

Sudden cardiac death in young people: risk factors, causes, morphological equivalents

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*«Sometimes death is a punishment; often a gift;
it has been a favour to many».*

Seneca

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Resume

This article reviews the literature on the causes of sudden cardiac death (SCD) in young people. The results of our own retrospective study of deaths of people under 39 years old based on forensic autopsies for 10 years have been presented. The structure and dynamics of the causes of death, risk factors, and the role of pre-existing disease, such as connective tissue dysplasia (CTD), in the development of terminal symptom complex have been studied. It has been found that the main mechanism of SCD in young people is arrhythmogenic, developing in response to such precipitating factors as physical activity, psychoemotional stress, and consumption of low alcohol drinks.

Keywords:

Pathology of the heart and blood vessels, sudden cardiac death, young age, risk factors, morphological features, connective tissue dysplasia

Definition of sudden death: the role of cardiac pathology

Sudden death (SD) in all age groups is a topical question, which needs studying by many medical professionals like pediatricians, cardiologists, neurologists, gerontologists, pathologists, forensic experts, and others. This is because of the main components of the conceptual signs, which are suddenness; surprise to others; no, at first glance, leading cause of death; and the time period during which all terminal stages implemented is very short. SD includes causes of death from diseases of the respiratory system, central nervous system, endocrine system, the gastrointestinal tract, etc. However, throughout the existence of medicine, the leading position (90%) in SD belongs to SCD, where the main etiological factor is hidden, not diagnosed during life, pathology of the heart and blood vessels or a disease of the cardiovascular system compensated by the time of death [1,2].

SCD is diverse and has been studied by many authors [3,4,5]. The 10th revision of the International Classification of Diseases (ICD) – 10 provides a clear definition of the SCD. It is a sudden cessation of cardiac activity, presumably due to ventricular fibrillation or asystole of the heart (when the heart stops beating), with the absence of signs allowing to make a different diagnosis.

A period of time between the beginning of the first signs of a heart attack and death, according to different authors, is wide [1,4,5,6]. Depending on an interval between the onset of a heart attack and the moment of death, there are instantaneous cardiac death (within a few seconds) and SCD (within an hour). Based on this time criteria, some authors propose the following definition of SCD (Myerburg and Castellanos, 2001): this is a non-violent death due to heart disease, manifested in a sudden loss of consciousness within 1 hour from the onset of acute symptoms, while prior heart disease may be known or unknown but death is always unexpected. However, the *WHO* experts have clearly defined the time criteria of SCD, where death is considered sudden within 6 hours of the first symptoms of heart disease.

Etiology of sudden cardiac death

According to statistics, SCD around the world happens in 50 to 90% of all cases of SD, and various heart disease cause it [2,3,6,7]. Among all cardiac causes, the leading and stable position for many years belongs to pathology of the heart, caused by stenotic coronary vessels and hypertension [7,8]. However, over the last 10 years, there have been certain changes in SCD in

terms of the age of the dead and nosology. When diagnosing the cause of death in people over 40–50 years old and in old people, cardiac cause of death is always obvious enough, but during autopsy studies of young people of working age (39 years old), it is often problematic to identify and establish the main pathology.

In people over the age of 40–50 years, the cause of SCD in 95% of cases is some form of coronary heart disease, manifested as acute myocardial ischaemia due to atherosclerotic stenosis of the coronary arteries. Moreover, atherosclerotic vascular disease has systemic nature, when during autopsy studies, the signs of vascular lesion of different localisation (the brain vessels, aorta, renal arteries with different degrees of stenosis) get revealed [1,7,8].

In young people (up to 39 years old), vascular lesion of atherosclerosis is either absent or only detected in the early stages (lipoidosis). The causes of SCD in young people are the different types of pathology of the myocardium and the conduction system of the heart, myocarditis, hypertrophic cardiomyopathy, aortic stenosis, rupture of the aorta, rupture of the thoracic aorta during Marfan's disease [9,10]. The causes of SCD in teenagers were chronic myocarditis (not diagnosed during their lives), long QT syndrome, aortic stenosis, coronary artery spasm without atherosclerosis, coronary artery abnormalities, ruptured aortic aneurysm [11,12]. The main cause of death, especially in teenagers died before 19 years old, is SCD (primary cardiac arrest) as a form of coronary heart disease. The onset of CD is most often due to ventricular fibrillation or asystole [13,15,16].

