https://russjcardiol.elpub.ru
doi:10.15829/1560-4071-2019-9-7-13

ISSN 1560-4071 (print)
ISSN 2618-7620 (online)

Association of stress with cardiovascular diseases and risk factors in a population (ESSE-RF in Kemerovo region)

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Aim. To assess the prevalence of stress and its association with socio-demographic characteristics, cardiovascular risk factors and cardiovascular diseases (CVD) in the Siberian population.

Material and methods. A cross-sectional study was performed in the framework of the Russian multicenter epidemiological study ESSE-RF in the Kemerovo Region in 2013. The presented study included 1628 individuals aged 25 to 64 years. Information was assessed on the presence of stress, some socio-demographic and economic characteristics, a history of CVD, as well as behavioral habits and quality of life. To eliminate the modifying effect of socio-demographic characteristics, a logistic regression analysis was used. The odds ratio (OR) and the 95% confidence interval (CI) were calculated.

Results. The prevalence of stress was 22,6%; stress was statistically significantly more often recorded in women (28,1%) than in men (11,7%). After adjusting for socio-demographic characteristics, stress was statistically significantly more often recorded in people with secondary and primary education compared with those with higher education (24,9% and 19,1%, p=0,006), as well as in people with middle and high financial affluence compared with low affluence (24,5% and 11,3%, p<0,001). This association is observed only at the expense of women. For unemployed participants, the stress rate is higher only among males — 18,8% versus 11,4% among workers (p=0,015). Stress was also statistically significantly more often recorded in groups with arterial hypertension, lack of sleep, quality of life on the EQ-VAS scale and on the EuroQol scale. Smokers are more likely to have stress (23,8% vs 22,0%) and have a history of stroke (35,3% vs 22,2%). Among all CVDs and their risk factors, an inverse association of stress with obesity was revealed only in men.

Conclusion. Study showed that people with stress are under large load of some cardiovascular risk factors. At the same time, ambiguous associations between stress and arterial hypertension and quality of life were obtained. This confirms the need for further study of the association of stress with other factors of cardiovascular risk, taking into account age and gender and socio-economic characteristics of the population.

Key words: stress, risk factors for cardiovascular diseases, epidemiological study.

Conflicts of Interest: nothing to declare.

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Received: 15.04.2019
Revision Received: 20.05.2019
Accepted: 31.05.2019

For citation: Shapovalova E. B., Maksimov S. A., Indukaeva E. V., Artamonova G. V. Association of stress with cardiovascular diseases and risk factors in a population (ESSE-RF in Kemerovo region). *Russian Journal of Cardiology*. 2019;24(9):7-13. (In Russ.)
doi:10.15829/1560-4071-2019-9-7-13

It is known that stress can act as a trigger for the development of cardiovascular disease, initiating a systemic inflammation, which may lead to adverse consequences especially for people with low socio-economic status [1]. However, the contribution of stress to the cause-effect relationships with socio-demographic, behavioral, and psychological risk factors for cardiovascular disease (CVD) is still a subject of discussion. That is because there is no definitive answer to the question of which mechanisms of initiation play the main role in triggering of complex stress-induced pathophysiological processes. The assessment of such a risk factor as stress may include several components and seems to be a laborious and complex process. The reason for this is the lack of a unified assessment of stress, which to some extent may affect the obtained associations [2, 3]. In addition, stress-induced complex body reactions can lead to the development of CVDs in the delayed observation period. INTERHEART study of a representative sample of 24767 people from 52 countries showed that stress doubles the risk of acute myocardial infarction, and this association did not depend on the region of residence, ethnicity, and gender [2]. Another prospective study of the effects of cumulative stress on cardiovascular risk shows association with age, ethnicity, marital status, as well as smoking and obesity, diabetes, depression, and anxiety [4]. As past studies have shown, it is important to take into account the interpretation of the events that have taken place when studying stress, as the same events can have a diametrically opposed meaning for different individuals. Despite differences in research methods (in samples differing in sex, age, and ethnic composition), the negative contribution of stress to the pathogenesis of CVDs has been undisputed for several decades [5]. Difficulties in studying the interaction of stress with cardiovascular risk (CVR) factors and CVDs have led to the accumulation of a vast array of epidemiological, clinical, experimental and pathophysiological studies. However, there are still unresolved issues in the literature regarding the cause-effect relationships between stress and CVDs. It is known that these associations are influenced by external factors (climatic and geographical conditions, legislative and social environment of the region), internal features of the organism (presence of comorbid pathology, certain socio-demographic and behavioral factors, individual susceptibility to stress). Taking into account that the life of any modern person is inseparably associated with stress, its study is given an important place as one of the modifiable CVR factors.

