Volume 5, Number 15, September 2017
ISSN: 2311-1623
http://www.heart-vdj.com

International Heart and Vascular Disease Journal

Journal of the Cardioprogress Foundation

Low physical activity as a behavioral risk factor in men of open urban population and its association with prevalence of coronary heart disease

Impact of omega-3 polyunsaturated fatty acids on arrhythmic activity of myocardium and characteristics of cardiac rhythm in patients with unstable angina

Results of the European Society of Cardiology Congress 2017

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CHINA HEART FEDERATION

GW-ICC

The 28th Great Wall International Congress of Cardiology

FIRST ANNOUNCEMENT

Date: October 12 - 15, 2017

Venue: China National Convention Center (CNCC) Beijing, China

Important Dates:

Abstract submission: January 1-April 30, 2017
Early-bird registration: May 1-August 20,2017

Congress Language:

English & Mandarin

Organized by:

China Heart Federation (CHF)
Organizing Committee of The Great Wall International Congress of Cardiology (GW-ICC)
China International Conference Center for Science and Technology

Congress Secretariat

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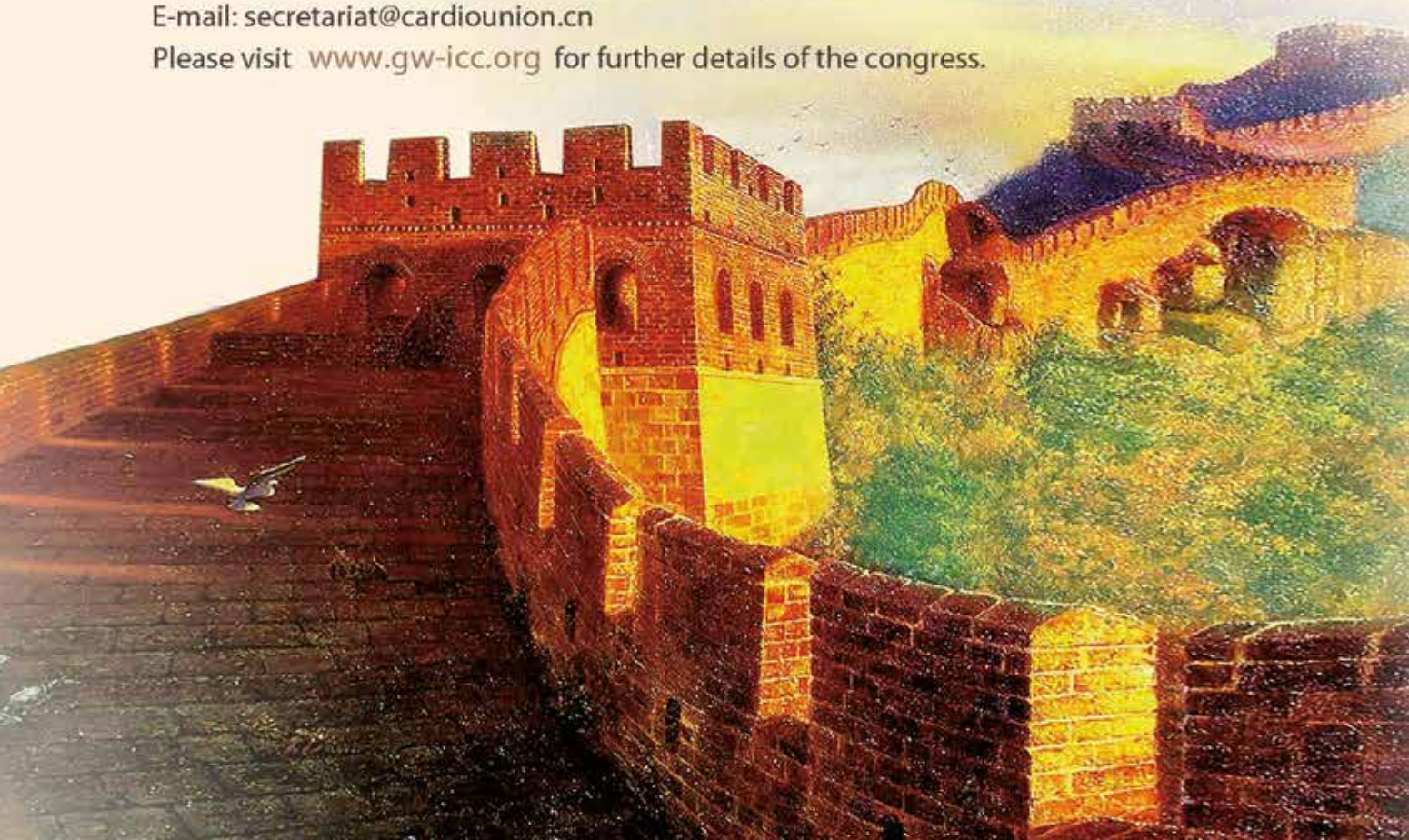

International Heart and Vascular Disease Journal
Journal of the Cardioprogress Foundation

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Cardioprogress Foundation and Editorial Office:
Room 213, Building 2, Prospect Gostinichny 6, Moscow 127106, Russia
Editorial Office tel.: (+7) 965 236 1600
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Editorial correspondence should be sent to: Mehman Mamedov, Deputy Editor, editor.ihvdj@gmail.com
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Printed in Russia

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International Heart and Vascular Disease Journal

Journal of the Cardioprogress Foundation

Volume 5, Number 15, September 2017

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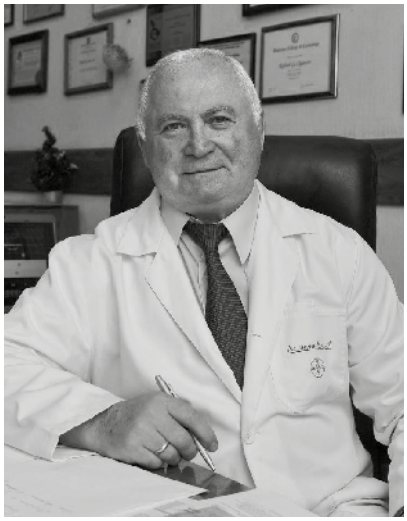

Editor's Welcome

Dear colleagues!

In the 15th issue of the International Heart and Vascular Disease Journal, there are the leading article, original and review articles, and the report on annual European Society of Cardiology Congress.

The leading article of this issue was done by the group of Tyumen Cardiology Research Center. The objective of this study was to determine the associations of low physical activity and ability to work in men of open urban population with high prevalence of coronary heart disease (representative group included 1000 men). It has been demonstrated that men aged 25-64 years with CHD detected using extended epidemiological criteria tried to make physical exercises more often comparing with the control group and estimated their physical activity as the passive one. At the same time these groups demonstrated lowered physical activity and work capacity.

Traditional "Original articles" section includes 4 works of authors from Russia and Azerbaijan. The study dedicated to estimation of the influence of omega-3 polyunsaturated fatty acids on myocardial arrhythmic activity and cardiac rhythm variability in patients with unstable angina involved 41 patients. It demonstrated that administration of this food supplementary decreased ventricular arrhythmic activity and increased general reserve of neurohumoral regulation. Another original article investigated clinical and biochemical features of metabolic syndrome in men. In order to achieve it the authors observed 299 men with metabolic syndrome. This study reported that men who developed obesity before reaching the age of 40 had higher number of metabolic syndrome components. The authors proposed detailed examination of patients who developed obesity before the age of 40 for early diagnostics of associated conditions.

The influence of seasonal variations of blood pressure measured at night and in the morning on patients with arterial hypertension had been studied during the period from 1996 to 2011. The authors of this study analyzed the results of 953 24h- blood pressure monitoring tests. They proved that the time of day and seasons influence systolic and diastolic BP and that the severity of these changes correlated reversely with parameters characterizing social support of patients with AH realized by relatives, friends and colleagues.

Another original work was done by the author from Azerbaijan. Clinical cohort study involved 523 patients with diabetes mellitus, 2 type and investigated the interrelation between education level and glycemic status, cardiovascular complications and their electrocardiographic criteria. According to the results of this study, it is necessary to perform adequate glycemic control of disease progression and improve the management of risk factors in all patients with diabetes mellitus type 2, independently on their education level.

Our "Review articles" section is present with the work of Russian authors and describes known data about evolution and pathogenesis of atherosclerosis. Authors propose their own point of view on atherosclerosis development.

In this issue we report the results of annual European Society of Cardiology Congress that was held in Barcelona (Spain) on August 26-30, 2017.

We invite everybody to collaborate with the journal. We are waiting for your original papers, review articles, discussions, and opinions about problems, treatment and prophylaxis recommendations.

Rafael G. Oganov

Editor-in-Chief

President of the "Cardioprogress" Foundation

International Heart and Vascular Disease Journal
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LEADING ARTICLE

Low physical activity as a behavioral risk factor in men of open urban population and its association with prevalence of coronary heart disease

Akimov A.M.*, Akimova E.V., Kayumova M.M., Kuznetsov V.A.

Tyumen Cardiology Research Center, Tomsk National Research Medical Center of the Russian Academy of Sciences, Tomsk, Russia.

Authors

Alexander M. Akimov, M.D., Ph.D., junior researcher in the laboratory of cardiovascular disease epidemiology and prevention, Tyumen Cardiology Research Center; Tyumen, Russia.

Ekaterina V. Akimova,M.D., Ph.D., doctor of sciences, head of the laboratory of cardiovascular disease epidemiology and prevention, Tyumen Cardiology Research Center; Tyumen, Russia.

Marina M. Kayumova, M.D., Ph.D., researcher in the laboratory of cardiovascular disease epidemiology and prevention, Tyumen Cardiology Research Center; Tyumen, Russia.

Vadim A. Kuznetsov, M.D., Ph.D., doctor of sciences, head of Tyumen Cardiology Research Center, Tyumen, Russia.

Summary

Objective

To determine the associations of low physical activity (LPA) and ability to work in men of open urban population with high prevalence of coronary heart disease (CHD)

Materials and methods

The study was conducted in the framework of cardiological screening among males aged 25-64 years in a representative sample (1000 people) taken from the electoral lists of one of the administrative districts of Tyumen, the response amounted to 85.0%. Selection of various forms of CHD was carried out based on standard methods used in epidemiological studies. CHD detection was performed according to extended epidemiological criteria and it included "certain" coronary heart disease (CCHD) and "possible" CHD (PCHD). Questioning of participants was conducted using WHO-MONICA questionnaire "Knowledge and attitude towards their health".

* Corresponding author. Tel.: +79829101778, E-mail: akimov_a_m@mail.ru

Results

According to the results, men aged 25-64 years with the presence of CCHD and CHD detected using extended epidemiological criteria tried to make physical exercises and estimated their physical activity as the passive one. At the same time, people with CHD had reduced physical activity and ability to work during the last 12 months.

Key words

Epidemiological study, open urban population, males, low physical activity, work capacity.

Introduction

According to epidemiological studies, low physical activity (LPA) is an independent cardiovascular disease (CVD) risk factor and it takes leading positions between reversible causes of total and cardiovascular mortality of the world population [1, 2, 3]. In the developed countries the consequences of scientific-technical revolution caused muscular deficiency, since physical activity in industry and routine life has reduced, physical work has been substituted by machines, and everyday life has become more comfortable [4, 5, 6]. As the consequence of LPA, hypokinesia impairs the functioning of organs and systems, weakens the immune system, reduces physical and intellectual work capacity, and in the end leads to the development of several diseases like CVD and to lifespan shortening [7, 8]. According with the World Health Organization (WHO), LPA together with unhealthy food and smoking are the leading causes of development of main non-infectious diseases like coronary heart disease (CHD) [9].

The objective of this study was to determine the associations of LPA and work capacity in men of open urban population with high prevalence of CHD.

Materials and methods

Single moment epidemiological study was conducted in the framework of cardiological screening among males aged 25-64 years belonging to the open urban population of Tyumen. A representative population that involved 1000 participants was taken from the electoral lists of one of the administrative districts of Tyumen, it included 250 men of each age group (25-34, 35-44, 45-54, 55-64 years), the response amounted to 85.0%. Questioning of participants was conducted using WHO-MONICA-psychosocial questionnaire [3]. The questionnaire "Knowledge and attitude towards their health" included 33 questions, the current study include questions related to LPA and work capacity.

Detection of various forms of CHD was carried out based on standard methods used in epidemiological studies (The WHO questionnaire for stable angina, electrocardiography (ECG) at rest and Minnesota coding). We selected "certain" coronary heart disease (CCHD) and "possible" CHD (PCHD).

In order to conduct correct comparative analysis with the results of other epidemiological studies, we performed standardization of variables using direct standardization method. To standardize obtained data during analysis we used the age structure of Russian urban population between 25 and 64 years. Statistical analysis was done using SPSS 11.5 Statistics, version 22.0 software.

Results and discussion

19.0% of male population answered positively to the question "Do you make any physical exercises apart from physical exercises at work?", and 22.1% of respondents answered negatively ("No, I don't need it) to this question. More than a half of male population of Tyumen (56.7%) did not use to make physical exercises, even if considered it necessary, and 15.0% tried to make efforts of physical activity that were useless. Minimal amount of participants (1.1%) reported medical contraindications for physical exercises (Table 1).

The answer: "I should have made physical exercises, but I don't make them" was significantly less frequent in the group of older people and there were significant differences between the age groups of 55-64 years with 25-34 years and 35-44 years (37.9% vs 56.5%, $p<0.01$ and 37.9% vs 52.6%, $p<0.05$, respectively) and with the frequency of this answer in general population (37.9% vs 48.1%, $p<0.01$). Unsuccessful attempts of physical activity were significantly more frequent in older generations of 45-54 years and 55-64 years, comparing with the younger age group of 25-34 years (9.0% vs 19.0%, $p<0.001$ and 9.0% vs 20.6%, $p<0.001$, respectively), and in general population (9.0% vs 16.6%, $p<0.001$) (Table 1).

Physical activity at free time increased with age, reached its maximum in the older age group (55-64 years), and it had significant differences with younger age groups (25-34 years and 35-44 years (31.8% vs 18.6%, $p<0.05$ and 31.8% vs 15.8%, $p<0.001$, respectively) and with general population (31.6% – 23.6%, $p<0.05$) (Table 1).

Table 1. **Attitude to physical activity of males aged 25-64 years depending on their age**

Question/attitude	Age groups										
	25-34		35-44		45-54		55-64		25-64		ASV
	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	%
Do you make physical exercises apart from physical exercises at work?											
Not, I don't need it	25	14,1	31	13,6	31	13,4	40	18,7	127	14,9	22,1
I should have made physical exercises, but I don't make them	100	56,5	120	52,6	108	46,8	81	37,9***	409	48,1**	56,7
I tried but unsuccessfully	16	9,0	37	16,2	44	19,0***	44	20,6***	141	16,6***	15,0
I make them regularly	34	19,2	38	16,7	47	20,3	44	20,6	163	19,2	19,0
According with the doctors, I have contraindications for making physical exercises	2	1,1	2	0,9	1	0,4	5	2,3	10	1,2	1,1
How do you spend your free time?											
Actively	33	18,6	36	15,8	64	27,7*	68	31,8***	201	*23,6	22,1
In different ways	107	60,5	140	61,4	113	48,9*	110	51,4	470	55,3	53,4
Physically passively (laying, sitting, watching TV, reading, writing, making crafts)	35	19,8	50	21,9	48	20,8	35	16,4	168	19,8	20,0
I have no hobbies	2	1,1	2	0,9	6	2,6	1	0,5	11	1,3	1,3
Did your physical activity (mobility, sports, etc) change during the last 12 months?											
Yes, it started to be more active	37	20,9	32	14,0	19	8,2**	18	8,4**	106	12,5*	14,2
It did not change	103	58,2	145	63,6	159	68,8*	115	53,7**	522	61,6	61,2
It started to be less active	37	20,9	49	21,5	53	22,9	81	37,9***	220	25,9**	24,4
How do you estimate your physical activity comparing with the other people of the same age?											
I started to be more active	23	13,0	20	8,8	30	13,0	27	12,6	100	11,8	11,8
I started to be a bit more active	49	27,7	61	26,8	69	29,9	59	27,6	238	28,0	27,9
I am as much active as the others	82	46,3	109	47,8	94	40,7	79	36,9*	364	42,8	43,9
I started to be a bit more passive	22	12,4	32	14,0	34	14,7	30	14,0	118	13,9	13,6
I started to be much more passive	1	0,6	6	2,6	4	1,7	19	8,9	30	3,5	2,8
Did your work capacity change during the last 12 months?											
It increased	31	17,5	20	8,8*	17	7,4**	10	4,7***	78	9,2*	10,8
It did not change	129	72,9	174	76,3	166	71,9	108	50,5***	577	67,9***	69,8
It decreased	17	9,6	31	13,6	39	16,9	68	31,8***	155	18,2*	16,0
It decreased significantly	0	0,0	3	1,3	9	3,9	28	13,1***	40	4,7***	3,4

Comment: Significance of differences between the age group of 25-34 years and other age groups is signed with * in the upper right corner of the table cell, significance of differences between the age group of 35-44 years and other age groups is signed with * in the lower right corner of the table cell, significance of differences between the age group of 45-54 years and other age groups is signed with * in the upper left corner, significance of differences between the age group of 55-64 years and other groups is signed in the lower left corner.
* - p<0,05, ** - p<0,01, *** - p<0,001; ASV – age-standardized variable.

Physical activity did not change during the last 12 months in the majority of men of Tyumen population (age-standardized variable (ASV) 61.2%), whereas one quarter of the population started to be less active (ASV 24.4%) and 14.2% of people started to be more active (Table 1).

The population looked more active due to the presence of young age groups. For example, the older age groups (age 45-54 and 55-64 years) and general population had significantly lower values of the dynamics of physical activity during the last year (8.2% vs 20.9%, p<0.01, 8.4% vs 20.9%, p<0.01, 12.5% vs 20.9%, p<0.05, respectively). The biggest number of "It did not change " answer was found in the age group of 45-54 years, and it had significant differences with the age groups of 25-34 and 55-64 years (68.8% vs 58.2%, p<0.05 and 68.8% vs 53.7%, p<0.01, respectively). The answer "I started to be less active" was present the most frequently in the group of more advanced age (55-64 years) and had significant differences with all the other age groups and the frequency in general population (37.9% vs 25.9%, p<0.01) (Table 1).

More than 80% of men of the population considered themselves more active or the same active comparing with the other people of the same age (ASV 39.7% and 43.9%, respectively). 16.4% of Tyumen men described themselves more passive comparing with the other people of the same age. Around 75% of men

answered, that their work capacity has not changed during the last 12 months, 10.8% of respondents said that their work capacity has increased, and 19.4% of men said that it has decreased (Table 1).

The frequency of increased or stable work capacity within the last 12 months decreased with age reaching minimum during the sixth decade of life. The biggest increase of work capacity within the last year was found in the age group of 25-34 years, and this value was significantly different from the other age groups and general population (17.5% vs 9.2%, p<0.05). The answer "It didn't change" was the least present in the age group of 55-65 years, where it had significant differences with the other three age groups and with the same value in general population (50.5% vs 67.9%, p<0.001). "Decreased" and "Significantly decreased" work capacity were the most frequent during the sixth decade of life (31.8% and 13.1%, respectively) and had significant differences with the other age groups and general population (Table 1).

