically 'unfavourable' friable plaques in carotid arteries is in direct correlation with the presence and variant of myocardial remodelling.

Keywords: arterial hypertension, common carotid arteries, myocardial remodelling, myocardial hypertrophy, remodelling of common carotid arteries, intima-media complex thickness, echo structure of atherosclerotic plaques.

Introduction

The wide spread of AH at the present stage endows the mentioned problem with very great relevance and social significance. According to epidemiological studies, the prevalence of AH among adults' ranges from 20 to 40%, increasing with age and being found in 50% of men and women over 60 years old and in 2/3 – over 70 years old [2; 8]. As AH progresses, elasticity of the walls of the main and smaller arteries decreases, their deformations, sclerosis and remodelling develop, which usually leads to various complications – cerebral circulatory disorders, strokes, myocardial infarctions, etc. In this regard, timely detection of patients with early changes in vessels (appearance of signs of atherosclerotic lesions of vessels with the formation of intravascular AP) in AH becomes very important. Introduction into clinical practice of modern instrumental methods of research, including ultrasound Doppler vascular imaging, has provided an opportunity to diagnose subclinical

vascular lesions at the earliest stages of atherosclerotic lesions. In addition, with the improvement of ultrasound equipment it became possible to differentiate differences in the ultrasound structure of formed intravascular APs with the definition of homogeneity or heterogeneity, weakening or strengthening of the ultrasound signal reflected from APs, changes in the integrity and structure of the intimal and adventitial layers of the vascular wall (presence of phenocrysts, calcifications and other inclusions) [15]. At present, as a result of analysis and comparison of the accumulated clinical and instrumental data, it has become clear that APs of different echo structure have different prognostic value in terms of the possibility of complications, their rupture, emboli, etc. [5; 7]. At the same time, it is known that along with vascular remodelling, the course of AH is almost always accompanied to a greater or lesser extent by cardiac remodelling, the main manifestations of which are changes in its geometry (increased myocardial mass (MM) of the left ventricle (LV), LV hypertrophy (LVH) of various degrees and other signs) [1; 3]. In the light of the above mentioned, the aim of the present study was to evaluate structural and functional changes of carotid arteries in patients with AH with absence and different types of cardiac remodelling.

Material and Methods

124 patients with AH of I-III degree aged from 31 to 62 years (mean age 55,66±1,01 years), 56 men (mean age 54,7±1,01 years) and 65 women (mean age 56,5±1,68 years) were examined. AH was diagnosed according to WHO criteria [16]. Inclusion criteria for the study were patients with AH I-III degree. The duration of AH was on average 8.36±0.37 years with fluctuations from 1 to 21 years; in the subgroup of men – 8.42±0.42 years with fluctuations from 2 to 21 years, in the subgroup of women – 8.21±0.74 years with fluctuations from 1 to 18 years. The presence of type 2 diabetes mellitus and metabolic syndrome, symptomatic forms of AH, acute myocardial infarction, cardiac rhythm and conduction disorders, blood diseases, oncological diseases, acute cerebral circulation disorder in the history, heart defects, respiratory, renal, hepatic and cardiac insufficiency were excluded in all examined patients. In order to study the influence of absence and different variants of cardiac remodelling on remodelling and nature of AP in CCA, the total number of the examined patients was also divided into 3 subgroups depending on the presence and type of cardiac remodelling according to the proposed classification [13] (Table 1).

Table 1: Distribution of patients depending on the presence and variant of cardiac remodelling

	Without remodelling	*Eccentric type*	*Concentric type*
Men	6 (4,84%)	34 (27,42%)	46 (37,1%)
Women	12 (9,68%)	14 (11,29%)	12 (9,68%)
Total	18 (14,52%)	48 (38,71%)	58 (46,77%)

