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Psychosomatic aspects in individuals with normal blood pressure and left ventricular hypertrophy

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Abstract

Objective. The objective was to study the relationship between psychological and emotional features, hormonal changes and left ventricular hypertrophy (LVH) in subjects with normal blood pressure (BP). **Design and methods.** The study included 107 practically healthy people of working age from an organized population, including 46 men (mean age 43.7 ± 11.5 years) and 61 women (mean age 43.1 ± 10.1 years). In all subjects, fasting blood samples for hormone level evaluation were taken, structural myocardial changes were assessed by echocardiography, BP measurement was performed according to the standard procedure, and validated psychological questionnaires were completed. **Results.** Subjects with LVH showed a high level of accumulated stress according to the Holmes-Rahe scale and low vitality according to the visual analog scale. They were also characterized by significant changes in the ratio noradrenaline/adrenaline, and by the elevated cortisol levels. Biochemical parameters and structural and functional myocardial characteristics correlated with the psychological factors in a gender-dependent manner. **Conclusions.** In psychoemotional stress, triggered stress reactions are accompanied by metabolic changes (involving neurotransmitter mechanisms, growth factors), and, as suggested, by structural myocardial changes. The investigation of stress reactions within the psychosomatic continuum is highly important in order to understand how the stress affects the development and the course of various diseases, as well as for the development of an integrated approach to prevent chronic non-communicable diseases.

Key words: psychological and emotional factors, hormonal status, growth factors, left ventricular hypertrophy

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Психосоматические аспекты изучения гипертрофии левого желудочка у лиц с нормальным уровнем артериального давления

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Резюме

Цель работы — изучить связь психоэмоциональных особенностей с гормональными изменениями и гипертрофией левого желудочка (ГЛЖ) у лиц с нормальным уровнем артериального давления (АД). **Материалы и методы.** В исследование включено 107 практически здоровых лиц трудоспособного возраста из организованной популяции, из них 46 мужчин (средний возраст — 43,7 ± 11,5 года) и 61 женщина (средний возраст — 43,1 ± 10,1 года). Всем обследуемым проводились исследования гормональных показателей венозной крови натощак, структурных изменений миокарда с применением эхокардиографии, измерение АД по стандартной процедуре, а также анкетирование с помощью валидизированных психологических опросников. **Результаты.** У лиц с наличием ГЛЖ отмечается значимо высокий уровень накопленного стресса по шкале Холмса-Рея и низкая жизнестойкость по визуально-аналоговой шкале. Группа обследованных с выявленной ГЛЖ характеризовалась значимым изменением отношения нор-адреналин/адреналин, повышенным уровнем кортизола. Установлены взаимосвязи как биохимических показателей, так и структурно-функциональных характеристик сердца с психологическими факторами; характер изученных связей имеет гендерные различия. **Выводы.** При психоэмоциональном стрессе запускаются стресс-реакции, сопровождающиеся метаболическими изменениями (медиаторных механизмов, системы ростовых факторов), а также, возможно, структурными изменениями миокарда. Изучение стресс-реакций в рамках психосоматического континуума существенно для раскрытия механизмов влияния стресса на развитие и течение заболеваний, разработки интеграционного подхода к профилактике хронических неинфекционных болезней.

Ключевые слова: психоэмоциональные факторы, гормональные показатели, ростовые факторы, гипертрофия левого желудочка

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Introduction

Left ventricular hypertrophy (LVH) is an independent risk factor of cardiovascular morbidity and mortality and of main preclinical manifestation of cardiovascular damage [1]. Recently, non-hemodynamic mechanisms of left ventricular hypertrophy were discussed. In particular, the role of acute and chronic psychoemotional stress is discussed. It triggers hyperactivation of the hypothalamic-pituitary-adrenal axis and autonomic dysregulation leading to the sympathetic activation and increase in the level of circulating catecholamines.

An increase in the left ventricular mass (LVM) is common in normotensive subjects, i. e. when there are no hemodynamic reasons. These LV changes are associated with the personal response to professional stress and autonomic dysregulation [2]. Moreover, in 10–30 % of cases, LVH is found in normotensive individuals with non-infectious diseases such as ulcer disease, chronic liver damage, chronic bronchial obstructive disease, etc. Stress-induced cardiomyopathy developed after an earthquake, military conflicts or other severe stresses is described [3]. Indeed, experimental studies provide evidence that chronic stress may lead to morphologic myocardial changes including the increase in the relative heart mass, decrease in the density of cardiomyocytes and capillary vessels [4]. Cardiovascular system is considered to reflect individual manifestations of a latent pathology.

However, correlation between notable psychoemotional stress and somatic organ stress response (like left ventricular hypertrophy) is controversial because of the lacking evidence (no prospective studies, methodology of quantitative measurement of everyday stress including the absence of validated stress questionnaires). In addition, the role of confounding factors such as gender differences in stress response type in a stressful situation still is to be defined.