One fifth part of men of 25-64 years had high level of physical activity (19.0% used to make physical exercises, and 22.1% preferred to spend free time actively), and people of older age (55-64 years) had higher frequency of active hobbies combined with decreased work capacity within the last 12 months, and younger age 25-34 years was characterized with increased physical activity and work capacity (Table 1).

The prevalence of CHD in the population of Tyumen men aged 25-64 years was 12.4%. Extended criteria demonstrated the increase of CHD with age and it was 14.4 times higher in the older age group. CHD frequency defined with strict criteria was 6.6%. This variable significantly increased with age from the forth(35-44 years) to the fifth (45-54 years) (3.5% vs 8.2%, p<0.05) and from the fifth (45-54 years) to the sixth (55-64 years) decades of life (8.2% vs 19.2%, p<0.01), and the frequency of "defined" CHD was 11.3 times higher in the oldest age group comparing with the youngest one [10].

Analysis of behavioral characteristics' impact on CVD development in the population of males aged 25-64 years demonstrated the correlation between CHD prevalence and attitude to physical activity and work capacity.

People with CCHD and PCHD mostly tried to make physical exercises but pointlessly comparing with the group without CHD (28.2% vs 15.4%, p<0.01; 23.1% vs 15.4%, p<0.05, respectively). Comparing with the control group, the majority of respondents with PCHD and CHD diagnosed with extended epidemiological criteria explained their refusal to make physical exercises with medical contraindications (5.1% vs 0.8%, p<0.01; 3.1% vs 0.8%, p<0.05, respectively) (Figure 1). There was no difference in free time physical activity between people with and without CHD. Dynamics of physical activity within the last 12 months was more significant in patients with all three grades of CHD comparing with the group without CHD (CCHD: 40.8% vs 56.6%, p<0.001; PCHD: 49.2% vs 56.6%, p<0.05; CHD: 44.6% vs 56.6%, p<0.001) (Figure 2). Since the frequency of the answer of the respondents to this question ("It became more passive") increased in all three groups with CHD comparing with the group without CHD (p<0.05), we can talk about negative dynamics of physical activity in the groups with CHD during the last 12 months. Men with CCHD (39.5%) and CHD diagnosed using extended epidemiological criteria (32.3%) estimated their physical activity comparing with other people of the same age as more passive one. There were significant differences between answers "A bit more passive" and "Much more passive" comparing with the group without CHD (p<0.001). The answers ("It increased" or "It did not change") to the question ("Did your work capacity change during the last 12 months?") were significantly more frequent in the group without CHD comparing with the same answers in the group with CCHD (10.3% vs 1.4%, p<0.05; 71.0% vs 42.3%, p<0.05, respectively) and PCHD (10.3% vs 3.1%, p<0.01; 71.0% vs 50.8%, p<0.001, respectively). The answer "It decreased" was registered significantly more often in the group without CHD comparing with the same answer in the groups with CCHD and CHD detected with extended epidemiological criteria (15.7% vs 38.0%, p<0.001; 15.7% vs 32.3%, p<0.001, respectively). The answer "It decreased significantly" was registered significantly less frequently in the group without CHD comparing with the same answer in all three groups with CHD (CCHD: 3.1% vs 18.3%, p<0.001; PCHD: 3.1% vs 8.5%, p<0.05; CHD: 3.1% vs 13.8%, p<0.001) (Figure 3).

Consequently, men of middle age (35-44 years and 45-54 years) can be considered more vulnerable due to low physical activity and high risk of CHD development, and there was neither high frequency of active rest nor increase of physical activity and work capacity. At the same time, numerous epidemiological studies proved the connection between low physical activity at work and at rest and high risk of CHD and CVD development and total mortality [11, 12].

According with the results of the current study, men of 25-64 years with CCHD and PCHD comparing

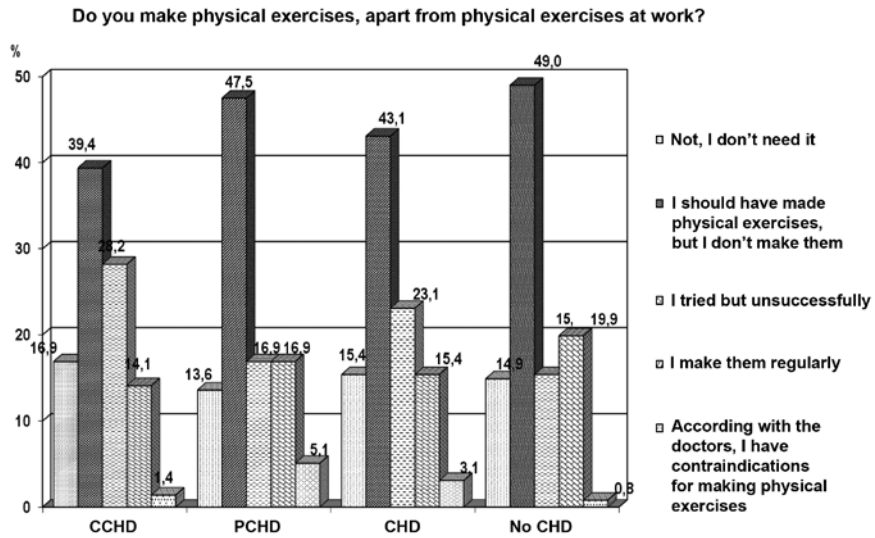

Figure 1. Attitude to physical activity in men aged 25-64 years with and without CHD, %

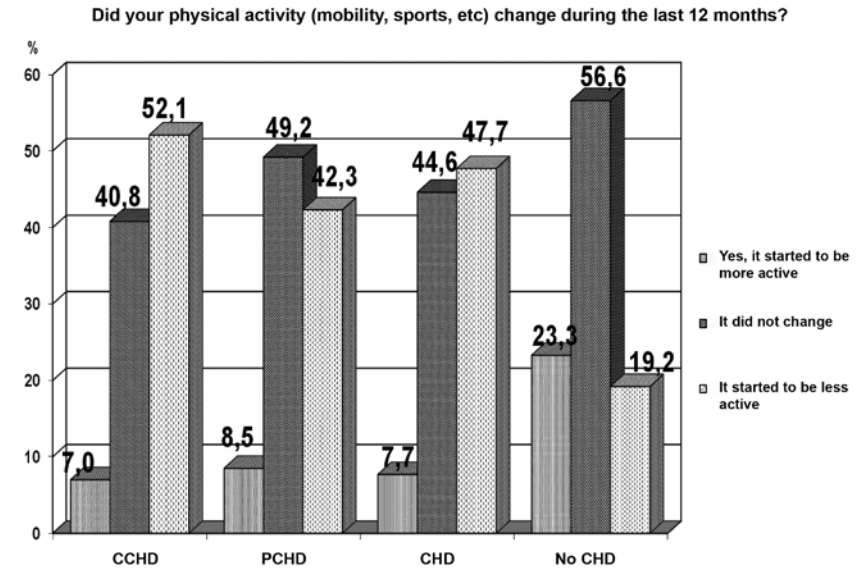

Figure 2. Dynamics of physical activity in men aged 25-64 years with and without CHD

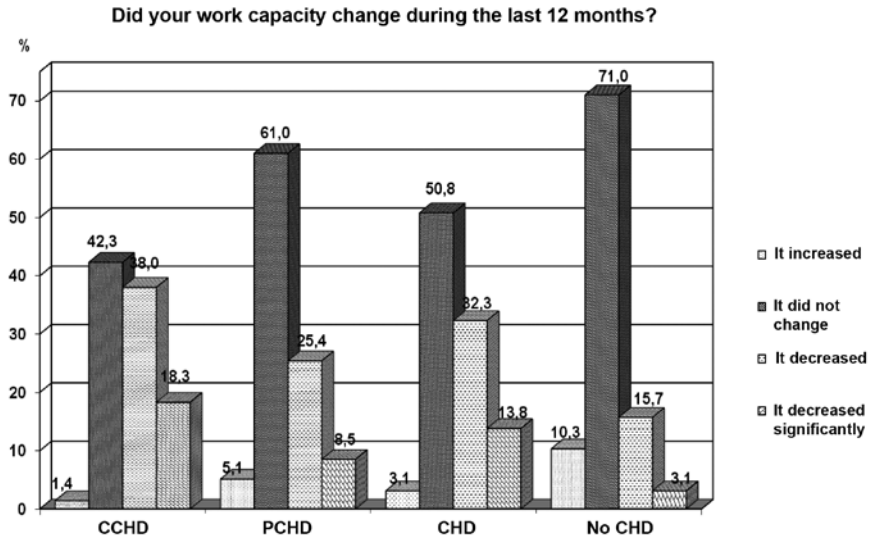

Figure 3. Dynamics of work capacity in men aged 25-64 years with and without CHD

with the group without CHD tried to make physical exercises more often and estimated their physical activity as the passive one, at the same time reduction of physical activity and work ability was registered in all groups with CHD within the last 12 months. This trend seems to be reasonable, since men with diagnosed CHD diminish their physical activity and work capacity, change their attitude to life values and put more efforts into following healthy lifestyle.

Conclusion

Analysis of behavioral characteristics' influence on CVD development in men aged 25-64 years and belonging to the open population demonstrated the correlation between CHD prevalence and attitude to physical activity and work capacity. In the open urban population males aged 25-64 years with the presence of CCHD and CHD detected using extended epidemiological criteria comparing to the group of persons without CHD, tried to make physical exercises more frequently and estimated their physical activity as the passive one. At the same time, people with CHD had reduced physical activity and ability to work during the last 12 months.

The results obtained in this study conducted in unorganized population of Tyumen may be used as the scientific basis for organizing complex socially oriented preventive programs in other moderately urbanized Siberian cities.

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Impact of omega-3 polyunsaturated fatty acids on arrhythmic activity of myocardium and characteristics of cardiac rhythm in patients with unstable angina

Mikhin V.P., Shveynov A.I.*, Kharchenko A.V.

Kursk State Medical University, Kursk, Russia

Autors

Vadim P. Mikhin, M.D., Ph.D., doctor of sciences, head of the department of internal medicine №2, Kursk State Medical University, Kursk, Russia.

Alexander I. Shveynov, Ph.D. student of the department of internal medicine №2, Kursk State Medical University, Kursk, Russia.

Alexander V. Kharchenko, M.D., Ph.D., assistant professor of the department of internal medicine №2, Kursk State Medical University, Kursk, Russia.

Summary

Objective

To evaluate the impact of omega-3 polyunsaturated fatty acids (PUSFA) on myocardial arrhythmic activity and characteristics of cardiac rhythm variability in patients with unstable angina

Materials and methods

We've conducted an open randomized trial that involved 41 patients aged 45-70 years and diagnosed with coronary heart disease (CHD): unstable angina. All patients underwent standard complex therapy. Patients were subdivided into two groups: omega-3 PUSFA supplement (1g/day) was added to the therapy in the first (main) group, whereas the patients of the second (control) group received standard therapy. Patients underwent 24-h electrocardiogram (ECG) monitoring with estimation of ventricular and supraventricular extrasystolic activity and main characteristics of cardiac rhythm variability on the 3rd and 14th days of treatment.

Results

Estimation of supraventricular activity during 24 hours revealed significant reduction of the number of extrasystoles both in the main and control groups (reduction from 40.5 (21.8-122.5) to 29.5 (6-68.3) in the main group (p<0.01) and reduction from 10 (0-18) to 7.5 (3.8-56.3) in the control group (p<0.05). Differences between groups were

* Corresponding author. Tel.: +7-906-573-08-02. E-mail: mr.shveynov@yandex.ru

statistically significant. In the main group the number of ventricular extrasystoles reduced significantly from 7.5 (1.8-31.8) to 1 (0-18.8), p<0.05. Comparison of cardiac rhythm variability parameters revealed significant increase of SDNN (by 38% and 28.7% in main and control groups, respectively, p<0.01) and HF in both groups (p<0.05), pNN50 and VLF in the main group by 41.4% and 21.5%, respectively (p<0.01, p<0.05).

Conclusion

Addition of omega-3 PUSFA (1g/day) supplement to the complex therapy of patients with unstable angina leads to reduction of ventricular arrhythmic activity and increases total reserve of neurohumoral regulation.

Key words

Omega-3 polyunsaturated fatty acids, unstable angina, arrhythmic activity, cardiac rhythm variability.

Introduction

Coronary heart disease (CHD) still keeps the leading position between the causes of morbidity and mortality in the majority of world countries. The risk of fatal arrhythmias development due to electric instability and damage of membranes of cardiomyocytes is one of factors that influence CHD outcomes, and in particular its acute forms. Due to this CHD treatment considers the use of antiarrhythmic therapy restricted to beta-blockers and amiodarone that should not be used for long-term treatment because of adverse effects related to iodine presence [5, 6].

The above-mentioned drawbacks explain the necessity of search for new drugs suitable for careful correction of proarrhythmic activity. Due to this it seems to be promising to use omega-3 polyunsatutated fatty acids (PUSFA) that positive influence on myocardial arrhythmic activity mediated by change of the structure of cardiomyocytal membranes has been proved by numerous studies. Omega-3 PUSFA also has positive effect on cardiac rhythm variability (CRV). CRV impairment precedes the development of fatal arrhythmias, and several CRV parameters can be predictors of sudden cardiac death [3, 7].

The **objective** of this study was to evaluate the impact of omega-3 PUSFA on myocardial arrhythmic activity and characteristics of cardiac rhythm variability in patients with unstable angina.

Materials and methods

We've conducted an open randomized trial that involved 41 patients aged 45-70 years and diagnosed with coronary heart disease (CHD): unstable angina (UA) based on clinical infestationsons and electrocardiography (ECG) results. All patients underwent standard complex therapy that included angiotensin-converting enzyme (ACE) inhibitors (enalapril 5-15 mg/day), beta-blockers (bisoprolol 2.5-10 mg/day), statins (atorvastatin 20-40 mg/day), antianginal drugs (long-acting nitrates: isosorbide-5-mononitrate 20-40 mg/day), anticoagulants (heparin 20000 U/day subcutaneously with consequent dose reduction), double antiplatelet therapy (aspirin 75 mg/day+clopidogrel 75 mg/day).

Inclusion criteria were the following: left ventricular ejection fraction (estimated with echocardiography) ≥45%, lack of intolerance of prescribed drugs, signed informed consent.

Exclusion criteria were the following: intolerance or adverse effects of a prescribed drug, cardiogenic shock, disseminated intravascular coagulation (DIC) syndrome; chronic renal and hepatic insufficiency, chronic kidney and liver failure, thrombolytic therapy, lack of signed informed consent.

Patients were subdivided into two groups: omega-3 PUSFA supplement (1g/day) was added to the therapy in the first (main) group, whereas the patients of the second (control) group received standard therapy.

Patients underwent 24-h ECG monitoring with estimation of single and paired ventricular (SVE and PVE, respectively) and supraventricular extrasystolic (SSVE and PSVE, respectively) activity on the 3rd and 14th days of treatment. We estimated the main characteristics of CRV: standard deviation of the NN interval (SDNN), a representative of parasympathetic and sympathetic regulation (pNN50), low frequency (LF) – a representative of sympathetic influences, high frequency (HF) – a representative of parasympathetic influences, very low frequency (VLF) – a representative of humoral influences. Since statistical analysis of data in both groups revealed non-normal distribution of arrhythmic episodes (according with Kolmogorov-Smirnov criterion, d_{max}<0.2), we used the methods of non-parametric statistics (sign test (ST), Mann-Whitney test). CRV parameters had normal distribution (Kolmogorov-Smirnov criterion d_{max}>0.25), and statistical analysis of results was performed using parametric methods (Student's test) ans Statistica 6.0 software.

Table 1. **Arrhythmic activity of myocardium in patients with UA estimated on the 3rd and 14th days of treatment**

Group	Day of monitoring	Characteristics	Median	25th percentile	75th percentile	Used statistical test and significance
Main group (n=24)	3rd	SSVE	40.5	21.8	122.3	-
		PSVE	3	0	3	-
		SVE	7.5	1.8	31.8	-
		PSVE	0.5	0	2	-
	14th	SSVE	29.5	6	68.3	ST, p<0.01
		PSVE	0	0	0.25	ST, p<0.05
		SVE	1	0	18.8	ST, p<0.05
		PSVE	0	0	0	ST, p<0.05
Control group (n=17)	3rd	SSVE	10	3.8	56.3	-
		PSVE	0	0	1	-
		SVE	1	0	1.25	-
		PSVE	0	0	0	-
	14th	SSVE	7.5	0	18	ST, p<0.05
		PSVE	0	0	0	Non significant
		SVE	1	0	78	Non significant
		PSVE	0	0	0	Non significant

Results

Patients of the main and control groups had initially high level of arrhythmic activity that had been reduced with higher or lower significance by the 14th day of treatment (Table 1).

Estimation of supraventricular extrasystolic activity within 24h revealed significant decrease of the number of extrasystoles in both main and control groups, but the statistical significance of the results was higher in the main group (reduction from 40.4 (21.8-122.5) to 29.5 (6-68.3) in the main group, p<0.01; reduction from 10 (3.8-56.3) to 7.5 (0-18) in the control group, p<0.05). The differences between the groups were statistically significant (p<0.05). The number of ventricular extrasystoles reduced significantly only in the main group (from 7.5 (1.8-31.8) to 1 (0-18.8) p<0.05.

The main parameters of CRV in patients with UA within 24 h are present in the Table 2.

Comparison of CRV parameters measured within 24 h in main and control groups reveals significant increase of SDNN (by 38 and 28.7% in the main and control groups, respectively, p<0.01). HF increased significantly (p<0.05) in both groups, and pNN50 and VLF increased by 41.4% and 21.5%, respectively, in the main group (figure 1, p<0.01, p<0.05, respectively).

