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Prognostic value of serum soluble ST2 in professional athletes
Valor pronóstico de ST2 soluble en suero en deportistas profesionales

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Abstract. Background: The predictive value of serum soluble ST2 (sST2) biomarker for diagnostics of cardiovascular pathologies is still poorly understood as well as the role of psychological stress on the risk of heart disease. Aim: This study aimed at determining the diagnostic significance of the sST2 level in athletes involved in speed-strength sports. In addition, stress as a risk factor for the development of cardiovascular pathology was assessed and analysed as well. Methods: A prospective study on Greco-Roman wrestlers was carried out at the Centre for Sports Medicine and Rehabilitation (Almaty, Republic of Kazakhstan). All participants (n = 30) were males aged 20 to 34 years. The control group consisted of volunteers (VO) (n = 30). Anthropometric and hemodynamic parameters of athletes were studied along with electrocardiography (ECG) and ECG tests. The sST2 level was determined before (BT) and immediately after (AT) training. The stress level was determined using The Perceived Stress Scale-10 (PSS-10). Results: The average age of the athletes was 26.57 ± 3.6 years. The total training experience was 14.57 ± 4.02 years. According to the ECG data, minor deviations from the norm (13.3%) and an abnormal ECG (33.3%) were identified. Echo-CG data showed «moderate» and «pronounced changes» in 23.3% and 53.3% of cases, respectively. The sST2 level of VO (337.1 ± 61.8 pg / mL) was lower than that of BT (548.1 ± 32.6 pg / mL) (p d» 0.001). The sST2 level of AT, it was significantly higher (830.01 ± 71.6 pg / mL) than BT (p d» 0.001). The average and high level of stress among athletes was in 43.3% and 56.7% of cases, respectively. Stress increased the likelihood of developing distinctly abnormal ECG (OR = 1.06, 95% CI 1.01–1.08; p = 0.02). The stress level showed a positive correlation with the sST2 level (r = 0.752, p = 0.01). The sST2 concentration and categorical echocardiography data demonstrated a dependent positive correlation (r = 0.6, p = 0.01). Conclusions: Athletes' sST2 levels exceeded thresholds both before and after training. Moreover, the relationship between an increase in sST2 levels and abnormal ECG abnormalities and a high level of stress in athletes was determined. sST2 concentration was associated with cardio-pulmonary stress triggered by the cumulative exercise dose as well as with lifelong psychological stress. Our findings indicate that the elevated sST2 concentrations in athletes could be used as the predictive value. However, clinical relevance and results validity require further intensive studies.

Keywords: solubleST2; biomarker; heart hypertrophy; stress; athletes.

