

Unresolved Cardiovascular Disease Prevention Issues

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Abstract— The prevalence of risk factors for cardiovascular diseases and the electrophysiological state of the myocardium in male patients with somatoform dysfunction of the vegetative nervous system was studied. Among the risk factors, the leading positions were taken by stress, low physical activity and smoking. A method has been developed for diagnosing prenosological changes in the electrophysiological state of the myocardium associated with the tension of the regulatory systems in male patients with somatoform dysfunction of the vegetative nervous system in order to identify prenosological conditions and increased risk of the cardiovascular disease. The correlation between the sum of points according to the developed method and indicators characterizing the state of the sympathetic section of the vegetative nervous system and the electrophysiological state of the myocardium have been proved. The threshold score for risk factors for the cardiovascular disease, corresponding to the presence of prenosological changes in the electrophysiological state of the myocardium in male patients with somatoform dysfunction of the vegetative nervous system is 8. The diagnostic sensitivity of the method in male patients with somatoform dysfunction of the vegetative nervous system with a threshold score of 8 was 80 %, specificity – 70.8 %.

Keywords — risk factors for cardiovascular diseases, prevention Introduction

I. INTRODUCTION

The importance of assessing the overall risk of the cardiovascular disease (CVD) is noted by all current recommendations for cardiovascular prevention, since it is proved that atherosclerosis develops against the background of the combined effect to risk factors (RF). Currently, there is an increasing scientific evidence that serious mental illnesses, such as bipolar disorder and schizophrenia, have a significant effect on the risk of developing CVD. This is due to the high

prevalence of behavioral RF, such as low physical activity (PhA), smoking, non-compliance with the principles of healthy eating among these patients, and low commitment to correct RF. In this regard, borderline mental disorders, neurotic, stress-related and somatoform, are attracting more and more attention of specialists in the field of practical medicine. Behavioral and psychosocial RF are widespread among these patients, but their commitment to correct them is higher than that in patients with serious mental illnesses, which may contribute to greater effectiveness of preventive interventions and, possibly, reduce the risk of developing CVD in these individuals. In this regard, it is of great interest to study the likelihood of developing prenosological conditions and an increased risk of diseases of the cardiovascular system in patients with somatoform dysfunction of the vegetative nervous system (VNSSD) with CVD RF. It is of great sensitivity to psychosocial RF and inadequate response of the CVS to ordinary and super-strong stimuli in patients with VNSSD. The transition from health to illness is associated with a decrease in the adaptive capacity of the body with a decrease in the ability to adequately respond to normal everyday workloads, and not only to social and labor ones. Transient conditions that occur on the border between health and disease are called prenosological. Long-term persisting or excessive stress can cause the phenomenon of incomplete adaptation in patients with VNSSD, followed by depletion of adaptation reserves and the initiation of prenosological states and somatic pathology in the "interested" organ or system. According to the researchers, the "concerned" organ or system is the cardiovascular system (CVS) [1–3]. Therefore, it seemed to us topical to study the likelihood of the development of prenosological conditions and, possibly, an increased risk of CVD in patients with VNSSD with CVD RFs. The purpose of the study is to study

the likelihood of development prenosological conditions and an increased risk of the cardiovascular disease in male patients with somatoform dysfunction of the vegetative nervous system with CVD risk factors.

Objectives of the study:

1. To study the structure of risk factors for the cardiovascular disease in male patients with somatoform dysfunction of the vegetative nervous system. 2. To develop a method for diagnosing prenosological changes in the electrophysiological state of the myocardium in male patients with somatoform dysfunction of the vegetative nervous system to identify prediction prenosological conditions. 3. To prove the correlation relationship between the sum of points for the developed method and the indicators characterizing the state of the sympathetic section of the vegetative nervous system and the electrophysiological state of the myocardium. 4. To determine the threshold score for risk factors for cardiovascular disease, corresponding to the presence of prenosological changes in the electrophysiological state of the myocardium in male patients with somatoform dysfunction of the vegetative nervous system.