Discussion

Estimation of myocardial arrhythmic activity in patients with UA reveals reduction of PVE and SVE, SSVE and PSVE in the main group, whereas in the control group just the number of SSVE decreased significantly. Our results go along with the results of other studies that demonstrated antiarrhythmic effect of

Table 2. **CRV parameters in the groups of patients with UA**

Parameters	Main group		Control group	
	3rd day	14th day	3rd day	14th day
SDNN	100.9±9.9	139.2±21.2**	104.1±12.1	134.0±9.5**
pNN50	3.44±2.09	6.61±1.77*	4.14±0.69	5.36±1.34
LF	493.3±86.1	482.5±81.2	497.2±50.0	501.0±77.1
HF	209.8±55.8	296.6±62.0*	278.1±51.5	343.1±98.4*
VLF	1582.5±152.0	1922.9±171.3**	1685.7±112.7	1887.2±141.5*

*- significant differences, p<0.05 ** - significant differences, p<0.01

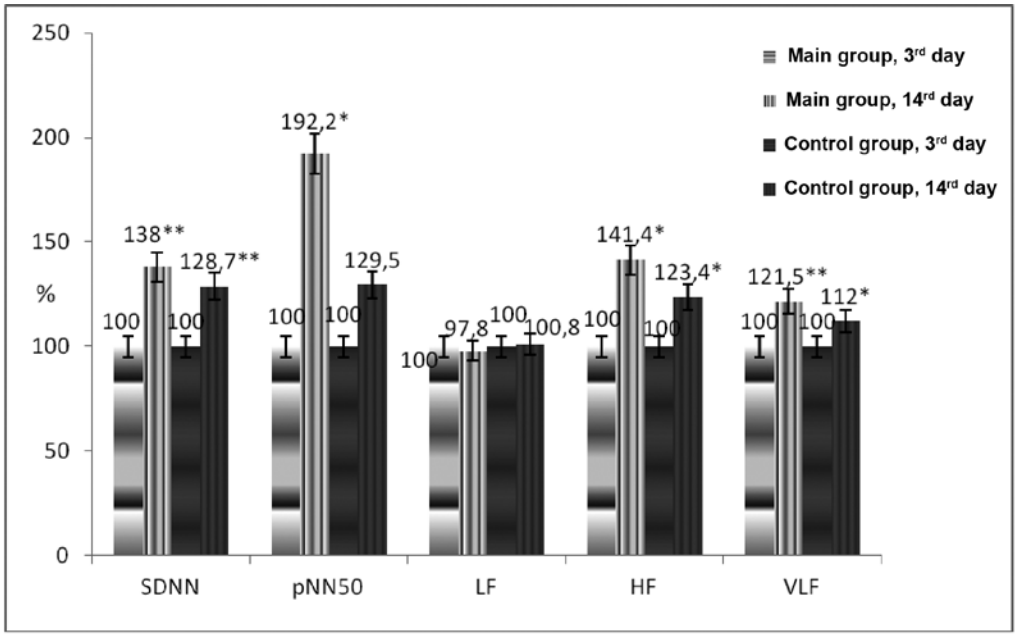

Figure 1. CRV parameters in the studied groups (* - p<0.05, ** - p<0.01)

omega-3 PUSFA in patients with CHD that resulted in reduced ectopic arrhythmic activity. Described mechanisms include as the stabilization of the membrane of cardiomyocytes as the influence on fast sodium and slow calcium channels [4]. Particular efficacy of this supplementary in patients with UA may be explained by susceptibility of cardiomyocytes to the therapy with omega-3 PUSFA, since there are no big necrotic areas in the myocardium in case of UA, unlike acute myocardial infarction. Patients that received omega-3 PUSFA demonstrated significant improvement of temporal CRV parameter pNN50, and frequency parameters HF and VLF increased significantly in both groups. These changes have high prognostic value, since increased values of CRV play an important role in the reduction of fatal arrhythmias risk [1, 2].

Conclusions

1. Addition of omega-3 PUSFA (1g/day) supplement to the complex therapy of patients with unstable angina leads to reduction of ventricular arrhythmic activity.
2. Omega-3 PUSFA increase total reserve of neurohumoral regulation and increase pNN50 values that is important for future prevention of fatal arrhythmic complications.

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Clinical and biochemical features of the metabolic syndrome in men

Solovieva A.V.

Ryazan State Medical University, Ryazan, Russian Federation

Author

Alexandra V. Solovieva, M.D., PhD, associate professor of the department of intermediate therapy with the course of endocrinology, clinical pharmacology, and occupational diseases, Ryazan State Medical University, Ryazan, Russian Federation.

Summary

Objective

To reveal clinical and biochemical particularities of the metabolic syndrome in men.

Materials and methods

The study included 299 men with metabolic syndrome aged from 31 to 89 years.

Results

We identified the presence of hypertriglyceridemia and increased quantity of low density lipids in young males, whereas carbohydrate metabolism disorders prevailed in middle-aged men. In 52% of cases metabolic syndrome was combined with overweight. The body mass index was significantly higher in men with manifestation of obesity before the age of 40 comparing to patients whose weight gain began after 40 years. Relatively early onset of arterial hypertension was discovered during the development of obesity at a young age. Men who developed obesity before the age of 40 years, had a higher number of metabolic syndrome components. Statistically significant increase in ALT and uric acid levels were revealed in men with newly diagnosed diabetes mellitus type 2, compared to those with previously diagnosed diabetes.

Conclusion

Clinical and biochemical particularities of the metabolic syndrome in men with different duration of obesity determine the need of advanced examination of individuals developing obesity before the age of 40 years for early diagnosis of associated conditions.

Key words

Metabolic syndrome, carbohydrate metabolism disorders, hyperuricemia

* Corresponding author: Tel. +71924433900, E-mail: vnutbolezni@mail.ru

Introduction

A lot of new data demonstrating controversial impact of metabolic abnormalities into metabolic syndrome (MS) development in men and women has been published during the last years. For example, Dallongeville J. et al. observed that body overweight, waist circumference, high density lipoprotein (HDL) levels have bigger impact on MS development in women, whereas in men systolic and diastolic blood pressure and apolipoprotein B levels are more important [1]. These data support the idea of different MS diagnostic criteria in men and women.

Epidemiological studies of the last years demonstrate a distinct interest to consequent manifestation of different MS syndromes in order to elaborate effective preventive strategy. According with several researchers, MS symptoms are characterized by distinct order of manifestation. For example, patients below 50 years often have abnormal carbohydrate metabolism and left ventricular myocardium remodeling, and patients above 50 years have dyslipidemia, abdominal obesity and arterial hypertension [2]. At the same time diabetes mellitus, 2 type (DM2) rarely occurs as the first manifestation of MS and is more common to develop after 50 years, when other components of MS have already appeared [3]. According with numerous studies, arterial hypertension (AH) is one of the dominating features of MS, and nowadays many researchers consider AH as part of MS [4].

Abdominal obesity (AO) is not always an early feature of MS, and the order of AH, carbohydrate metabolism disorders (CMD), and dyslipidemia manifestation can differ. According to population study made in Taiwan, abnormal lipid spectrum appears before the other MS components in both genders [5]. Another research group from Taiwan discovered gender differences in the sequence of MS manifestation: women start to have AO in adolescent age that develops into DM2 later, and young males initially demonstrate AO, increased levels of triglycerids (TG) and decreased levels of HDL, AH is added in middle age, and after all they develop DM2 [6]. Several studies demonstrated that MS components like AH, increased body weight, impaired glucose tolerance, and burdened family history may act as risk factors predisposing prediabetes change into evident DM [7].

The question of interrelation between ureic acid (UA) levels and DM are actively discussed in publications of the last years [8], and hyperuricemia is considered to be a DM2 predictor, increased UA concentration is present in the early stages of ICM and is related to micro- and macrovascular complications in the advanced stages of diabetes. Study made on Iranian population of patients with DM2 revealed direct correlation of MS components with UA levels [9]. The study of Rancho Bernardo[10] demonstrated that all causes of mortality are independently related to hyperuricemia, but mortality due to cardiovascular diseases (CVD) is connected with hyperuricemia just in people with impaired glucose tolerance. Epidemiological study of cardiovascular diseases and their risk factors in different regions of the Russian Federation (ESSE-RF) demonstrated independent association of all metabolic factors and hyperuricemia [11].

The knowledge of age, gender, clinical and biochemical features of metabolic syndrome, stages of its development and symptoms' manifestation would allow to perform effective preventive measures.

The aim of this study was to identify clinical and metabolic features of MS in males.

Materials and methods

299 men with MS aged 31-89 years underwent examination in the department of internal medicine of Ryazan Regional clinical hospital. All patients signed informed consent for participation in this study. This study was approved by local Ethic committee of Ryazan State Medical University. Inclusion criteria were the following: the presence of MS according with the criteria of Russian Society of Cardiology (2009) and signed informed consent.

Exclusion criteria were the following: DM1, severe kidney disorders (glomerular filtration rate (GFR)<30 mL/min quantified using CKD EPI), severe chronic heart failure, severe respiratory insufficiency, viral or alcohol liver lesions, autoimmune connective tissue disorders, congenital valve disease, mental disorders that could interfere with the contract between doctor and patient, patient's refusal of treatment.

Apart from history taking and standard physical examination patients underwent waist circumference (WC) and body mass index (BMI, quantified using Quetelet's formula). Laboratory tests included glucose detection using glucose oxidase method, oral glucose tolerance test, blood lipid spectrum (total cholesterol (TC), HDL, low density lipoproteins (LDL), TG) estimation was performed using enzymatic techniques and biochemical analyzer "Olympus AU-400" (Japan) that was also used for alanin aminotransferase (ALT) and aspartate aminotransferase (AST),

UA and creatinine detection. Transthoracic echocardiography (EchoCG) was done using ultrasound scanner Sequoia 512 (Siemens) in duplex mode, 2D mode, M-echo mode, tissue harmonic imaging and tissue doppler imaging. Abdominal ultrasonography was performed using LOGIQ Book XP (GE Medical Systems, China) ultrasound imaging system.

Statistical analysis of obtained data was done using Statistica 10.0 software. Data are present as median and 25-75 quartiles. Quantitative comparison of two independent groups was performed using Mann-Whitney U-test. Analysis of correlation between two variables was done using Spearman's rank correlation test (r). The level of significance (p) was taken as 0.05.

Results and discussion

The values of WC, the main component of MS, were 107.2 (100; 113) cm in men.

Patients were subdivided into the following age categories according to the WHO classification: aged 25-44 years referred to the young age, aged 44-60 years referred to the middle age, aged 60-75 years referred to the elderly age, aged 75-90 years referred to the very old age. Age distribution is present at the Figure 1.

Average BMI was 29.9±4.2 kg/m^2. BMI distribution of male patients with MS can be seen at the Figure 2.

52% of all patients had body overweight, and 9 men had AO combined with normal body weight.

Talking about additional MS diagnostic criteria, all patients had AH II-III degrees, and 87% of patients had it combined with coronary heart disease (CHD).

MS components representing abnormal lipid spectrum were the following: TG — 1.71 (1.23;2.47) mmol/L; HDL — 1.02 (0.89;1.22) mmol/L, LDL — 3.54 (2.8;4.39) mmol/L.

CMD that characterize one additional MS component were present in 41.7% and included: impaired fasting glycemia (IFG) — 33 patients (11%), impaired glucose tolerance (IGT) — 22 patients (7.3%), and DM2 — 70 patients (23.4%).

Age-related MS features in men (Figure 3) are characterized mostly by hypertriglyceridemia in young age (65.2%) with gradual decrease of its frequency in old age (17.4%). The frequency of CMD was

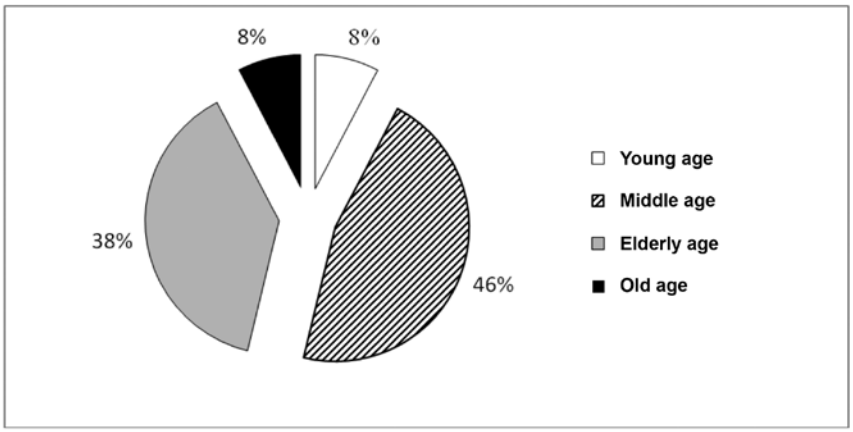

Figure 1. Age distribution of males

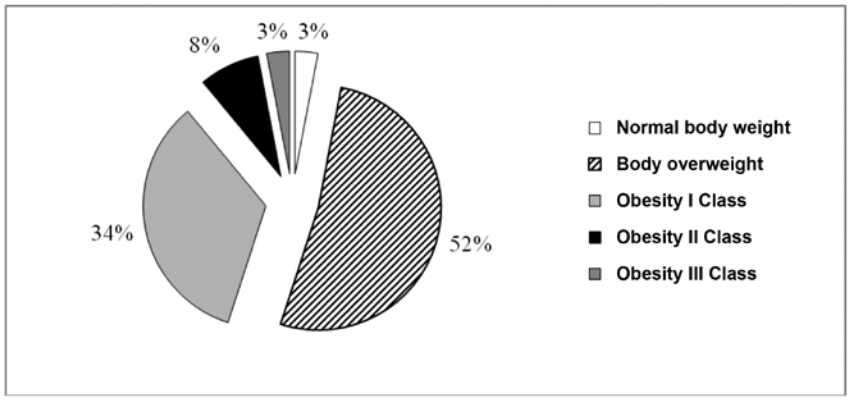

Figure 2. BMI distribution of males

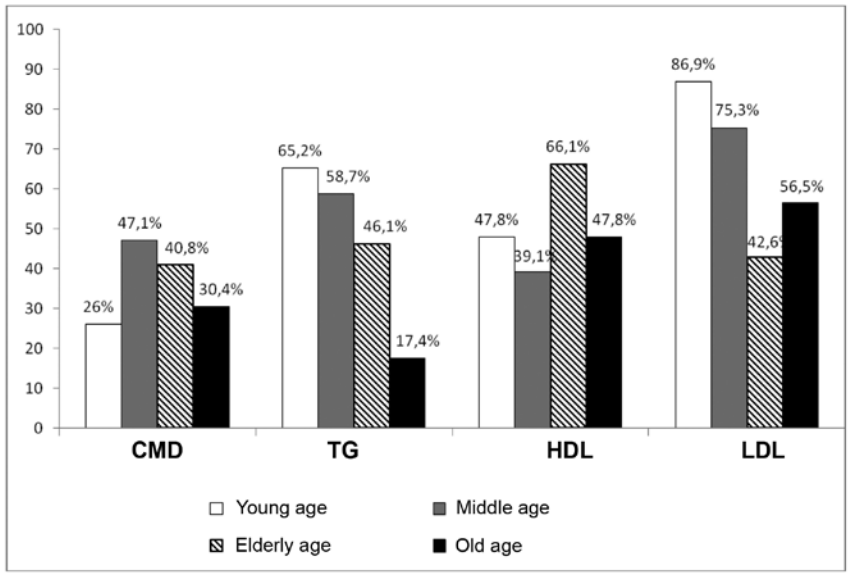

Figure 3. Age-related frequency of MS components in men

Table 1. **Comparison of patients in relation to the age of obesity onset**

Characteristic	Group 1 (n=168)	Group 2 (n=131	p
Age, years	49 (43.5; 54.5)	59 (57; 62)	0.000001
WC, cm	115.5 (105; 121)	112.5 (104; 117.5)	>0.05
MBI, kg/m^2	33 (31; 36.67)	31.4 (28; 33.7)	0.05
Duration of obesity, years	20 (10; 26.5)	8 (5; 15)	0.00002
Duration of AH, years	8 (5; 20)	8 (5; 20)	>0.05
Duration of DM2, years	2.5 (1; 6)	4 (4; 15)	>0.05
TC, mmol/L	5.9 (5.2; 7)	5.6 (4.6; 6.59)	>0.05
HDL, mmol/L	1 (0.87; 1.21)	1.13 (0.9; 1.33)	>0.05
LDL, mmol/L	4.1 (3.4; 4.9)	3.62 (2.8; 4.7)	>0.05
TG, mmol/L	1.88 (1.45; 1.56)	1.8 (1.25; 2.63)	>0.05

maximal in middle age (47.1%). HDL reduction is the most frequent in elderly man, and the occurrence of elevated LDL is maximal in young age (86.9%) and goes down in elderly age.

In men AO duration correlated directly with AH duration (r=0.3, p=0.025), with the sickness of interventricular septum (IVS, r=0.27, p=0.048) and had a reverse correlation with HDL levels (r=-0.34, p=0.011).

In order to study the features of MS development in men we subdivided them into the groups according with the age when the overweight started: Group 1 — 168 people reported to start body overweight before reaching 40 years, Group 2 — 131 patients reported the start of body weight after 40 years. Comparison of these two groups is present at Table 1.

The first group included significantly younger males with significantly higher BMI and obesity duration 2.5 times longer than in the second group. There were no statistically significant differences of WC between the groups. DM2 and burdened family history of DM2 was more frequent in the Group 1 (27.9% versus 17.5% and 40% versus 6.8%, respectively). Family history of obesity was more present in the Group 1 comparing with the Group 2 (32.2% versus 25.9%), whereas the family history of AH was found in the half of patients of both groups. More advanced obesity was combined with hepatomegaly: oblique vertical height of liver was 165.5 (153.5; 176) mm in the Group 1 versus 151 (144; 160) mm in the Group 2 (p=0.04), and other signs of non-alcoholic fatty liver disease were detected. According with the Table 1, there were no significant differences of lipid spectrum between groups.

Analyzing the number of MS components in two groups of men (Figure 4), we identified that increase of body weight in young age (Group 1) is combined with the higher number of MS components, even if the age of patients of the Group 2 was significantly higher.

According with the diagram (Figure 5), the most frequent combinations of MS components in the Group 1 include AO+AH+↑LDL (19.6%) and AO+AH+↓HDL+↑LDL+↑TG (17.8%), and the combination of AO+AH+↑LDL prevails also in the Group 2

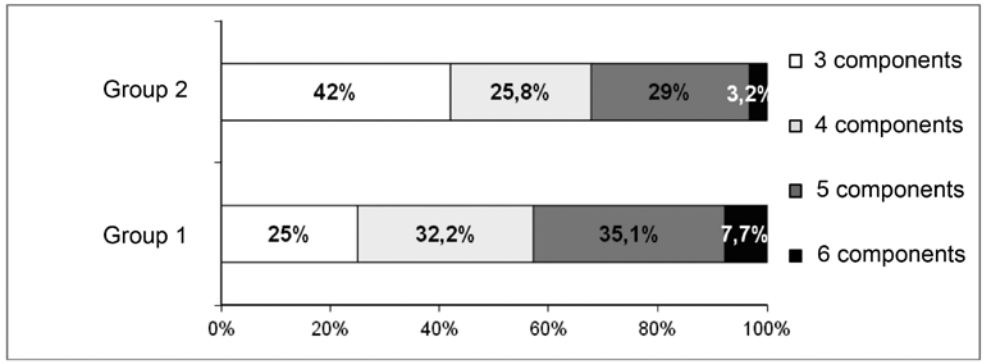

Figure 4. The frequency of different combinations of MS components

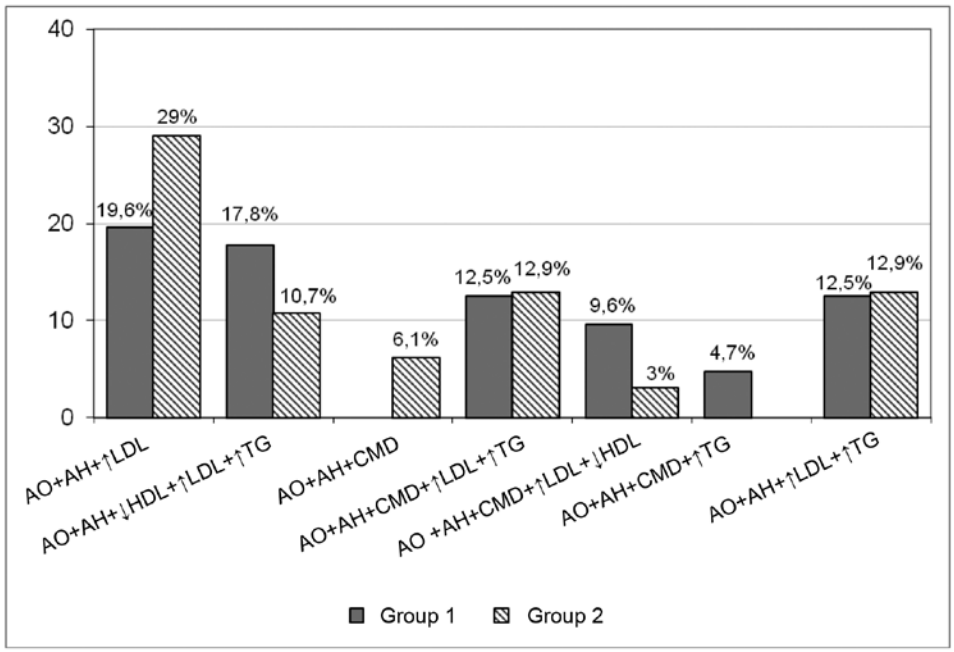

Figure 5. The frequency of various MS components in males (%)

(29%). The frequency of AO+AH+CMD+↑LDL+↑TG and AO+AH+CMD+↑TG combinations is equal in both groups. AO+AH+CMD is not present in the Group 1, and there is no AO+AH+CMD+↑ТГ combination in the Group 2. All combinations of MS components including ↑TG prevail with the same or higher frequency in the Group 1 that was proved with negative correlation between TG level and age of males (r=-0.33; p=0.000001).

