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Relation of the Atherosclerotic Process with the Manifestation of Oxidative Stress in Arterial Hypertension Patients Combined with Rheumatoid Arthritis

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Abstract

Introduction. When arterial hypertension (AH) is combined with rheumatoid arthritis (RA), there are significant imbalances between the production of lipid peroxidation (LP) derivatives and the ability to neutralize these reactive substances.

Aim of the study: To investigate the lipid profile, the thickness of the intima-media complex (TIMC) of common carotid arteries in patients with rheumatoid arthritis in combination with arterial hypertension, and to correlate these indicators with the manifestations of oxidative stress, and the antioxidant system.

Materials and methods: The results of the study are based on a comprehensive survey of 96 patients with stage 2 hypertension in combination with RA, 45 patients with stage 2 hypertension and 31 healthy volunteers.

Research results. The stage of hypertension significantly influenced the manifestations of atherosclerotic process and oxidative stress, average TIMC indexes of the right CCA 1.28 (1.08; 1.30) mm and left CCA 1.29 (1.06; 1.30) mm in patients with RA in combination with stage 2 AH were significantly higher by 24.2% and 24%, respectively, against rates of RA patients in combination with grade 1 AH ($p < 0.01$). The detection rate of atherosclerotic plaques in the subgroup of RA patients

in combination with grade 2 AH was significantly higher 10 times, compared to the subgroup of RA patients in combination with stage 1 AH ($p < 0.01$).

Significant relation between LP products indices and manifestations of atherosclerotic process in patients with hypertension in combination with RA, direct linear correlation of medium strength between indices of malonic aldehyde and LDL R = + 0,57, TG R = + 0,56, TIMC R = + 0.55, respectively ($p < 0.05$), diene ketones and TG R = + 0.52, TG R = + 0.55, respectively ($p < 0.05$).

Conclusions. The highest predictive value for the detection of atheromatous plaques in the CCA system had malonic aldehyde (AUC 0.870, 95% CI AUC 0.784 to 0.931) at the optimum distribution point > 5.25 nmol/ml, sensitivity 88.73%, and specificity 90.43%, and diene ketones (AUC 0.869, 95% CI AUC 0.784 to 0.930) sensitivity 90.36% and specificity 88.87% at the optimum distribution point > 5 c.un./ml.

Keywords: arterial hypertension, rheumatoid arthritis, intima-media complex thickness, oxidative stress, lipid peroxidation products.

Introduction

When arterial hypertension (AH) is combined with rheumatoid arthritis (RA), there are significant imbalances between the production of lipid peroxidation products (LP) and their derivatives and the ability to neutralize these reactive substances. Lipid peroxidation products - isolated double bonds, diene conjugates, diene ketones, chiffon bases and malonic aldehyde accumulate in biological organisms and under reduced endogenous antioxidant protection disrupt processes of synthesis. Penetrating into the bilipid layer of membranes LP products initiate chain reactions of oxidation, resulting in damage of endothelial cells, which leads to endothelial dysfunction and progression of atherosclerosis process [10,12]. Oxidative stress impairs endothelial dysfunction, and endothelial dysfunction worsens ischemia and leads to even more intense formation of peroxide radicals [7,5].

Increased mortality in RA is caused by the high prevalence of cardiovascular diseases (CVD) and its complications, which are mainly associated with the atherosclerosis process [13,4]. RA is recognized as an independent risk factor for CVD, with additional specific mechanisms for vascular wall damage and atherosclerosis [8]. In conditions of chronic inflammatory process and intense oxidative stress, there is an increase in the penetration of small lipid particles into the subendothelial layer, which leads to an increase in the thickness of the intima-media complex (TIMC) [6,2]. TIMC determines not only the functionality of the artery, but also the development of atherosclerosis. TIMC and the presence of atheromatous plaques (AP) are predictors of CVD development, both in the general population and

in patients with RA [1,9]. Early detection of vascular affection predictors and early correction of modified risk factors may reduce the rate of cardiovascular complications in patients with AH in combination with RA. The aim of the study**:** to investigate the lipid profile, the thickness of the intima-media complex of common carotid arteries in patients with rheumatoid arthritis in combination with arterial hypertension, and to correlate these indicators with the manifestations of oxidative stress, and the antioxidant system.