The aim of the study was to assess the prevalence of stress and its associations with socio-demographic characteristics, CVR factors and CVDs in the Siberian population.

Material and methods

The study was carried out as part of the Russian multicenter epidemiological ESSE-RF study in the Kemerovo region in 2013. It included 1628 surveyed persons aged 25 to 64 years.

The questionnaire survey provided information on socio-demographic characteristics (sex, age, education, marital status, employment), stress, behavioral habits (alcohol, smoking, lack of sleep and low physical activity), history of CVD (arterial hypertension, coronary artery disease (CAD), cerebrovascular accident, diabetes mellitus), economic conditions (financial wealth), quality of life.

The criterion of arterial hypertension was considered to be the level of blood pressure $\geqslant$140/90 mm Hg, or lower against the background of hypotensive therapy. CAD presence was assessed on the basis of three epidemiological criteria: coding of electrocardiographic changes according to Minnesota code, Rose questionnaire and history of myocardial infarction.

Obesity was defined as value of body mass index >29 kg/m^2. Hypercholesterolemia was diagnosed with total cholesterol levels >5,0 mmol/l, as well as taking of lipid-lowering drugs (mainly statins) in the history. Fasting hyperglycemia was diagnosed with plasma glucose level of venous blood >5,6 mmol/l.

Alcohol consumption was estimated based on the frequency, volume and type of drink consumed. The volume of alcohol consumed per year was calculated and converted to average daily values in grams of ethanol. Those who consumed more than 24 grams of ethanol per day were considered as alcohol abusers.

Smokers were those who smoked at least one cigarette a day or quit smoking less than 1 year ago.

The Perceived Stress Scale was used to determine susceptibility to stress. This scale consists of 10 questions that determined how stressful the previous month was [6]. The order of series obtained was used to calculate the 75th percentile, the values above were considered as a risk factor (5 points and above).

Insufficient sleep was considered to be night's sleep at duration of <7 hours. Insufficient physical activity was taken in case of activity <5 times per week for 30 min (moderate) or physical activity <3 times per week for 20 min (intensive). The level of physical activity was considered to be low

if it was below the minimum recommended level of 150 minutes of moderate or 75 minutes of intensive aerobic exercise per week for adults (medium or high speed walking, or equivalent exercise).

The EUROQOL-EQ-5D international questionnaire and EQ-VAS visual analogue scale were used to assess the quality of life. It was used to score 5 components of the quality of life (mobility, self-care, usual activity, pain/discomfort, anxiety/depression). Each component was assigned 0 points for the absence of disorders, 1 point for moderate disorders and 2 points for severe disorders. The sum of the scores was used as a quantitative assessment of the quality of life. According to the visual analogue scale, interviewers assessed their health status in scores from 0 to 100.

The study was conducted in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Research Institute for Complex Issues of Cardiovascular Diseases. Prior to inclusion in the study, written informed consent was obtained from all participants.

The analysis of stress prevalence depending on socio-demographic characteristics of the sample, presence of cardiovascular diseases and CVR factors was carried out using the Pearson's Chi-square test. Differences in quantitative parameters (age, quality of life according to EQ-VAS and EUROQOL scales) in persons with/without stress were assessed using the Mann-Whitney test and were represented by mean values and standard deviation.

Significant differences in stress prevalence depending on socio-demographic characteristics may affect the association of stress with CVDs and SSR factors. Logistic regression analysis was used to eliminate the modifying effect of socio-demographic characteristics. At the same time, the associations studied were adjusted for the impact of gender, age, employment, level of education, marital status, urban/rural residence, and financial well-being. The odds ratio (OR) and 95% confidence interval (CI) were calculated.

A critical level of statistical significance was 0,05.

Results

Association of stress prevalence with socio-demographic characteristics. The prevalence of stress was 22,6%, and in women (28,1%) it was statistically significantly higher than in men (11,7%), respectively (OR=0,37, 95% CI=0,28-0,49).

