Original Article

Data analysis of autoimmune bioindicators in the context of predicting cardiomyocyte damage

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ABSTRACT

This study was aimed at assessing the diagnostic significance of Anti-ACTC1, Anti-MYH7B, and Anti-cTnI autoantibodies at the molecular level, as well as their relationship with the results of electrocardiography in predicting damage to the heart muscle in athletes under conditions of physical stress. A medical examination was conducted on 35 men aged 8 to 25 years divided into 2 groups: proffessional basketball players and participants with the usual amount of total motor activity. The study included consultation with medical specialists, physical development research; psychological questionnaires; laboratory screening; and instrumental diagnostics. The values of blood parameters in athletes exceed the reference intervals: the content of erythrocytes by 15.8%, hemoglobin by 11.25%, and hematocrit by 9.1%. The concentration of testosterone in athletes is within the normal range, but during training, it can decrease by 35.5%, indicating anabolism and muscle growth, or overstrain or negative factors. It was found intense stress and emotional stress can cause myocardial stress, microtrauma, and inflammation in the heart muscles, stimulating the immune response and expression of serum antibodies anti-ACTC1, anti-MYH7B, anti-cTnI, as a result of pathophysiological remodeling of the myocardium.

Keywords: Autoantibodies to cardiomyocyte proteins, Exercise, Sex hormones, Cardiospecific immunoglobulins

Introduction

The pathophysiology of morphofunctional myocardial injuries under conditions of physical and psychoemotional stress is the most frequent and rapidly progressing problem of public health and sports medicine. Morphofunctional myocardial damage refers to diseases such as coronary heart disease, strokes, arterial hypertension, arrhythmias, and other cardiovascular abnormalities [1].

Cardiovascular diseases (CVD) occur due to various factors, including prolonged stressful effects of physical overload on the heart. The INTERHEART study showed that physical stress is one of the factors contributing to the development of CVD. The combination of factors associated with physical stress plays an important role in the occurrence of damage to the heart and blood vessels and is the basis for the development of myocardiodystrophy, hypotrophy, heart attack, coronary spasm, and sudden cardiac death (SCD) [2].

In persons engaged in professional sports, myocardial hypotrophy is one of the main reactions of the heart to physical activity. In 90% of cases, this causes the development of SCD and sudden cardiac arrest in athletes [3-8]. It should be noted that the number of cases of SCD among athletes is 2-3 times higher than that among people with normal motor activity [9].

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Between 1994 and 2006, 1,290 cases of SCD were reported, and 576 cases between 1989 and 1993. During the entire period from 1966 to 2004, 1,101 cases of sudden death of athletes under the age of 35 were documented [5]. The results of foreign studies have revealed significant gender differences in the incidence of SCD: in men, the frequency of SCD is more than 9 times higher than that of women [10]. At the same time, football is the most common occurrence of SCD among athletes, followed by basketball [11, 12].

It is believed that a high percentage of cases of SCD among basketball players is associated with some features of their anthropometric data [13, 14]. One of these features is the high height of most basketball players. They also have the phenomenon of a "big heart", which serves to provide the necessary blood supply and oxygen delivery to the muscles during intense physical activity. Intensive training and competitions create stress for the heart of basketball players, a constant increase in heart rate and blood pressure puts additional stress on the heart and increases the risk of heart problems.

It should be noted that in Russia there is no systematic monitoring of the incidence of SCD in people involved in sports. Consequently, there are no official recommendations for the early detection of athletes at increased risk of developing SCD. Without such data and recommendations, it becomes difficult to identify athletes who may be at risk and require more thorough examination and monitoring.

The introduction of monitoring and systematic collection of data on SCD among athletes would be of great importance to ensure the safety of athletes and prevent cases of SCD. This would make it possible to develop effective strategies and recommendations for early detection and intervention in relation to athletes at risk and would improve the overall safety of sports activities.

This issue is very relevant due to the growing number of cases of CVD in athletes. Intense physical activity, especially with high training volumes and intensity, can lead to the development of various disorders and pathological conditions of the cardiovascular system.