Materials and methods. The study was conducted on the basis of the Department of Clinical Pharmacology and Endocrinology of the "Zaporizhzhya Medical Academy of Postgraduate Education of the Ministry of Health of Ukraine", and the selection of patients was carried out in the rheumatology and therapeutic department of KU "Zaporizhzhia City Clinical Hospital No. 10" of Zaporizhzhia City Council from 2016 to 2018. The results of the study are based on a comprehensive survey of 96 patients with stage II hypertension in combination with RA, 45 patients with stage 2 hypertension and 31 practically healthy individuals.

Inclusion criteria of the study: persons of both genders aged from 45 to 65 years inclusive; presence of proved diagnosis of stage 2 hypertension; presence of proved diagnosis of RA that developed after the onset of hypertension (for patients of the main group); informed consent of patients for follow-up; stable selection of basic RA therapy (at least 6 months before enrollment) for patients of the main group;

Exclusion criteria of the study: diagnosis of coronary heart disease; stage 3 hypertension; secondary forms of hypertension; clinical signs of heart failure II B - III stages, hemodynamically significant disturbances of rhythm and cardiac malformations; diabetes mellitus and hypothyroidism; renal dysfunction GFR <60 ml / min / 1.73 m; obesity 3 - 4 stages; oncological diseases.

In carrying out diagnostic measures I grounded on the protocols of the MH of Ukraine according to the order from 11.04.2014 "Unified clinical protocol of primary, secondary, tertiary care and medical rehabilitation of patients with rheumatoid arthritis" [14]; the recommendations of the Association of Rheumatologists of Ukraine and ACR / EULAR 2018; diagnosis and treatment protocol in accordance with Order № 384 of May 24, 2012 "On approval and implementation of medical and technological documents on standardization of care in arterial hypertension", recommendations of the Ukrainian Association of Cardiologists and ESC 2018.

The main first group (group I) included 93 patients with the stage 2 hypertension in combination with RA, including 15 (16.13%) men and 78 (83.87%) women. There were 63 patients with hypertension 1 and 30 patients with stage 2 hypertension. The average age was 56 (51; 61) years. The average duration of hypertension in patients of group I was 9 (8; 10) years, the average duration of RA was 6 (4; 7) years. Activity on the DAS 28 scale was 4.64 (4.24; 4.88) points corresponded to the average activity of the process. The control second group (group II) included 45 patients with stage 2 hypertension, including 10 (20%) men and 36

(80%) women, the average duration of hypertension was also 9 (8; 10) years. The average age was 56 (54; 59) years. 30 patients with stage 1 hypertension and 15 patients with stage 2 hypertension. The control third group (group III) included 31 practically healthy persons, 7 (22.58%) men and 24 (77.42%) women. The average age was 56 (54; 59) years. 30 patients with stage 1 hypertension and 15 patients with Stage 2 hypertension. The control third group (group III) included 31 practically healthy persons, 7 (22.58%) men and 24 (77.42%) women. The average age was 54 (51; 58). The groups were age- and gender-matched ($p > 0.05$).

All patients were tested for lipid profile, total cholesterol (TCL), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG) and atherogenic index (AI). Common carotid arteries (CCA) ultrasound imaging scans were performed on an ULTIMA PRO-30 scanner (Ukraine) with a 7.5 MHz sensor. The course of carotid arteries, blood flow, presence and number of atheromatous plaques (AP) were evaluated, and their location on the sites of available imaging. The thickness of the intima-media complex (TIMC) was measured in the frozen image mode, in the distal segment of the CCA system along the posterior wall of the right and left CCA.