Objective of the study is to examine possible correlation of psychoemotional characteristics with hormonal changes and LVH in normotensive subjects.

Design and methods

Cross-sectional study of employees of an industrial enterprise was carried out as a part of the prophylactic medical examination of adult population (the Order of the Ministry of Public Health of Russia No. 1006 N dd. 03.12.2012). The study included 107 apparently healthy subjects (based on the results of the prophylactic medical examination), among them 46 males aged 23–60 years (43 %) (average age 43.7 ± 11.5 years old) and 61 females aged 25–60 years (57 %) (average age 43.1 ± 10.1 years old).

Normal BP level was stated based on the data from outpatient records (retrospective assessment of long-term prophylactic medical examinations), office BP measurements (BP level < 140/90 mm Hg), and self-control BP data (BP level < 130–135/85 mm Hg).

Office BP was measured three times in the sitting position after a 5-minute rest according to a standard protocol by a mechanical calibrated tonometer and universal cuff. Arithmetic average of three measurements was included in the analysis.

In patients with diagnosed LVH, 24-hour BP monitoring was performed by the device MnSDP-1 (BPLab, Russia).

Exclusion criteria were as follows: professional sports activities; intake of medications that can affect BP, LVH, psychoemotional state.

The study was approved by the local ethics committee of the South Ural State Medical University (protocol No. 10 dd. 02.09.2011).

Blood tests were carried out using an automatic immune-enzyme assay (Personal Lab, Adaltis, Italy). Fasting venous blood samples were taken for the hormone analysis: serum cortisol by immune-enzyme assay of Diagnostics Biochem Canada Inc. (Canada); serum insulin-like growth factor-1 (IGF-1 Elisa) by immune-enzyme assay of Immunodiagnostic systems (UK); separate quantitative measurement of dopamine, adrenalin (epinephrine) and noradrenalin (norepinephrine) in blood plasma by the reagents of IBL International Gmbh (Germany).

Echocardiography (Echo) was recorded by an ultrasound scanner Logic-5 XP (GE, USA) with a 3.5 MHz transducer with the patient lying on his/her left side at an angle of 45° according to standard methods. The main values were measured: left ventricular posterior wall thickness (LVPWT) in diastole, interventricular septum thickness (IVST) in diastole, left ventricular end-diastolic (EDD) and end-systolic (ESD) diameters, left ventricular end-diastolic (EDV) and end-systolic (ESV) volumes according to the algorithm “area-length”, aorta diameter, maximal size of the left atrium, left ventricular posterior wall and interventricular septum excursion. Left ventricular mass (LVM) was calculated using R. Devereux and N. Reichek formula: LVM = 1.04 × ((IVST + LVPWT + EDD)3 — (EDD)3) — 13.6 [5, 6]. LVM index (LVMI — LVM to the area of body surface) was calculated, the following criteria of LVH were applied: LVMI > 115 g/m^2 for males and > 95 g/m^2 for females [6]. Left ventricular ejection fraction was calculated according to the formula (EDV — ESV)/EDV.

Psychological diagnostics was conducted with the help of standardized scales: State and Trait Anxiety Scale by Spielberger–Khanin [7]; Depression Evaluation Scale of the US Center of Epidemiologic Studies (CES-D), adapted by M. Yu. Drobizhev [8]. CES-D scale shows high accuracy for diagnosing mild, moderate and severe depressive states. The optimal cut-off value is ≥ 18 points [8]. Final verification of the depressive disorder was carried out by a professional psychiatrist on the basis of diagnostic criteria of the International classification of diseases, revision 10. Out of 19 subjects with clinically relevant depression severity according to the CES-D scale (total ≥ 18 points) the diagnosis was verified in 10 patients including 7 subjects with the “mild depressive episode” and 3 subjects with the “moderate depressive episode”.

Experimental psychological tests included “Level of social frustration” by L.I. Vasserman et al. [9]; Holmes and Rahe scale [10]; visual analogue scale (VAS) for the self-assessment of health, everyday stress, viability (modified version of Dembo–Rubinstein method) [11]. In the latter one three vertical graphic scales were used. For more convenient result formalization all the examined persons were asked to mark a point on the 10-cm-long line graded into 1-cm intervals. The assessment was made in points from 0 to 100. Instruction before the test was as following: “Let us assume that people from all over the world are here on this line: here at the top (demonstration) are the healthiest and there at the bottom (demonstration) are the most ill. Where is your place among all these people according to your health condition? Mark a point with the pencil where you are, in your opinion.” [11].