To prevent or minimize the development of heart pathology in athletes, it is necessary to understand the mechanisms of its formation. Research in this area can help identify factors contributing to the development of pathology, such as genetic predisposition, congenital and acquired abnormalities, environmental exposure, etc. This will allow taking measures to prevent the occurrence of pathology or its further progression.

In addition, it is necessary to develop new approaches and tools for early diagnosis of heart pathology in athletes. Traditional diagnostic methods such as ECG, echocardiography, and stress tests may not be sensitive enough and specific enough to identify the initial stages of myocardial pathology. The development of new research methods, such as laboratory molecular indicators, may make it possible to detect pathological changes in the myocardium at an earlier stage and take timely measures to correct them.

In general, it is important to conduct comprehensive studies of the mechanisms of formation of heart pathology in athletes and work on the development of new approaches and tools for early diagnosis. This will make it possible to more effectively control and prevent the development of cardiovascular problems in athletes while maintaining their health and ability to train and compete.

The method of determining the serum content of autoantibodies (auto-AT) to cardiomyocyte proteins (cTnI, ACTC1, MUN7B) can be an informative method for the prenosological diagnosis of emerging disorders in the myocardium [15-17].

Pathophysiological changes in conditions of physical overload lead to breakdowns of the cardio-contractile apparatus in proteins with myofibril filaments, where death or dramatization of myocytes is inevitable, where intracellular proteins are released from the cytoplasm of cardiomyocytes [18]. The released intracellular proteins can cause an inflammatory response and activation of pathological processes in the heart muscle, which can lead to cardiac dysfunction and insufficiency in general. The determination of the serum auto-AT content to cardiomyocyte proteins makes it possible to detect the presence of these antibodies in the patient's blood. If such antibodies are present, this may indicate autoimmune processes in which the immune system attacks its heart cells [19].

Thus, the method of early diagnosis of myocardial condition in athletes, based on the analysis of products of damage to cardiomyocytes and the content of serum autoantibodies, presents a prospect for identifying possible health problems and taking preventive measures. If problems are identified at an early stage, preventive measures can be taken to prevent the deterioration of the condition and ensure the continued performance of the athlete.

Various experimental studies have revealed a clear link between the immune system response and changes occurring in the heart muscle during adaptation to various physical activities, depending on their duration and intensity [20, 21].

The results of the conducted experimental studies suggest that the determination of auto-AT to cardiomyocyte proteins in athletes is an informative method for determining the nature of adaptive processes at different stages of sports activity, including pathological damage to cardiomyocytes.

The main purpose of this study was to identify how molecular autoimmune indicators can be used to predict damage to the heart muscle in athletes. To achieve this goal, a comparative study was conducted, which studied the relationship between the content of autoantibodies to troponin I, alpha-actin 1, and the heavy chain of beta-myosin 7B in the blood and the results of electrocardiography in professional basketball players at various stages of the training and competition period.

Materials and Methods

An ideal model for studying the effects of chronic physical overstrain on the myocardium is athletes who experience regular physical overloads during training and, especially, in conditions of competitive activity. As part of this work, we conducted a medical examination of 35 men with different amounts of total motor activity, who were divided into groups.

The experimental group 1 consisted of 15 studied men aged 18-22 years. All members of this group are members of the national basketball team at the North Caucasus Federal University (Stavropol, Russia). All participants were in active sports training and trained at least 4 times a week.

Control group 2 included 20 practically healthy men aged 18 to 25 years, with the usual amount of total motor activity.

Before the experiment, the subjects were carefully examined by doctors of various specialties of the City Polyclinic No. 1 (Stavropol, Russia): therapist, cardiologist, neurologist, and endocrinologist. There were no chronic diseases or functional disorders of individual organs and systems. During the research process, the subjects did not take medications. During the examination, during the training and competition process, no complaints from the cardiovascular system were registered in athletes.

A questionnaire was used to collect data, which included socio-demographic information and health-related data, as well as anamnesis, including information about chronic and past illnesses, bad habits, and drug use. All patients received their voluntary, informed consent to participate in the study, in full accordance with the principles of the Helsinki Declaration of the World Medical Association [22]. This work has been reviewed and approved by the Ethics Committee of the North Caucasus Federal University.