We should notice that DM2 was firstly diagnosed in 25 men (35% of patients with DM2). According with this, we aimed to identify the differences with firstly and previously diagnosed DM2. We found out that patients with the onset of DM2 were younger and had shorter duration of obesity. We should not ignore the important biochemical features of firstly diagnosed DM2 in males like significantly higher levels of ALT and UA (Table 2).

Table 2. **Differences between male patients with different DM2 duration**

Characteristic	Firstly diagnosed DM2	Previously diagnosed DM2	p
Age, years	52 (50; 61)	60 (55; 69)	0.02
Obesity duration, years	4.75 (5; 9)	19 (15; 30)	0.03
ALT, U/L	36.5 (27; 46)	26 (18; 33)	0.005
UA, μM/L	451 (435; 461)	339 (308; 376)	0.023

Hyperuricemia was detected in 32.1% of males with MS (according to the ESSE-RF study, the same value in men aged 25-64 was 25.3% [11]). MS hyperuricemia was associated with TG levels (r=0.27, p=0.025). According to the results of several other studies, UA is related to TG levels, but independently from fasting insulin levels and obesity, thus demonstrating that the underlying mechanism is partially connected with insulin resistance and obesity [12].

In respect to elevated serum ALT levels in patients with firstly diagnosed diabetes, elevated ALT level was considered to be DM2 predictor in patients with AH [13] in one of available studies. Another one, published in 2016, demonstrated that border values of serum ALT and γ-GT (but not AST) levels were independent predictors of IFG and DM2 [14]. Several other studies have proved the connection between elevated serum ALT levels with DM2 risk [15, 16].

Conclusion

The analysis of clinical and biochemical features of MS in men allowed identifying of hypertriglyceridemia and elevated LDL levels in young age and maximal frequency of carbohydrate metabolism disorders in middle age patients. In 52% of cases MS was combined with body overweight in the studied group of male patients.

Men who manifested AO before the age of 40 (Group 1) had significantly higher BMI (but not WC) comparing with the patients who started to increase their body weight after reaching 40 years, and it demonstrates different fat tissue distribution in these groups. The same duration of AH in groups of men and significantly younger age of males of the Group 1 indicate earlier manifestation of AH in case of early development of obesity. Although the patients of the Group 1 were significantly younger, development of obesity before the age of 40 was characterized with higher number of MS components.

Men with firstly diagnosed DM2 had statistically significant increased ALT and UA serum levels comparing with the people with previously diagnosed DM. Our results go along with the results of several other studies and prove the role of these biochemical markers in early diagnostics of impaired carbohydrate metabolism.

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Interrelation between severity of seasonal changes of blood pressure at night and in the morning and life quality characteristics in patients with arterial hypertension

Andreeva G.F.*, Deev A.D.

National Research Centre for Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia

Authors

Galiya F. Andreeva, M.D., Ph.D., senior researcher of the laboratory of the use of outpatient diagnostic techniques for chronic non-invectious diseases, National Research Centre for Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia.
Alexander D. Deev, Ph.D., head of the laborarory of biostatistics, National Research Center for Preventive Medicine of the Ministry of Healthcare of the Russian Federation, Moscow, Russia.

Summary

Objective

To identify the interrelation between the severity of seasonal changes of blood pressure (BP) at night and in the morning and life quality (LQ) characteristics in patients with AH.

Materials and methods

We analyzed databases of different studies that had been hold in our Center during the period from 1996 to 2011 and included the results of 953 24-h BP monitoring (24h-BPM) tests. We analyzed the results of studies with similar design and inclusion criteria. We estimated 24h-BMP in patients without serious concomitant diseases who underwent BP monitoring during one week withdrawal of antihypertensive therapy.

Results

We demonstrated that seasonal dynamics of diastolic BP (DBP) measured at night and in the morning was similar: maximal values of DBP were registered in winter and minimal ones – in summer, and it was typical for seasonal dynamics of DBP in general. The values of systolic BP (SBP) measured in the morning were minimal in winter and

* Corresponding author. E-mail: gandreeva@gnicpm.ru

maximal in autumn, but there were no significant differences between seasons. Average values of night SBP were minimal in spring and maximal in autumn (p<0,05).
Statistical analysis of obtained results performed using generalized linear models and Fisher criterion (F) demonstrated that severity of seasonal BP changes was reversely correlated with the level of social support for seasonal changes of SBP measured at night and in the morning and for DBP measured in the morning. Apart from it, seasonal SBP changes depended on sex and gender: males and elderly people had more evident seasonal changes of SBP (F=5,01, p<0,03 and F=5,05, p<0,03, respectively).

Conclusions

We demonstrated that severity of seasonal changes of SBP and DBP in the morning and at night was reversely correlated with characteristics of AH patients' social support provided by relatives, friends, colleagues (one of LQ elements). Seasonal dynamics of DBP measured in the morning and at night was typical: BP levels were maximal in winter and minimal in summer. The highest values of morning SBP were detected in autumn, and the lowest ones were measured in winter. The values of night SBP were minimal in spring and maximal in autumn.

Key words

Arterial hypertension, seasonal dynamics of blood pressure, life quality

It is well known that climatic factors have much influence on humans. The change of seasons leads to functional changes in many organs and organ systems, behavior and mood [1-3]. Numerous studies conducted in Europe during the last years demonstrated seasonal fluctuations of clinical and home-measured levels of blood pressure (BP) [4] registered using automatic gadgets for 24-h BP monitoring (24h BPM) and BP self-monitoring (BPSM). It has been shown that clinical, average 24-hour (measured at home) and daily levels of BP are maximal in winter and minimal in summer, and average night BP is maximal in summer and minimal in winter [5, 6, 7, 8]. According with several studies, the degree of night BP reduction was the most evident in winter and the less noticeable in summer [9]. Another major study demonstrated that morning levels of BP (during awakening and 2 hours after it) were the highest at cold time of the year [10].

In this study we estimated seasonal dynamics of average night and morning BP levels (measured between 6 and 8 a.m.). It is necessary to mention that the features characterizing the degree of morning increase and night decrease of BP, absolute values of morning and night BP have prognostic value for cardiovascular complications and mortality, target organ lesions, and increase of carotid arteries' intima-media thickness [11-21]. Life quality (LQ) of patients is one of the main factors connected with BP levels. Numerous studies demonstrated that clinical levels of BP (degree of BP reduction at night, BP variability) correlated with several elements of LQ of patients with AH. The objective of this study was to identify the interrelation between the severity of seasonal changes of BP at night and in the morning and life quality (LQ) characteristics in patients with AH living in Moscow region.

Materials and methods

We analyzed a database of different studies that had been hold in our Center during the period from 1996 to 2011 and had similar inclusion criteria and study protocols. We selected 953 24-h BPM tests performed with the use of SpaceLabs equipment in patients with AH and without severe concomitant diseases after withdrawal of antihypertensive therapy. We included just the results of 24h-BPM that satisfied the following criteria: 1) the number of effective BP measurements was not less than 50; 2) there were no pauses longer than 1h in 24h-BPM protocols; 3) 24-h BPM device was fitted in the morning between 09.15 and 10.15 a.m. and it was removed the day after at the same time; 4) the age of patients was between 20 and 80 years; 5) average daytime BP was >135/85 mm Hg and ≤160/110 mm Hg, and patients with white coat hypertension (WCH) had BP>140/90 mm Hg measured in clinical setting (the percentage of WCH patients did not exceed 10-15% in total and for each season in particular); 6) patients had not been receiving antihypertensive therapy for 1 week at the moment of monitor fitting; 7) 24h-BMP was performed using SpaceLab90207 and 90317 devices.

We analyzed 953 24h-BPM that met the inclusion criteria. According with the results of 24h-BMP, we quantified average BP values in the following time periods: morning (m) — from 6 a.m. to 8 a.m.; night (n) — from 0 a.m. to 6 a.m.; daytime (d) — from 8 a.m. to 22 p.m.; 24 hours (24).

After 24h BPM patients underwent LQ estimation. We used "General Well-Being Questionnaire" (GWBQ) developed by the research group from Marburg university (Siegrist J et al, 1989) and further adapted for Russian population [29, 30]. The questionnaire is based on self-estimation of personal condition by patient and it includes 8 clinical scales: I — physical well-being (complaints), II — work capacity, III — positive (III) or IV — negative psychological well-being, V — psychological capacities, VI — social well-being, VII — ability to make social contacts, VIII – sexual capacity in men. Estimating the dynamics of GWBQ scales, we considered that reduction of the values of scales I-IV and increase of the values of all other scales corresponded to improved LQ. The scale VIII was not analyzed since both men and women took part in this study.

Statistical analysis of the results was done using SAS (version 6.15) software. Fisher's criterion (F) was quantified using generalized linear model. Severity of seasonal BP increase was quantified as the value characterizing the increase of BP at one exact day comparing with the reference (average annual) BP level. 24h-BPM values were quantified using APBM-FIT software [31].

Results

Average annual BP values in patients with AH detected with 24h BPM. We analyzed results of 953 24h BPM that met the inclusion criteria. 51% of 24h-BPM results belonged to female patients, and 49% of results were male ones. The average age of the patients was 55,2±12,3 years, the average duration of AH was 11,97±10,7 years, the average height was 168,3±8,1 cm, the average weight was 81,7±14,2 kg.

The average annual values of systolic BP (SBP) were the following (Table 1): the average daytime SBP (dSBP) was 141,5±15,5 mm Hg, the average night SBP (nSBP) was 124,9±16,4 mm Hg, the average 24h SBP (SBP24) was 137,7±15,0 mm Hg. Diastolic BP (DBP) had the following values: the average daytime DBP (dDBP) was 89,1,5±10,7 mm Hg, the average night SBP (nSBP) was 74.3,9±10,9 mm Hg, the average 24h SBP (SBP24) was 85,7±10,4 mm Hg.

Table 1. **Average annual SBP and DBP levels in patients with stable AH (M±SD)**

Time intervals	DBP (mm Hg)	SBP (mm Hg)
24 h	85.7±10.4	137.7±15,0
Daytime	89.1±10.7	141.5±15.5
Nighttime	74.3±10.9	124.9±16.4
TI for 24h	38.6±28.1	48.4±30.1
TI for daytime	46.3±32.6	50.4±33.2
TI for night	30.3±30.5	56.5±36.6
HR	74.9±9.5	

Comment: DBP, SBP – average diastolic/systolic BP, TI – time index, HR – heart rate.

Comparison of social-demographic characteristics of patients who participated in 24h BPM at different seasons did not reveal any significant differences of sex, age, height, weight and AH duration in all four groups. We analyzed the results of 953 24h-BPM, between them 230, 262, 208, 253 24h-BPM were performed in winter, spring, summer and autumn periods, respectively (Table 2).

Seasonal changes of home-measured BP values. Average home-measured *mDBP* had minimal values in summer and maximal ones in winter, but there were no significant differences between seasons.

We identified that average dDBP and DBP24 of patients with AH were maximal in winter and minimal in summer ($p<0,05$). Average home-measured nDBP levels had the same trend of seasonal changes, but there were no statistically significant changes between seasons (Table 3, Figure 1).

Average home-measured mSBP had the lowest and the highest values in winter and in autumn, respectively, but there were no significant changes between seasons.

Analysis of seasonal changes of main SBP characteristics (Table 3, Figure 1) measured in patients with

Table 2. **Characteristic of patients who underwent 24h-BPM during different seasons**

Characteristics	Demographic characteristics of patients who participated in 24h-BPM in winter (n=230) (M±SD)	Demographic characteristics of patients who participated in 24h-BPM in spring (n=262) (M±SD)	Demographic characteristics of patients who participated in 24h-BPM in summer (n=208) (M±SD)	Demographic characteristics of patients who participated in 24h-BPM in autumn (n=253) (M±SD)	Significance of differences (p<0,05)
Age (years)	55.7±12.4	56.1±10.9	54.4±12.5	55.3±11.9	Ns
Height (cm)	168.6±7.9	168.1±14.0	166.9±8.9	168.7±15.1	Ns
Weight (kg)	82.6±13.3	81.1±14.7	80.0±14.2	82.8±15.2	Ns
AH duration	12.8±11.3	11.1±11.24	11.7±10.1	12.0±10.3	Ns
Gender %(m/f)	49/51	50/50	50/50	49/51	Ns

Comment: ns – not significant

Table 3. **Seasonal changes of home-measured BP (M±SD)**

Seasons / 24h-BPM results	Winter	Spring	Summer	Autumn	Significance of differences p< 0.05
Seasonal changes of main home-measured BP characteristics					
DBP24	87.5±10.8	85.5±10.4	84.1±9.9	86.2±9.7	** - between winter and summer
dDBP	91.4±11.4	89.0±10.7	86.3±10.0	89.8±10.6	***- between winter and summer
nDBP	75.6±14.1	73.6±10.4	72.5±10.4	75.2±11.5	Ns
SBP24	138.5±15.2	137.3±14.9	136.0±15.0	138.6±14.8	Ns
dSBP	142.6±15.6	141.3±15.2	139.3±15.6	142.4±15.3	Ns
nSBP	125.2±15.7	123.0±15.8	124.6±15.8	126.3±16.9	** - between spring and autumn
Seasonal changes of morning home-measured BP characteristics					
mSBP	131.8±17.6	132.4±14.8	132.8±19.2	133.3±18.7	Ns
mDBP	83.5±13.7	81.5±13.4	80.2±11.5	82.25±12.3	Ns

Comment: Ns – not significant ** - p<0,05, *** - p<0,01.

AH demonstrated that average dSBP and SBP24 levels were maximal in winter and minimal in summer. The differences between seasons were not significant. Average home-measured nSBP were minimal in spring and maximal in autumn (p<0,05).

Concluding the results mentioned above (Figure 1), we can say that mSBP levels were maximal in autumn and minimal in winter. The highest values of mDBP were detected in summer and the lowest ones were detected in winter. Seasonal changes of BP24, dBP, and nBP in patients with AH who did not receive antihypertensive therapy were similar, with maximal BP levels in winter and minimal BP values in summer. The lowest levels of nSBP were registered in spring and the highest ones were detected in autumn.

We estimated influence of several independent variables on the severity of seasonal changes of 24h-BM using dispersion analysis and generalized linear models and quantifying Fisher's criterion (F) for these variables.

As can be seen at the Table 4, age and gender were important for morning seasonal SBP changes (F=5,01, p<0,03 and F=5,05, p<0,03, respectively).

We observed reverse correlation between several LQ features and severity of SBP fluctuations during year. Improved social support from family, friends, colleagues (scale VI — social well-being) was connected with reduced severity of SBP seasonal changes at day, night and in the morning (Table 4).

Seasonal DBP changes did not depend on gender and age. Several components of patients' LQ correlated reversely with the severity of DPB seasonal changes. Increased social support (Scale VI) correlated with decreased severity of seasonal changes of DBP in the morning, at daytime and during 24h (Table 5).

Therefore, decreased social support (one of LQ components) was combined with increased severity of seasonal DBP and SBP changes in the morning and at night in patients with AH. Seasonal mSBP changes were more evident in men and elderly pa-

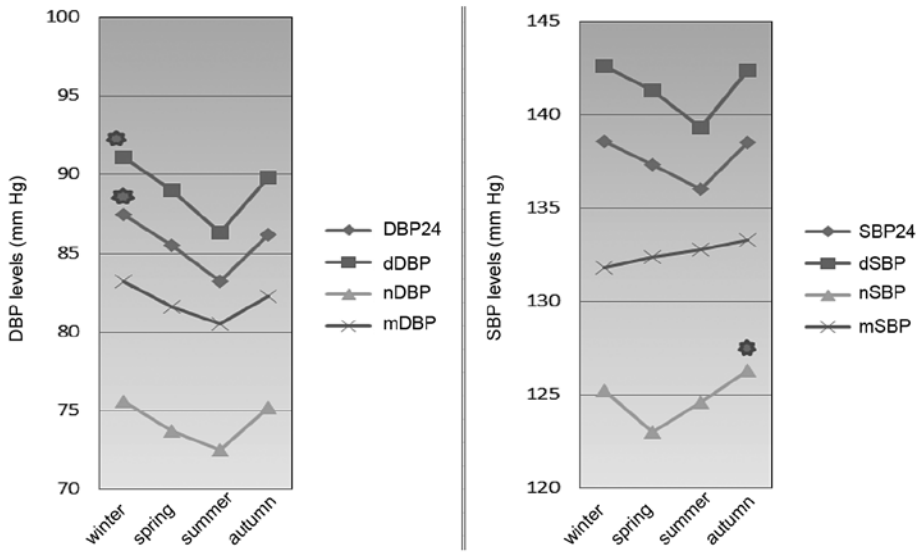

Figure 1. Comparison of seasonal changes of morning and night BP in patients with AH
* - significant differences (p<0,05)

Table 4. **Interrelation between LQ, age, gender and severity of seasonal SBP changes (based on Fisher's criterion (F))**

Social-demographic characteristics / 24h-BPM	Age	Gender	LQ characteristics (Scale VI)
SBP24	Ns	Ns	F=11,34, (p<0,001)(-)
dSBP	Ns	Ns	F=11,91, (p<0,001)(-)
nSBP	F=4,13, (p<0,04)(+)	Ns	F=5,04, (p<0,002) (-)
mSBP	F=5,01,(p<0,03)(+)	F=5,05, (p<0,03)	F=11,29, (p<0,001)(-)

Comment: Ns – not significant; F – Fisher's criterion; SBP24 – average SBP measured within 24h, dSBP – average daytime SBP, nSBP – average night SBP, mSBP – average morning SBP; The scales of LQ-estimating questionnaire: VI – social well-being, + positive connections, - negative connections.