II. MATERIALS AND METHODS

The study was performed at the Department of Polyclinic Therapy and General Medical Practice of the Voronezh State Medical Academy N. N. Burdenko. 58 male patients with VNSSD (age 22.9 ± 1.6 years) were the object of the study. The control group included 51 healthy men (22.8 ± 2.0 years old). The age of 20–30, the absence of concomitant diseases were the criteria for inclusion in the study. All the respondents signed the personal informed consent. The study was conducted after the approval of the ethics committee of Voronezh State Medical Academy named after N. N. Burdenko. The diagnosis of VNSSD was made in accordance with the criteria of neurocirculatory asthenia proposed by V. I. Makolkin and S. A. Abakumov (1996). In accordance with the National Recommendations for Cardiovascular Prevention developed by the Committee of Experts of the All-Russian Scientific Society of Cardiologists and the National Scientific Society "Cardiovascular Prevention and Rehabilitation" (2011), the CVD RF were detected in patients with VNSSD [4]. To assess the functional reserves the state of the physiological norm, the prenosological and premorbid states, and the breakdown of the adaptation mechanisms were distinguished according to the classification proposed by R. M. Baevsky. Dispersion mapping (DM) of an electrocardiogram (ECG) was used as a method of prenosological diagnostics. Electrophysiological state of the myocardium (MEPhS) was assessed using an integral indicator (II): "Myocardium". The value of II "Myocardium" $\leq 14\%$ at rest and $\leq 17\%$ with physical activity (PhA) was interpreted as normal. II "Myocardium" 15–19 %, 20–25 % and more than 25 % reflected the borderline state associated with the MEPhS stress of (prenosological state), overstrain (premorbid state) and depletion of myocardial function reserves – development of signs of pathology, respectively [5]. Two functional tests were performed: a test with PhA and the active orthostatic test (AOCT). On the eve of the study, the consumption of strong tea, coffee, and alcohol was prohibited.

The study was conducted from 10 to 11 o'clock in the afternoon. The test procedure for PhA was as follows: initial examination for 60 seconds at rest (T1), after PhA (T2), 2 (T3) and 4 (T4) minutes after PhA. The method of conducting AOCT: initial examination lying (T5), in orthostasis (T6), after 2 (T7) and 4 (T8) minutes of being in orthostasis lying (T9), 2 (T10) and 4 (T11) minutes after the transition to a horizontal position. Statistical data processing was carried out using the STATISTICA personal computer software package in Windows and IBM SPSS Statistics 20.0. A value of $p=0.05$ was taken as the threshold level of statistical significance. Using the Shapiro-Wilkes criterion, the conditions for the normality of the analyzed data and equality of variances of distributions of characters in the compared groups were checked. In the distribution of the studied traits in accordance with the normal law, the average value (M) was taken as the most typical indicator for the sample, and the standard deviation (s) was taken as the measure of dispersion. As a measure of the central tendency and a measure of dispersion, the median and interquartile range were used if the studied signs did not obey the normal law. The relationship of quantitative normal signs was studied using the Pearson method, otherwise – Spearman R correlation. Logistic regression was used to theoretically test the methods developed and determine the threshold score. Using the ROC analysis, the predictive power of the methods and sensitivity and specificity analysis were evaluated.

III. RESULTS AND DISCUSSION

Among the RFs of CVD in males with VNSSD, the leading positions were taken by stress, low PhA and smoking, in 71, 59 and 57 % of cases, respectively. The following CVD RFs are arranged in descending order: excess BM and obesity, anxiety, low consumption of vegetables and fruits, negative history of additional aerobic PhA, excessive alcohol consumption, depression, total cholesterol ≥ 5 mmol/l and heart rate ≥ 80 beats/min, in 43, 41, 36, 36, 34, 26, 23 and 9 % of cases, respectively. To develop a method for diagnosing prenosological changes of MEPhS in male patients with VNSSD, we estimated the severity of the studied CVD RFs in points from 0 to 3. If the stress level (Reeder L. G. et al, 1969) was 1-2, 2 points were assigned, 2.01-3 – 1 point, 3.01-4 – 0 points. The level of PhA was detected using the Potemkina R. A. test, with a positive answer to questions 1-4, 5-6 and 7-8, 2, 1 and 0 points were assigned respectively. 2 points were assigned when smoking ≥ 1 cigarettes per day, < 1 cigarette per day – 1 point, with a negative smoking status – 0 points. The BM index values of 18.5–24.9, 25–29.9 and ≥ 30 kg/m² were regarded as 0, 1 and 2 points, respectively. The overall response to the anxiety subscale (HADS) 0-5, 6-9, ≥ 10 was rated as 0, 1 and 2 points, respectively. The cumulative response to the depression subscale (HADS) 0-5, 6-9, ≥ 10 was rated as 0, 1 and 2 points, respectively. When the heart rate in a patient VNSSD 50-59 beats/min, assigned 0 points. Heart rate 60–69 beats/min, 70–79 beats/min and ≥ 80 beats/min were estimated at 1, 2 and 3 points, respectively. Office blood pressure $\leq 129/84$ mm Hg., 130-139 mm Hg. for the SAP assigned 0 and 1 point, respectively. Wen blood pressure was $\geq 140/90$ mm Hg., 2 points were put. With daily alcohol intake < 2 servings, 0 points were assigned, 2 servings, and > 2 were