The state of the LP processes was evaluated on the basis of the primary and secondary products of the LP: Schiff bases, diene conjugates, diene ketones and malonic aldehyde. Diene conjugates were determined according to a method of V.B. Havrylov (1988) using a SF-46 spectrophotometer. Lipid hydroperoxides were extracted from plasma with a mixture of heptane-isopropyl spirit. The concentration of malonic aldehyde was determined in reaction with 2-thiobarbituric acid to form a three-minute complex with a maximum absorption of 532 nm, a molar extinction coefficient of 1.58×105 M cm. The obtained data were calculated per 1 ml of plasma. Photoelectrocolorimeter KFK-2 was applied to obtain results.

In order to study the antioxidant system, the levels of vitamins A and E were determined using Thomson's method in modification of R.G. Chernyauskine (1983). The method was based on the determination of fluorescence of tocopherol and retinol in serum hexane extract. Vitamin concentration was calculated per 1 ml of serum.

Statistical processing was performed on a personal computer using the PSPP application package (version 0.10.2, GNU Project, 1998-2016) and Apache OpenOffice (version 4.1, GNU GPL licenses). Data are presented as the median and interquartile range Me (Q25; Q75). When testing the statistical hypotheses, the null hypothesis was rejected at the level of statistical significance (p) below 0.05. The relationship of the two traits was evaluated by the results of correlation analysis. To determine parametric distribution the Pearson method (r) was applied, and at the distribution other than normal the method of Spearman rank correlation (R) was applied. For dichotomous variables an analysis was performed (Receiver Operating Characteristic curve analysis). The ROC analysis was used to determine the optimal point of separation, while calculating the area under the ROC curve (AUC) and its

95% confidence interval (CI), sensitivity (Se) and specificity (Sp). Detection of the optimal separation point was performed using the Youden index.

Results

In the study of lipid profile in the surveyed persons, it was found that the median values of TCL 5.9 (5.32; 6.54) mmol/l, LDL 3.76 (3.2; 4.42) mmol/l, TG 2.3 (1.99; 2.7) mmol/l and IA 4.06 (3.46; 5.2). And in patients with hypertension combined with RA the lipid profile test results were significantly higher by 6.8%, 10.6%, 19.6% and 11.6%, TCL 5.5 (4.88; 6.05) mmol/l, LDL 3.36 (2.95; 3.86) mmol/l, TG1.85 (1.51; 2.12) mmol/l, IA 3.59 (2.93; 3.88) comparing to the group of patients with hypertension ($p < 0.05$). And the median HDL of 1.12 (1; 1.25) mmol/l was significantly lower by 13.9%, compared to HDL of 1.3 (1.1; 1.4) mmol/l group of patients with hypertension ($p < 0.05$). The results are presented in the table 1.

Table 1: Lipid profile test results of the surveyed persons (Me [25; 75], n = 163).

Test results, units of measure	Patients with hypertension + RA (n = 93)	Patients with hypertension (n = 45)	Almost healthy individuals (n = 31)	P value
	I	II	III	
TCL, mmol / l	5.9 [5.32; 6.54]	5.5 [4.88; 6.05]	4.2 [3.7; 4.5]	$p_{1-2} = 0.02$ $p_{2-3,\ 1-3} < 0{,}001$
HDL, mmol / l	1.12 [1.0; 1.25]	1.3 [1.1; 1.4]	1.54 [1.38; 1.68]	$p_{1-2} = 0.036$ $p_{2-3,\ 1-3} < 0.001$
LDL, mmol / l	3.76 [3.2; 4.42]	3.36 [2.95; 3.86]	2.0 [1.81; 1.68]	$p_{1-2} = 0.034$ $p_{2-3,\ 1-3} < 0.001$
IA	4.06 [3.46; 5.2]	3.59 [2.93; 3.88]	1.71 [1.47 1.8]	$p_{1-2,\ 2-3,\ 1-3} < 0.001$
TG, mmol / l	2.3 [1.99; 2.7]	1.85 [1.51; 2.12]	1.12 [0.84; 1.36]	$p_{1-2} = 0.002$ $p_{2-3,\ 1-3} < 0.001$