Stress prevalence and its association with socio-demographic characteristics are presented in Table 1. Univariate analysis shows differences in stress prevalence depending on gender, employment, level of education, marital status and financial well-being. Thus, stress is statistically significantly more often registered in the unemployed, compared to those who have job (27,2% and 21,0%, p=0,009), persons with secondary and primary education, compared to those with higher education (24,9% and 19,1%, p=0,006), individuals without a family, compared to those with a family (26,5% and 19,8%, p<0,001), participants with medium and high income, compared to those with low income (24,5% and 11,3%, p<0,001).

After adjustment for socio-demographic characteristics, the association with stress became statistically insignificant for such parameters as employment and marital status. In other cases, the regularities remained the same.

Association of CVR factors with stress in different gender groups. An analysis of CVR factors and stress relationships in men and women revealed an association between stress and secondary and primary education, as well as financial well-being (only for women). Thus, stress is more often recorded in women with secondary and primary education (33,4%) compared with higher education (24,2% (p=0,002)), and less often in women with low incomes — 13,5% versus 32,2% (p=0,001). For unemployed, the stress prevalence is higher only among males — 18,8% versus 11,4% (p=0,015). The adjustment for socio-demographic characteristics did not change the above associations.

Association of stress with CVDs and CVR factors. Univariate analysis showed differences in associations between stress prevalence and arterial hypertension, CAD, as well as factors such as sleep adequacy, alcohol abuse, and average quality of life (both EQ-VAS and EUROQOL) (Table 2). The stress frequency is lower in persons with arterial hypertension than without it (19,7% and 24,8%, p=0,012, respectively), as well as in alcohol abusers, compared to those who do not abuse alcohol (18,9% and 25,6%, p<0,001). In contrast, the stress rate was higher in the group with lack of sleep (29,0% vs. 20,0%, p<0,001) and CAD (30,7% vs. 20,9%, p<0,001). The quality of life of persons with recorded stress, as compared to those without it, was higher on both the EQ-VAS scale (67,9±16,1 vs. 59,6±16,8, p<0,001) and the EUROQOL scale (1,36±1,34 vs. 2,52±1,53, p<0,001).

Adjustment for socio-demographic characteristics has not changed the importance of associations with

Table 1

Associations of stress with socio-demographic characteristics

Characteristics		N	Stress		Logistic regression		
			%, M±SD	P	OR	95% CI	P
Sex	Males	700	11,7	<0,001	0,37	0,28-0,49	<0,001
	Females	928	28,1				
Age	Stress	367	45,6±11,4	0,10	1,00	0,99-1,01	0,86
	No stress	1258	47,6±11,2				
Age groups (years)	25-34	331	21,2	0,20	–	–	–
	35-44	332	19,1				
	45-54	434	25,1				
	55-64	531	23,6				
Employment	Yes	255	21,0	0,009	0,84	0,63-1,11	0,22
	No	112	27,2				
Secondary education	Yes	245	24,9	0,006	1,37	1,05-1,78	0,019
	No	122	19,1				
Lack of family	Yes	172	26,5	<0,001	1,08	0,84-1,39	0,56
	No	191	19,8				
Rural residence	Yes	66	23,9	0,6	0,96	0,69-1,32	0,79
	No	300	22,5				
Low income	Yes	27	11,3	<0,001	0,42	0,27-0,65	<0,001
	No	340	24,5				

stress in the groups: with arterial hypertension (OR=0,75, 95% CI 0,57-0,98), lack of sleep (OR=1,72, 95% CI 1,33-2,22), quality of life on the EQ-VAS scale (OR=0,07, 95% CI 0,96-0,98) and on the EUROQOL scale (OR=1,66, 95% CI 1,51-1,82). Associations of stress with alcohol abuse and CAD were not statistically significant. On the contrary, there were statistically significant associations of stress with smoking and stroke in the history: stress was observed more likely in smokers (OR=1,61, 95% CI 1,21-2,14) and persons with stroke in the history (OR=2,21, 95% CI 1,04-4,73).

Association of stress with CVDs and CVR factors in different sexual groups. Among all CVDs and their CVR factors, only males have an inverse relationship between stress prevalence and obesity. Thus, association of stress prevalence with obesity in men was statistically significantly lower (8,7% vs. 14,7%, respectively, p=0,03), After adjustment for socio-demographic characteristics the significance of the association has not changed (OR=0,54, 95% CI 0,30-0,95). No other associations between stress and CVDs depending of sex were found.

Discussion

Thus, according to the survey results, the prevalence of stress was 22,6%. In women, stress was statistically significantly recorded almost 2 times more often than in men. The high prevalence of stress in women was also observed in the Swedish national study [7], which may indicate a strong association between stress and female sex.