Statistics was carried out with the help of software SPSS v. 17.0 (SPSS Lab., USA). Non-parametric quantitative criteria are given as medians and interquartile range. To verify the type of data distribution, Kolmogorov–Smirnov test was applied. Since distribution was not normal, Mann–Whitney U-test was applied in further analysis. Nominal (categorical) variables were compared using Pearson $\chi 2$ test. Correlation analysis and Spearman’s rank correlation coefficients (r) were performed. LVM and lVMI as dependent variables, and independent predictors (studied risk factors of cardiovascular diseases, psychological factors and hormone values) were included in a multiple regression analysis. The differences and correlations were considered significant at p-level 0.05 or less.

Results

The prevalence of LVH in normotensive people was 25 % (n = 27) including 11 % (n =12) in males and 14 % (n = 15) in females ($\chi^2 = 0.06$, $p = 0.81$). Groups with and without LVH were matched by age, height, body mass and body mass index (Table 1). Subjects with LVH had no relevant valve abnormalities according to Echo.

The levels of cortisol and noradrenalin levels differed significantly in groups with and without LVH independently of sex (Table 2). In males with LVH, noradrenalin level was lower compared to males without LVH: 440.3 [265.6; 615.0] and 756.5 [561.8; 951.2] pg/ml, respectively ($p = 0.03$). In females with LVH, plasma adrenalin level was increased compared to females without LVH — 157.5 [84.2; 230,9] vs 73.6 [23.4; 123.7] pg/ml ($p = 0.004$).

Subjects with and without LVH showed different psychological parameters: level of health and viability self-assessment according to VAS, accumulated stress according to the Holmes and Rahe scale (Table 3).

Gender was an important confounding factor in a correlation analysis.

For example, in males VAS-based viability level correlated with LVM and LVMI ($r = –0.45$, $p = 0.02$ and $r = –0.65$, $p = 0.001$, respectively). Besides, trait anxiety correlated with LVMI ($r = 0.45$, $p = 0.03$). In females with normal BP, the quantitative level of the accumulated stress according to the Holmes and Rahe’s scale

Table 1

CHARACTERISTICS OF THE GROUPS WITH AND WITHOUT LEFT VENTRICULAR HYPERTROPHY

Characteristics	With LVH M [95% CI] n = 27	Without LVH M [95 % CI] n = 80	p
Age, yr	40.4 [37.1; 43.7]	40.6 [38.1; 43.0]	0.80
Height, m	1.7 [1.6; 1.7]	1.7 [1.6; 1.7]	0.95
Weight, kg	76.2 [71.1; 81.4]	71.3 [68.6; 73.9]	0.12
Body mass index, kg/m^2	27.6 [25.0; 29.3]	25.7 [24.9; 26.5]	0.11

Note: LVH — left ventricular hypertrophy; CI — confidence interval.

Table 2

BIOCHEMICAL PARAMETERS AND GROWTH FACTORS DEPENDING ON THE LEFT VENTRICULAR HYPERTROPHY

Characteristics	With LVH M [95% CI] n = 27	Without LVH M [95 % CI] n = 80	p
Dopamine, pg/ml	26.1 [22.0; 30.2]	24.3 [20.3; 28.3]	0.52
Epinephrine, pg/ml	116.8 [90.3; 143.4]	90.0 [58.9; 121.1]	0.10
Norepinephrine, pg/ml	425.4 [334.9; 515.9]	642.3 [516.9; 767.7]	0.004
Cortisol, mcg/dl	22.9 [21.6; 24.2]	20.2 [18.0; 22.4]	0.03
IGF-1, mcg/l	156.4 [130.8; 182.0]	131.0 [112.7; 149.2]	0.21

Note: LVH — left ventricular hypertrophy; CI — confidence interval; IGF-1 — insulin-like growth factor 1.

Table 3

PSYCHOEMOTIONAL CHARACTERISTICS IN GROUPS WITH AND WITHOUT LEFT VENTRICULAR HYPERTROPHY

Characteristics, point	With LVH M [95% CI] n = 27	Without LVH M [95 % CI] n = 80	p
VAS (health)	54.7 [46.1; 63.3]	68.0 [63.0; 73.1]	0.01
VAS (stress)	45.4 [34.9; 55.9]	43.5 [37.1; 49.9]	0.93
VAS (vitality)	48.9 [36.9; 60.8]	66.2 [60.3; 72.2]	0.01
LSF	2.1 [1.7; 2.4]	1.8 [1.6; 2.0]	0.19
Depression	15.2 [12.3; 18.1]	13.1 [11.6; 14.5]	0.14
RA	37.0 [32.0; 42.0]	36.5 [33.5; 39.5]	0.82
TA	42.0 [37.6; 46.3]	41.7 [39.6; 43.8]	0.85
Accumulated stress	156.2 [148.1; 194.4]	136.0 [115.0; 147.1]	0.04

Note: LVH — left ventricular hypertrophy; CI — confidence interval; VAS — visual analogue scale; LSF — level of social frustration; RA — reactive anxiety; TA — trait anxiety.

positively correlated with LVM and LVMI with the equal correlation coefficients ($r = 0.31$, $p = 0.04$). Depression value positively correlated with LVMI ($r = 0.30$, $p = 0.04$).