Resumen. Antecedentes: El valor predictivo del biomarcador ST2 soluble en suero (sST2) en la enfermedad cardiovascular aún no se conoce bien, así como el papel del estrés psicológico en el riesgo de enfermedad cardiovascular. Objetivos: Este estudio tuvo como objetivo determinar la importancia diagnóstica del nivel de sST2 en atletas involucrados en deportes de velocidad-fuerza. Además, también se evaluó y analizó el estrés como factor de riesgo para el desarrollo de patología cardiovascular. Métodos: Se llevó a cabo un estudio prospectivo sobre luchadores grecorromanos en el Centro de Medicina y Rehabilitación del Deporte (Almaty, República de Kazajstán). Todos los participantes (n = 30) eran hombres de entre 20 y 34 años. El grupo de control estaba formado por voluntarios (VO) (n = 30). Se estudiaron los parámetros antropométricos y hemodinámicos de los atletas junto con las pruebas de electrocardiografía (ECG). El nivel de sST2 se determinó antes (BT) e inmediatamente después (AT) del entrenamiento. El nivel de estrés se determinó utilizando la Escala de Estrés Percibido-10 (PSS-10). Resultados: La edad promedio de los deportistas fue de 26,57 ± 3,6 años. La experiencia de formación total fue de 14,57 ± 4,02 años. Según los datos del ECG, se identificaron desviaciones menores de la norma (13,3%) y un ECG anormal (33,3%). Los datos de Echo-CG mostraron cambios «moderados» y «pronunciados» en el 23,3% y el 53,3% de los casos, respectivamente. El nivel de sST2 del grupo VO (337,1 ± 61,8 pg / mL) fue menor que el de BT (548,1 ± 32,6 pg / mL) (p d» 0,001),). El nivel de sST2 en AT fue significativamente mayor (830.01 ± 71.6 pg / mL) que en BT (p d» 0.001). El nivel medio y alto de estrés entre los deportistas fue del 43,3% y el 56,7% de los casos, respectivamente. El estrés aumentó la probabilidad de desarrollar un ECG claramente anormal (OR = 1,06; IC del 95%: 1,01-1,08; p = 0,02). El nivel de estrés mostró una correlación positiva con el nivel de sST2 (r = 0,752, p = 0,01). La concentración de sST2 y los datos de la ecocardiografía categórica demostraron una correlación positiva dependiente (r = 0,6, p = 0,01). Conclusión: Los niveles de sST2 de los atletas excedieron los umbrales tanto antes como después del entrenamiento. Además, se determinó la relación entre un aumento en los niveles de sST2 y anomalías anormales del ECG y un alto nivel de estrés en los atletas. La concentración de sST2 se asoció con el estrés cardiopulmonar desencadenado por la dosis acumulativa de ejercicio, así como con el estrés psicológico de por vida. Nuestros hallazgos indican que las concentraciones elevadas de sST2 en los atletas pueden usarse como valor predictivo. Sin embargo, se requieren más estudios.

Palabras clave: soluble ST2; biomarcador; hipertrofia cardíaca; estrés; atletas.

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Introduction

The assessment of specific biomarkers is critical for the prediction of the risk of developing heart disease (Albert, 2011). One of these biomarkers is the ST2 receptor for interleukin 1, also known as the interleukin-1 receptor-like 1 (IL1RL-1) (Pascual-Figal & Januzzi, 2015). Previous studies have demonstrated the importance of determining the level of sST2 as a biomarker of various pathological processes (Kakkar & Lee, 2008). It has been shown that the concentration of sST2 in the blood increases in many inflammatory diseases (Mueller & Jaffe, 2015). For instance, Weinberg et al. (2003) showed that the levels of circulating serum sST2 might be employed for the assessment of patients with chronic severe heart failure.

Taking into account that symptoms of cardiovascular pathology can be hidden due to adaptive mechanisms, heart diseases can develop asymptomatically (Lee, Chandel, & Simon, 2020; Nakamura & Sadoshima, 2018; Shevchenko, Bohmat, Holovko, & Demianenko, 2019). The pathways leading from biomechanical overload to cardiac remodeling are of primary clinical importance, but this process remains not fully defined (Weinberg et al., 2002).

Therefore, there is a need to expand the choice of diagnostic tools for the timely detection of cardiac disorders and the prevention of possible complications (Kovacs & Baggish, 2016). Aengevaeren et al. (2019) showed that the change in the concentration of sST2 in the blood could be used as a predictor of cardiovascular disease in runners (before and after exercise). However, it must be noted that this study did not compare the level of this biomarker in people who are not involved in sports.

Given the fact that there is a different classification of physical activity depending on the type of sport (Garcia, Muñiz, Rodriguez, & Suarez, 2016; Holfelder, Klotzbier, Eisele, & Schott, 2020; Howley, 2001; Schnell, 2019), it can be assumed that changes in the cardiovascular system of athletes may significantly vary (Barbas et al., 2011). In turn, the concentration of sST2 in various types of sports can also differ. In this regard, prolonged physical activity in athletes can trigger an increase in the size of the heart by 10-20% (Sharma, Merghani, & Mont, 2015). Athletes engaged in strength sports develop pure concentric hypertrophy of the left ventricle leading to an increase in both absolute and relative wall thickness and a significant increase in the diameter of the left ventricle (Pluim, Zwinderman, van der Laarse, & van der Wall, 2000). Apart from that, it should be noted that cardiac fibroblasts and cardiomyocytes produce circulating ST2 in response to stress and overload (Weinberg et al., 2002).