rated at 1 and 2 points, respectively. The positive history of additional aerobic PhA in childhood and/or adolescence was rated as 0 points, negative – 1 point. Negative family history of coronary artery disease or CVD in first-degree relatives (for men <55 years and for women < 65 years) – 0 points, positive – 1 point. 0 and 1 points were assigned, respectively, with the consuming of ≥ 5 servings of vegetables and fruits per day (not including potatoes) and <5 servings «table 1».

TABLE I. A METHOD FOR DIAGNOSING PRENOSOLOGICAL CHANGES OF MEPhS FOR INDIVIDUAL PREDICTION OF PRENOSOLOGICAL CONDITIONS AND INCREASED RISK OF DEVELOPING CVD IN MALE PATIENTS WITH VNSSD

The Risk factor	The severity of the characteristic in points		
	0	1	2
1. office resting heart rate (beats/min)	50-59	60-69	≥ 70
if the office resting heart rate ≥ 80 , 3 points were assigned			
2. depression level (HADS)	0-5	6-9	≥ 10
3. anxiety level (HADS)	0-5	6-9	≥ 10
4. history of smoking (cigarettes/day)	negative	<1	≥ 1
5. office blood pressure (mm Hg.)	$\leq 129/84$	130-139/85-89	$\geq 140/90$
6. level of physical activity (Potemkin R. A. test)	answers 7-8	answers 5-6	answers 1-4
7. stress level (Reader test)	3.01-4	2.01-3	1-2
8. BMI (kg/m^2)	18.5-24.9	25-29.9	≥ 30
9. alcohol consumption by males (senior dose/ day)	< 2	2	> 2
10. anamnesis of additional aerobic PhA in childhood and/or adolescence	negative	positive	-
11. family history of coronary heart disease or CVD in first-degree relatives (males <55 years and females < 65 years)	negative	positive	-
12. the consumption of vegetables and fruits per day (not counting potatoes)	≥ 5 servings	< 5 servings	-

We had to prove statistically significant correlations between the sum of points for all CVD RFs and RRNN value in T (8), then, between the of RRNN value in T (8) and the II "Myocardium" at T (2), and finally, between II "Myocardium" in T (2) and the sum of points for the CVD RFs. As reference positions, we chose the RRNN value after 4 min of stay in orthostasis T (8) and the value of the II "Myocardium" after the PhA (T2), based on the data that the RRNN value is the reciprocal of the HR. The value of RRNN after 4 minutes of stay in orthostasis (T8) reflects the increase in heart rate due to the activation of the sympathetic division of the VNS and the release of catecholamines in the blood. And the value of the II "Myocardium" after PhA (T2) allows one to assess the nature of the response of the CVS to the daily PhA, and to identify transient changes in the CVS in young people without clinical manifestations of CVD.

A statistically significant correlation dependence between the sum of points for all CVD FRs and RRNN value in T (8) was inverse, moderate: $r = -0.41$ ($p = 0.0012$). Consequently, the greater the sum of points for the CVD RF, the lower the RRNN value in T (8), i.e. the higher the activity of the sympathetic division of the VNS. The correlation between RRNN in T (8) and II "Myocardium" in T (2) in male patients with VNSSD was moderate: $r = -0.25$ ($p = 0.0500$). Thus, we

proved that the higher the activity of the sympathetic division of the VNS, the more the II "Myocardium" after PhA (T2). At the last stage, we proved the presence of a direct moderate correlation dependence between the sum of points for the CVD RFs and the II "Myocardium" in T (2) in male patients with VNSSD: $r = 0.54$ ($p = 0.00001$). So the II "Myocardium" after PhA the higher, the higher the sum of the points for the CVD RFs. We found in male patients with VNSSD that the value of II "Myocardium" $\geq 18\%$ after the PhA reflecting the tension of regulatory systems and the development of prenosologic states correspond to the sum of the scores by CVD RFs >8 . The theoretical test of the developed method was carried out by binary logistic regression, where the presence of prenosological changes of MEPhS in male patients with VNSSD and only predictor was the total score for the method developed by us in «table I».