Sleep disorders, like stress, are an important problem in modern society.

A number of studies have found that sleep disorder increases the risk of various diseases, including CVDs. A nationwide Japanese study of the relationship between sleep disorders and stress showed that people who felt high levels of stress were more prone to sleep disorder [8]. In study of Alosaimi FD, et al. (2015) a similar positive association of stress with lack of sleep was observed [9]. Our study obtained a statistically significant direct relationship between insufficient sleep and stress. Behavioural habits such as drinking and smoking were also positively related to sleep disorders. Smoking, as a strategy for correction of sleep disorder, is known to contribute significantly to sleep pathologies. Smokers are more likely to experience sleep disorders such as night apnea, defect sleep quality, insomnia, which, in turn, are risk factors for the development of many chronic diseases of modern civilization (obesity, CVDs, diabetes) [10].

In this study, a statistically significant association of bad habits (smoking and alcohol abuse) with stress

Table 2

Associations of stress with CVR and CVD factors

Risk factors		N	Stress		Logistic regression		
			%, M±SD	P	OR	95% CI	P
Lack of sleep	Yes	135	29,0	<0,001	1,72	1,33-2,22	<0,001
	No	232	20,0				
Low physical activity	Yes	92	22,3	0,9	1,16	0,86-1,56	0,91
	No	265	22,4				
Smoking	Yes	118	23,8	0,42	1,61	1,21-2,14	<0,001
	No	249	22,0				
Alcohol	Yes	139	18,9	<0,001	0,99	0,75-1,30	0,92
	No	228	25,6				
Quality of LIfe (EQ-VAS)	Stress	367	67,9±16,1	<0,001	0,97	0,96-0,98	<0,001
	No stress	1258	59,6±16,8				
Quality of life (EUROQOL)	Stress	367	1,36±1,34	<0,001	1,66	1,51-1,82	<0,001
	No stress	1258	2,52±1,53				
Hypercholesterolemia	Yes	194	22,6	0,97	0,91	0,71-1,18	0,48
	No	171	22,7				
Hyperglycemia	Yes	59	21,2	0,53	0,88	0,63-1,24	0,47
	No	306	22,9				
Arterial hypertension	Yes	139	19,7	0,012	0,75	0,57-0,98	0,032
	No	228	24,8				
Coronary artery disease	Yes	83	30,7	<0,001	0,99	0,98-1,01	0,12
	No	280	20,9				
Stroke	Yes	12	35,3	0,074	2,21	1,04-4,73	0,040
	No	351	22,2				
Obesity	Yes	124	21,7	0,53	0,80	0,61-1,04	0,099
	No	242	23,1				
Diabetes mellitus	Yes	13	20,6	0,71	0,92	0,48-1,76	0,80
	No	350	22,6				

has been identified among both smokers and alcohol abusers. However, after adjustment for socio-demographic factors, the significance of the stress relationship remained only for smokers.

Stress has long been recognized as a risk factor for smoking. There is ample evidence, both epide-miological and clinical, of the direct association between stress and substance use behaviour. Stress also relates to both smoking addiction and its successful cessation. For example, past studies have shown that smokers have a higher level of stress than non-smokers and former smokers [11].

It is known that the quality of life directly depends on socio-demographic, anthropometric, anamnestic, psychological factors, as well as the current morbid status. However, there is still no consensus on the factors influencing the quality of life. At the same time, certain nosologies are characterized by their own set of the most studied factors influencing the quality of life. In this study, the reverse association of stress with quality of life is obtained both on the EUROQOL-EQ-5D scale and on the EQ-VAS scale. In this study, people with stress have a higher quality of life than those without it. Thus, stress has been associated with higher quality of life values, which indicates a complex relationship between quality of life and stress.

The study found an association of stress with obesity only in men. Obesity was statistically significantly less common in men with stress than in men without stress. According to the literature, the evidence of the relationship between stress and body mass index is rather contradictory. On the one hand, given the relationship between stress and the addictions underlying many chronic diseases, stress contributes to weight gain, including obesity [10]. On the other

hand, a meta-analysis of data from 1,617,46 participants in 13 European studies (49% of men, mean age 43,7 years) showed that stress associated with hard work can be associated with both weight gain and loss, reflecting a U-shaped association of stress and body mass index [12]. In the study by Boyce JA, et al. (2014) examining stress and body mass index in New Zealand freshmen showed that students with high levels of stress gained weight if they had an initial high body mass index, and lost weight in case of initial low body mass index [13].