The examination was conducted in accordance with the recommendations for conducting a phased medical examination of cyclical sports athletes, including consultation with medical specialists, physical development research, a questionnaire, laboratory screening, and instrumental diagnostics.

To exclude possible causes of increased autoimmune antibodies to cardio-specific proteins, the presence of concomitant diseases such as chronic renal failure, cancer, diabetes mellitus, undergoing cardiac surgery, systemic hypoxia in certain pathological conditions (such as severe anemia, respiratory failure, and others), as well as damage to the central nervous system and other non-cardiac and system states.

The study of physical development was conducted with the collection of data on various anthropometric indicators. This included measuring the height and weight of athletes, as well as determining parameters such as lung capacity and maximum oxygen consumption. These indicators help to assess the physical fitness of athletes and their ability to effectively use oxygen during physical activity.

Two questionnaires were used to study the general physical and mental condition of athletes. The first is the rating scale of psychological state (POMS), which allows athletes to assess their current psychological state by indicators such as anxiety, irritability, fatigue, and others. The second is the Athlete Fatigue Symptoms Questionnaire (ABQ), which helps identify early symptoms of overwork and burnout in athletes.

During the examination of patients, the following laboratory tests were performed during different periods of intense stress:

1. A general blood test was performed using the XN SYSMEX hematology analyzer (Beckman Coulter, USA). The following indicators were determined: the number of erythrocytes, leukocytes and platelets, hematocrit, and hemoglobin levels, as well as other parameters that can provide information about the patient's health status.
2. The quantitative index of the sex hormone testosterone was determined by immunochemistry analysis on an automatic immunochemical analyzer Unicel Dxi 800 (Beckman Coulter, USA).
3. Various laboratory methods were used to measure the cardiophysiological marker of troponin, which included the use of two different analysis methods.

   The first method was carried out using the PATHFAST immunochemistry analyzer (LSI Medicine Corporation, Japan). This method made it possible to qualitatively determine the concentration of troponin I.

   The second method was carried out quantitatively using immunochemistry analysis on an automatic immunochemical analyzer Unicel Dxi 800 (Beckman Coulter, USA).

   Thus, the use of two different analysis methods made it possible to confirm and compare the results of determining the concentration of troponin I to ensure the purity of the experiment.
4. Cardiospecific autoimmune globulins to troponin I (cTnI), to alpha-actin 1 (ACTC1), and the heavy chain of beta-myosin 7B (MUN7B) were quantified by solid-phase enzyme immunoassay using kits from Cloud Clone Corp (China). Using equipment: microplate photometer for scientific research hermo Scientific Multiskan FC, shaker ST-3L, automatic microplate washer Thermo Scientific.

For laboratory analysis, blood was taken from the ulnar vein in the morning from 8:00 to 10:00, in a state of hunger and without intense muscle exertion during the previous 24 hours. In the group of athletes, blood was collected at the initial stages of the experiment, as well as after the preparatory, competitive, and transitional stages of training. The examination of the control group participants and blood collection were carried out once at the initial stages of the study.

To assess the heart rate (HR), the presence of abnormalities, and monitoring of electrical activity, including myocardial pathology during training, the ATES MEDICA Easy ECG ECG device with 12-channel parameters was used.

The above-mentioned manipulations were carried out based on the City Clinical Polyclinic No. 1 (Stavropol, Russia), with the participation of qualified medical specialists with appropriate permits to practice medicine.

The data obtained were processed using methods of variational statistics using the statistical packages "Statistics for Windows" v.6.0 and Biostat (version 4.03). To assess the statistical significance of the differences between the groups of subjects, the Student's t-test and the Mann-Whitney test were used.

Results and Discussion

A comparative analysis of anthropometric and physiometric studies revealed a significant superiority (P <0.001) in height and body weight of basketball players compared to the control group. In group 1, there was a significant superiority in lung vital capacity by 46.24%, and maximum oxygen consumption by 42.81% compared to representatives of group 2.

Athletes who completed the Psychophysical Condition Index (POMS) questionnaire and the ABQ questionnaire did not show any abnormalities in their physical and mental condition. No signs of overwork, emotional fatigue, or instability were found (P <0.001).