An important role in diagnosing and finding the causes of SCD belongs to morphological studies, which are aimed at clarifying the role of certain pathological processes (coronary atherosclerosis, impaired microcirculation, early ischemic myocardial injury, alcoholic cardiomyopathy) in the pathogenesis of SD. However, in cases of SCD in young people, it is important to study adrenergic and cholinergic innervation of the heart, extracardiac ganglia, the cardiac conduction system, and to identify structural changes in conducting pathways [16,17,18,19,20,21].

In SCD, there are features according to sex. SCD in young men is seen in 70% of cases. At the age of 45–64 years, SCD in men is recorded 7 times more often than in women, and only at the age of 65–74 years, the frequency of SCD in men and women has 2:1 ratio. However, to date, the frequency of SCD has a tendency of «rejuvenating» and remains higher among men than women [19].

Table 1. Indicators of sudden death for the 2004–2013 period

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Nonviolent death (cases per year)	3,454	3,649	4,425	3,692	3,992	4,013	3,922	3,793	3,750	3,561
Death from diseases of the cardiovascular system (cases per year)	2,395	2,612	3,179	2,887	2,922	3,143	3,038	2,973	3,027	2,644
%	69.33	63.35	71.84	78.19	73.1	78.32	77.46	78.38	80.7	74

Over the past 20 years, the problem of SD in athletes and young people actively involved in sports has been closely studied. In the literature, there is an increasing number of described cases of SD in athletes during training or immediately after it [15]. These cases are registered among the top athletes in such sports as hockey, basketball, volleyball, and others. In this case, sport activity as psychophysical stress of increased intensity is the causative or subsidiary causative factor of SD. Until now, there is no single time criterion when determining SD in people involved in sports. The majority of authors in describing the cases of SD during exercise, stick to the following definition: death occurs within an hour of the onset of acute symptoms and coincides with the sport activity in the absence of external factors, which themselves could be the cause of death [11,15]. The latter creates some difficulties in determining the cause of death in athletes, because death comes suddenly at overall health.

An autopsy of cases of SD in young people is quite complicated, because usually there are no expressed pathological changes in young people, and so the study of each case is based on a comprehensive approach to finding the causes of death taking into consideration all preceding events.

Study of causes of death according to forensic autopsies

The aim of our study was to investigate causes and patterns of SD in people under 39 years old, risk factors and establishment of pathomorphological symptoms.

To address these goals, we investigated cases of non-violent deaths over the 2004–2013 period, which were studied in the *Bureau of Forensic Expertise* in Omsk. Of the whole array of the dead, there were specifically investigated the cases of SD in people under the age of 39 years. All cases were subject to forensic autopsy, during which the following methods were used: sectional, anthropometric, pathomorphological, histological, and chemical.

In the study of sectional cases of SD of young people, who died suddenly, it was found that the SD usually occurs outside hospitals. In addition, a significant number of SCD in young people occur without wit-

nesses, and precise determination of the conditions of death is extremely difficult.

During a 10-year period, it was found that diseases of the cardiovascular system occupied the leading position among all cases of SD and accounted for on average of 74% (Table 1).

During those 10 years, respiratory diseases accounted for 9% of all cases of SD; diseases of the central nervous system for 3%; digestive system for 4%; neoplasms for 3.6%; and infectious diseases for 6.4%. Among infectious diseases, some forms of tuberculosis with complications were stated as the main cause of death, which were, in some cases, undiagnosed during people's life. Typically, this cause of death was observed in people engaged in anti-social way of life, with some signs of cachexia and attributes of organ pathology, reflecting chronic alcohol intoxication.