Table 5. **Interrelation between LQ, age, gender and severity of seasonal DBP changes (based on Fisher's criterion (F))**

Social-demographic characteristics / 24h-BPM	Age	Gender	LQ characteristics (Scale VI)
DBP24	Ns	ns	F=4,06, (p,<0,04)(-)
dDBP	Ns	ns	F=5,17, (p,<0,02)(-)
nDBP	Ns	ns	Ns
mDBP	Ns	Ns	F=4,29, (p<0,04)(-)

Comment: Ns – not significant; F – Fisher's criterion; DBP24 – average DBP measured within 24h, dDBP – average daytime DBP, nDBP – average night DBP, mDBP – average morning DBP; The scales of LQ-estimating questionnaire: VI – social well-being, + positive connections, - negative connections.

tients. Seasonal mDBP dynamics was typical: BP levels were maximal in winter and minimal in summer. At the same time, the highest values of mSBP were registered in autumn and the lowest ones were detected in winter.

Discussion

In our study we estimated a new additional parameter that characterized morning BP levels measured at home (mBP) apart from well-known ones. mBP was quantified as average value of BP measured between 6 and 8 a.m. We selected this time period because it corresponds to the first time period associated with increased general and cardiovascular mortality [23]. Apart from it, this time period was associated with highest mortality in hospitals without intensive care units (ICU) (In case of ICU presence mortality peaks have different timing) [24]. Our approach of BP evaluation (average BP values measured between 6 and 8 a.m.) in the morning is enough simple to perform, since many devices for 24h-BPM have settings that allow to choose a distinct time interval and quantify average values of BP measurements made at this time period. As we have already mentioned before, parameters that characterize the severity of mBP increase, absolute values of mBP and night BP (nBP) have a prognostic value for estimation of the risk of stroke development, cardiovascular complications and mortality, and also for target organs lesions and increased thickness of carotid arteries' intima-media [11-21].

Our study demonstrated that low levels of social support (one of LQ elements) correlated with increased severity of seasonal variations of mBP and nBP in patients with AH. Many studies demonstrated that social support is one of the main psychosocial factors influencing the prognosis of cardiovascular diseases [32]. More than that, social support is also connected with some characteristics of home-measured BP. The study of Fortmann A.L. et al reported the association between the level of social support and the degree of BP dipping at night (comparative analysis of 297 studies [33]. Another study proved the important role of social support in BP dipping at night. This study involved 171 persons, both people with normal BP and AH [34]. Our results suggest that patients with low social support (lonely people or people living in retirement homes) should undergo more detailed estimation of BP and antihypertensive therapy efficiency during periods of seasonal BP fluctuations in order to improve the efficacy of complex antihypertensive treatment.

This study demonstrated that average home-measured systolic and diastolic values of BP24, dBP, nBP, and mBP had similar seasonal variations: maximal BP levels were registered in winter, and minimal BP levels were detected in summer. Numerous studies that had been conducted in Europe during the last years demonstrated that clinical [4] and home-measured BP levels obtained using 24h-BPM and blood pressure self-monitoring (BPSM) were characterized with increased BP levels during cold periods of the

year [5, 6, 7, 8]. In our research center we also estimated seasonal changes of BP in different regions of European Russia (Ivanovo, Saratov, Moscow) and received similar results [35, 36]. Seasonal variations of BP characteristics differ between nighttime and daytime periods. Many studies demonstrated that average nBP levels were maximal not in winter, but in summer, and they had the lowest values in winter [5, 6, 7]. Another major study reported that mBP levels (measured before awakening and 2 hours after it) were the highest during the cold period of the year [10]. In our study nSBP and mSBP were minimal in spring and winter, respectively, and maximal in autumn. It is possible that such differences between our study and the works of our foreign colleagues may be explained by the fact that in the Moscow region the weather of the beginning and in the middle of spring is similar with the winter one. Possibly, if we had performed analysis of seasonal BP changes taking into account not formal change of seasons but real weather changes, our results would have been more similar with the results of other studies.

Conclusions

1) Severity of seasonal changes of SBP and DBP in the morning and at night was reversely correlated with characteristics of AH patients' social support provided by relatives, friends, colleagues (one of LQ elements).

2) Seasonal dynamics of mDBP was typical: BP levels were maximal in winter and minimal in summer. The highest values of mSBP were detected in autumn, and the lowest ones were measured in winter. Gender and age were significant just for seasonal variations of mSBP

3) The values of nDBP were maximal in winter and minimal in simmer, whereas the levels of nSBP were maximal in autumn and minimal in spring

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Characteristics of glycaemic status and cardiovascular complications in relation to education level in patients with diabetes mellitus type 2

Mehdiyev S.Kh.
Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev

Authors
Samir Kh. Mehdiyev, M.D., Ph.D., associate professor of the department of internal medicine, Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev.

Summary

Objective
To investigate the relation between education level, glycaemic status, and cardiovascular complications and their electrocardiogram (ECG) criteria in patients with diabetes mellitus type 2 (DM 2).

Materials and methods
This study included 523 patients with DM2. Patients underwent questioning that allowed to estimate their education level and obtain information about the presence of arterial hypertension (AH), coronary heart disease (CHD), chronic heart failure (CHF), and history of myocardial infarction (MI). Apart from it, we performed ECG registration in order to detect left ventricular hypertrophy, MI and CHD, and estimated fasting levels of glucose and glycated hemoglobin in venous blood.

Results
Systolic AH was more frequently present in patients with incomplete secondary education comparing with the patients with higher education, and diastolic AH was more frequent in persons with vocational education. Use of ROSE questionnaire allowed to detect angina pectoris 2.5 times more frequently comparing with routine patient's questioning, and ECG identified signs of precedent MI 2 times more frequently than normal questioning. Patients with secondary education demonstrated significantly lower occurrence of MI history, various arrhythmias and CHF, and ECG signs of MI were more frequent in patients with secondary and vocational education, in comparison with patients with higher education ($p<0.05$). We identified reverse correlation between education level and

* Corresponding author. Tel.: +9940513744890. E-mail: smehdiyev@mail.ru

glycemia in persons with secondary education comparing with the patients with higher education (76.3±2.9% and 64.8±3.7%, respectively, p<0.05). The least favorable control of disease progression was found in patients with incomplete secondary education (55.5±8.2%), and the most favorable one was demonstrated by patients with secondary education (14.2±2.4%).

Conclusion

It is necessary to perform adequate control of disease progression and improve risk factors' management in all patients with DM 2 independently from their education level in order to prevent cardiovascular complications.

Key words

Diabetes mellitus type 2, education level, glycaemic status, cardiovascular complications.

Introduction

Education level is considered to be a significant modifiable and non-modifiable risk factor (RF) that influences the health of population [1, 2, 3, 4]. Although results of numerous studies that proved the influence of education on cardiovascular complications have been published in scientific literature, this relation has never been studied in patients with diabetes mellitus type 2 (DM2) depending on their gender[5, 6, 7, 8, 9].

It is known that education level influences lifestyle, smoking, obesity and other RF in people of both genders, and this, in its turn, increases the risk of complications in patients with DM2 [6]. There are enough evidences of direct correlation between education level and health condition of patients [4, 6, 9]. Education status significantly reduces the risk of DM2 and arterial hypertension (AH) development in women, but not in men. Women with secondary education had elevated both AH occurrence and BMI, consequently, it increases the risk of coronary heart disease (CHD) development. It is known that men with low education have 7-8 times higher risk of cardiovascular pathology development [6].

Efficacy of antihypertensive therapy is lower in men with higher education having tachycardia and obesity and consuming excessive amount of alcohol [5]. Other studies demonstrated direct correlation between education level and AH just in young women [6].

The level of education has negative correlation with cardiovascular complications and influences also the lifespan. Thus, men with higher education have longer lifespan in respect to men with secondary education. Although men's lifespan has increased during the last 25 years comparing with women, its gender differences in relation to education levels have not been studied [10]. During the last years it has been noticed that that people with lower education level had shorter lifespan, and it was tightly connected with social conditions and complications, in particular, with cardiovascular ones [9].

It is worth to mention that smoking and its bad impact are more frequent in people with low education level that, in its turn, increases the risk of cardiovascular disease development and progressing of their complications [10].

High frequency of cardiovascular complications in people with low education level can be explained by their restricted knowledge about negative influence of RF. At the same time, during the last years the level of knowledge about preventive measures in women has increased comparing with men [7]. Education level increases the risk of cardiometabolic changes, and it is differently regulated in men and women. The frequency of cardiovascular complications is different between both genders [6].

Taking into account the facts mentioned above, we aimed to study the correlation between education level and cardiovascular complications in patients with DM2.

Materials and methods

This study involved 523 patients aged 30-69 who were admitted to endocrinological department of the Republican Clinical Hospital named after Mirkasimov or who had to visit endocrinologist at the Republican Clinical Hospital outpatient department or Republican endocrinological center. 165 patients (31.5%) were males, and 358 (68.5%) were females. Average age of patients was 53.9±0.4 years.

All patients had to fill ARIC questionnaire established by the World Health Organization (WHO) professionals and being used for clinical epidemiological studies. This questionnaire contained a section dedicated to educational status of patients. All patients underwent blood pressure (BP) measurement us-

ing mercury sphygmomanometer with accuracy of 2 mm Hg in sitting position for two times with 5-minute break between them. For further analysis we used an average value of three BP measurements.

All patients filled ROSE questionnaire that reported the presence of stable angina, AH, CHD, the history of myocardial infarction (MI), and chronic heart failure (CHF). AH was diagnosed if BP levels were ≥140/90 mm Hg, left ventricular hypertrophy (LVH), MI and CHD were diagnosed using electrocardiography (ECG) criteria. 24-hour ECG monitoring was used for arrhythmias diagnosis, and CHF was diagnosed based on transthoracic echocardiography results.

Blood used for glycaemic status determination was taken from cubital vein. If glucose concentration in blood was ≥7 mmol/L, hyperglycemia was considered, and glycated hemoglobin concentration ≥7% indicated inadequate DM control.

Results

It is known that AH is the most studied complication of DM2 (Table 1). It was demonstrated that patients with DM2 and higher, professional and secondary education had the same frequency of AH, and the lowest frequency of AH was present in people with incomplete secondary education. At the same time no one of them had statistically significant values.

Although the patients with DM2 and incomplete secondary education had lower occurrence of AH, they had ECG signs of LVH more often ($p>0.05$). The highest occurrence of systolic AH was found in the patients with DM2 and incomplete secondary education comparing with the people having higher education ($p<0.05$). Even if the occurrence of AH in patients with higher education, systolic AH was present in few patients. Diastolic AH was less common in patients with higher education, and its frequency was lower comparing with people with professional education.

According to the questionnaires, stable angina was the least frequent in patients with university education, and it was 2.5 higher if assessed with ROSE questionnaire. The frequency of this CHD form was relatively lower in patients with DM2 and higher education comparing with the patients with secondary and professional education.

ECG signs of CHD were present in 10.6% of patients, but these characteristics had no statistically significant difference between groups of patients with different education levels.

Questioning revealed MI in every one out of ten patients, and every fifth one had ECG signs of MI. Instrumental examination and patients' history demonstrated that the lowest number of MI was found in patients with secondary education, and comparing with the people with higher education this difference was statistically significant.

The biggest number of arrhythmias was detected in patients with DM2 and higher education, and the lowest one was found in people with secondary education.

The same situation was fair for patients with CHF, since 1/3 part of patients had its clinical and echocardiographic signs, and people with university education had relatively higher frequency of this condition comparing with the people with secondary education ($p<0.05$).

Table 1. **The occurrence of glycemia, cardiovascular complications and their ECG criteria depending on education level (%)**

Characteristic	Higher education (n=165)	Professional education (n=111)	Secondary education (n=211)	Incomplete secondary education (n=36)
AH	80±3.1	82.8±3.5	80.1±2.7	69.4±7.7
CHD (angina)	6.7±1.9	13.5±3.2	14.2±2.4**	11.1±5.2
Stable angina (ROSE questionnaire)	16.3±2.8	27.0±4.2*	22.3±2.8	16.6±6.2
MI	9.7±2.3	4.5±1.9	3.3±1.2**	5.5±3.8
Arrhythmia	15.1±2.8	11.7±3.0	8.5±1.9**	13.9±5.7
CHF	33.9±3.7	27.0±4.2	22.3±2.8**	22.2±6.9
LVH (ECG)	71.5±3.5	64.8±4.5	62.5±3.3	72.2±7.4
MI (ECG)	21.2±3.2	10.8±2.9*	11.4±2.2**	16.6±6.2
CHD (ECG)	12.7±2.6	14.4±3.3	11.4±2.2	13.9±5.7
Glycemia (≥7mmol/l)	64.8±3.7	66.6±4.4	76.3±2.9**	77.7±6.9
HbA1c (≥7%)	33.9±3.7	20.7±3.8*	14.2±2.4**	55.5±8.2***
Systolic AH	49.1±3.9	56.7±4.7	54.0±3.4	66.6±7.8***
Diastolic AH	30.9±3.6	42.3±4.8*	32.7±3.2	36.1±8.0

Comment: * - Difference between patients with higher and professional education ($p<0.05$); ** - Difference between patients with higher and secondary education ($p<0.05$); *** - difference between patients with higher and incomplete secondary education ($p<0.05$).

There was a negative correlation between education level and glucose concentration in blood. Inadequate glucose control (plasma levels ≥7 mmol/L) were more frequent in patients with incomplete secondary education and present the least in patients with higher education. Comparison of this parameter between patients with DM2 and higher education and patients with DM2 and secondary education was statistically significant.

It is interesting to notice that the highest values of poorly controlled glycaemia were detected in people with incomplete secondary education, and relatively good control of glycaemia was characteristic for patients who had higher education. Inadequate glycemic control was present in 1/3 part of patients with DM2 and higher education and in 1/5 part of patients with professional education. The difference between HbA1c levels was statistically significant depending on education levels. Patients with DM2 and higher education had poorer glycemic control comparing with the patients with DM2 and professional or full secondary education, whereas patients with incomplete secondary education had relatively good glycemic control.

Discussion

It is known that AH is one of the most frequent concomitant diseases in patients with DM2 [5, 8]. Our results were a bit controversial, and they demonstrated that education level did not change significantly AH prevalence. But it is worth to notice that the studies mentioned above were performed in patients with AH without DM2 [5, 8]. Educated patients had no adequate DM compensation, apart from it preventive measures aiming to target RF have not been performed in this group, and in the end it has led to significant increase of AH prevalence.

The probability of low AH frequency in people with incomplete secondary education can be explained by their high physical activity, and high AH values can be explained by the lack of knowledge about the presence of disease and consequent insufficient therapy. According with our results, this trend was exactly the opposite in the patients with higher education.

ECG signs of LVH were a frequent pathology between the patients of this study. LVH prevalence in general population is around 16-19%, and in patients with AH this value is above 60% [11]. The frequency of LVH in our population was 67.7% independently from education level, and it raises particular concerns. It is known that the risk of arrhythmias, CHF, sudden death and other cardiovascular complications is high enough in patients with LVH, and it requires performing immediate preventive measures [12, 13].

Stable angina was detected 2.5 times more often if the ROSE Angina questionnaire was used, comparing with routine history taking. In this questionnaire patients have to answer particular questions that facilitate establishing the diagnosis. Low detection of CHD in people with higher education can be explained by sufficient knowledge about the complications of this disease, by more precise following a hypolipidemic diet, by adequate actions against RF. Taken together, these things indicate that these people followed healthy lifestyle.

ECG signs of myocardial infarction were detected 2-3 more often that can be explained by diabetic cardiomyopathy [14]. Although clinical manifestations of MI was less present in the history of patients with secondary education comparing with the other groups, the frequency of MI ECG symptoms was 3 times higher. These results demonstrate that painless forms of CHD prevails over clinical manifestations of MI in patients with DM2 [15, 16, 17]. It can be explained by the fact that CHD is more often diagnosed in educated people and that preventive measures are well-timed in this group of patients. Our results can be proved by similar studies that have been conducted in past [6, 7, 9].

Frequent detection of arrhythmias in patients can be explained not by improved education level but by early diagnosis of this pathology. The frequency of CHF in patients with DM2 goes up together with the increase of education level, and it stimulates developing preventive programs.

Table 1 demonstrates reverse correlation between venous blood glycaemia and HbA1c levels. It proves once more the fact that the control of DM course should be performed using HbA1c levels. The worsening of DM control with the increase of education level can be considered negative, and it does not go along with other studies that have been conducted in other regions [6].

Conclusion

Thus, reasonable correlation between education level and cardiovascular complications were not detected in the studied cohort of patients. Otherwise, it is recommended to improve DM2 RF prophylaxis independently on patients' education in order to prevent cardiovascular complications and perform adequate glycemic control.

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Phylogenetic theory of general pathology.
Atherosclerosis and atheromatosis as two different processes: aphysiological implementation of biological function of trophology and endoecology

Titov V.N.*, Rozhkova T.A., Kaminnaya V.I.

Russian Cardiology Research-and-Production Complex, Ministry of Health of the Russian Federation, Moscow

Authors

Vladimir N. Titov, M.D., Ph.D., professor, doctor of sciences, head of the laboratory of lipid metabolism clinical biochemistry, A.L.Myasnikov Institute of Clinical Cardiology, Russian Cardiology Research-and-Production Complex, Ministry of Health of the Russian Federation, Moscow.

Tatyana A. Rozhkova, M.D., Ph.D., researcher of the department of atherosclerosis problems, A.L.Myasnikov Institute of Clinical Cardiology, Russian Cardiology Research-and-Production Complex, Ministry of Health of the Russian Federation, Moscow.

Violetta I. Kaminnaya, M.D., Ph.D., junior researcher of the department of atherosclerosis problems, A.L.Myasnikov Institute of Clinical Cardiology, Russian Cardiology Research-and-Production Complex, Ministry of Health of the Russian Federation, Moscow.