All examined patients underwent echocardiographic cardiac examination, color duplex scanning of CCA on both sides. To evaluate central hemodynamics and myocardial contractile function, transthoracic EchoCG, pulse-wave Doppler on Vivid S5 3ScRS (USA) with 3.5 MHz transducer with pulse mode and color Doppler were performed. We used standard EchoCG accesses (parasternal on long and short axes, apical and subcostal) with estimation of left ventricular (LV) end-diastolic (EDD) and systolic (ESD) dimensions, LV end-diastolic (EDV) and systolic (ESV) volumes, interventricular septum (IVS) thickness and LV posterior wall thickness (LV PWT). Cardiac contractile function and central haemodynamics were calculated using the biplane method of Simpson et al. (1972). EchoCG parameters analysis included calculation of central and cardiac haemodynamics parameters: stroke volume (SV), ejection fraction (EF) according to generally accepted methods. LV myocardial mass (LV MM) was calculated according to M-mode EchoCG data using the previously proposed formula [11]. Ultrasound scanning of the right and left CCA in B-mode combined with Dopplerography and color mapping of intravascular blood flow through the arteries was performed on a Seividi device (manufactured in Hong Kong) using a 7 mHz linear transducer. The arteries of the cervical region were visualized with sighting of the CCA on both sides in 3 planes. The presence of arterial tortuosity, wall structure changes (calcification, calcifications, aneurysms), intravascular APs was detected [4]. The echo structure of the intima-media complex was studied according to the recommendations of the international consensus [15]. Quantitative assessment of IMCT was performed at the distal part of CCA 1-1.5 cm from the bifurcation, outside the area of AP along its posterior wall, averaging three maximum measurements. The cursor was set at the boundary 'artery-intima-vessel lumen' and at the boundary 'media-adventitia'. The image was synchronised with diastole. The presence of structural changes in CCA was documented on the basis of detection of initial atherosclerotic changes in the form of its increased IMCT more than 0.9 mm [6]. When APs were detected, their size, shape, surface character (smooth, irregular), echogenicity (normo-, hypo-, hyper- or hetero-), haemodynamic significance were determined in accordance with the recommendations [4].

Laboratory examination included determination of plasma glucose, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) using kits 'Human' (Germany) and Erba (European Union) on a biochemical analyzer Multi+ (Poland). The content of low-density lipoprotein cholesterol LDL-C was calculated according to the formula [12], the content of very-low-density lipoprotein cholesterol LVLD-C by the formula: (TC

– HDL-HDL-C – TG)/2.2, because the TG level in all subjects was less than 35.37 mmol/l; atherogenicity coefficient (AC) by the formula: AC = (TC – HDL-C)/ HDL-C. Methods of descriptive statistics included calculation of mean values (M), standard error of mean (m), minimum and maximum for normal distribution. Results were presented as M±m. Since quantitative signs in variation series were normally distributed in all compared groups, comparison of two independent groups with was performed using Student's t-test for independent samples. The critical level of significance (p) was taken as 0.05. Statistical processing of the obtained data was carried out using the statistics 12.0 programme.

Results and Discussion

IVS, LV PWT and ESD indices were significantly higher in patients with eccentric (EH) and concentric hipertrophy (CH) compared to the subgroup without hipertrophy (WH) (ESD differences between the subgroups of EH and CH patients reached statistical significance). The mean values of LV EDD, EDV and ESV were also comparatively higher in patients with EH and CH. The values of EF were not significantly different, whereas the values were significantly higher in the subgroup WH compared to both EH and CH patients. The EF was significantly higher in the CH patients compared to the EH patients, and there were no significant differences between the subgroups of EH and CH patients in other parameters. The highest values of LV MM and myocardial mass index (MMI) were in the subgroup with CH, significantly exceeding those in the subgroups with EH and WH, with these values in the subgroup with EH significantly exceeding those in the subgroup with WH. Out of 124 examined patients with AH of I-III degrees, IMC thickening (over 0.9 mm) was detected in 99 patients in the right and 101 patients in the left CCA, at that 14 patients (11 men and 3 women) had increase of CCA IMC thickness on one side, in other 87 patients – on both sides (in the right and left CCA). APs were detected in 2 patients (2 men) in the right CCA and in 18 patients (15 men and 3 women) in the left CCA. To investigate the relationship between the presence and type of cardiac and vascular remodelling, we studied the frequency of detection and echo structure of detected APs depending on the presence and different variants of myocardial remodelling (Tables 2 and 3).

Table 2: Comparative characteristics of myocardial functional state indices in patients with AH without cardiac remodelling and with different variants of LV remodelling (M ± m)