The results of multiple examinations of athletes during a year of training and competition cycles did not reveal any obvious differences in the measured indicators of physical and psychological condition. These results indicate a higher overall physical performance of athletes compared to individuals with a normal level of physical activity.

According to the hematological blood test, athletes had a higher hematocrit level (by an average of 26.0%), an increased red blood cell count (by an average of 41.2%), and hemoglobin levels in the blood and the cell (by an average of 27.2%) compared with the data of the control group, who had the results of a general blood test they did not exceed the generally accepted normative values.

The listed blood parameters in athletes were also higher than the established reference intervals: the content of red blood cells by an average of 15.8%; the level of hemoglobin in blood and cells by an average of 11.25%; the level of hematocrit by an average of 9.1%. This indicates a high physiological oxygen capacity of the blood, which arose as a result of long-term sports training. The concentration of testosterone in the blood of the experimental group, determined in the preparatory period, was within the physiological norm for this age group. A decrease in testosterone concentration by 35.5% during the training and competition process may indicate the predominance of anabolism processes. That is, the body is more focused on muscle growth and development, recovery, and adaptation after training [23, 24]. However, a decrease in testosterone levels may also be the result of overexertion or other factors that can negatively affect an athlete's health [25].

When comparing the values of biomarkers of necrosis and ischemia of Cardiac troponin I (cTn I) in blood samples, using two different methods, at all stages of the annual cycle, there were no diagnostically significant deviations between the studied. However, in some cases, the level of cTn I cardiomarkers may remain within the normal range, even in the presence of cardiac problems. This may be caused by the following factors:

1. Timing: The level of cardiomarkers may increase only after a certain period of time after the onset of heart damage. If the examination is carried out in the first hours or days after the incident, the level of cardiomarkers may be within the normal range.
2. Heterogeneity of damage: Sometimes damage to the heart muscle can be heterogeneous, and this can lead to insufficient release of cardiomarkers into the blood.

It should be noted that cTn I is used to diagnose and confirm the existing pathology of the heart-myocardial infarction [26]. There is no data on the use of laboratory analysis of cTn I in the blood as an early marker of myocardial damage for athletes not associated with acute myocardial infarction. **Table 1** shows the dynamics of laboratory parameters in the blood serum of athletes, determined during the end of annual training cycles.

Table 1. Dynamics of laboratory parameters in the blood serum of athletes determined during the end of annual training cycles

Defined indicators	Rapid examination of the level of Cardiac troponin I (semi-quantitative)	Cardiac troponin I (quantitative)
Reference values / Units of measurement	Negative < 0.5 ng/L	0-1 ng/l
Data at the beginning of the research		
Group 1 (experimental) (n=15)	< 0.5	< 0.20
Group 2 (control) (n=20)	< 0.5	< 0.20
p-value	< 0.001	< 0.001
Data from group 1 (experimental), determined during the end of one-year training cycles		
Preparatory period (n=15)	< 0.5	< 0.20
Competition period (n=15)	< 0.5	< 0.20
Transition period (n=15)	< 0.5	< 0.20
p-value	< 0.001	< 0.001

The results of a comparative analysis of autoantibodies provided the following picture: it was found that individuals engaged in sports activities during the preparatory period had a high content of antibodies associated with troponin I (Anti-cTnI) and the heavy chain of beta-myosin 7B (Anti-MYH7B), and Anti-ACTC1 were also detected in a larger volume, where anti-ACTC1 is higher by 13.8%; anti-MYH7B by 63.4%; anti-cTnI-29.4%. This phenomenon in athletes is associated with myocardial adaptation and increased metabolism, as a result of the formation of physiological remodeling of the myocardium [27].

In the competitive period, under conditions of physical and psychoemotional overexcitation, the level of autoantibodies tended to increase; and Anti-ACTC1 by 18.0%, Anti-MYH7B by 20.1%, Anti-cTnI-40.9% compared with the indicators of the preparatory period. Such values may be caused by myocardial stress, which leads to microtrauma and inflammatory processes in the heart muscles, which in turn provoke an immune response and an increase in autoantibody levels [28, 29].