In fact, focussing on the development of strength can lead to exceeding the recommended limit of physical activity, and developing possible complications (Kovacs & Baggish, 2016).

Unfortunately, not only excessive physical activity in athletes (Gustafsson, Sagar, & Stenling, 2017) is a risk factor for cardiac disorders. It has been shown that psychological distress during competitions is an important negative factor as well (Villarreal-Angeles, Rodriguez Vela, Tapia Martínez, Gallegos Sanchez, & Moncada-Jimenez, 2021). Hence, the constant fear of failure and loss also potentiates the impact of psycho-emotional stress on physical health (Proietti et al., 2011). The negative role of emotional stress as a trigger for the development of acute coronary disorders was described by Wilbert - Lampen et al. (2008). It was demonstrated that the incidence of cardiovascular complications was doubled not only among athletes, but also among spectators (during the sports matches).

It has been shown that stress may be the most important factor, but it is not the only a cause for the development of cardiac complications in people with pre-existing cardiovascular disorders (Rafanelli, Roncuzzi, Ottolini, & Rigatelli, 2007). However, it is worth noting that psycho-emotional stress is still one of the main factors in the development of cardiovascular diseases (Steptoe & Kivimäki, 2012) and damage of cardiomyocytes (Alevizos, Karagkouni, Panagiotidou, Vasiadi, & Theoharides, 2014). In this regard, the purpose of this study was to identify the diagnostic significance of the sST2 level in athletes engaged in sports (focused on 'speed-strength'). In addition, the study aimed at the assessment of stress as a risk factor for the development of pathology of the cardiovascular system.

Materials and Methods

Participants

This is a prospective non-randomized study with the participation of 30 male athletes aged 20-34 years (Greco-Roman wrestling) with an experience of 5 years or more continuous training and competition. The study was conducted on the basis of the Centre for Sports Medicine and Rehabilitation (Almaty, Republic of Kazakhstan). During preparation, athletes adhered to a standard diet in accordance with standard time ranges corresponding to normal competitions.

As a control group (VO), the study included 30 volunteers aged 20-34: young people who are not involved in professional sports.

Ethical issues

The study was approved by the Ethical Committee of Kazakh Medical University of Continuing Education, Almaty, Kazakhstan. All athletes were fully informed about the experimental procedures, the possible risks and benefits associated with their participation in the study.

General information

Depending on their age, the study participants were sub-divided into 3 age categories: 20-24 years old, 25-29 years old and 30-35 years old. The athletes possessed the following official sports qualifications, including Master of Sports (MS), Master of Sports of International Class (MSMK) and Honoured Master of Sports (ZMS). The level of systolic blood pressure (SBP) and diastolic blood pressure (DBP) at rest was determined according to the ACC / AHA guidelines (Drawz et al., 2020). The pulse rate at rest (Alexis, 2010), level of VO_{2max} (Hawkins, Raven, Snell, Stray-Gundersen, & Levine, 2007), weight and height (SECA, model M20812, Hamburg, Germany), body mass index (BMI) were calculated according to the standard formula (Wan Nudri, Wan Abdul Manan, & Mohamed Rusli, 2009).

ECG Data Analysis

Before the ECG study, athletes kept a horizontal position for 5 minutes, to adapt to environmental conditions. The study was carried out in the morning time at an air temperature of at least 22 ° C (Sharma et al., 2017). ECG analysis was performed in 12 leads, recording speed 50 mm / s, in the supine position, using the BTL Cardiopoint ECG C600 (UK) apparatus. ECG data were analysed at the Research Institute of Cardiology and Internal Medicine (Almaty, Kazakhstan) by two independent cardiologists and divided into three subgroups (normal, mildly abnormal, and abnormal) according to a previous study (Koch, Cassel, Linné, Mayer, & Scharhag, 2014).

Echocardiographic Data Analysis

Echocardiography was performed using an ACUSON S1000 ultrasound machine of the HELX Evolution series (Germany). In accordance with the recommendations of the American Society of Echocardiography (Churchill et al., 2020) the following parameters were determined: LV volume, mass, relative wall thickness, mitral flow velocity, tissue Doppler velocity, LAV, LVEF. Left atrial deformity and global longitudinal LV deformity were measured using 2D speckle tracking software (Cameli et al., 2017).