Previous studies have proven the role of chronic stress in the formation and progression of arterial hypertension in particular and CVDs in general, directly potentiating systemic inflammation, as well as indirectly influencing behavioral changes. In a study by Lu X, et al. (2019) shows that the association of stress with arterial hypertension changed by gender and ethnicity [14]. Asian-American men with high levels of stress were significantly more likely to develop arterial hypertension than men with low stress. There was no association between perceived stress and hypertension for females. In our study of the relationship between stress and arterial hypertension, no association was found for both men and women. On the contrary, persons with normal blood pressure were more likely to experience stress than persons with hypertension. After adjustment for socio-demographic factors, the statistically significant relationship between hypertension and stress did not change.

Work and stress are inseparably associated in modern society, affecting each other. The results of the research show that people with jobs were less stressed than unemployed people. The unemployed had a higher prevalence of stress only because of their male counterparts, which suggests that stress was more related to unemployment among men than women. This is confirmed by the literature, where a cohort study by Mæhlisen MH, et al. (2018) found that domestic stress almost doubled the risk of unemployment [15].

It is known that chronic stress increases the risk of CAD [1, 2]. INTERHEART's study in a representative sample of 52 countries showed that stress doubles the risk of myocardial infarction, regardless of gender, race, or region of residence. In this study, people with CAD were more likely to have stress than people without CAD, but this association was not strong in case of elimination the modifying effects of socio-demographic characteristics. Thus, we did not get a significant association of stress with CAD. The REGARDS's study showed that groups of people with high levels of stress were at increased risk of CAD, but only for those with below average income [16].

Poverty is known to be a source of chronic stress and can have a negative impact on both physical and mental health. At the same time, it can be ambiguously perceived by the population, as indicated by study of Hjelm L, et al. (2018) examining the impact of state poverty alleviation programmes on stress among poor households in Zambia, South Africa. The study found that financial programmes did not change the frequency of stress, but that this improved food security associated with improved food quality, resulting in an indirect reduction in the prevalence of stress [17]. Absence of associations of financial income with stress was also noted in another study [9]. However, persons over 60 years old have an association between low income and higher levels of stress [7], which indicates a modifying effect of age. In the present study, stress was almost twice as rare in low-income individuals as in middle- and high-income individuals. Adjustment for socio-demographic factors did not change the importance of association. However, this association was observed only at the expense of women.

A statistically significant association of secondary education and stress is obtained. Thus, among individuals with secondary education stress prevalence is higher than with higher education. Moreover, this association is observed among women. Thus, women with secondary education were statistically significantly more likely have stress. For men, the association of the level of education with stress was not found in our study. In the study by Hjelm L, et al. (2018) among poor households in Zambia, the level of education also did not show a strong association with stress among both men and women [17].

However, in a population study examining the prevalence of stress after 65 years of age, higher average levels of d stress were associated with low levels of education [7].

Stress was less common among married people than among single people, but the adjustment for socio-demographic factors led to a leveling of this relationship. The absence of a relationship between marital status and stress was also noted in the study by Alosaimi FD, et al. (2015) [9]. At the same time, in a population study, singlehood was statistically significantly associated with stress in older persons [7].

Conclusion

Thus, when studying the relationship of stress with CVD risk factors, it was revealed that stress is

more often recorded in women and in people with lack of sleep. Socio-demographic factors such as secondary education and financial well-being are also closely related to stress.

It has been shown that people with stress have a large load of some CVR factors. At the same time, ambiguous associations of stress with arterial hypertension and quality of life were obtained.

It is noteworthy that these associations remained after the adjustment for the socio-demographic factors. This confirms the need for further study of the association of stress with other CVR factors, taking into account the sex, age and socio-economic characteristics of the population, to identify the effects of stress on the cardiovascular system.

Limitations. An important limitation due to the cross-sectional design of the study is the inability to draw conclusions about the cause-effect associations. We have also not studied the contribution of depression, which in itself can cause stress and, conversely, lead to additive effect. We have not studied the modifying effects of age and socioeconomic status, although there is evidence that age may influence the associations obtained, and low socioeconomic status is an aggravating factor for stress. In addition, stress levels were not graded, which could lead to ambiguous interpretation of the results.

Conflicts of Interest: nothing to declare.

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