Of course, circumstances and place of death (home death, hospital death), disease duration, and lifetime diagnosis affect the structure of SD. For example, a low percentage of SD from cancer in our study was due to statutory rights of relatives to refuse an autopsy if the cancer was verified during patient's life (Article 67 of the Federal Law of the Russian Federation № 323). Moreover, cases of long-lasting illnesses of the central nervous system (hemorrhagic cerebral infarction, ischaemic cerebral infarction, and their consequences) are, as a rule, subjected for autopsy, and are not grounds for forensic examination.

Thus, forensic studies helped reliably examine the cases of SCD, which met such basic criteria as suddenness, surprise, and fast progression of terminal condition.

Analysis of cases of SD according to sex revealed the predominance of deaths among men. In the age group under 39 years, men represented 78% of all cases of SD, while in the age group over 40 years, men represented 57% and women 43%, respectively. In the age group of 60 years and older, they were almost equal, with the prevalence of women (Table 2).

Based on the analysis of the structure of SD, it is clear that over the last decade, diseases of the circulatory system have been ranked first among other reasons. A decline in 2013 was not due to an absolute decrease in mortality from diseases of the cardiovas-

Table 2. Sex and age characteristics of sudden death

	14–39 years old	40–59 years old	Over 60 years old
Men	78%	57%	54%
Women	22%	43%	56%

cular system, but due to a change of methodological approaches to statistical account of a number of diseases acting in conjunction with the basic pathology of the cardiovascular system, mainly in the age groups of patients over 40–60 years. In view of these circumstances, diseases such as diabetes, asthma with the presence of pulmonary heart disease and signs of decompensation, obesity and its consequences (Pickwickian syndrome) have become the main causes of death, while diseases of the heart and vascular bed moved to the second (background) position. Thus, an annual growth of SCD should be stated with a gradual expansion in predictors of SD, reduction in age indicators, and changes in reasons of SCD.

Of particular interest are the cases of SCD in young people under 39 years. During the sectional study using normal macro- and microscopic examination of the heart and major vessels, their pathological changes are nearly absent or insignificant. The difficulty of such investigation, in some cases with public outcry, is due to the lack of any medical information on individual's lifetime monitoring and his/her visits to a doctor.

There are particularly difficult cases of SD in the age group under 29 years at the time of sports activities, namely during training, warm ups, sports competitions, or physical education. Smolenskiy AV and Lubina BG offered to interpret SD in sports as a death, which occurs during an hour after acute symptoms and coincides with sports activities (before start, during competition, immediately after finish) in the absence of external factors, which themselves could be a cause of death.

In our study, the death during exercise (before, during and after training) was recorded in 23 cases. Physical activity as a provoking factor of the onset of SD was found in 4 cases of sexual activity, 7 cases of heavy lifting (lifting weights, furniture transportation, work at their summer cottages, etc.), and 12 cases of active sports. Analysis of all these cases allowed to consider physical activity as a major provoking factor of SD associated with the heart. In all the cases of SD due to physical activity, the basic pathological changes were detected in the heart, the cardiac conduction system, and coronary vascular bed.

Pathomorphological changes of the heart usually reflect the main, arrhythmic, mechanism of

SCD. The main causes of arrhythmic death were ventricular arrhythmias (80% of cases), intraventricular or atrioventricular blocks. Asystole was much rarer (20%), and it reflected the atrioventricular block or sinus node dysfunction. In some cases, emergency doctors, arrived before biological death of people, recorded from their electrocardiograms (ECGs) episodes of paroxysmal tachycardia, the presence of extrasystoles, followed by atrial flutter and atrial fibrillation, which enabled experts to identify and establish the main cause of death.