Plasma / Serum IL1RL1 (ST2) Determination

Blood samples were taken on an empty stomach, according to standard protocol rules (Giavarina & Lippi, 2017), from the antecubital vein (10 ml), 30 minutes before exercise (BT) and within two hours after exercise (AT). Blood samples were placed in test tubes (Ayset, Turkey) and centrifuged at 300g for 10 min, then frozen, and stored at -70 ^{0} C for the analysis (Boisot et al., 2008). The sST2 concentration was determined using a commercial human sST2 ELISA kit (Westang Biotech Co., Shanghai, China) according to the manufacturer's instructions (Chen et al., 2018).

It has been shown that an intensive trainings can affect the occurrence of haematological changes in blood (for example, on the level of haemoglobin, haematocrit) (Santos, 2018). Hence, to calculate changes in plasma volume by determining the levels of haemoglobin and haematocrit (to assess the degree of dehydration), 2 ml of venous blood was additionally taken before and after training for evaluation according to the previously described method (Dill & Costill, 1974).

The analysis was carried out in a certified (ISO 15189-2015) scientific clinical diagnostic laboratory of the Scientific Research Institute of FPM named after B. Atchabarov (Almaty, Kazakhstan).

Characteristic of physical activity

The standard training of the study participants consisted of a set of 3-hour exercises for sequential execution. In addition, daily training included outdoor walking, warm-up for 15 minutes before the main set of exercises. The main routine of physical activity consisted of several types of exercises related to general and special physical training. In terms of the complex of general physical training, exercises were performed on gym machines (1.5 hours), such as a horizontal bar (4 sets x 25 reps), parallel bars (4 sets x 30 reps), and exercises to strengthen the muscles of the back (4 sets x 20 reps), the press (4 sets x 25 reps) and jumping out with a pancake (4 sets x 20 reps). According to the special physical training exercises, the athletes practiced wrestling techniques (1.5 hours).

Evaluation of level of stress

The level of perceived stress and subjective perception of the level of tension in athletes was assessed using the «The Perceived Stress Scale-10» («PSS-10») questionnaire. The PSS-10 questionnaire consists of 10 questions and determines how stressful people think the previous month of their life (Anwer, Manzar, Alghadir, Salahuddin, & Abdul Hameed, 2020). Answer options are scored on a 5-point Likert scale (0-4), with scores as follows: 4: never, 3: rarely, 2: sometimes, 1: often, 0: always. It should be noted that items 4, 5, 7 and 8 were calculated positively. An overall score of 13 corresponds to normal stress levels, and a score of 20 or higher indicates 'high-stress' levels requiring therapeutic intervention (Cohen, 1988).Thus, the results obtained can be interpreted as follows: normal score (0-13), average score (14-20) and high score: (> 20)[33].In our study, we used an adapted version of the PSS-10 questionnaire in Russian language.The choice of version 10 of the PSS questionnaire in comparison with other available versions such as PSS-7 and PSS-14 was justified by the fact that the analysis of previous studies shows higher psychometric properties of the PSS-10 questionnaire (Lee, 2012).

Statistical analysis

Statistical analysis was performed using SPSS Statistics 25 programme (SPSS Inc., Chicago, Illinois, USA). Data normality was verified using the Kolmogorov-Smirnov test and the homogeneity of variances (Levene test) were confirmed (p> .05). Once the normal distribution was confirmed, studying groups were compared using the unpaired and paired Student s t test. The statistical significance was set at $p<0.05$.

Results

The average age of athletes was 26.57 ± 3.6 years (Table 1). By age groups, athletes aged 20-24 years accounted for 33% (n = 10), 25-29 years were in 50% (n = 15), 30-35 years was 16.7% (n = 5). The total training experience was 14.57 ± 4.02 years. According to anthropometric data, the average weight and height were equal to 80.03 ± 18.9 kg and 174.02 ± 9.5 cm, respectively, the BMI was 26.03 ± 3.49 kg / m^2. The median plasma volume change was 0% (-5% to 4%).