Indices	*WH (n = 18)*	*EH (n = 48)*	*CH (n = 58)*
IVS thickness	0,97 ± 0,02*1;^1 (0,7 – 1,1)	1,25 ± 0,02*1 (0,9 – 1,4)	1,25 ± 0,02^1 (1,0 – 1,5)
LV PWT	0,96 ± 0,02*2;^2 (0,71 – 1,12)	1,1 ± 0,02*2;#1 (0,8– 1,5)	1,21 ± 0,02^2;#1 (0,9 – 1,5)
LV EDD	4,95 ± 0,1 (4,4 – 6,1)	5,07 ± 0,07 (3,8 – 5,9)	5,13 ± 0,06 (4,2 – 6,0)
LV ESD	3,39 ± 0,11^3 (2,9 – 4,9)	3,54 ± 0,07 (2,5 – 4,8)	3,7 ± 0,06^3 (2,6 – 4,8)
LV EDV	106,7 ± 4,84 (78 – 161)	114,0 ± 2,85 (62 – 168)	117,8 ± 2,79 (77 – 168)
LV ESV	45,0 ± 4,52 (30 – 103)	49,19 ± 1,99 (22 – 99)	53,24 ± 1,69 (31 – 95)
LV SV	58,6 ± 2,55 (36,03 - 71,17)	57,31 ± 0,93#2 (40,15 - 69,0)	64,52 ± 1,84#2 (34,0 - 97,0)
LV EF	58,6 ± 2,55 (36,03 - 71,17)	57,31 ± 0,93 (40,15 - 69,0)	54,78 ± 0,9 (38,95 - 68,04)
DS%	31,58 ± 1,06^4 (19,7 – 38,2)	30,31 ± 0,66#3 (18,64 – 38,2)	28,01 ± 0,69^4; #3 (17,86 – 39,53)
LV MM	173,4 ± 7,19*3;^5 (118,7 - 233,9)	241,7 ± 6,34*3;#4 (150,6 - 320,2)	260,0 ± 6,07^5; #4 (180,5 - 386,1)
MMI	87,76 ± 3,18*4;^6 (65,2 - 108,7)	115,5 ± 2,94*4 (72,96 - 155,2)	123,5 ± 3,07^6 (82,01 - 186,9)

Notes to Table 3: WH – without LV hypertrophy, EH – eccentric LV hypertrophy; CH - concentric LV hypertrophy. * - reliability of differences between WH and EH subgroups; ^ - reliability of differences between WH and CH; # - reliability of differences between EH and CH; *1-p=0.0000000001; Student's t-test, 9.90 (number of degrees of freedom f=64); *2-p=0.000006; Student's t-test, 4.95; *3-p=0.00000000000001; Student's t-test, 7.12; *4-p=0.00000000000001; Student's t-test, 6.41; ^1-p=0.0000000001; Student's t-test, 9.90 (number of degrees of freedom f=74); ^2-p=0.00000000001; Student's t-test, 8.84; ^3-p=0.015683; Student's t-test, 2.47; ^4-p=0.006134; Student's t-test, 2.82; ^5-p=0.000000000000001; Student's t-test, 9.20; ^6-p=0.00000000000001; Student's t-test, 8.09; #1-p=0.000178; Student's t-test, 3.89 (number of degrees of freedom f=104); #2-p=0.000695; Student's t-test, 3.50; #3-p=0.017781; Student's t-test, 2.41; #4-p=0.039548; Student's t-test, 2.08; ^2 - p=0.0000000000001; Student's t-test, 8.84; ^3 - p=0.025909; Student's t-test, 2.27; ^4 - p=0.015417; Student's t-test, 2.48; #1-p=0.000048; Student's t-test, 4.24 (number of degrees of freedom f=104); #2-p=0.020313; Student's t-test, 2.36; #3-p=0.003736; Student's t-test, 2.97.

Table 3: Comparative characteristics of indices of structural and functional state (remodelling) of common carotid arteries and vasomotor function of endothelium in patients with AH without cardiac remodelling and with different variants of LV remodelling (M ± m)

Indices	*WH (n = 18)*	*EH (n = 48)*	*CH (n = 58)*
Different character of AP and pathologically changed indices in right and left CCA (n = 248)			
AP (right +left CCA)	1 (0,4%)	6 (2,4%)	11 (4,4%)
AP (right CCA)	0 (0,0%)	0 (0,0%)	2 (0,8%)
AP (left CCA)	1 (0,4%)	6 (2,4%)	9 (3,6%)
AP (h/is)	1 (0,81%)	5 (2,0%)	9 (3,6%)
AP (h/s)	0 (0,0%)	1 (0,4%)	2 (0,8%)
High echogenety			
Totally	1 (0,4%)	5 (2,0%)	4 (1,6%)
Low echogenety			
Totally	0 (0,0%)	0 (0,0%)	5 (2,0%)
Heterogenic echogenety			
Totally	0 (0,0%)	1 (0,4%)	2 (0,8 %)
Plaque edges are jagged			
Totally	0 (0,0%)	0 (0,0%)	6 (2,4%)