Summary

We believe that seven biological functions have formed during phylogenesis. They are: 1) trophology, 2) homeostasis, 3) endoecology, 4) adaptation, 5) reproduction, 6) locomotion, 7) cognitive function, including intellect. The function of trophology (feeding) is realized via the biological reaction of exotrophy (external feeding) and endotrophy (internal feeding). The function of endoecology provides the maintenance of all vital parameters within physiological range. This function is realized through the reactions of inflammation and excretion. Etiological factors of atherosclerosis are: 1) oleic monounsaturated fatty acid (MFA) that is more actively utilized in biochemical reactions than palmitic fatty acid, 2) in the ocean all animals were carnivorous (fish eating), after millions of years of living on dry land Homo sapiens became herbivorous, 3)insulin plays the major role in transition from

* Corresponding author: Tel. +7 495 4146310. E-mail: vn_titov@mail.ru

carnivorous to herbivorous belongs, since this hormone is involved in conversion of endogenous saturated palmitic (SFA) into oleic MFA, 4) phylogenetically insulin does not initiate in vivo conversion of exogenous palmitic SFA into oleic MFA, and 5) in the ocean, biologically active eicosanoids are synthesized from eicosapentaenoic polyenic FA (PFA); on dry land this acid is not available. Excessive eating of meat by herbivorous Homo sapiens provides the basis for atherosclerosis. Blocked bioavailability of PFA leads to their deficiency in cells. Insulin-initiated transport of oleic MFA as oleic triglycerides (TG) in oleic apoE/B-100 very low density lipoproteins (VLDL) occurs without LDL formation; transport of SFA in palmitic apoE/B-100 VLDL is blocked at the stage of nonligand palmitic VLDL→LDL formation, glycolipoprotein formation and high level of LDL-cholesterol. Incomplete utilization of palmitic VLDL→LDL by monocytes leads to atheromatosis in the intima of elastic arteries. Polyenic FA metabolites which were not internalized via apoB-100 endocytosis are the major constituents of atheromas. Atherosclerosis, hyperlipoproteinemia and high content of LDL-cholesterol result from impaired function of trophology, while atheromatosis is associated with impaired biological function of endoecology.

Key words

Atherosclerosis, atheromatosis, insulin, biological functions, LDL-cholesterol, arterial intima.

New epochs, new theories, new concepts of medicine, disease etiology and pathogenesis create thoughts about the necessity of developing a new theory of general pathology after the cellular theory of R. Virchow. These thoughts appear the most often during observation of phylogenesis of difference between etiological factors and pathogenetic unity of metabolic pandemias, the diseases of the civilization that became widespread in populations of developed countries. We select [1] seven metabolic pandemias:

1. Atherosclerosis and atheromatosis;
2. Metabolic essential arterial hypertension (AH);
3. Insulin resistance (IR) syndrome;
4. Metabolic syndrome;
5. Obesity;
6. Non-alcoholic fatty liver disease;
7. Endogenous hyperuricemia. Their differences are determined by the specificity of etiological factors that have formed during phylogenesis of these non-physiological processes. The World Health Organization (WHO) specialists do not consider all metabolic pandemias as nosological forms of diseases, instead only systemic, etiologically specific ones and widespread in vivo metabolic abnormalities can be considered metabolic pandemias.

All metabolic pandemias excluding endogenous hyperuricemia, are characterized by in vivo (at organism level) impairment of fatty acids (FA) metabolism. Simultaneously they affect:

a) functions of cellular structures;

b) regulatory and

c) energetic basics of FA metabolism in phylo- and ontogenesis.

Etiological factors of metabolic pandemias have been consequently formed during the stages of phylogenesis. If the frequency of non-infectious, non-physiological process in population exceeds 5-7%, we suppose that its etiological cause is based on impaired biological functions and reactions. We suggest that the phylogenetic theory of general pathology would become a biologically proved successor of cellular theory of R.Virchow. There is nothing more difficult then changing well-established ideas of people. It is fair even for scientific terminology; sometimes terms start to exist independently from the meaning that the investigators put into them in the beginning. We have been using the term "cardiovascular system" for 400 years, starting from the times of William Garraway, but as soon as we start to discuss the regulation of circulation and in vivo circulatory pathologies we should rationally remember that vasculary-cardiac system has been formed phylogenetically. Similar changes happen with the words atherosclerosis and atheromatosis. We can about the atherosclerosis of coronary arteries as much often as about the atheromatosis of elastic arteries' intima. What is the real difference of ideological, phylogenetic, pathopysiological meaning between the terms "atherosclerosis" and "atheromatosis"? How do the specific different etiological factors and atheromatosis have been formed during the stages of phylogenesis, and in which tissues these non-physiological (physiological?) processes are localized, which is their order of appearance, which is the common part of their pathogenesis? Which term is it more correct to use talking about arterial intima: "atherosclerosis" or "atheromatosis"?

Careful investigation of etiological factors of metabolic pandemias that include:

a) hyperlipoproteinemia (HLP);

b) plasma concentration of non-esterified FA (NEFA);

c) clinical manifestations of coronary heart disease (CHD);

d) variants of abnormal lipoprotein (LP) metabolism;

e) difference of topological variants of coronary sclerosis, may help to establish a reasonable point of view that inhabited terms "atherosclerosis" and "atheromatosis" for real express two FA metabolism abnormalities with different etiology and equal pathogenesis.

It is possible to understand the difference of etiological factors of atherosclerosis and atheromatosis if we start to observe them from the positions of our phylogenetic theory of general pathology [2].

We suppose that impaired regulatory activity of insulin underlies atherosclerosis pathogenesis; atherosclerosis is a non-physiological reaction of HLP formation, impaired metabolism of FA, lipids, triglycerids (TG, esters of triatomic alcohol glycerol and insulin-dependent phylogenetically young ApoE/B-100 very low density lipoproteins (VLDL)) at first. Being expressed as the target of insulin, they started to transfer ω-9 C18:1 oleic acid, monounsaturated FA (MFA) endogenously synthesized in hepatocytes from exogenous glucose in the form of oleic TG phylogenetically late.

When ApoE/B-100 LP start to transfer to cells big amounts of exogenous C16:0 palmitic saturated FA (SFA) derived from food in case of impaired biological function of trophology (feeding), it blocks the bioavailability and cell uptake of polyunsaturated FA (PUFA) as part of low density LP (LDL). PUFA are the substrate for the synthesis of biologically active phylogenetically old humoral mediators eicosanoids, that include prostacyclines, prostaglandines, thromboxanes and leukotriens. This is atherosclerosis and it is initiated by impaired biological function of trophology (feeding), biological reaction of exotrophy (external feeding), by excessive amounts of consumed and present in vivo palmitic SFA and impaired biological activity of insulin.

From the point of view of phylogenetic theory of general pathology, biological role of insulin consists at first of FA metabolism regulation and at second of mediating the regulation of glucose metabolism.

Atheromatosis is a generally physiological process of compensation of abnormal FA metabolism, in particular HLP, realization of biological function of endoecology, unfortunately in vivo conditions it often does not reach its functional ending. In this condition it leads to formation of inflammatory-destructive non-physiological process called atheromatosis of elastic (or mixed type) arteries' intima in phylogenetically late part of arterial system. Atheromatous masses of arterial intima are consisted of palmitic ligandless ApoE/B-100 VLDL→LDL impossible to be absorbed by cells by ApoE/B-100 endocytosis due to excess of exogenous palmitic SFA.

The main part of atheromatous masses of intima is made of PUFA esters of cholysterol (PUSChE) that cells were unable to take together with ligandless palmitic VLDL→LDL via ApoE/B-100 endocytosis.

Phylogenetic theory of general pathology

The main approaches of general biology and medicine include:

1. Unity of structure and function;

2. Unity of the main stages of phylo- and ontogenesis;

3. The same technology of functional systems formation in ontogenesis;

4. Use of systemic approach of general biology for explanation of events happening in vivo. We suggest completing this list with other two biological approaches;

5. Continuity of formation of biological functions and reactions in phylogenesis, and 6. Methodological approach of biological subordination.

Development of biological functions and reactions during phylogenesis occurs not as creation of something principally new, this way is more characteristic for mutations, of high or low significance or neutral by now. According to biological subordination, newly formed humoral (hormonal) mediator in vivo is organically built upon earlier ones, it interacts with them functionally, but no new mediator, even more perfect one, can change the action of phylogenetically older mediators.

If the frequency of non-infectious disease in population exceeds 5-7% we suggest that:

a) this metabolic pandemia is etiologically based on impaired biological functions and reactions;

b) it is necessary to build rational pathogenesis in the aspect of phylogenesis; and

c) these abnormalities should undergo pharmacological correction only in case of development of complications. We suggest rational estimating all that has happened and is happening in vivo from the point of biological functions and reactions. We suppose that seven biological functions have been formed during

phylogenesis not simultaneously millions of years ago. These seven functions include:

1. Biological function of trophology;
2. Biological function of homeostasis;
3. Biological function of endoecology;
4. Biological function of adaptation;
5. Biological function of continuation of the species;
6. Biological function of locomotion, and
7. Cognitive biological function, and intellect is its upper point.

Biological function of homeostasis is aimed to fulfill the following position: intercellular medium in vivo should contain enough of everything for all cells at any point of time. The function of homeostasis should not allow the reduction of analytes (physical and chemical parameters) concentration in intercellular medium below the lower limit of physiological interval. Dozens of biological reactions fulfill the function of homeostasis according to the number of biochemical (physical-chemical) analytes in intercellular medium.

Biological function of trophology (feeding) is realized via two biological reactions: a) biological reaction of exotrophy — exogenous feeding (hydrolysis, absorption of exogenous nutrients, complicated process of nutrients' deposition) and b) biological reaction of endotrophy that provides cells with all necessary substrates during food deprivation at night, during hibernation and forced fasting. It is more difficult to release FA from adipose cells rather than to deposit them. Trophology is the science about food, feeding, trophic connections in vivo and food assimilation [3]. It seems to be interesting for researchers that pathogenesis of non-physiological processes in vivo can be based on impaired biological function of trophology and feeding.

Biological function of endoecology is aimed to prevent analytes from exceeding upper limits of normal (physiological) intervals in physiological (non-physiological) conditions. Biological function of endoecology considers elevated amounts of analytes as lack of "cleanness" of intercellular environment, its "pollution" with endogenous phlogogens with high molecular weight (>70 kDa, big phlogogens) initiating biological reaction of inflammation. Glucose and Na+ can become small molecular weight phlogogens (<70 kDa, small phlogogens) in case of hyperglycemia and hypernatremia. Palmitic VLDL→LDL can act as big phlogogens n vivo when they don't form ApoE/B-100 ligand and cannot be absorbed by all insulin-dependent cells via physiological ApoE/B-100 endocytosis.

Two non-specific biological reactions are responsible for the function of endoecology: a) biological reaction of excretion and b) biological reaction of inflammation. If molecular weight of small endogenous phlogogens in intercellular environment is not higher than molecular weight of albumin their excretion goes through realization of biological reaction of excretion in kidney nephrons and urine formation. If endogenous phlogogens are big as exogenous ones or can be infectionally pathogenic (lipopolysaccharide + specific binding protein) and have higher molecular weight than albumin, their collection and utilization occur in vivo and in situ through the realization of biological reaction of inflammation. Main function of biological reaction of inflammation is to maintain "cleanness" of intercellular environment in vivo, collection and utilization of big endogenous phlogogens and exogenous pathogens in situ. The meaning of biological function of endoecology is that "intercellular environment should be always clean". Accumulation of big endogenous phlogogens is the main condition for activation of biological function of endoecology in vivo. Realization of biological function of endoecology does not depend on etiological factors, from the character of endogenous phlogogens: apoptotic bodies, products of cellular autophagy, antigen/antibody complexes, exogenous infectious pathogens like polysaccharides of Gram-negative bacteries [4]. Excretion is determined by the size of fenestrae on the membrane of glomerulus between the feet of podocytes on the basal membrane.

The main tests that detect abnormalities of biological function of endoecology are microalbuminuria and C-reactive protein (CRP) — monomer and pentamer. The test for microalbuminuria can demonstrate:

a) "pollution" of intercellular environment with small phlogogens;

b) prevalence of active glomerular filtration over passive reabsorption in proximal tubules of nephrons, and

c) activation of angiotensin-II secretion by the cells of juxtaglomerular cluster of nephron via the mechanism of reverse feedback and decreased filtration after compensatory spasm of afferent arteriole.

Increased urinary excretion of microquantities of albumin often goes along with increased plasma levels of:

a) pro- and anti-inflammatory interleukins;

b) increased oxidation of proteins with reactive oxygen species (ROS) (physiological process of protein denaturation) [5].

Increased concentration of CRP monomers and pentamers is a sign of "pollution" of intercellular environment with big endogenous phlogogens, apoptotic bodies, products of biological reaction of autophagy and inflammatory reactions [5]. Biological role of CRP consists from formation of vector, directed FA transfer, providing substrates for production of energy (FA in the form of TG as part of VLDL) just in the cells that should fulfill biological reaction of inflammation.

Biological reactions that participated in realization of biological function of endoecology include also:

1. Reaction of hydrodynamic arterial pressure (BP);

2 Physiological denaturation of endogenous proteins with ROS;

3. Biological reaction of transcytosis throw endothelial monolayer;

4. Reaction of hyperthermia;

5. Biological reaction of apoptosis;

6.Reaction of opsonization by complement components;

7. Biological reaction of innate and

8. Acquired immunity;

9. Reaction of systemic inflammatory response, and

10. Biological reaction of autophagy.

To activate biological reaction of excretion it is necessary to increase hydrodynamic (hydraulic) pressure on basal membrane of glomerules. That's why accumulation of small endogenous phlogogens in intercellular environment initiates BP elevation and increases filtration in glomerules of nephrons independently of phlogogens' etiology, and these abnormalities can occur in physiological range for a long time.

After formation of closed circulatory system cells continued to excrete big phlogogens from cytoplasm into the bloodstream, in the local pool of intravascular intercellular environment as it used to be millions of years before. In this case evolutionally late pull of collection and utilization of big phlogogens from intravascular pull of intercellular environment is located directly after the endothelial monolayer in elastic arteries' intima.

Activation of biological reaction of inflammation for excretion of big phlogogens from the local pool of intravascular intercellular environment to elastic arteries' intima requires activation of biological reaction of transcytosis (pinocytosis, endo- + exocytosis) through endothelial cells monolayer. Since the formation of closed circulatory system was evolutionally late, the only way of transcytosis activation is the increase of hydrodynamic pressure in the distal part of arterial system made of precapillary muscular arterioles. And if a patient has increased plasma levels of CRP monomers or pentamers for a long time it is always accompanied with elevated BP, it occurs within physiological values of BP more frequently, but constantly and during long time periods. It is followed by impairment of biological function of endoecology and slow formation of essential metabolic AH.

Biological function of adaptation is realized through the following mechanisms:

1. Biological reaction of stress;

2. Reaction of compensation;

3. Biological reaction of compensatory anti-inflammatory protection, and

4. Reaction of innate and acquired immunity. Biological stress reaction is evolutionally old, it is realized even at autocrine level (inside cells) through the synthesis of chaperone proteins [6].

Chaperones are the heat shock proteins, the "clips" synthesized by each and every cell for realization of biological stress reaction in order to preserve functional conformation (ternary and quaternary structure) of the most functionally important proteins through physical-chemical interaction with chaperones [6].

Biological reactions of compensation in vivo are various, and they are realized as at cellular level as at the level of paracrine regulation of cellular communities. The syndrome of compensatory anti-inflammatory response also participates in the realization of biological function of adaptation; it controls in vivo the consistency between biological inflammatory reactions and action of initiating factors like endogenous phlogogens or exogenous pathogens.

After each biological reaction of stress, even after emotional one, intercellular environment contains many chaperons including the ones with high molecular weight (65-130 kDa). Loose connective tissue (LCT) cells utilize chaperons in vivo through realization of biological reaction of inflammation, and this is the function of "sedentary", resident macrophages. Each episode of any stress including emotional one is followed by biological reaction of inflammation:

a) synthesis of chaperone family proteins;

b) their collection and elimination from intercellular environment, and

c) their utilization via inflammatory reaction in elastic arteries' intima. Due to this even emotional AH is always accompanied with biological reactions of BP and inflammation.

From functional point of view arterial intima is a single pool that collects and utilizes in vivo multiple endogenous phlogogens, exogenous infectious pathogens and various xenobiotics, alien substances that enter circulation during pharmacological treatment; intima also regulates utilization — the final step of generalized biological function of endoecology and inflammatory reaction. Biological function of endoecology, reaction of inflammation occurs in vivo every minute and second, as it happens with biological reaction of excretion in glomerules of nephrons.

Independently from etiology, every disease is based on initial or acquired impairment of biological functions. Only the therapy that overcomes (eradicates) undesirable endogenous and exogenous influences and brings back the processes to their natural course can be called effective. Adaptation of organism to non-physiological conditions can be considered as the unity of adaptation mechanisms (formation of optimal changes) and compensation of physiological processes. It is necessary to note that compensation can be physiological and non-physiological.

Biological function of locomotion

Realization of locomotion during phylogenesis that requires movement due to reciprocal contraction of evolutionally late skeletal myocytes was accompanied with formation of: a) closed circulatory system; b) heart started to work as the central pump in the proximal part of arterial system; c) differentiated function of millions of local peristaltic pumps like muscular arterioles, formation of "peripheral" heart in the distal part of arterial system. The system of insulin-dependent cellular pools has been formed: striated myocytes, cardiomyocytes' syncytium, subcutaneous insulin-dependent adipocytes, periportal hepatocytes, specialized Kupffer cells in liver, ß-cells of Langerhans islets in pancreas; d) vector transfer of oleic MFA synthesized in situ de novo from glucose in hepatocytes in the form of oleic TG as the part of oleic ApoE/B-100 VLDL that do not turn to LDL. They are absorbed by insulin-dependent cells via vector ApoE/B-100-dependent endocytosis of ligand oleic VLDL.

Cognitive biological function

The term "cognitive function" arises from Latin word "cognition" — knowledge; cognosere – to know, to estimate the environment, to look around. The terms like recognition of abnormalities, estimation (of metabolism) and outer condition (environment) have the same etymology [7]. As we suppose, cognitive function includes: a) the ability of an individual to focus on metabolism regulation in vivo and combine regulation of all cellular community function in vivo in all three levels of relative biological "perfection" [7]. It can be related to:

1) Autocrine regulation of each cell;
2) All cellular communities, organs, organ system s receiving paracrine regulation;
3) Organism in general [8] in vivo, and
4) Microbiota that lives together with organism during all its life [9].

Realization of cognitive function means adequate self-positioning in outer environment, space and being surrounded by other individuals in conditions of constantly changing, severe, not always positive influences of environmental factors. This can be also applied to physiology of organism that is an optimal combination between dominating multicellular system and local bacterial ecosystem of facultative anaerobic organisms of the large intestine [9].

We suppose that cognitive biological function is the combined, single, neurohumoral vegetative regulation of metabolism at the third level of relative biological perfection, at the level of organism. It occurs during:

a) combined function of all organs [10] and systems;

b) dynamic formation of metabolic unity in vivo;

c) changes of the environment [11].

Whatever were the parameters (1), however fast the environmental changes occurred (2), cognitive biological function of subcortical brain structures would be responsible for optimal changes of metabolism [12]. During phylogenesis imperfection of cognitive biological function sometimes used to create so imperfect in vivo conditions even for Homo sapiens ancestors that the majority of population members died [13].

Impaired cognitive function during the formation of metabolic pandemias that are tightly connected with each other from pathogenetic point of view includes pathology of biological functions of trophology, homeostasis, endoecology and adaptation. Restricted pool of cells independent from insulin action that includes visceral omental adipose cells and unlimited number of insulin-dependent subcutaneous adipocytes participate in the formation of pathology and lo-

cal abnormalities of paracrine communities, tissues and organs in vivo [14].