With intense physical exertion, an increase in autoantibodies to myocardial contractile proteins is observed long before it manifests itself in external indicators. Their increase can serve as a warning signal about potential pathological processes that are not yet clinically manifested.

These results highlight the importance of regular monitoring of the level of autoantibodies to myocardial sarcomere proteins in athletes, especially those who engage in intensive training. This allows us to identify possible heart health problems at an early stage and take appropriate measures to prevent or treat them early [30].

During the competition period, changes in the electrocardiogram were detected **(Table 2)**. There is an initial and secondary moderate bradycardia, this is due to an increase in the tone of the vagus nerve as a result of long-term training. Athletes with a high level of physical fitness may have pronounced bradycardia, especially during prolonged exercise. The severity of bradycardia in athletes is used as one of the indicators of their fitness, especially in sports where endurance is needed [31].

Individuals with high total activity have a vertical position of the electrical axis of the heart, this phenomenon in basketball is the result not only of anatomy but also of training, physical training, and movement techniques. When interpreting the ECG data obtained, an increase in the ST segment is noted in leads V2-V3, which indicates a possible violation of the processes of repolarization of the myocardium of the septum of the left ventricle, probably due to its hypertrophy. In addition, there is an increase in the degree of ST elevation, in leads V2-V4, which indicates the spread of changes to the pre-perinatal department and the transition to the top.

The width of the QRS complex in the studied sports group at the second stage increased compared to the results of the first stage and exceeded the norm by 17.0%. This indicates the appearance of a violation of intraventricular conduction, most likely due to myocardial hypertrophy of the septum of the left ventricle (interventricular septum), as well as a trough-like rise of the ST segment with a bulge facing down from the terminal j notch, which indicates signs of early ventricular repolarization syndrome. This phenomenon can lead to interventricular and/or intraventricular asynchronism [27].

Shortening the QT interval by 0.08 ms (27.5%) and QTc by 80 ms (30.3%) in athletes during the competitive period may be a physiological adaptive response to regular physical training. However, shortening the QTc and QT interval in athletes during intense physical training may be associated with an increased risk of arrhythmias, including life-threatening arrhythmias such as ventricular flutter (ventricular fibrillation).

Prolongation of the PQ interval by 0.03 ms (15%) in athletes during the competitive period, is associated with intense physical activity and training. These adaptations may include changes in the automatism of the sinus node and conduction in the heart. However, it should be noted that a slowdown in the PQ interval may indicate a blockage of conduction in the atrioventricular node, where there is a delay in signal transmission between the atria and ventricles.

Table 2. Dynamics of the electrocardiogram in athletes, determined during the end of annual training cycles

Indicator	Units of measurement	Norms	Experimental group (athletes) (n=15)			The control group (n=20)
			Stage 1	Stage 2	Stage 3	
Heart rate	min^{-1}	60-90	58.57 ±11.12	65.42 ±15.13	60.41 ±12.11	72.4 ±10.29
RR	msec	1.0-0.67	1.064 ±0.150	0.982 ±0.025	1.050 ±0.149	0.839 ±0.125
P	sec. 1 mm.	0.08-0.10	0.10 ±0.001	0.13 ±0.009	0.11 ±0.001	0.085 ±0.010
PQ	msec	0.12-0.20	0.20 ±0.012	0.23 ±0.008	0.21 ±0.013	0.18 ±0.019
QRS	msec	0.8-0.10	0.094 ±0.013	0.11 ±0.019	0.099 ±0.014	0.83 ±0.007
Q-T	sec	0.35 – 0.44	0.37±0.010	0.29±0.011	0.35±0.009	0.352 ±0.021
QTc	sec	340-450[1]	344±13.32	264±12.29	340±10.29	420 ±13.02
Q	msec	<0.04	without features	without features	without features	without features
T	–	+ I, II, III, AVL, AVF	+	+	-	+
p-value	–	–	<0.01	<0.01	<0.01	<0.01

Note: QTc values are calculated using the Bazett formula

No significant deviations were found in the remaining measurements of the complex and the intervals. The indicators of PQ, ST, QRS, and QT on an electrocardiogram may reflect the adaptive mechanisms of the cardiovascular system during physical exertion. An increase or change in these parameters may indicate a temporary adaptation of the myocardium to increased psycho-physical stress. However, a direct correlation with the level of autoantibodies also indicates the possibility of detecting incipient destructive changes in the myocardium [32].