Ultrasound examination of common carotid arteries has not revealed a significant difference between TIMC indicators of right and left CCA in patients with hypertension in combination with RA and patients with hypertension ($p > 0.05$). Atheromatic plaques were detected in 23 (24.7%) patients with hypertension combined with RA, and in 9 (20%) patients with hypertension. The detection rate of atherosclerotic plaques was higher by 19% in patients with hypertension in combination with RA ($p = 0.04$). The median TIMC indices of the right CCA 1.03

(0.89; 1.13) mm and the left CCA 1.01 (0.90; 1.12) mm were significantly higher in patients with hypertension in combination with RA by 19.4% and 17,8% respectively against indicators of the group of healthy persons (p <0.01). TIMC indices of common carotid arteries in patients with hypertension in combination with RA were analyzed depending on the stage of hypertension. The median TIMC indices of the right CCA 1.28 (1.08; 1.30) mm and TIMC of the left CCA 1.29 (1.06; 1.30) in RA patients combined with stage 2 AH were significantly higher by 24.2 % and 24%, respectively, against the indicators of TIMC of the right CCA 0.97 (0.88; 1.09) mm and TIMC of the left CCA 0.98 (0.88; 1.08) mm of RA patients in combination with stage 1 hypertension (p <0.01). The detection rate of atheromatous plaques in the subgroup of RA patients in combination with stage 2 AH was significantly 10-times higher, compared to the subgroup of RA patients in combination with stage 1 AH (p <0.01). The results are presented in the table 2.

Table 2: Indicators of thickness of the intima-media complex of common carotid arteries in patients with hypertension in combination with RA depending on the stage of hypertension (Me [25; 75], n = 93).

Test results, units of measure	Patients with hypertension + RA stage 1 AH (n = 63)	Patients with hypertension + RA stage 2 AH (n = 30)	P value
	1	2	
TIMC of the right CCA, mm	0.97 [0.88; 1.09]	1.28 [1.08; 1.30]	p < 0.001
TIMC of the left CCA, mm	0.98 [0.88; 1.08]	1.29 [1.06; 1.30]	p < 0.001
Presence of AB, number of persons (%)	4 (6.3 %)	19 (63.3%)	p < 0.001

In patients with hypertension, in combination with RA, the median of isolated double bonds were 26.2 (21.3; 29.1) c.u./ml, diene conjugates 28.5 (22.7; 31.4) c.un./ml, diene ketones 4.8 (4.1; 5.3) c.u./ml, Schiff bases 17 (14; 19) c.u./ml, and malonic aldehyde 4.66 (3.94; 5.25) nmol/ml. Above results were significantly higher by 26.7%, 31.6%, 31.3%, 17.6% and 28.3%, respectively, against isolated double bond rates 19.2 (18.1; 20.3) c.u./ml, diene conjugates 19.5 (18.3; 20.4) c.u./ml, diene ketones 3.3 (3.1; 3,7), chiffon bases 14 (12; 16) c.u./ml, and malonic aldehyde 3.34 (3.11; 3.54) nmol/ml in patients with hypertension (p <0.01). Median Vitamin A results were 1.51 (1.22; 1.79) μmol/l, Vitamin E 11.03 (8.98; 13.1) μmol/L and Catalase 16.4 (13.8; 19.1) mcat/l. Above results were significantly lower by 31.4%, 42.1%, and 29.3%, respectively, against vitamin A 2.2 (1.99; 2.32) μmol/l, vitamin E 19.1 (17.2; 20.98) μmol/l, and catalase 23.2 (20.7; 24.6) mcat/l in patients with hypertension (p <0.01).