In psychology "cognition" means the ability to acquire and fulfill knowledge, perception, thinking, speech, conscience and memory [15]. The terms "cognitive skills" and "cognitive capacities" usually characterize individual capacities through realization of which person can perceive knowledge, information and successfully fulfill them. During evolution the action of leptin, adiponectin, and acetyl-CoA [16] and biological cognitive function have not created in vivo system [17] that would have informed subcortical nuclei of hypothalamic area of the brain about the end of physiological food intake and aphysiological continuation of meal using the mechanism of reverse negative feedback [18].

The unity of pathogenesis of atherosclerosis, impaired biological function of trophology and endoecology

Etiological factors of atherosclerosis that have been formed during the early stages of phylogenesis include the following ones:

1. Oleic MFA is more active in chemical reactions than palmitic FA [19];

2. When animals used to live in the ocean, they were carnivorous (they used to eat fish). After the reduction of the ocean level, forced life on the ground during millions of years and adaptation to new environmental conditions made Homo sapiens become herbivorous [20].

3. Biological role of insulin consists of providing substrates for energy production, first of all, for biological function of locomotion, to provide organism with energy (ATP) through combined use of two substrates: FA and glucose. Insulin expresses transformation of C 16:0 palmitic SFA endogenously synthesized from glucose to ϕ-9 C18:1 oleic MFA. Insulin expression increased kinetic parameters in vivo [21].

4. At the same time evolutionally late insulin cannot initiate in vivo transformation of all exogenous palmitic SFA of meat (carnivorous food) to oleic MFA. Herbivorous organisms realize oleic variant of FA metabolism under the action of insulin, and after meat food consumption they shift to palmitic variant of FA metabolism.

5. During the life in the ocean all animals used to synthesize biologically active mediators eicosanoids from the fish fat, from ϕ-3 C20:5 eicosapentaenoic PUFA (eicosa) [22]. There was no PUFA synthesis system on the ground.

High consumption of carnivorous food (meat) by evolutionally herbivorous Homo sapiens is the most frequent pathogenetic factor of atherosclerosis. It leads to formation of:

a) alimentary deficiency of PUFA [23] due to its blocked bioavailability and its absorption by cells in the form of polyunsaturated cholesteryl ester (PUSChE) activates biological reaction of compensation and in vivo synthesis of non-physiological eicosanoids that impairs in vivo regulation of many aspects of metabolism [24];

b) evolutionally late insulin is unable to transform exogenous palmitic SFA to oleic MFA; in this case palmitic variant of FA metabolism starts to prevail in vivo and it impairs providing cells with energy comparing with oleic variant; meat contains several times more palmitic SFA than fish [25];

c) Vector transfer of oleic MFA in the form of oleic TG as part of oleic ApoE/B-100 VLDL initiated by insulin does not lead to LDL formation, and ligand oleic VLDL are directly consumed by insulin-dependent cells via ApoE/B-100 endocytosis.

d) Phylogenetically late ApoE/B-100 FA transport cannot transfer palmitic SFA in the form of palmitic TG as part of palmitic VLDL, the blockade occurs at the stage of formation of ligandless palmitic VLDL→LDL. Cells cannot absorb ligandless VLDL in receptor-mediated way, and these particles become big endogenous phlogogens forming retention HLP and high levels of LDL-cholesterol [26].

Increase of LDL cholesterol occurs first of all due to increased concentration of non-esterified cholesterol in polar monolayer of palmitic VLDL→LDL. They block cellular absorption of PUFA as part of physiological linoleic and linolenic LDL in the form of PUSChE via ApoB-100 endocytosis. Instead of highly effective oleic variant of energy production by cells blocked action of insulin leads to non optimal palmitic variant of FA metabolism that is characterized with constant deficiency of energy in the form of ATP in vivo.

Atherosclerosis, alimentary deficiency of PUFA in cells and compensatory synthesis of non-physiological eicosanoids

Eicosapentaenoic and docosahexaenoic PUFA, so called Omega-3 FA (and this name is normally applied just to them and not to all ω-3 FA) are biologically active components of fish fat, substrates for synthesis of evolutionally early humoral mediators eicosanoids in humans [27]. Plasma concentrations of

docosahexaenoic PUFA is several times higher than eicosapentaenoic PUFA; the first one is the form of PUFA for PUFA deposing in phospholipids (PL) of intracellular membranes. ϖ-3 C20:5 eicosapentaenoic acid (name is derived from a Greek word "eikosa" that means twenty) is the only biologically active predecessor for synthesis of eicosanoids-3 (three double bonds in eicosanoid molecule) (Figure 1).

When animals entered the ground environment that lacked of eicosapentaenoic PUFA cells started to produce less active eicosanoids of the second group from such physiological predecessor like ω6 C20:4 arachidonic PUFA. During the life in the ocean cells started to produce evolutionally early highly active prostaglandins belonging the group of prostacyclins, thromboxans, and leukotriens of the third groups that have three double bonds in the molecule from C20:5 PUFA. During the life on the ground animals started to synthesize less active humoral mediators from C20:4 arachidonic PUFA; these eicosanoids have two double bonds in their molecules. In case of atherosclerosis cells lack both C20:5 eicosapentaenoic and C20:4 arachidonic PUFA and start to produce eicosanoids not from PUFA, but from endogenously synthesized C20:3 dihomo-γ-linolenic UFA, mead acid; these non-physiological eicosanoids have one double bond in their molecules.

Synthesis of non-physiological eicosanoids of the first group is the cause of many metabolic abnormalities in vivo in atherosclerosis:

a) non-physiological role of prostacyclins of the first group in regulation of biological reactions of endothelium-dependent vasorelaxation and impaired circulation in distant parts of arterial system, dysfunction of biological reaction metabolism↔microcirculation; all this creates conditions for metabolic AH;

b) absence of PUFA in the structure of aminophospholipids causes the change of function of all integral proteins of cell membrane including glucose trasporters, Na^+/K^+ ATPase, various receptors, acyltransferases, and biological reaction of endo-exocytosis (transcytosis) [28];

c) synthesis of thromboxanes of the first group from endogenous predecessors instead of its inhibition activates adhesion of all cells including platelets in vivo [29];

d) synthesis of non-physiological leukotrienes of the first group is the condition for activation of synthesis of mostly proinflammatory cytokines that augment biological reaction of inflammation in vivo [30], thus initiating impairment of biological reaction metabolism↔micrucirculation.

Atheromatosis is the impairment of biological function of endoecology, collection from circulation and utilization of palmitic VLDL→LDL in arterial intima

Etiological factors of atheromatosis include:

a) evolutionally late pool of collection and utilization of big endogenous phlogogens (exogenous pathogens) from circulation for realization of biological function of endoecology was localized directly behind endothelial monolayer in elastic arteries' intima [31];

b) when too many endogenous phlogogens are concentrated in the collection pool of arterial intima, a restricted number of polyfunctional resident macrophages of LCT in situ are responsible for utilization

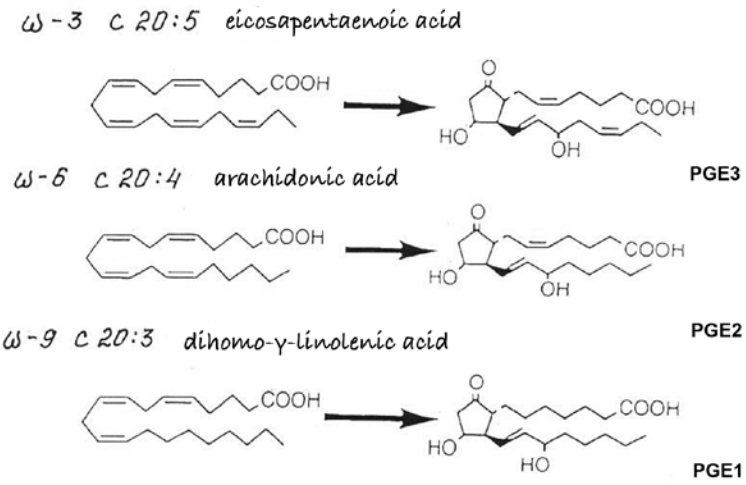

Figure 1. Structural formulas of FA – substrates and highly active prostaglandins PGE3, less active PGE2, and absolutely non-physiological PGE1.

of phlogogens, and numerous recruited monocytes of hematogenous origin [32];

c) bone marrow-derived monocytes have less expression of PUSChE than resident macrophages [33].

Atheromatous masses of elastic arteries' intima are partially catabolized physiological ϖ-3, ϖ-6 and non-physiological ϖ-9 PUFA in the form of non-polar PUSChE. Cells were unable to absorb these PUFA from blood in the form of PUSChE as part of linoleic and linolenic LDL via ApoB-100 mediated endocytosis in physiological way. The more severe is PUFA and physiological eicosanoids synthesis deficiency in cells, the more evident is atheromatosis in intima of phylogenetically late mixed type and elastic arterioles in the proximal part of arterial system. Therefore, a) atherosclerosis is the impairment of biological function of trophology and biological reaction of exotrophy, the pathology of PUFA and SFA transport as part of LP and their metabolism; b) atheromatosis is a non-physiological realization of compensatory function of endoecology and biological reaction of inflammation in the pool of collection and utilization of palmitic VLDL→LDL from the local pool of intravascular system in elastic arteries' intima.

Insulin is required to provide all cells responsible for locomotion function with substrates for energy production. The systems of FA transport in non-polar TG have been consequently developed in vivo during phylogenesis:

a) in carnivorous animals consuming meat food it looked like: enterocytes →ApoE/B-48 chylomicrons →lymphatic vessels→hepatocytes→ApoB-100 VLDL →ApoB-100 LDL→ApoB-100 receptor-mediated endocytosis;

b) in herbivorous animals consuming plant food: transport was much shorter in case of endogenous synthesis of oleic MFA and insulin action: hepatocytes→ligand oleic VLDL — ApoE/B-100 endocytosis by insulin-dependent cells; herbivorous animals do not form oleic LDL if they consume mostly vegetal and fish food.

c) Insulin cannot transform palmitic SFA into oleic MFA in herbivorous animals consuming meat food and big amounts of exogenous palmitic SFA; many ligandless palmitic VLDL→LDL are accumulated in blood during transport, cells do not absorb them, and these particles pollute intravascular pool of intercellular environment forming HLP.

If we start to compare phylogenetic variants of FA transport in carnivorous animals (1), in herbivorous animals consuming vegetal food (2), and in herbivorous animals on carnivorous diet (3), we can observe the following mechanisms:

1) enterocytes→chylomicrons→hepatocytes→VLDL→LDL→ApoB-100 endocytosis;

2) hepatocytes — VLDL→ApoE/B-100, and

3) hepatocytes — palmitic VLDL→LDL→ApoB-100 endocytosis blockade→HLP→increased concentration of TG and LDL cholesterol.

In this case all steps of HLP formation after impairment of biological function of trophology start to look clear. We can see why the system of oleic UFA as part of oleic VLDL transport cannot be functional with palmitic VLDL.

It leads us to understanding that herbivorous animals producing mostly oleic MFA, oleic TG and oleic VLDL from glucose in hepatocytes form physiologically minimal amounts of palmitic LDL and LDL cholesterol in blood. The more animal food evolutionally herbivorous Homo sapiens consumes, the more palmitic TG, palmitic VLD and non-physiological VLDL→LDL he has in blood. Excessive consumption of non-physiological amount of meat food and excess of palmitic UFA are the main reasons of elevated concentration of LDL cholesterol [20].

Palmitic ligandless VLDL→LDL that haven't been absorbed by cells via insulin-dependent ApoE/B-100 endocytosis become the substrate for atheromatosis of intima [34]. Non-physiological palmitic VLDL→LDL unite pathogenesis of atherosclerosis and atheromatosis [35]. Palmitic VLDL→LDL are formed during realization of atherosclerosis as non-physiological process, in case of atheromatosis ligandless palmitic LP are removed from blood, unfortunately it occurs in not absolutely physiological [36] or in non-physiological way [37]. Palmitic VLDL→LDL induce atheromatosis in elastic arteries' intima [38]. Excessive amount of palmitic SFA in food is the main cause of lipoidosis in all insulin-dependent cells: sceletary myocytes, cardiomyocytes, periportal hepatocytes, Kupffer cells and ß-cells of Langerhans islets.

Phylogenesis and biological bases of atherosclerosis and atheromatosis primary prevention

Biological action of insulin determined the transformation of carnivorous animals to herbivorous ones. At first it required the expression of insulin-like growth factor, then glucagon was added, and in the end of phylogenesis humoral mediator insulin appeared. And if during phylogenesis every cell synthesized just palmitic UFA from acetyl-CoA before the appearance

of insulin, this hormone has added two biochemical reactions to FA synthesis: C16:0 palmitic UFA→C18:0 stearic UFA→ ω-9 C18:1 oleic UFA. It accompanied the development of herbivorous animals on the ground, since previously carnivorous animals started to be herbivorous after leaving ocean for ground. The same thing happened with Homo sapiens.

Insulin initiated formation of functionally new cells in vivo. These cells were:

1. Striated myocytes;
2. Syncytium of cardiomyocytes;
3. Pool of subcutaneous adipocytes;
4. Periportal hepatocytes, and
5. Resident liver macrophages – Kupffer cells, and
6. Pancreatic β-cells of Langerhans islets.

Since hepatocytes and not enterocytes were the starting point for FA transport in vivo in herbivorous animals, insulin can be considered phylogenetically late. The transport of oleic MFA, first of all, in the form of oleic TG as part of oleic VLDL was the shortest vector way. Hepatocytes→oleic VLDL→lypolysis and ligand oleic VLDL→ApoE/B-100 endocytosis without formation of oleic LDL. Only palmitic VLDL→LDL are accumulated in blood, and they lead to increased concentration of LDL cholesterol in blood.

Unwillingness of patients to consume animal (fish) food is non-physiological [39]. For millions of years ancestors of human used to be carnivorous. From this period people inherited: a) every animal cell synthesizes just palmitic UFA from acetyl-CoA; b) biological functions and reactions are regulated with highly active humoral mediators that cells synthesize from exogenous essential PUFA [40] from the components of fish fat; c) many herbivorous animals feed their children with animal food milk. Milk consists ov of palmitic, saturated animal fat, we call it butter without any reasonable background. Without any reasonable background doctors recommend animal palmitic butter for eating and prevent patients from consuming vegetal oleic palm oil [41]. From the position of atherosclerosis and atheromatosis prevention, vegetal oils are better than any animal fat, including butter [42].

Refusal of fish consumption and alimentary deficiency of essential eicosapentaenoic and docosahexaenoic PUFA always lead to atherosclerosis; and atheromatosis in this case will not be so evident [43]. We can reasonably suppose that atherosclerosis formation in vivo depends on cellular deficiency of ω-3 PUFA. Atheromatosis of arterial intima occurs in parallel with excess of meat with high contents of palmitic UfA, cholesterol and palmitic VLDL→LDL (LDL cholesterol) in food consumed by herbivorous animals.

Exogenous hypercholesterolemia in the experiments of S.S. Khalatov and N.N. Anichkov is a particular case of general law of biology: rabbit is a herbivorous animal, and exogenous alcohol cholesterol represents excess of animal food. By now it was impossible to reproduce aorta atheromatosis in exogenous hypercholesterolemia in carnivorous rats [44]. Every single excess of animal food in the diet of herbivorous human (animals) leads to formation of locus minoris resistentia. Palmitic ApoE/B-100 VLDL form ligands very slowly, ligandless palmitic VLDL→LDL are accumulated in blood, and they increase the concentration of LDL cholesterol.

Ligandless palmitic VLDL→LDL that have not been absorbed by cells are transported via biological reaction of transcytocis through endothelium of proximal part of arterial system to the pool of collection and utilization of big endogenous phlogogens in arterial intima. Since utilization of palmitic VLDL→LDL in intima is performed not by polyfunctional resident intima macrophages, but by functionally overloaded monocytes originated from peripheral blood, realization of inflammation leads to intima atheromatosis [45]. Oleic MFA prevents the action of palmitic UFA excess and impaired mitochondrial function during IR. It has been shown that C16:1 palmitoleic MFA can influence the function of resident macrophages [46].

Physical and chemical properties of oleic MFA, oleic TG, and oleic VLDL are very different from palmitic UFA, palmitic TG, and palmitic VLDL [47]. Etiological factors of atherosclerosis incude:

a) excessive, non-physiological consumption of animal food by herbivorous Homo sapiens, and

b) lower involvement of C16:0 palmitic UFA in all biochemical reaction in vivo comparing with high parameters of C 18:1 oleic MFA.

Atheromatosis is in vivo catabolism (utilization) of PUFA that were not absorbed by cells from blood being part of palmitic LDL; they are PUFA in the form of non-polar PUSChE. PUFA collection and utilization from LDL occurs in arterial intima, only partial catabolism of PUSChE under the action of hematogenous monocytes [48] forms atheromatous lipid depositions (plaques), and leads to stenosis of elastic arteries with CHD manifestations and brain ischemia. If together with high levels of LDL cholesterol blood plasm has elevated concentrations of TG, atherothrombosis occurs simultaneously in arterial intima;

it is characterized with formation of soft plaques that contain much TG and have high risk of rupture.

Conclusion

We said nothing about such etiological factors of atherosclerosis and atheromatosis like innate disorders of metabolism, familiar HLP [49], pathologies of ApoE isoforms, and formation of HLP, III type [50]. Etiologically different abnormalities of primary structure of apoproteins are characterized with low affinity to non-polar lipids. Abnormal activity of hydrolases and esterases of glycerol and cholesterol esters, blockage of palmitic SFA transport through inner mitochondrial membrane promote the formation of atherosclerosis. In the situations difficult for our metabolism it is necessary to follow optimal diet since it is the most effective way to prevent atheromatosis complications and atheromatosis of elastic arteries in the proximal part of arterial system, formation of AH, acute coronary system and ischemic circulatory disorders of the brain. We have no other alternative for phylogenesis; it is important to remember that Homo sapiens is phylogenetically herbivorous.

Conflict of interest: None declared.

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International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Results of the European Society of Cardiology Congress, 2017

Another annual congress of the European Society of Cardiology (ESC) took place in Barcelona, Spain, on August 26-30, 2017. The ESC Congress is one of three most important and visited international cardiological scientific meetings. More than 30000 participants from 140 countries and 5 continents took part in the Congress.

Scientific program of the ESC Congress comprised wide variety of themes and included more than 500 symposiums and sessions that involved both well-known international experts and clinical specialists and young researchers from different countries. The Congress has covered 163 topic of cardiology and related conditions that have been divided into 9 main directions (fundamental science, arterial hypertension, heart valve disease, arrhythmias/implantable pacemakers, coronary heart disease, chronic heart failure, prevention/rehabilitation, vascular surgery, cardiovisualization) and related events were hold in thematic "Villages".

The most visited Hot Line sessions of the ESC Congress traditionally took place in the main congress hall (Barcelona hall). This year there were 4 Hot Line sessions of Late-Breaking Clinical trials and 2 Hot Line sessions: Late Breaking Registry Results that presented the results of new major studies in different directions of cardiology. 10 multicenter projects were been discussed in the format of "Meeting with Trialists" (principal investigators of major studies).

For the first time scientific program included two new formats: "Expert advice" and "Great debates".