Notes to Table 4: *WH – without LV hipertrophy, EH – LV eccentric hipertrophy; CH – LV concentric hipertrophy*

Table 4: Mean values of blood lipid profile parameters in patients with AH without cardiac remodelling and with different variants of LV remodelling (M ± m)

Indices	*WH (n = 18) 6/12*	*EH (n = 48) 34/14*	*CH (n=58) 46/12*
CC (mmol/l)	5,13 ± 0,18 (3,8 - 6,7)***1**;^1	5,7 ± 0,21 (3,0 - 11,2)***1**	5,66 ± 0,14 (4,2-11,0)^1
Male	5,33 ± 0,35 (4,5 - 6,7)	5,76 ± 0,27 (3,0 - 11,2)	5,69 ± 0,17 (4,2 - 11,0)
Female	5,03 ± 0,17 (3,8 - 6,5)	5,54 ± 0,31 (4,0 - 7,4)	5,56 ± 0,21 (4,7 - 6,7)
HDLP (mmol/l)	1,01 ± 0,04 (0,8 - 1,3)	1,11 ± 0,04 (0,7 - 1,8)	1,06 ± 0,03 (0,7 - 1,8)
Male	1,04 ± 0,07 (0,88 - 1,3)	1,11 ± 0,04 (0,7 - 1,8)	1,06 ± 0,03 (0,75 - 1,8)
Female	1,0 ± 0,04 (0,8 - 1,2)	1,12 ± 0,06 (0,8 - 1,6)	1,04 ± 0,08 (0,7 - 1,6)
LDLP (mmol/l)	3,37 ± 0,18 (2,06 - 4,87)	3,74 ± 0,17 (1,72 - 7,49)	3,73 ± 0,12 (1,51 - 7,3)
Male	3,56 ± 0,41 (2,29 - 4,87)	3,78 ± 0,21 (1,72 - 7,49)	3,72 ± 0,14 (1,51 - 7,3)
Female	3,28 ± 0,16 (2,06 - 4,48)	3,64 ± 0,28 (2,25 - 5,28)	3,75 ± 0,21 (2,56 - 5,18)
VLDLP (mmol/l)	0,75 ± 0,03 (0,42 - 0,96)	0,84 ± 0,05 (0,36 - 1,91)	0,88±0,07 (0,36 - 4,36)
Male	0,74 ± 0,08 (0,42 - 0,96)	0,87 ± 0,06 (0,36 - 1,91)	0,91 ± 0,09 (0,36 - 4,36)
Female	0,75 ± 0,03 (0,59 - 0,96)	0,78 ± 0,07 (0,46 - 1,55)	0,77 ± 0,05 (0,55 - 1,09)
TG (mmol/l)	1,65 ± 0,07 (0,93 - 2,1)	1,86 ± 0,11 (0,8 - 4,2)	1,93 ± 0,16 (0,8 - 9,6)
Male	1,62 ± 0,17 (0,93 - 2,1)	1,91 ± 0,14 (0,8 - 4,2)	1,99 ± 0,19 (0,8 - 9,6)
Female	1,66 ± 0,06 (1,3 - 2,1)	1,72 ± 0,15 (1,0 - 3,4)	1,69 ± 0,1 (1,2 - 2,4)
AI (units)	4,2 ± 0,25 (2,46 - 5,71)	4,21 ± 0,17 (2,01 - 7,2)	4,54 ± 0,17 (1,63 - 8,57)
Male	4,28 ± 0,49 (2,46 - 5,71)	4,24 ± 0,19 (2,08 - 7,2)	4,49 ± 0,17 (1,63 - 7,5)
Female	4,17 ± 0,25 (2,46 - 5,56)	4,12 ± 0,39 (2,07 - 6,44)	4,72 ± 0,5 (2,0 - 8,57)

Notes to Table 4: *WH – without LV hipertrophy, EH – LV eccentric hipertrophy; CH – LV concentric hipertrophy*
* - reliability of differences between WH and EH subgroups: p=0.043452; Student's t-test - 2.06 (number of degrees of freedom f=64); ^ - reliability of differences between WH and CH: p=0.022900; Student's t-test - 2.32 (number of degrees of freedom f=74)