Indicators of LP and antioxidant system in patients with hypertension in combination with RA were also analyzed depending on the presence of atheromatous plaques in the CCA system. In the subgroup of patients with hypertension combined with RA with the presence of AP in the CCA (n = 23), the median rates of isolated double bonds were 29.3 (27.5; 32.2) c.u./ml, diene conjugates 31.6 (30.3; 35.6) c.u./ml, diene ketones 5.65 (5.2; 6.1) c.u./ml, chiffon bases 19.5 (18.0; 22) c.u./ml and malonic aldehyde 5.74 (5.02; 6.22) nmol/ml were significantly higher by 16%, 16.5%, 22.1%, 23.1% and 24, 2%, respectively, against the subgroup of patients with hypertension combined with RA without AP in the CCA system (p <0.001). Median Vitamin A results were 1.16 (0.62; 1.32) μmol/l, Vitamin E 7.36 (4.76; 8.99) μmol/l and catalase 13 (9.4; 14.8) mcat/l in the subgroup of patients with hypertension in combination with RA with the presence of AP in the CCA were significantly lower by 27%, 38.4% and 25.3%, respectively, against the subgroup of patients with hypertension combined with RA without the AP in the CCA (p <0.001). The results are shown in the table 3.

Table 3: Indicators of LP products in patients with hypertension in combination with RA depending on the presence of atheromous plaques in the CCA (Me [25; 75], n = 93).

Test results, units of measure	Patients with hypertension + RAwithout AP in the CCA (n = 70)	Patients with hypertension + RA with the presence of AP in the CCA (n = 23)	P value
Malone aldehyde, nmol/ml	4.35 [3.74; 4.88]	5.74 [5.02; 6.22]	p < 0.001
Isolated double bonds, c.un./ml	24.6 [20.3; 27.6]	29.3 [27.5; 32.2]	p < 0.001
Diene conjugates, c.un./ml	26.4 [19.6; 29.6]	31.6 [30.3; 35.6]	p < 0.001
Diene ketones, c.un./ml	4.4 [3.9; 4.9]	5.65 [5.2; 6.1]	p < 0.001
Schiff bases, c.un./ml	15.0 [13.0; 18.0]	19.5 [18.0; 22.0]	p < 0.001
Vitamin A, μmol/l	1.59 [1.45; 1.91]	1.16 [0.62; 1.32]	p < 0.001
Vitamin E, μmol/l	11.95 [9.25; 13.55]	7.36 [4.76; 8.99]	p < 0.001
Catalase, mcat/l	17.4 [15.5; 19.6]	13.0 [9.4; 14.8]	p < 0.001

Correlation analysis was conducted between the parameters of LP products and the antioxidant system with the indicators of lipid profile and TIMC of CCA in patients with hypertension in combination with RA. There was linear dependence of medium strength between CHD and malonic aldehyde R = + 0.53, CHD and diene conjugates R = + 0.51, CHD and diene ketones R = + 0.52 (p <0.05). Significant linear correlations of medium strength were also observed between LDL and malonic aldehyde R = + 0.57, LDL and isolated double bonds R = + 0.54 (p <0.05), between

TG and malonic aldehyde R = + 0.56, TG and diene ketones R = + 0.58, TG and Schiff bases R = + 0.52 (p <0.05). Also, reliable linear correlation was found between TIMC and malonic aldehyde R = + 0,55, TIMC and isolated double bonds R = + 0,51, TIMC and diene ketones R = + 0,55, TIMC and Schiff bases R = + 0.53 (p <0.05). Medium-strength inverse correlations were found between TIMC and vitamin A R = - 0.53, TKIM and vitamin E R = - 0.51, TKIM and catalase R = - 0.51 (p <0.05). The data are presented in table 4.

Table 4: Correlations between indicators of lipid profile, thickness of intima-media complex of CCA and indicators of LP and antioxidant system in patients with hypertension in combination with RA (Me [25; 75], n = 93).