The combination of autoantibodies and electrocardiogram data can serve as an indicator of possible defects and changes in cardiomyocytes. The presence of high levels of autoantibodies, combined with abnormal parameters of the electrocardiogram, may indicate incipient pathophysiological processes in the heart tissue, possibly associated with disruption of the adaptive mechanisms of the cardiovascular system [33, 34].

The assumption of the expression of cardiospecific autoantibodies in even minor pathophysiological abnormalities in the myocardium emphasizes the importance of the immune response in the context of heart disease. This may indicate that the body reacts to structural and functional changes in the heart by producing autoantibodies, which, in turn, may be associated with possible cardiovascular pathology [35].

Based on the analysis of electrocardiogram data and the level of anti-cTnI, anti-ACTC, and anti-MYH7B autoantibodies, it can be assumed that this combination may be a useful tool for detecting adaptive and pathological changes in the myocardium. However, for a more accurate interpretation of the results, it is necessary to conduct additional studies and take into account many other factors affecting the state of the cardiovascular system.

Conclusion

The obtained research results confirm the importance and informative value of cardiospecific autoantibodies such as cTnI, ACTC 1, and MYH7B in the context of early diagnosis and detection of myocardial damage. In comparison with traditional methods based on troponin I evaluation, antibodies against sarcomere contractile proteins demonstrate significant superiority in accuracy and informativeness.

The study of the relationship between ECG data and the level of anti-cTnI, anti-ACTC, and anti-MYH7B autoantibodies makes it possible to identify significant aspects of the functioning of the cardiovascular system and possible myocardial pathologies under conditions of intense physical exertion.

The conducted studies have shown that during the intensive training period of the competition period, there is an increase in the Anti-ACTC1 antibody content by 18.0%, Anti-MYH7B by 20.1%, and Anti-CTnI by 40.9%. These changes are accompanied by electrocardiographic abnormalities, such as disturbances in the processes of cardiac repolarization, intraventricular conduction, and interventricular conduction due to hypertrophy.

Despite the absence of pronounced fatigue, complaints from the cardiovascular system, and clinical manifestations in athletes, the data obtained indicate the possible presence of myocardial stress, which is accompanied by microtrauma, inflammatory processes in cardiomyocytes, and pathological remodeling of the heart, which in turn provokes an immune reaction and an increase in the level of autoantibodies, as a result of the body's immune response to these pathophysiological changes.

There is reason to believe that even minor destructive pathophysiological abnormalities in the myocardium of the heart are accompanied by the expression of cardiospecific auto-antibodies anti-cTnI, anti-ACTC 1, and anti-MYH7B. The direct relationship between electrocardiogram data and the level of anti-cTnI, anti-ACTC, and anti-MYH7B indicates a potential link between disorders and interruptions in the work of the heart and the immunological response of the body. This may have a double meaning: adaptation of the cardiovascular system to intense physical exertion and/or the presence of myocardial pathology.

The interpretation of the data as predictors of the possible development of destructive pathophysiological changes in the myocardium is based on the identification of comparable changes in antibodies (cTnI, ACTC, MYH7B) and ECG parameters. These changes may indicate disturbances in the adaptive mechanisms of the heart under intense stress, which, in turn, can lead to pathological changes in the myocardium in the long term.

Based on the data obtained during the research, it can be stated that cardio-specific immunoglobulins to myocardial proteins is an informative diagnostic method in the early diagnosis of functional and structural changes of the heart and can provide significant assistance in situations with an atypical clinical picture and the absence of diagnostic changes on the electrocardiogram.