According to the data presented in Table 2, it can be seen that LV EDD, ESD, as well as LV EDV and ESV were significantly higher in CH patients (at that, it was reliable with the CH subgroup in terms of LV ESD). The DS% were significantly higher in WH patients, whereas LV SV and EF were not significantly different. The highest LV MM and MMI were in the subgroup with CH, significantly exceeding the same in the subgroups with EH and WH, at the same time, the index

of LV MMI in the subgroup with CH significantly exceeded the similar index in the subgroup with EH, and they were minimal in the subgroup with WH, significantly differing by both indices from the subgroups with different type of myocardial remodelling. The overwhelming majority of the examined patients showed signs of atherosclerotic lesion of the CCA walls on one or both sides, consisting in IMC enlargement, differentiation of arterial wall IMC into separate clearly defined layers with increase or decrease of their echogenicity. According to the data presented in Table 3, we can see that the number of detected APs was the lowest in the subgroup of WH patients, maximum high – in the subgroup with CH, among the patients with EC – occupied an intermediate position; the differences in this indicator were not reliable. In the subgroup of WH patients, APs in CCA were detected comparatively less frequently when assessed from both sides. In the EH subgroup, they were detected in the left CCA in 6 patients, in 11 patients with CH (2 - in the right, 9 - in the left CCA). APs were detected more frequently in men both in the subgroup with EH (6 (2.4%) vs. 0 (0.0%)) and with CH (9 (3.6%) vs. 2 (0.8%)). When comparing the detected APs according to the degree of narrowing of the vessel lumen, it was demonstrated that relatively more frequent APs were hemodynamically insignificant (his) versus hemodynamically significant (hs): in the subgroup of patients with EH (5 (2.0%) vs. 0 (0.0%), in the subgroup of patients with CH (9 (3.6%) vs. 2 (0.8%)). In the subgroup of WH patients, 1 (0.4%) AP was detected in a woman who had more than 70% stenosis of the CCA, i.e., was hs. When comparing the detected APs by the degree of echogenicity of the reflected ultrasound signal, we distinguished the structure of APs as homogeneous (high and low echogenicity) and heterogeneous. In the WH subgroup the echogenicity of the detected AP was high, in the EH subgroup 5 (2.0%) APs had high echogenicity with a smooth surface; in the CH subgroup 7 (2.8%) patients had high echogenicity, with the surface of the AP being smooth, in 2 (0.8%) patients the echogenicity of the AP was low, although in 1 case the edges of the APs were smooth and well delineated, in 1 case the edges were indistinct and loosened. Thus, according to our data, there was a certain correlation between the variant of myocardial remodelling and the character of formed APs in CCA. When comparing the main blood lipid profile parameters (Table 4), no significant differences were found between the subgroups of patients without and with LVH, with the exception of CC indices, the mean values of which were significantly lower in the WH subgroup compared to both EH and CH patients. At the same time, there was a distinct non-significant tendency to increase LDLP, VLDLP and TG in patients with different types of LVH in comparison with patients in the WH subgroup. There was also a trend towards increased AI in patients WH. Thus, the differences in the structure and character of AP described in the first part did not depend on the lipid profile of blood plasma of the examined patients.

Discussion

It is known that the earliest marker of atherosclerotic lesions development in CCA is an increase in IMCT, as well as additional ultrasound signs in the form of differentiation into separate layers, increased or partial change in echogenicity, hyperechogenic inclusions, and at later stages of atherosclerosis – formation of AP, also differing in their echo structure [6]. According to our data, in patients with LV myocardial remodelling of eccentric or concentric type, the signs of atherosclerotic lesion of CCA with the formation of APs in them were detected more often. Similar data were obtained in the studies of other authors. Thus, it was shown that damage to the vascular wall due to increased systolic BP increases its susceptibility to atherosclerosis development by the mechanism caused by the pathological effect of LDL-C [14]. In addition, other authors revealed the relationship between LV myocardial remodelling (mainly of concentric type) with more frequent formation of heterogeneous and unstable AP, deformation of extracranial sections of brachiocephalic arteries, which reflected a higher risk of cerebrovascular complications in hypertensive patients [7]. According to our data, loosened APs with low echogenicity, which, according to numerous studies, have poor prognostic significance with a high risk of embolism development even at a small degree of narrowing of the arterial lumen [9; 10], were detected more often in hypertension, especially in CH type. It is necessary to conduct further studies aimed at studying the nature and interrelation of structural changes in the walls of the main arteries and the heart in cause-and-effect relations in the aspect of the development of life-threatening complications of AH.

Conclusion

- A large number of patients with AH have cardiac and vascular remodelling (exemplified by CCA).
- In eccentric and to an even greater extent in concentric type of LV hypertrophy detected APs have low or heterogeneous echo structure, which is an unfavourable prognostic sign in the aspect of thromboembolism development and plaque rupture.

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