Morphological characteristics of sudden cardiac death

Morphological findings were revealed during the autopsy, at the detailed study of the myocardium in the projection of the cardiac conduction system such as bundle of His and its branches. During macroscopic examination of the myocardium, there was detected severe disturbance of blood supply in the interatrial and interventricular septa, in the projections of the atrioventricular node and bundle of His. This was presented by irregular blood supply to the myocardium with alternation of ischaemic foci and sharp plethora of the myocardium, the mottled myocardium during serial cross-sections of the septum, and in some cases, the formation of small foci of hemorrhage (Figure 1). During the pathohistological study, pieces of the heart from different levels of the interatrial and interventricular septa, lateral surfaces of the right and left atria, and walls of the left ventricle were examined. There were identified acute ischaemic myocardial lesions, mild perivascular sclerosis, fragmentation and uneven hypertrophy of cardiomyocytes,

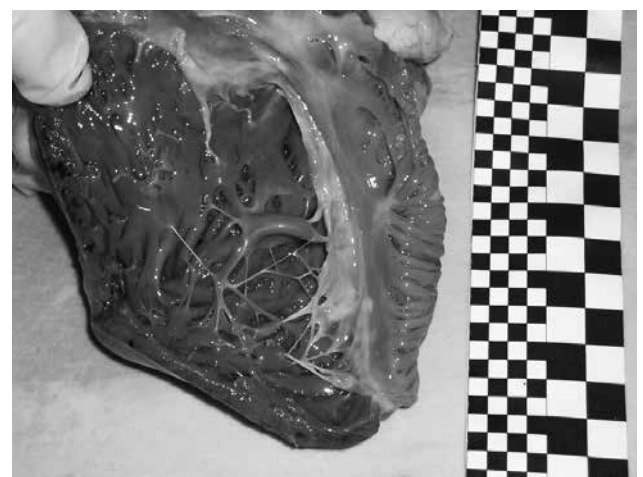


Figure 1. Left side of the heart. In the area of the atrial and ventricular septa, there is an alternation of sharp hyperemia and ischaemia, and a presence of small focal hemorrhages into the myocardium. Multiple abnormally placed chords of the left ventricle. Sudden cardiac death of a 23-year old man during physical exercise

Table 3. Indicators of sudden death in the age group under 39 years

Years	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Number of cases	127	199	159	175	182	211	299	154	166	183
Men	97	166	127	146	153	179	216	111	123	139
Women	30	33	32	29	29	32	83	43	43	44
Ratio of men, %	76.3	83.4	79.87	83.42	84	84	72.24	72.07	74.09	75.9
Ratio of women, %	23.7	16.6	20.13	16.58	16	16	27.76	27.93	25.91	24.1

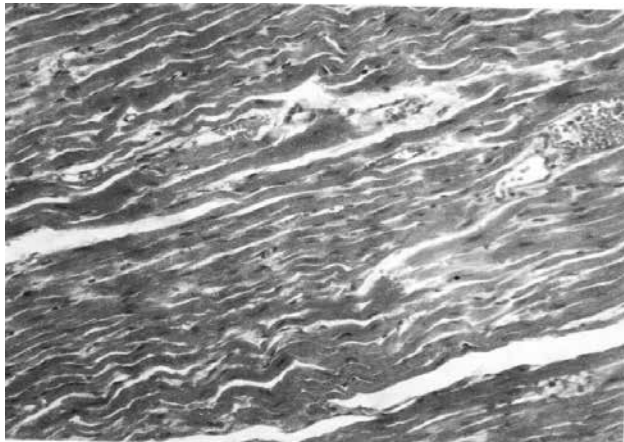


Figure 2. Fragmentation of cardiomyocytes in the bundle of His, contracture, pronounced microcirculatory disorders. Sudden cardiac death occurred by arrhythmogenic mechanism

and expressed changes of the microcirculatory bed, namely spasms in arterioles and small arteries, and irregular blood supply (Figure 2).

Thus, the main mechanism of the onset of SCD in young people is fatal arrhythmias, where physical activity and psychoemotional stress act as a provoking factor. A number of pathogenetic links contribute to the development of the terminal symptom complex of arrhythmia. They include coronary artery spasm and a sudden increase in myocardial oxygen demand during increased physical activity or emotional stress, accompanied by changes in neural control of the cardiovascular system, violation in the cardiac conduction system, and an increase in myocardial susceptibility to ischemia. All of these conditions develop quickly, without having to cause marked morphological manifestations and changes in the cardiovascular system, detected by a usual sectional study. However, a detailed study of the cardiac conduction system, sinus and atrioventricular nodes, the bundle of His, intracardiac ganglia and nerves, as well as small coronary arteries, allows to detect signs of one's lifetime myocardial electrical instability and life-threatening arrhythmias.