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References

1. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016;13(6):368-78. doi:10.1038/nrcardio.2016.25
2. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet. 2004;364(9438):937-52. doi:10.1016/S0140-6736(04)17018-9
3. Narayanan K, Bougouin W, Sharifzadehgan A, Waldmann V, Karam N, Marijon E, et al. Sudden cardiac death during sports activities in the general population. Card Electrophysiol Clin. 2017;9(4):559-67. doi:10.1016/j.ccep.2017.07.007
4. Harmon KG. Incidence and causes of sudden cardiac death in athletes. Clin Sports Med. 2022;41(3):369-88. doi:10.1016/j.csm.2022.02.002
5. Maron BJ, Haas TS, Ahluwalia A, Murphy CJ, Garberich RF. Demographics and epidemiology of sudden deaths in young competitive athletes: From the united states national registry. Am J Med. 2016;129(11):1170-7. doi:10.1016/j.amjmed.2016.02.031

6. Rajan D, Garcia R, Svane J, Tfelt-Hansen J. Risk of sports-related sudden cardiac death in women. Eur Heart J. 2022;43(12):1198-206. doi:10.1093/eurheartj/ehab833
7. Compagnucci P, Volpato G, Falanga U, Cipolletta L, Conti MA, Grifoni G, et al. Myocardial inflammation, sports practice, and sudden cardiac death: 2021 update. Medicina (Kaunas). 2021;57(3):277. doi:10.3390/medicina57030277
8. Quinn R, Moulson N, Wang J, Isserow S, McKinney J. Sports-related sudden cardiac death attributable to myocarditis: A systematic review and meta-analysis. Can J Cardiol. 2022;38(11):1684-92. doi:10.1016/j.cjca.2022.07.006
9. Jouven X, Bougouin W, Narayanan K, Marijon E. Sudden cardiac death and sports. Eur Heart J. 2017;38(4):232-4. doi:10.1093/eurheartj/ehw669
10. Jiménez-Pavón D, Artero EG, Lee DC, España-Romero V, Sui X, Pate RR, et al. Cardiorespiratory fitness and risk of sudden cardiac death in men and women in the united states: A prospective evaluation from the aerobics center longitudinal study. Mayo Clin Proc. 2016;91(7):849-57. doi:10.1016/j.mayocp.2016.04.025
11. Bohm P, Kästner A, Meyer T. Sudden cardiac death in football. J Sports Sci. 2013;31(13):1451-9. doi:10.1080/02640414.2013.796064
12. Bassi MD, Farina JM, Bombau J, Fitz Maurice M, Bortman G, Nuñez E, et al. Sudden cardiac arrest in basketball and soccer stadiums, the role of automated external defibrillators: A review. For the BELTRAN Study (BaskEtbaLl and soccer sTadiums: Registry on Automatic exterNal defibrillators). Arrhythm Electrophysiol Rev. 2023;12:e03. doi:10.15420/aer.2022.30
13. Shames S, Bello NA, Schwartz A, Homma S, Patel N, Garza J, et al. Echocardiographic characterization of female professional basketball players in the US. JAMA Cardiol. 2020;5(9):991-8. doi:10.1001/jamacardio.2020.0988
14. Zhao K, Liu Y, Dong L, Gao B. Echocardiographic myocardial work in pre-adolescent male basketball players: A comparison with cardiopulmonary exercise test-derived aerobic capacity. Front Physiol. 2022;13:913623. doi:10.3389/fphys.2022.913623
15. El-Kased RF. Immuno-analytical approach and its application for cardiac disease marker detection. J Immunoassay Immunochem. 2018;39(5):538-50. doi:10.1080/15321819.2018.1518241
16. Pang H, Han B, Li ZY, Fu Q. Identification of molecular markers in patients with hypertensive heart disease accompanied with coronary artery disease. Genet Mol Res. 2015;14(1):93-100. doi:10.4238/2015.January.15.12
17. Banfi C, Gugliandolo P, Paolillo S, Mallia A, Gianazza E, Agostoni P. The alveolar-capillary unit in the physiopathological conditions of heart failure: Identification of a potential marker. Eur J Prev Cardiol. 2023;30(Suppl 2):ii2-8. doi:10.1093/eurjpc/zwad227
18. Müller D, Klamt T, Gentemann L, Heisterkamp A, Kalies SMK. Evaluation of laser induced sarcomere micro-damage: Role of damage extent and location in cardiomyocytes. PLoS One. 2021;16(6):e0252346. doi:10.1371/journal.pone.0252346
19. Ryabkova VA, Shubik YV, Erman MV, Churilov LP, Kanduc D, Shoenfeld Y. Lethal immunoglobulins: Autoantibodies and sudden cardiac death. Autoimmun Rev. 2019;18(4):415-25. doi:10.1016/j.autrev.2018.12.005
20. Mastorakos G, Pavlatou M, Diamanti-Kandarakis E, Chrousos GP. Exercise and the stress system. Hormones (Athens). 2005;4(2):73-89.
21. Perna FM, Schneiderman N, LaPerriere A. Psychological stress, exercise and immunity. Int J Sports Med. 1997;18 Suppl 1:S78-83. doi:10.1055/s-2007-972703
22. World Medical Association. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4. doi:10.1001/jama.2013.281053
23. Cupka M, Sedliak M. Hungry runners - low energy availability in male endurance athletes and its impact on performance and testosterone: Mini-review. Eur J Transl Myol. 2023;33(2):11104. doi:10.4081/ejtm.2023.11104
24. Hackney AC, Hooper DR. Reductions in testosterone are not indicative of exercise performance decrement in male endurance athletes. Aging Male. 2020;23(1):33-4. doi:10.1080/13685538.2019.1574736
25. Belyaev NG, Rzhepakovsky IV, Timchenko LD, Areshidze DA, Simonov AN, Nagdalian AA, et al. Effect of training on femur mineral density of rats. Biochem Cell Arch. 2019;19(2):3549-52.
26. Duque-Ossa LC, García-Ferrera B, Reyes-Retana JA. Troponin I as a biomarker for early detection of acute myocardial infarction. Curr Probl Cardiol. 2023;48(5):101067. doi:10.1016/j.cpcardiol.2021.101067
27. Houthuizen P, Bracke FALE, van Gelder BM. Atrioventricular and interventricular delay optimization in cardiac resynchronization therapy: Physiological principles and overview of available methods. Heart Fail Rev. 2011;16:263-76. doi:10.1007/s10741-010-9215-1
28. Maisch B. Cardio-immunology of myocarditis: Focus on immune mechanisms and treatment options. Front Cardiovasc Med. 2019;6:48. doi:10.3389/fcvm.2019.00048
29. Rzhepakovsky I, Anusha Siddiqui S, Avanesyan S, Benlidayi M, Dhingra K, Dolgalev A, et al. Anti-arthritic effect of chicken embryo tissue hydrolyzate against adjuvant arthritis in rats (X-ray microtomographic and histopathological analysis). Food Sci Nutr. 2021;9(10):5648-69. doi:10.1002/fsn3.2529
30. Khandia R, Pandey MK, Zaki MEA, Al-Hussain SA, Baklanov I, Gurjar P. Application of codon usage and context analysis in genes up- or down-regulated in neurodegeneration and cancer to combat comorbidities. Front Mol Neurosci. 2023;16:1200523. doi:10.3389/fnmol.2023.1200523