Test results, units of measure	TCL, mmol/l	HDL, mmol/l	LDL, mmol/l	AI	TG, mmol/l	TIMC thickness, mm
Malone aldehyde, nmol/ml	R= + 0.53*	R= - 0.39*	R= + 0.57*	R= + 0.49*	R= + 0.56*	R= + 0.55*
Isolated double bonds,. c.un./ml	R= + 0.45*	R= - 0.40*	R= + 0.54*	R= + 0.39*	R= + 0.35*	R= + 0.51*
Dieneconjugates, y.o./ml	R= + 0.51*	R= - 0.25*	R= + 0.48*	R= + 0.35*	R= + 0.46*	R= + 0.46*
Diene ketones, c.un./ml	R= + 0.52*	R= - 0.31*	R= + 0.47*	R= + 0.41*	R= + 0.58*	R= + 0.55*
Schiff bases, c.un./ml	R= + 0.45*	R= - 0.27*	R= + 0.41*	R= + 0.37*	R= + 0.52*	R= + 0.52*
Vitamin A, μmol/l	R= - 0.47*	R= + 0.29*	R= - 0.31*	R= - 0.37*	R= - 0.29*	R= - 0.53*
Vitamin E, μmol/l	R= - 0.46*	R= + 0.17	R= - 0.39*	R= - 0.34*	R= - 0.31*	R= - 0.51*
Catalase, mcat/l	R= - 0.39*	R= + 0.19*	R= - 0.29*	R= - 0.39*	R= - 0.44*	R= - 0.51*

Note*p <0.05 is a valid result.

Using the ROC analysis, the values of the test results of LP products and the antioxidant system for the detection of AP in the CCA system in patients with RA were determined. The largest area under the ROC curve, a sensitivity of 88.73% and a specificity of 90.44%, respectively, for the detection of atherosclerotic plaques in the CCA was determined from the malonic aldehyde index (AUC 0.870, 95% CI AUC 0.784 to 0.931) at the optimum distribution point> 5.25 nmol/ml, and at the diene ketone index (AUC 0.869, 95% CI AUC 0.784 to 0.930) sensitivity 90.36% and specificity 88.87% at the optimum distribution point> 5 c.un./ml.

Table 5: Evaluation of gender, catalase, Vitamin A and E indicators for detection of atheromatous plaques in Common Carotid Artery in Patients with AH in combination with RA based on ROC Analysis.

Test results, units of measure	Cut off point	AUC	95% CI AUC	Se, %	Sp, %
Malone aldehyde, nmol/ml	>5.25	0.870	0.784 to 0.931	88.73	90.44
Isolated double bonds, c.un./ml	>26.5	0.831	0.739 to 0.901	90.91	69.01
Dien conjugates, c.un./ml	>29.1	0.838	0.747 to 0.906	95.45	70.42
Diene ketones, c.un./ml	>5.0	0.869	0.784 to 0.930	90.36	88.87
Schiff bases, c.un./ml	>18.0	0.815	0.721 to 0.888	68.18	78.87
Vitamin A, μmol/l	≤ 1.39	0.810	0.754 to 0.931	80.91	83.1
Vitamin E, μmol/l	≤ 9.05	0.809	0.819 to 0.952	80.01	70.28
Catalase, mcat/l	≤ 15.3	0.831	0.739 to 0.900	86.36	76.06

Discussion

Screening for asymptomatic AP using ultrasound imaging of the CCA is considered by European Antirheumatic League experts as an important part of the risk assessment of CVD in patients with RA [1]. The combination of RA with hypertension is associated with adverse prognosis and faster progression of atherosclerotic processes. Increased blood pressure stimulates the development of hypertrophy and rigidity of the vascular wall [3, 11]. In our study, the degree of arterial hypertension also significantly influenced the manifestations of atherosclerotic process in patients with hypertension in combination with RA. The average TIMC indices of the right CCA were 1.28 (1.08; 1.30) mm and of the left CCA were 1.29 (1.06; 1.30) mm in patients with RA combined with stage 2 AH were significantly higher by 24.2 % and 24%, respectively, against the rates in patients with RA in combination with stage 1 hypertension ($p < 0.01$). The detection rate of atheromatic plaques in the subgroup of patients with RA in combination with stage 2 AH was significantly 10-times higher, compared with the subgroup of patients with RA in combination with stage 1 AH ($p < 0.01$). Ambrosino P. et al. conducted a meta-analysis of the 59 studies results (n = 4317 patients with RA and control group n = 3606) which revealed that in patients with RA TIMC of CCA and the rate of AP in the CCA system were significantly higher than in the general population that is associated with a chronic inflammatory process and a pronounced manifestation of oxidative stress [2]. Our study has also found a reliable relation of the atherosclerotic process with pronounced manifestations of oxidative stress in hypertensive patients in