Causes of death due to pathology of the cardiovascular system

Analysis of cases of SCD in the age group under 39 years revealed certain patterns according to sex (Table 3).

Table 4. Dynamics and comparative analysis of causes of sudden cardiac death in the age group under 39 years

Causes of death	2004	2013
Heart defects	4%	2%
Sudden cardiac death	6%	3.8%
Cardiomyopathies	26%	41.2%
Other myocardial lesions (myocarditis, myocardiodystrophy)	7%	9%
Acute coronary insufficiency	39%	21%
Vascular pathology	18%	23%

As shown in table 3, there has been an upward trend in the incidence of SCD among young men of working age compared to women.

Analysis of mortality allowed to reveal certain changes in the causes of SCD during this 10 year period (Table 4).

As shown in the table 4, SCD from valve problems (mitral valve prolapse, congenital heart defects) tends to decrease, thanks to developments in the healthcare of the Russian Federation; growth of diagnostic and therapeutic measures; introduction of new advanced methods of treatment in cardiac surgery; and increase in quality of life of these patients. At the same time, an increase in SCD, caused by cardiomyopathy with distinct morphological signs of myocardial lesions with hypertrophy, expansion of cavities of the heart, and development of symptom complex of arrhythmia at the onset of death. This fact may be due to an increase in consumption of alcoholic beverages (beer) among teenagers and young adults up to 23 years. The mechanism of the damaging effect of which is in violation of metabolic processes of the myocardium, and in direct toxic effect on cardiomyocytes (cobalt).

We have paid particular attention to a group of people who died from vascular events due to pathology of large and medium vessels. It was found during autopsy that in this group there were diagnosed external and internal signs of systemic pathology such as connective tissue dysplasia (CTD).

The results obtained in recent years on the diagnosis of pathological conditions and diseases associated with CTD allowed to consider this pathology as one of the risk factors for SD among young people. Many studies, devoted to understanding the function of the

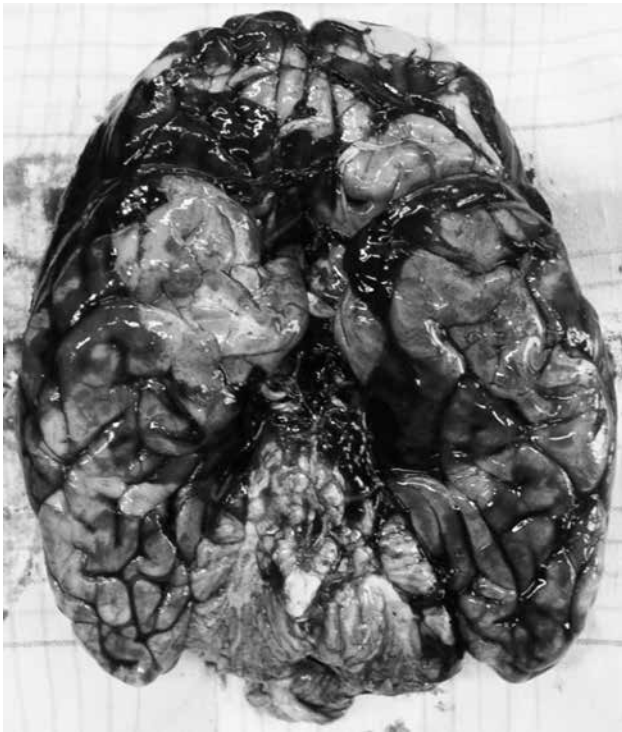


Figure 3. Basal subarachnoid hemorrhage at rupture of congenital aneurysm of the anterior cerebral artery during physical exercise (weight lifting)