31. Azevedo LF, Perlingeiro PS, Hachul DT, Gomes-Santos IL, Brum PC, Allison TG, et al. Sport modality affects bradycardia level and its mechanisms of control in professional athletes. Int J Sports Med. 2014;35(11):954-9. doi:10.1055/s-0033-1364024
32. Martinez MW, Kim JH, Shah AB, Phelan D, Emery MS, Wasfy MM, et al. Exercise-induced cardiovascular adaptations and approach to exercise and cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol. 2021;78(14):1453-70. doi:10.1016/j.jacc.2021.08.003
33. Korça E, Piskovatska V, Börgermann J, Navarrete Santos A, Simm A. Circulating antibodies against age-modified proteins in patients with coronary atherosclerosis. Sci Rep. 2020;10(1):17105. doi:10.1038/s41598-020-73877-5
34. Li J. The role of autoantibodies in arrhythmogenesis. Curr Cardiol Rep. 2020;23(1):3. doi:10.1007/s11886-020-01430-x
35. Wang L, Lv XB, Yuan YT, Wang N, Yao HY, Zhang WC, et al. Relationship between β1-AA and AT1-AA and cardiac function in patients with hypertension complicated with left ventricular diastolic function limitation. Cardiovasc Ther. 2023;2023:7611819. doi:10.1155/2023/7611819