The regression equation is:

$$p = \frac{1}{1+e^{8,000-0,767x}} \quad (1)$$

where p – the theoretical possibility of prenosological changes of MEPhS according to the method we developed in male patients with VNSSD, x – the value of the total score of the method developed by us «table I» in a specific patient with VNSSD.

In male patients with VNSSD this regression model predicts the risk prediction of the development of MEPhS donosological changes with accuracy of 89.7 % (Cox and Snell determination coefficient $R^2 = 0.269$; R^2 Nagelkerka = 0.447; -2Log Likelihood = 35.178; $\chi^2(1) = 18.146$, $p < 0.001$; the level of statistical significance of the regression coefficients $r < 0.05$. With the independent inclusion of predictors in the regression model, the accuracy of the prognosis male patients with VNSSD with CVD RFs was the same as in the model based on the total score, and was at 89.7 %. However, with slightly large R^2 Cox and Snell it equals 0.330 of determination coefficients; R^2 Nagelkerka = 0.549, -2Log Likelihood = 30.109; $\chi^2(13) = 23.216$, $p < 0.05$; the level of statistical significance of the regression coefficients ($p > 0.05$). Consequently, the total scores, which acts as the only integral categorized predictor, gave us an exact model.

The theoretical probability of the presence of prenosological changes in MEPhS for each patient was calculated using equation (1) (Fig. I).

Then, mean probabilities for each male patient with VNSSD were calculated, and a theoretical probability range was found at which the prenosological changes of MEPhS in the sample were practically not detected, which corresponded to the range from 0.0061 to 0.2095. The graph in figure I revealed that this corresponds to a range from 0 to 9 points, and the average value of this probability (0.1078) falls on the interval from 8 to 9 points. Determination of the threshold score for male patients with VNSSD, its diagnostic sensitivity and specificity was carried out further by the method of ROC-analysis.

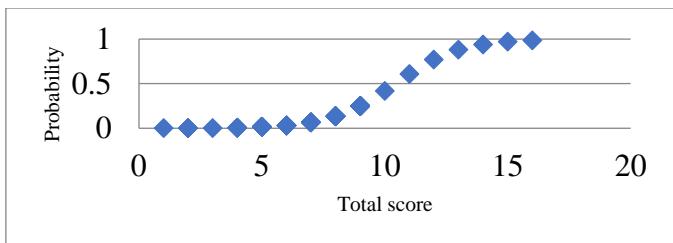


Fig. 1. Scatterplot. The dependence of theoretical probability of the presence of prenosological changes in MEPhS male patients with VNSSD RFs of cardiovascular diseases on the total score according to the method developed by us.

When using the ROC-analysis of sensitivity and specificity of the method of predicting the risk of MEPhS prenosologic changes in male patients with CVD and building a characteristic curve, a good prognostic ability of this model was found. The area under curve was 0.846 ± 0.076 (95 % confidence interval is 0.696-0.996, $p < 0.0001$). With a threshold score of 8, diagnostic sensitivity was 80 %, specificity – 70.8 % (Fig. 2, 3).

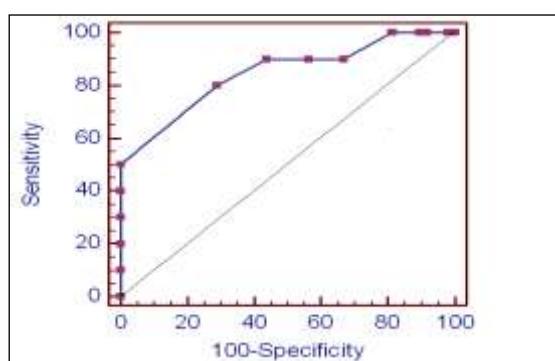


Fig. 2. ROC-curve of the method of diagnosing prenosological changes of MEPhS for individual prediction of prenosological conditions and increased risk for developing CVD in male patients with VNSSD.