combination with RA. In the subgroup of patients with hypertension combined with RA with the presence of AP in the CCA system, the average levels of isolated double bonds 29.3 (27.5; 32.2) c.un./ml, diene conjugates 31.6 (30.3; 35,6) c.un./ml, diene ketones 5,65 (5,2; 6,1) c.un./ml, chiffon bases 19.5 (18.0; 22) c.un./ml and malonic aldehyde 5.74 (5.02; 6.22) nmol/ml were significantly higher by 16%, 16.5%, 22.1%, 23.1% and 24.2%, respectively, against indicators of a subgroup of patients with hypertension combined with RA without AP in the CCA ($p < 0.001$). In the subgroup of patients with hypertension combined with RA with the presence of AP in the CCA indicated a significant decrease in the activity of the antioxidant system. Average levels of Vitamin A 1.16 (0,62; 1.32) μmol/l, Vitamin E 7.36 (4.76; 8.99) μmol/l and Catalase 13 (9.4; 14,8) mcat/l in patients with hypertension in combination with RA with the presence of AP in the CCA system were significantly lower by 27%, 38.4% and 25.3%, respectively, against the subgroup of patients with hypertension in combination with RA without AP in the CCA system ($p < 0.001$).

The highest predictive value for the detection of atheromatous plaques in the CCA had malonic aldehyde (AUC 0,870, 95% CI AUC 0,784 to 0,931) at the optimum distribution point> 5.25 nmol/ml, sensitivity 88.73%, and specificity 90.44%, and diene ketones (AUC 0.869, 95% CI AUC 0.784 to 0.930) sensitivity 90.36% and specificity 88.87% at the optimum distribution point> 5 c.un./ml. Also were found significant direct linear correlations of medium strength between the indices of malonic aldehyde and LDL R = + 0,57, malonic aldehyde and TG R = + 0,56, malonic aldehyde and TIMC R = + 0.55, diene ketones and TG R = + 0.52, diene ketones and TIMC R = + 0.55 ($p < 0.05$).

Conclusions

The degree of arterial hypertension significantly influenced the manifestations of atherosclerotic process and oxidative concussion, the median TIMC indicators of the right CCA of 1.28 (1.08; 1.30) mm and left CCA of 1.29 (1.06; 1.30) mm of patients on RA in combination with stage 2 AH were significantly higher by 24.2% and 24%, respectively, against rates of patients with RA in combination with stage 1 AH ($p < 0.01$). The detection rate of atheromatous plaques in the subgroup of RA patients in combination with stage 2 AH was significantly 10 times higher, compared to the subgroup of RA patients in combination with stage 1 AH ($p < 0.01$). A reliable relationship between lipid peroxidation indices and manifestations of atherosclerotic process in patients with arterial hypertension in combination with rheumatoid arthritis has been revealed. Also there was detected a direct linear correlation of medium strength between indices of malonic aldehyde and LDL R = + 0.57, TG R= + 0.56, TIMC R = + 0.55 respectively ($p < 0.05$), diene ketones and TG R = + 0.52, TIMC R = + 0.55 respectively ($p < 0.05$). The highest predictive value in detection of

atheromatous plaques in CCA had indices of malonic aldehyde (AUC 0.870, 95% CI AUC 0.784 to 0.931) at the optimum distribution point> 5.25 nmol/ml, and diene ketones (AUC 0.869, 95% CI AUC 0.784 to 0.930), a sensitivity of 90.36% and a specificity of 88.87% at an optimum distribution point> 5 c.un./ml.

Future studies

Oxidative stress underlies the pathogenesis of both hypertension and RA. Therefore, further in-depth study of the pathogenetic linkages of lipid peroxidation with the manifestations of atherosclerotic process in patients with hypertension in combination with RA will allow to improve approaches to the early diagnosis of possible complications and valid medical treatment.

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