The SBP level was 119.67 ± 7.64 mm Hg, the DBP was 79.50 ± 6.9 mm Hg, the pulse rate was 65.6 ± 9.5 beats / min., the average maximum oxygen uptake was 67.3 ± 4.2 ml / kg / min. In the sports category, the overwhelming majority of athletes' n = 19 (63.3%) were Master of International Sports, n = 9 (30%) were Master of Sports and n = 2 (6.7%) were Honoured Master of Sports.

Table 1
General characteristics of research participants

Data (N -30)	**Average**	**SD**	**Min**	**Max**
Age	26.57	3.569	20	34
20-24 n(%)		10 (33)		
25-29 n(%)		15 (50)		
30-35 n(%)		5 (16.7)		
Experience (years)	14.5	4.0	10	22
Weight (before training)	80.0	18.9	57	127
Weight (after training)	78.2	17.5	56	127
Height	174.0	9.5	160	201
Body Mass Index (kg/ m^2)	26.0	3.4	20.7	35.2
Systolic blood pressure (rest)	119.6	7.6	105	140
Diastolic blood pressure (rest)	79.5	6.9	70	90
Pulse (rest)	65.6	9.4	55	89
VO_{2max} (ml / kg / min)	67.3	4.2	58	72
Sports qualifications n(%)				
Master of Sports		9 (30)		
Master of International Sports		19 (63.3)		
Honoured Master of Sports		2 (6.7)		

ECG data showed that, R or S wave 25–29 mm in n = 21 (70%) cases, R or S wave equal to 30–34 mm in n = 2 (6.6 %) cases, R or S wave 35 mm and 30 ° d»QRS axise»110 ° in n = 3 (10%) cases, sinus bradycardia < 60 bpm in n = 12 (40%) cases, flat / tall T wave n = 3 (10%) and Q wave 2-3 mm n = 4 (13.3%), left bundle branch block (LBBB) only n = 1 (3.3 %) case. Analysis of ECG data (Table 2) for three subgroups (normal, with minor deviations and abnormal) demonstrated a normal ECG in n = 16 (53.4%), with minor deviations in n = 4 (13.3%) and in n = 10 (33.3 %) cases are abnormal.

Table 2
Distribution of study participants according to ECG data into three subgroups

Normal ECG n(%) – 16		Mildly abnormal ECG n(%) – 4		Distinctly abnormal ECG n (%) – 10	
R or S wave 25–29 mm	21(70)	R or S wave 30–34 mm	2(6.6)	R or S wave 35 mm	7(23.3)
ST segment elevation	00)	Flat/tall T wave	3(10)	T wave inversion	0(0)
Incomplete RBBB	3(10)	Q wave 2–3 mm	4(13.3)	Q wave _4 mm	0(0)
PR interval >0.20 s	2(6.6)	Incomplete R wave progression V1 to V3	0(0)	30°=QRS axis=110°	3(10)
				LAD/RAD	0(0)
Sinus bradycardia<60 bpm	12(40)	PQ interval =0.12 s	0(0)	LBBB	1(3.3)
		RBBB	0(0)	WPW	0(0)

Notes: Incomplete RBB: incomplete right bundle branch block. RBBB: right bundle branch block. LBBB: left bundle branch block. LAD: left axis deviation. RAD: right axis deviation. WPW: Wolff-Parkinson-White syndrome. Values presented as n (%);

The results of echocardiography in athletes (Table 3) showed the mean left atrial diameter (LAD) was 38.9 ± 6.2 ml, the size of the interventricular septum (IVS) was 1.1 ± 0.19 cm, the thickness of the posterior wall (PW) was 1.03 ± 0.15 cm, and the diameter of the aortic root (AO) was 3.04 ± 0.46cm. The ratio of left ventricular diastolic diameter / body surface area / (LV EDD / BSA) was 48.2 ± 20.6 mm / cm2, left ventricular diastolic diameter was 4.9 ± 0.28 cm. EDW and ESV were 117.6 ± 15.58cm and 41.6 ± 7.3cm, respectively. The EF percentage was 64.9 ± 3.08%.