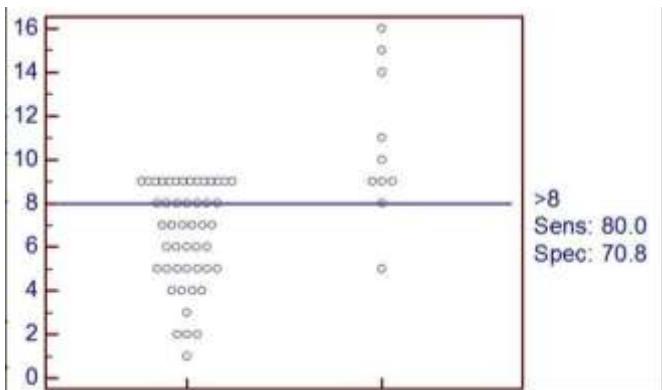


Fig. 3. Optimal cut-off thresholds for the method of diagnosing prenosological changes of MEPhS for individual prediction of prenosological conditions and increased risk of developing CVD in male patients with VNSSD depending on the distribution of patients according to the risk level and the total score

IV. CONCLUSIONS AND FINDINGS

1. Among the RFs of the CVD in male patients with VNSSD, stress, low PhA and smoking prevailed.

2. The diagnostic sensitivity of the method for determining changes in MEPhS for individual prediction of the prenosologic conditions and increased risk of developing CVD in male patients VNSSD with a threshold score of 8 was 80 %, specificity – 70.8 %.

3. The inverse moderate correlation was registered between the sum of points for all CVD RFs and the RRNN in T (8): $r = -0.41$ ($p = 0.0012$) and between the RRNN in T(8) and the II "Myocardium" in T(2): $r = -0.25$ ($p = 0.0500$). The direct moderate correlation dependence was between the sum of the scores for the RFs of CVD and the II "Myocardium" in T(2) in male patients with VNSSD: $r = 0.54$ ($p = 0.00001$).
 4. In male patients with VNSSD, the sum scores for CVD >8 reflects the tension of regulatory systems and the development of prenosological conditions.

It should be noted that throughout the entire period of the study of VNSSD, the attention of researchers has always been paid to the question of the relationship between mental disorders and somatic disorders. At different stages of the study of VNSSD, biologically and mentally oriented theories have contributed to the development and study of the psychosomatic direction of medicine. In foreign medicine, biologically and mentally oriented areas were also presented, and in practical medicine in Russia, for a long time, a biologically oriented direction prevailed. During each of these stages of the study of pathology, cardiovascular symptoms that occur in patients, scientists studied their causes most closely. The main result of the first period of study, which began in the XIX century in 1867, describing the symptoms of "irritated heart" among the soldiers of the British army in North America in McLean, was the idea of the leading role of psychological and physical overstrain in the development of the disease, its benignity polymorphism of complaints. With the introduction of the concept of "neurosis of the heart", the second period of the study of VNSSD began. B.S. Oppenheimer concluded that the multiple somatic symptoms that disturb patients are associated with impaired nervous regulation of the CVS and suggested the term "neurocirculatory asthenia." Studies of neurocirculatory asthenia, conducted in this period in Russia, led to the conclusion that this pathology, significantly affecting the working capacity of patients, has a favorable long-term prognosis and does not lead to fatal outcomes. The disease was classified as a disease of the CVS, developed classification criteria. The pathogenesis of suffering was actively studied, which allowed N. A. Kurshakov (1947) to make an assumption about the likelihood of "biochemical" disorders that underlie possible pathophysiological changes in the myocardium. Thus, the issue of the strength of the stressor capable of causing the transition of "functional" changes to "organic" changes in neurocirculatory asthenia was actively studied, and, consequently, the question of whether the disease was benign was questioned. The third period in the development of neurocirculatory asthenia is associated with an increase in the pace of life, the urban population, the development of functional diagnostics, the emergence of the concept of risk factors and the study of the influence of risk factors on human health. A group of scientists led by GF. Lang actively studied the cardiac component of the disease.

The result of this study was the concept of the possible development of myocardial dystrophy in a patient with neurocirculatory asthenia, i.e. view of the pathogenesis of the disease has changed. During this period, Soviet scientist V. Makolkin contributed greatly to the study of pathology. Abakumov, who believed that neurocirculatory asthenia should be treated by general practitioners, paid great attention to the differential diagnosis of suffering among other diseases of the CVS. The predominance of ideas about neurocirculatory asthenia, as a disease of psychogenic nature, was marked by the fourth period. Interest in the disease has declined. According to the International Classification of Diseases in 10 revisions, neurocirculatory asthenia is included in V section "Mental and behavioral disorders" and has the code F45.30 – somatoform dysfunction of the autonomic nervous system of the heart. In the US, VNSSD is included in the DSM-IV a manual, the genesis of the disease is considered from the position of the leading role of mental disorders. In DSM-V, the perspective on the diagnosis of somatoform disorders has changed [10, 11]. Currently, the term undifferentiated somatoform disorder has been replaced by a disorder that manifests itself with somatic symptoms, specifying that the patient has inadequate, excessive reactions to somatic symptoms. Perhaps we can talk about the fifth period of the study of borderline mental disorders, in connection with the proven prevalence among these patients psychosocial and behavioral risk factors. In our study, we tried to study the pathogenesis of VNSSD in patients with RFs CVD