We also analysed correlations of hormone values and growth factors with structural and functional characteristics of the heart in persons with diagnosed LVH in general and with regard to the gender differences.

There was a positive correlation between adrenalin, relative wall thickness and LVMI ($r = 0.58$, $p = 0.01$ and $r = 0.54$, $p = 0.02$, respectively), as well as between cortisol and left atrial size in systole ($r = 0.53$, $p = 0.02$).

In apparently healthy males with LVH, insulin-like growth factor-1 was associated with interventricular septum thickness in diastole ($r = 0.90$, $p = 0.04$). There were correlations between cortisol and left ventricular posterior wall thickness ($r = 0.47$, $p = 0.04$), LVM and LVMI ($r = 0.45$, $p = 0.04$ and $r = 0.50$, $p = 0.03$, respectively). Multiple regression analysis confirmed the role of cortisol for LVM and LVMI in normotensive males ($R^2 = 0.34$, $\beta = 0.58$, $p = 0.001$ and $R^2 = 0.41$, $\beta = 0.64$, $p = 0.001$, respectively). Standard regression coefficients of other independent variables were non-significant.

Discussion

Stress reactions include a number of stereotypic genetically fixed processes in cells, tissues and organs. The investigation of emotion-mediated physiological mechanisms as a part of the whole psychosomatic system is of exceptional interest. Previously we found associations of psychological factors (stress, anxiety, depression, irrational coping strategies, social frustration) with the indicators of protein biological oxidation [12], lipoprotein metabolism [13], endothelial function [14], and local vessel wall stiffness [15].

In our opinion, LVH in normotensive individuals can be regarded as a somatic disorder resulted from psychoemotional stress that cannot be coped with at the psychological level. This statement is consistent with the study by P. Palatini [16] who claims that LVH is a result of increased sympathetic activity and initially is not associated with persistent increase in BP. A number of experimental studies showed that, in the simulated chronic adrenergic stress, catecholamines may cause a dose-independent LVH [17]. In addition, a 18-year long prospective study showed that cardiovascular and catecholamine stress-responsiveness is a stable characteristic of a person over extended periods of time [18].

To conclude, we assume that maintaining the noradrenalin/adrenalin ratio within the physiological range is beneficial for the structural and functional state of the myocardium and can increase the organ capability to adapt to challenges that emerge in stressful situations [19]. A gradual suppression of the adaptive and trophic function of the heart takes place due to the initial activation of the sympathoadrenal system, accompanied by increased noradrenalin release, decrease of its spare synthesis, and growing discrepancy between synthesis and release of this mediator.

A prospective study showed a significant correlation between stress-induced cortisol production and arterial hypertension incidence (probability of approximately 59 %) in initially normotensive males and females [20]. The authors believe that even moderate stress (psychophysiological testing) is sensitive enough for the hypothalamic-pituitary-adrenal axis hyperresponsiveness and increased cortisol production independent of traditional cardiovascular risk factors including BP level. Cortisol may directly impact on the central nervous system affecting brain BP controlling regions (hypothalamus, limbic system). In addition, glucocorticoid receptors are present in the heart, smooth muscles of resistance vessels and kidneys, therefore they directly influence the BP.

Among the cellular factors — modulators of angiogenesis and remodeling processes in organs and tissues, growth factors, and in particular, the system of insulin-like growth factor, are of special interest. Low concentrations of IGF-1 and –2 are associated with high incidence of cardiovascular events [21]. Vice versa, increased blood level of these factors is associated with favourable outcomes in patients with vascular risk factors [22, 23]. One of the studies showed that the LVM increase in patients with untreated arterial hypertension ($n = 230$) is inversely related to the insulin-like growth factor level [24].

Conclusions

In people with LVH, relevantly high level of accumulated stress according to Holmes and Rahe's scale and low VAS-based viability were found. The subjects with diagnosed LVH are characterized by relevant change of the noradrenalin/adrenalin ratio and increased cortisol level. Both biochemical parameters and structural/functional heart characteristics correlate with the psychological factors. These correlations are gender-specific. Psychoemotional stress triggers stress reactions that are accompanied by metabolic changes (in mediator mechanisms, growth factor system) and probably by structural changes in the myocardium. Study of stress reactions as a part of the psychosomatic continuum is essential for the elucidation of the mechanisms of stress impact on the disease progression, as well as for the development of an integrative preventive approaches.

Conflict of interest

The authors declare no conflict of interest.

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