The average left ventricular mass (LV mass) was 188.27 ± 37.5 gr, and the LVM was 105.7 ± 26.3 gr / m^2. The E-wave / A-wave (E / A) ratio was 1.29 ± 0.26, and the relative wall thickness (RWT) was 0.38 ± 0.07.

Table 3
Cardiac dimensions (M ± SD) and upper reference limits (URL)

Characteristics	Diaposon	Min	Max	Average	Standard deviation
LAD (ml)	22	26	48	38.9	6.2
IVS (cm)	0.7	0.7	1.4	1.12	0.1
PW (cm)	0.6	0.8	1.4	1.03	0.1
LV EDD/BSA (mm/cm^2)	73	14	87	48.23	20.6
LV EDD (mm)	1.2	4.3	5.5	4.98	0.2
? O (cm)	1.5	2.3	3.8	3.04	0.4
EDW (ml)	65	83	148	117.6	15.5
ESV (ml)	29	27	56	41.63	7.3
EF (%)	13	59	72	64.93	3.0
LV mass (gr)	157	116	273	188.27	37.5
LVMi (gr/m^2)	111	50	161	105.70	26.3
E/A	1.5	1.1	1.5	1.293	0.2
RWT	0.47	0.32	0.47	0.3843	0.07

Notes: URL: upper reference limit. LRL: lower reference limit. LV EDD: left ventricular end-diastolic diameter. BSA: body surface area. IVS: interventricular septum, PW: posterior wall thickness. RWT: relative wall thickness. E: E-wave. A: A-wave. LAD: left atrial diameter. AO: aortic root diameter. RV EDD: right ventricular end-diastolic diameter. Echocardiographically determined cardiac dimensions presented as M ± SD;

sST2 level in the blood sample

To determine the level of sST2 expression in blood serum, first the serum sST2 level in VO at rest and in athletes in BT was analysed. The results showed (Figure 1) that sST2 levels were significantly higher (*p* d™ 0.001) in the BT 548.1 ± 32.6 pg / mL group than in the VO 337.1 ± 61.8 pg / mL. Serum sST2 level for AT 830.01 ± 71.6 pg / mL was significantly higher than BT (*p* d™ 0.001) (Figure 2).

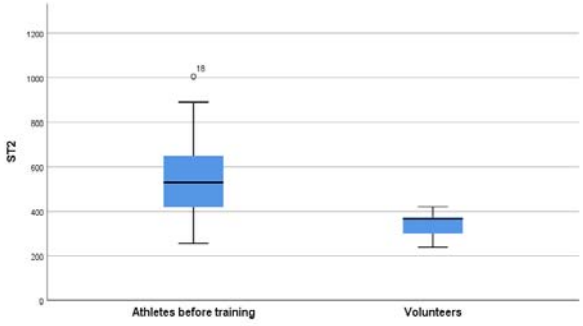

Figure 1
Analysis of serum sST2 levels in volunteers (VO) (n = 30), athletes before training (BT) (n = 30)
Data presented as median (IQR); *p*=0.001; BT compared to VO;

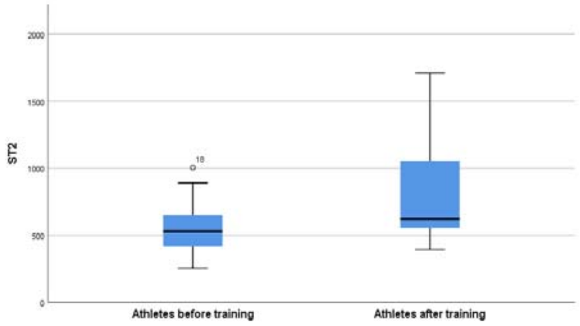

Figure 2
Analysis of serum sST2 levels in athletes before (BT) (n = 30) and athletes after training (AT) (n = 30). Data presented as median (IQR), p=0.001, BT compared to AT;

Evaluation of the results of perceived stress PSS-10 (Table 4) showed that the absence of athletes with normal stress levels, n = 13 (43.3%) was at an average level and n = 17 (56.7%) experienced a high level of stress. The average score on the stress scale was 24.0 ± 6.7.