Thus, we have proved that with the sum of the scores >8 for the CVD risk according to the method developed by us, prenosological conditions develop in male patients with VNSSD, which is a response to daily physical activity associated with the voltage of the electrophysiological state of the myocardium. One of pathogenetic mechanisms is an increase the activity of section of the VNS with the release into the blood of catecholamines and increase in heart rate [6,7]. Consequently, psychosocial RFs in combination with behavioral and biological RFs CVD through an increase in the activity of the sympathetic VNS and an increase in heart rate lead to hemodynamic and neurohumoral shifts in the functioning of the CVS. With the continued action of psychosocial, behavioral and biological CVD RFs, the adaptation reserves of the "interested" organ, in our study- the cardiovascular system, are depleted as a result of impaired neurohumoral regulation, and the pathological stage of general adaptation syndrome with CVD development is realized [8,9].

Modern scales that are used to assess cardiovascular risk (CVR) have a limited set of RFs. The method we have developed includes psychosocial RF, a family history of early CVD, overweight BM and obesity. According to the latest recommendations on cardiovascular prophylaxis, these RFs of cardiovascular diseases have reclassifying potential, i.e. can increase the CVR in their presence and reduce it. Thus, an interdisciplinary approach to the management of patients with VNSSD with the participation of doctors of different specialties is necessary.

References

- [1] N. Garganeeva, M. Belokrylova, "Clinical and socio-psychological background and determinants of the formation of "functional" cardiovascular disorders", Mental disorders in general med., vol. 01-02, pp. 36–43, 2016.
- [2] E. Anikina, N. Balabina, "Prevalence, risk factors, and the clinical course of autonomic dysfunction syndrome", Siberian Med. J. vol. 102, no. 3, pp. 23–27, 2011. Irkutsk.
- [3] V. Makolkin, "Neurocirculatory dystonia: myth or reality", Kardiologiiia, vol. 48, no 4, pp. 62–65, 2008.
- [4] Cardiovascular prophylaxis. National recommendations of the Committee of experts of the All-Russian Scientific Society of Cardiology, Cardiovascular therapy and prevention, vol. 10, no. 6, Appendix 2, p. 64, 2011.
- [5] G.G. Ivanov, R.M. Baevskii, E.Iu. Bersenev, V.B. Rusanova, I.M. Larina, L.Kh. Pastushkova, "Indices of electrocardiogram dispersion mapping during 5-day exposure in dry immersion", Aviakosm. Ekolog. Med., vol. 45, no 6, pp. 44–48, 2011.
- [6] E.Yu. Esina, V.V Lyutov, V.N. Tsigan, A.A. Zuykova, "Prevention of cardiovascular disease in patients with somatoform dysfunction of the vegetative nervous system", The EPMA J., vol. 8, no. S1, pp. 38–39, 2017.
- [7] E. Esina., A. Zuykova, Prevention of cardiovascular diseases in persons with mental illness Preventive medicine, vol. 21, no. 2-2, p. 51Y, 2018.
- [8] F.B. Ortega, M. Sánchez-López, M. Solera-Martínez, A. Fernández-Sánchez, M. Sjöström, V. Martínez-Vizcaino, "Self-reported and measured cardiorespiratory fitness similarly predict cardiovascular disease risk in young adults", Scand. J. Med. Sci. Sports, vol. 23, no. 6, pp. 749–757, 2013.
- [9] R. Seabra-Gomes, "Increased heart rate as a cardiovascular risk factor", Eur. J. Intern. Med., vol. 26(4), pp. 217–222, 2015.
- [10] S.M. van Geelen, P.A. Rydelius, C. Hagquist, "Somatic symptoms and psychological concerns in a general adolescent population: Exploring the relevance of DSM-5-somatic symptom disorder", J. Psychosom Res., vol. 79, no. 4, pp. 251–258, 2015.
- [11] C.M. van der Feltz-Cornelis, B. van Houdenhove, "DSM-5: from 'somatoform disorders' to 'somatic symptom and related disorders'", Tijdschr Psychiatr, vol. 56, no. 3, pp. 182–186, 2014.