The "Expert advice" section consisted of educational sessions in important clinical topics and lectures of worldwide-known experts:

- Endocarditis — The role of imaging
- Cardiomyopathy, sudden cardiac death
- Cardiogenic shock update
- Problems with statin treatment
- Managing complications in acute cardiac care
- Imaging for TAVI
- Unusual coronary pathology: what to do
- Heart failure patients have more than one problem: how to manage comorbidities
- Image Interpretation with the Masters — Cardiac CT
- Optimising cardiac resynchronization therapy
- Assessing left ventricular function in clinical practice
- Finding the right measure: how to tailor rehabilitation to cardiac interventions
- Making an impact: optimal secondary prevention following acute coronary syndromes
- Hypertension in 90 minutes
- Risk and management of pregnancy in women with cardiac diseases
- Image Interpretation with the Masters – Cardiac MRI
- How to interpret laboratory tests in acuter heart failure
- Clotted veins: pill or drill?
- Septal reduction therapies in hypertrophic obstructive cardiomyopathy

The "Great debates" section included the following sessions for wide discussion:

- Left atrial appendage occlusion
- Are vasodilators useful in the treatment of acute heart failure?
- Do we need PCSK9 inhibitors in post-MI patients?
- Viability in clinical decision making
- Blood pressure targets: is 120 too low?
- Inflammation and cardiovascular disease
- Left main is now a domain of interventional cardiology
- Secondary mitral regurgitation requires invasive therapy to improve outcome
- Aspirin for life

This year the scientific program consisted of numerous joint symposiums. It included 38 joint symposiums with international and national societies of Northern and Southern Africa, Asia and European societies of other profiles. Worldwide known cardiology journals (Circulation, The Lancet, The Journal of the American Medical Association, European Heart Journal) organized 8 symposiums.

Joint symposiums with national cardiology societies-members of ESC were organized as part of the scientific program in 2017. These symposiums were dedicated to distinct scientific topic. Russian symposium organized by the Russian Society of Cardiology presented the theme of ""Atrial fibrillation ablation – The "Big picture"". The mentioned below specialists took part in this symposium:

- E.V. Shlyakhto (Saint Petersburg), academician of the Russian Academy of Sciences
- S.T. Matskeplishvili (Moscow), corresponding member of the Russian Academy of Sciences
- D.V. Duplyakova (Samara), professor
- E.I. Baranova (Saint Petersburg), professor
- E.N. Mikhailov (Saint Petersburg), M.D., Ph.D., doctor of sciences
- A.V. Ardashev (Moscow), professor
- A.B. Romanov (Novosibirsk), professor.

The members of the Russian Academy of Sciences E.V.Shlyakhto and S.T. Matskeplishvili were co-chairmen of this symposium.

Scientific program of the Congress included 26 satellite symposiums that involved international manufacturers of medicines and medical equipment.

Poster session was the important part of the scientific program. Poster presentations were divided into 9 directions and two formats: traditional posters and electronic posters. It is worth to mention that Russian scientists participated actively in this session and presented more than 60 works. Young Russian cardiologist Angela Solovieva (People's Friendship University of Russia) won the certificate for the best poster in the "Heart failure" section.

The Conference book included more than 10 000 abstracts, a part of them was selected for oral presentations.

According to the tradition, the Congress presented updated clinical guidelines:

- Management of acute myocardial infarction in patients presenting with ST-segment elevation (ESC)
- Diagnosis and treatment of peripheral arterial disease (ESC and European Society for Vascular Surgery)
- Management of valvular heart disease (ESC and European Association of cardiothoracic surgery).
- Focused update on Dual Antiplatelet Therapy (DAPT) in coronary heart disease (ESC and European Association of cardiothoracic surgery)

New highlights of diagnostics and treatment of cardiovascular diseases were presented at the exhibition that involved manufacturers of medicines and medical equipment.

The ESC Congress underwent the accreditation of the European Accreditation Council for Continuing Medical Education (EACCME) and received 26 credits.

More detailed information on the ESC Congress can be found on its official website www.escardio.org

The review of new European clinical guidelines and the results of major international studies that were present at the Congress will be published on the official website of the Cardioprogress Foundation www.cardioprogress.ru

The next ESC Congress will be held in Munich (Germany), on August 25-29, 2018.

International Heart and Vascular Disease Journal
Volume 5, Number 15, September 2017

Journal of the Cardioprogress Foundation

Guidelines for authors

International Heart and Vascular Disease Journal
Requirements for Submission and Publication

(version 2017)

The requirements for submission and publication in the I**nternational Heart and Vascular Disease Journal** are based on the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals', developed by the *International Committee of Medical Journal Editors* (ICMJE), which can be found at www.ICMJE.org

These requirements form the basis for relations between the Editors of the **International Heart and Vascular Disease Journal**, further called «the Editors», and an author who submits a manuscript for publication, further called «the Author».

The **International Heart and Vascular Disease Journal** publishes reviewed articles that cover all aspects of cardiovascular diseases, including original clinical research, experimental research with clinical relevance, reviews on current problems in cardiology, and clinical case studies. Usually 4 issues are published annually (one issue every 3 months).

This is an open access journal, which means that all content is freely available without charge to the user or his/her institution. Users are allowed to read, download, copy, distribute, print, search, or link to the full texts of the articles in this journal without asking prior permission from the publisher or the author. This is in accordance with the *Budapest Open Access Initiative* (BOAI) definition of open access.

1. Submission requirements and publishing policy

1.1. A manuscript should be submitted to the following e-mail address: submissions@inbox.ru

Editorial Office tel.: +7(965) 236-16-00

1.2. A manuscript is accepted for further consideration only if the manuscript, or any substantively similar version, has not been submitted to and published in any other journal, or disseminated via any other media, such as the Internet.

1.3. The Author, submitting the manuscript to the Editor, assigns the Editor to publish it. The Editors have the right to incorporate within the manuscript any illustrated or text material, including advertisements. The Editors may allow third parties to put such content into the manuscript.

1.4. Submission of the manuscript to the Editors implies that the Author agrees to transfer the exclusive property rights for the manuscript and other objects of the copyright, like photos, drawings, graphics, tables, etc., to the Editors. The Editors obtain the right to reproduce (partly or fully) all the content submitted, including objects of the copyright, in press and on the Internet; to distribute; to translate the manuscript and other provided content into any language; to export and import copies of the issue where the article of the Author was published; and to revise the manuscript.

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1.6. The Editors have the right to transfer the rights received from the author to a third party or to prohibit any use of materials published in the journal by a third party.

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1.8. The Author retains the right to use the published material or its parts for personal use, includ-

ing scientific and educational purposes. The Author retains the right to publish extracts from the published material or its parts in other journals, on the condition that reference is made to the original publication in the **International Heart and Vascular Disease Journal**.

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1.11. The Editors are obliged to provide the Author with one copy of the issue in which the article is published. The Author(s) should provide his/her full postal address(es) including post code(s) at the end of the manuscript.

1.12. Manuscripts may be reviewed by independent experts. Manuscripts which are reviewed will be reviewed on a double blind basis: Authors will not know the identity of reviewers and reviewers will not know the identity of Authors. The name of the institution where an Author works or conducts research also remains confidential. The reviewer(s) comments and opinions will be sent to the Author and the Author invited to make any changes and/or corrections. In the case of an Author not returning changes and/or corrections to the Editors by an agreed date, the Editors have the right to make their own changes and/or corrections, or permit changes and/or corrections suggested by the reviewers, or to refuse to publish the manuscript. Editing, shortening and correction of the manuscript, and changes to a graph, picture or table design are made in order they comply the format and standards of the **International Heart and Vascular Disease Journal**.

1.13. The Editors are not responsible for the accuracy of information presented in the manuscripts.

1.14. The Editors recommend that submitted manuscripts conform with the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals', developed by the *International Committee of Medical Journal Editors* (ICMJE), and available on the **International Heart and Vascular Disease Journal** website www.cardioprogress.ru, in the 'For Authors' section.

1.15. Adhering to the standards outlined in this document will lead to faster reviewing, editing, and publishing of manuscripts accepted for publication. Manuscripts submitted outside the standards on design and formatting for this journal may not be accepted by the Editors.

2. General recommendations for submission of original scientific works

2.1. The Editors recommend that results of randomized controlled trials conform to the 'Consolidated Standards of Reporting Trials' (CONSORT) guidelines. Information on these standards are available on the CONSORT website: www.consort-statement.org

2.2. A manuscript should be typed using the Times New Roman font (12 points, double spacing; with 2 cm at the top, bottom, left and right margins). The length of a manuscript, including references, schedules, drawings and tables, should not exceed 12 standard typewritten pages (1 page is 1800 letters or symbols, including spaces). A case study should not exceed 6 standard pages. Reviews and lectures should not exceed 25 standard pages.

2.3. Manuscripts should be organized as follows: 1) title page; 2) structured summary and keywords; 3) list of abbreviations; 4) text; 5) acknowledgements (if applicable); 6) references; 7) names and legends of pictures, tables, graphics, and photocopies in the order they appear in the manuscript; 8) drawings, tables, graphics, and photocopies should be submitted on separate pages in the order they appear in the manuscript. Numeration of pages should begin from the title page.

2.4. If the manuscript contains pictures, tables, graphics, or photocopies that have been published previously, reference to the author(s) and publication is necessary. It is the Author's responsibility for determining whether permission is required for the duplication of material, and for obtaining relevant permission.

2.5. Manuscripts based on reviews of original research works should contain the following sections: Introduction (reflecting the urgency of a problem and research goals); Material and methods; Results; Discussion of the obtained results and Conclusion. The text should be clear, brief and without repetition.

3. Publication of uncontrolled trials results

3.1. An uncontrolled trial is a research without a control group.

3.2. Manuscripts based on uncontrolled trials results will be accepted for publication in the 'Practical Experience' column only if the uncontrolled design of the study is described in the Material and methods and Discussion sections. It is important not to exaggerate the significance of results in the Conclusion' section.

4. Ethical aspects

4.1. Trials should be conducted in accordance with principles of «good clinical practice". Participants of a trial should be informed about the purpose and main aims of the trial. They must sign to confirm their written informed consent to participate in the trial. The

«Material and methods» section must contain details of the process of obtaining participants informed consent, and notification that an Ethics Committee has approved conducting and reporting the trial. If a trial includes radiological methods it is desirable to describe these methods and the exposure doses in the «Material and methods» section.

4.2. Patients have the right to privacy and confidentiality of their personal data. Therefore, information containing pictures, names, and initials of patients or numbers of medical documents should not be presented in the materials. If such information is needed for scientific purposes, it is necessary to get written informed consent from the research participant (or their parent, their trustee, or a close relative, as applicable) prior to publication in print or electronically. Copies of written consent may be requested by the Editors.

4.3. Animal trials must conform to the 'International Guiding Principles for Biomedical Research Involving Animals', adopted by the Council for International Organizations of Medical Sciences (CIOMS) in 1985.

5. Authorship

5.1. Each author should significantly contribute to the work submitted for publication.

5.2. If more than 4 authors are indicated in the author's list, it is desirable to describe the contribution of each author in a covering letter. If the authorship is attributed to a group of authors, all members of the group must meet all criteria for authorship. For economy of space, members of the group may be listed in a separate column at the end of the manuscript. Authors can participate in the submitted manuscript in the following ways: 1) contributing to the concept and research design or analyzing and interpreting data; 2) substantiating the manuscript or checking the intellectual content; 3) providing final approval for the manuscript. Participation solely in collection of data does not justify authorship (such participation should be noted in the Acknowledgements section). Manuscripts should be submitted with a covering letter containing the following information: 1) the manuscript has not been submitted to any other media; 2) the manuscript has not been published previously; 3) all authors have read and approved the manuscript's content; 4) the manuscript contains full disclosure of any conflict of interests; 5) the author/authors confirm responsibility for the reliability of the materials presented in the manuscript. The author responsible for the correspondence should be specified in the covering letter.

6. Conflict of interests/financing

6.1. It is desirable for authors to disclose (in a covering letter or on the title page) any relationships with industrial and financial organizations, which might be seen as a conflict of interest with regard to the content of the submitted manuscript. It is also desirable to list all sources of financing in a footnote on the title page, as well as workplaces of all authors (including corporate affiliations or employment).

7. Manuscript content

7.1. Title page

7.1.1. It should include the name of the article (in capital letters); initials and last names of the authors; the full name of the institution which supported the manuscript, together with the city and country, and full mailing address with postal code of that institution.

7.1.2. A short title of the article (limited to 45 letters or symbols).

7.1.3. Information about the authors, including full names (last name, first name, patronymic name, if applicable; scientific degrees and titles, positions at main and secondary jobs, including corporate posts).

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7.2.1. Summary (limited to 300 words) should be attached to the manuscript. It should include the full title of the article, last names and initials of the authors, the name of the institution that supported the manuscript, and its full postal address. The heading of the summary should contain the international name(s) of any drug(s) mentioned.

7.2.2. Original studies summary should contain the following sections: Aim, Material and methods, Results, and Conclusion. The summary of a review should provide the main themes only. A manuscript must contain all data presented in the summary.

7.2.3. 5-6 keywords of the article should be given at the end of the abstract.

7.3. List of abbreviations and their definitions

7.3.1. To conserve space in the journal, up to 10 abbreviations of general terms (for example, ECG, ICV, ACS) or names (GUSTO, SOLVD, TIMI) can be used in a manuscript. List of abbreviations and their definitions should be provided on a separate page after the structured summary (for example, ACS – aortocoronary shunting). Only words generally accepted in scientific literature should be used.

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7.4.1. Original studies should be structured as follows: Introduction, Material and methods, Results, Discussion and Conclusion.

7.4.2. Case studies, reviews and lectures may be unstructured, but it is desirable to include the following paragraphs: Discussion and Conclusion (Conclusions and Recommendations).

7.4.3. Please, use international names of drugs in the title. Exceptions are possible when use of trade names is well-founded (for example, in studies of bio- or therapeutic equivalence of drugs). It is possible to use a trade name in the text, but not more than once per standard page (1800 symbols including spaces).

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7.4.7. References in the text must be numbered in Arabic figures, and provided in square brackets.

7.5. Statistics

7.5.1. All submitted materials may be revised to ensure relevance and accuracy of statistical methods and statistical interpretation of results. The Methods section should contain a subsection with detailed description of statistical methods, including those used for generalization of data; and of methods used for testing hypotheses (if those are available). Significance value for testing hypotheses must be provided. Please indicate which statistical software was used to process results and its version if you use more complex statistical methods (besides a t-test, a chi-square, simple linear regression, etc.).

7.6. Acknowledgements

7.6.1. The Acknowledgements section or Appendix should not exceed 100 words.

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7.7.3. The list of references should not include any dissertations, theses published more than two years ago, or information that is impossible to check (local conference materials, etc.). If material is taken from a thesis, please, mention that in brackets — (thesis).

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Periodicals

Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk factors in Atrial Fibrillation (ATRIA) Study. JAMA. 2001; 285(18):2370-5.

Sources in Russian with transliteration:

Baevskiy RM, Ivanov GG, Chireykin LV, et al. Analiz variabel'nosti serdechnogo ritma pri ispol'zovanii razlichnyh jelektrokardiograficheskih sistem (metodicheskie rekomendacii) [Analysis of heart rate variability using different ECG systems (guidelines)]. Vestnik aritmologii. 2002;24:65-86. Russian.

Please provide initials after the last names of authors. Last names of foreign authors are given in the original transcription. Names of periodicals can be abbreviated. Usually such abbreviations are accepted by the Editors of those periodicals. These can be found on the Publisher's site or in the list of abbreviations of Index Medicus.

Punctuation in the list of references should be considered. A comma should not be put between the name of the journal and the year of its release. After the year of release a semicolon is put without a space, then a colon follows the volume number, and finally page numbers are given. There are no indications like "volume", "№", «pages». Russian periodicals often have no indication of volume or numbering of pages within a year. In this case the number of an issue should be specified in brackets.

If the total number of authors exceeds four people, please provide the names of the first three authors and put "et al." afterwards. If there are not more than 4 authors, the full list of authors should be provided.

Chapters in a book

Swanton RH, Banerjee S. Cardiac Failure. In: Swanton RH, Banerjee S., editors. Swanton's Cardiology: A concise guide to clinical practice. 6th ed. Oxford: Blackwell Publishing; 2008. p. 255-309.

Sources in Russian with transliteration:

Belenkov YuN. Kardiomiopatii [Cardiomyopathies]. In.: Chazov EI, Belenkov YuN., editors. Racional'naja farmakoterapija serdechno-sosudistyh zabolevanij: Rukovodstvo dlja praktikujushhih vrachej [Rationale for drug therapy of cardiovascular diseases: A guide for medical practitioners]. Moscow: Litterra; 2006. p. 431-452. Russian.

Reference to a book chapter should be arranged in the following order: authors of the corresponding chapter; name of the chapter; «In:»; editors (title authors) of the book; name of the book; number of issue, publisher; city of publishing; year of publishing; pages of the corresponding chapter. Punctuation should be considered. There are no quotation marks.

Books

Sources in Russian with transliteration:

Shlyakhto EV, Konradi AO, Tsyrlin VA. Vegetativnaja nervnaja sistema i arterial'naja gipertenzija [The autonomic nervous system and hypertension]. St. Petersburg (Russia): Meditsinskoe izdatelstvo; 2008. Russian.

Websites

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WHO. Severe Acute Respiratory Syndrome (SARS) [Internet]. [place unknown: publisher unknown]; [updated 2010 June 1; cited 2010 June 10]. Available from: http://www.who.int/csr/sars/.

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- The article needs additional review by another specialist;
- The article can not be published in the journal.

8.3. If the review contains recommendations for correcting and finalizing the article, the editorial board of the journal sends the author a text of the review with a proposal to take them into account when preparing a new version of the article, or to argue them (partially or completely) with arguments. The finalization of the article should not take more than 2 months from the moment of sending an electronic message to the authors about the need to make changes. The article refined by the author is sent again for review.

8.4. In the event of the authors' refusal to modify the materials, they must, in writing or verbally, notify the editorial office of their refusal to publish the article. If the authors do not return the revised version after 3 months from the date of sending the review, even if there is no information from the authors refusing to modify the article, the editorial board removes it from the register. In such situations, the authors are notified of the removal of the manuscript from the registration in connection with the expiration of the time allotted for revision.

8.5. If the author and reviewers have unresolved contradictions regarding the manuscript, the editorial board is entitled to send the manuscript for additional review. In conflict situations, the decision is made by the editor-in-chief at a meeting of the editorial board.

8.6. The decision to refuse publication of the manuscript is taken at a meeting of the editorial board in accordance with the recommendations of reviewers. An article not recommended by a decision of the editorial board for publication is not accepted for reconsideration. The notice of refusal of publication is sent to the author by e-mail.

8.7. After the editorial board accepts the decision to admit the article for publication, the editorial office informs the author about it and specifies the terms of publication.

8.8. The presence of a positive review is not a sufficient basis for the publication of the article. The final decision on publication is made by the editorial board. In conflict situations, the decision is made by the editor-in-chief.

8.9. The original of the reviews is kept in the editorial office of the journal for 3 years.

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