In the age category 20-24 years old n = 4 (30.8%) athletes scored 14-20 points, above 20 points in this age category were determined in n = 6 (35.3%) participants. Athletes aged 25-29 received 14-20 points in n = 7 (53.8%) cases, and a high level of stress was identified in n = 8 (47.1%) respondents.

Table 4
Indicators for assessing perceived stress PSS-10, depending on age

Characteristics	Score PSS-10 n(%)			
	0-13	14-20	20and more	M ± SD
Stress scale	0(0)	13(43.3)	17(56.7)	24.0±6.7
20-24years	0(0)	4(30.8)	6(35.3)	24.4±6.1
25-29years	0(0)	7(53.8)	8(47.1)	23.8±6.7
30-35years	0(0)	2(15.4)	3(17.6)	23.6±9.0
Physical exertion*	13.50±5.368			
Resistance*	10.50±2.776*			

Notes: PSS-10: The Perceived Stress Scale-10. * Data presented M ± SD;

In univariate analysis, perceived stress increased the likelihood of prevalence of Distinctly abnormal ECG (OR = 1.06, 95% CI 1.01–1.08; *p* = 0.02).

The assessment of the stress level depending on the three components of the ECG study (normal, with minor deviations and abnormal) indicated that the level of perceived stress was significantly higher in athletes with distinctly abnormal ECG 23.9 ± 1.2 versus 19.7 ± 0.7 (*p* = 0.05) in Mildly abnormal and against 17.4 ± 1.2 (*p* = 0.001) in Normal ECG.

The sST2 concentration and categorical echocardiography data demonstrated a dependent positive correlation (r = 0.6, *p* = 0.01) The level of the stress showed a positive correlation with the sST2 level (r = 0.752, *p* = 0.01) (Figure 3).

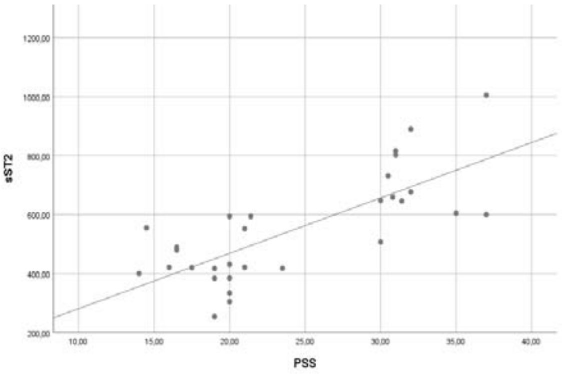

Figure 3
Correlation of stress level (PSS) and sST2 concentration in athletes
Data are presented as median (IQR), r = 0.752, p = 0.01

Discussion

To the best of our knowledge, this is the first study on the assessment of the concentration of sST2 as a possible indicator of the development of heart disorders in athletes engaged in strength sports. The results obtained showed a comparatively high level of sST2 in combat athletes before training in comparison with the control group. In addition, we observed an increase in the concentration of sST2 after training. Our data are consistent with previous reports, where sST2 scores were above cut-off values in 48% of professional runners before the start of a marathon and in 92% after a marathon run (Aengevaeren et al., 2019).

It has previously been shown that young athletes under 35 years old, in comparison with their peers who are not athletes, had an increased risk of sudden death due to cardiovascular diseases (Corrado, Basso, Rizzoli, Schiavon, & Thiene, 2003). Adaptive mechanisms that develop during intense physical exertion lead to functional and structural changes in the cardiovascular system (Dickhuth, Röcker, Mayer, König, & Korsten-Reck, 2004). Moreover, the thickness of both the septum and the posterior wall of the heart increases to the same extent as the internal volume (van de Schoor et al., 2016). The ratio of mass to volume and, therefore, the maximum systolic wall stress remains constant, in contrast to the pathological forms of hypertrophy (Dickhuth et al., 2004). These findings indicate the need for dynamic monitoring of the state of the cardiovascular system of athletes.

It should be noted that compared to other biomarkers such as natriuretic peptides and troponins (Aimo et al., 2019; Berg, Ruff, & Morrow, 2021; Cediel et al., 2021; Perrone et al., 2020; Wallentin et al., 2021), sST2 concentration is independent on the age, renal function or body mass index (Dieplinger et al., 2009). These findings were confirmed in our study as well.

The pathophysiological explanation for the increase in the concentration of sST2 in the blood serum can be linked to the susceptibility of the sST2 gene to the mechanical stress in cardiac myocytes (Weinberg et al., 2003). However, the question of whether sST2 is an indicator of structural changes in the myocardium remains controversial. Some researchers have come to the conclusion that the concentration of sST2 in non-ischemic heart failure reflects the level of hemodynamic stress, but the pathogenic processes in the myocardium (Broch et al., 2015). In addition, sST2 concentration is dependent on endothelial cells, but not in cardiomyocytes (Demyanets et al., 2013).

Apart from that, the concentration of sST2 level can be high in other various pathologies as well (Socrates et al., 2010; Tajima et al., 2007). However, the concentration of sST2 is associated with cardiac fibrosis, and some experiments have shown that sST2 has been expressed in mechanically stressed cardiomyocytes (Weinberg et al., 2002).

According to the PSS-10 questionnaire, all athletes had a medium or high level of stress, of which 57.6% of athletes with scores above 20 on this scale had indirect indications for therapeutic assistance. Cardiovascular changes caused by stress associated with the secretion of catecholamine are similar to those observed during exercise (Gavrilovic, Spasojevic, & Dronjak, 2012; Hammadah et al., 2017; Sarvasti et al., 2020; Webb, Rosalky, McAllister, Acevedo, & Kamimori, 2017).

In the situation when the heart rate and myocardial contractility increase, peripheral vasoconstriction leads to a significant elevation of arterial pressure (Shephard, 1997). In addition, it is necessary to note the important role of not only activation of the sympathetic nervous system in response to stress factors, but also a decrease in cholinergic activity. It can result in an increase in cortisol levels and a decrease in glucocorticoid sensitivity. In turn, it may lead to vascular complications causing cardiovascular pathologies (Wirtz & von Känel, 2017).

In a previous study, echocardiographic findings did not show any pathological correlation between elevated sST2 levels and left ventricular function (Quick et al., 2015), its diameter or mass, but this relationship was found out in another study (Shah, Chen-Tournoux, Picard, van Kimmenade, & Januzzi, 2009). In the present study, distinctly abnormal changes in the ECG were detected, which had a statistically significant relationship not only with an increase in sST2 concentration ($p = 0.01$), but also with the level of stress perception ($p = 0.01$). The results obtained indicate the importance of the sST2 concentration in the diagnosis of the cardiovascular system; however, due to its narrow specificity, it is not possible to assert the full role of increasing the sST2 concentration as a predictor of cardiovascular pathology.

The stress associated with participating in multiple sports tournaments can also potentiate the chances of developing cardiovascular disorders, although this influence is largely indirect (Ogilvie et al., 2016). Therefore, there is a need to pay attention to psychotherapeutic support as one of the important components of preventive measures. Our findings indicate that regular monitoring (biochemical and psychological) of the level of stress in athletes can help to optimize the physical activity in the early stages (González-Boto, Salguero, Tuero, González-Gallego, &

Márquez, 2008).

Study limitations

This prospective study has some limitations, including a small study sample. Further randomized controlled studies with a longer observational period of changes in a relatively large sample of athletes are needed to interpret the full mechanism of the development of adaptive processes and structural changes in cardiac tissue during the stress. It should encompass an accurate determination of the relationship between stress and the level of sST2 concentration in sportsmen.

Conclusions

Our data showed that athletes' sST2 levels exceeded thresholds both before and after exercise. Moreover, the relationship of increased sST2 levels with abnormal ECG abnormalities and high-stress levels in athletes was determined. The sST2 concentration is associated with cardiopulmonary stress induced by the cumulative exercise dose as well as psychological stress. The role of elevated sST2 level in athletes under the stress requires further intensive studies.

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Conflicts of Interest

The authors declare no conflict of interest.

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