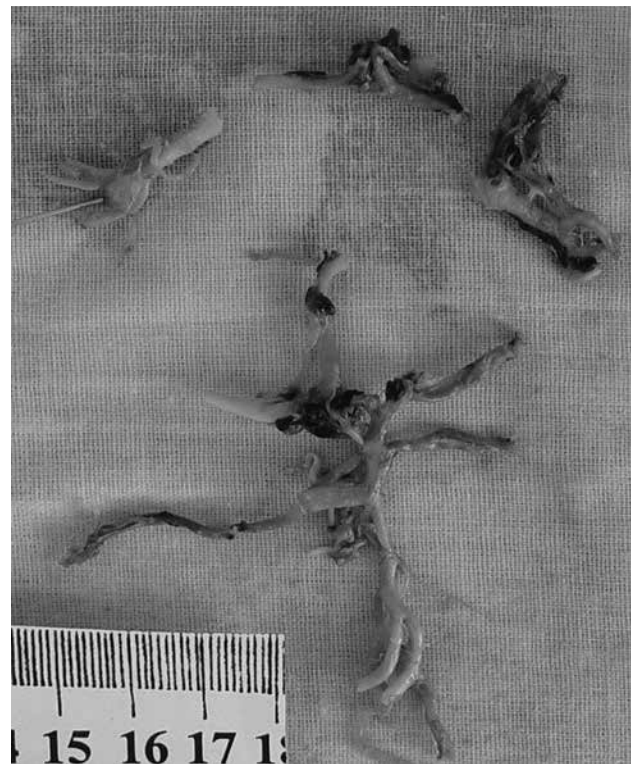


Figure 4. Blood vessels at the base of the brain. Tortuosity of the blood vessels, focal thinning of the walls, aneurysm formation

myocardium and central hemodynamics in patients with CTD, allowed to form a view that pathology of the cardiovascular system in patients with CTD is the most common and cardiovascular disorders are the leading causes of shortening the patients' life [12,20].

Despite evidence of lots of cases of CTD in the population, including among those who consider themselves relatively healthy, the problem of early lifetime detection of the main manifestations of CTD, and hence the problem of early detection of signs of lesions of the cardiovascular system, which are the main cause of SD among young people, remain very relevant and have been confirmed in our study.

Ninety seven percent of people, who suddenly died from vascular events, had signs of CTD. They included asthenic type: tall, asthenic chest, poor development of the subcutaneous adipose tissue; and violation in development of the musculoskeletal system: pathologies of the spine (scoliosis, kyphoscoliosis, lordosis), pathology of the sternum (deformities like funnel chest and keeled chest), elongation of the upper extremities, arachnodactyly, valgus deformities of the feet, various forms of flat feet and other small signs.

The main manifestations of this systemic pathology are the lesions of the cardiovascular system, such as valvular heart disease (mitral valve prolapse), cerebral aneurysms, anomalous origin of the coronary

vessels and formation of their aneurysms, as well as pathology of the aorta in the form of hypoplasia and ascending and aortic arch aneurysms.

According to our research, the immediate causes of death in patients with signs of CTD and cardiovascular syndrome were massive basal subarachnoid hemorrhage with a breakthrough into the ventricular system of the brain due to rupture of congenital aneurysms of the cerebral arteries (Figure 3 and Figure 4); pulmonary embolism with varicose veins; hemorrhagic shock due to rupture of a congenital aneurysm of the thoracic aorta; profuse bleeding due to rupture of small arteries of the internal organs of the stomach and esophagus. The following are the main pathogenetic links of the vascular aneurysm formation in patients with CTD: congenital defect in the muscle layer of the vascular wall; damage to the internal elastic membrane; change of collagen fibers of blood vessels; and hemodynamic disturbances arising along with such provoking risk factors as physical activity, psychoemotional stress, smoking, excessive consumption of low alcohol drinks (beer, energy drinks).

Another striking vascular pathology, reflecting systemic connective tissue pathology, is aortic malformations, which, unfortunately, are usually diagnosed only post-mortem. These defects include aortic hypoplasia, a double-barreled aorta with wall rupture, and aneurysms of the arch or the thoracic aorta.

The following signs of anomalies of the coronary arteries, when death occurs suddenly due to increased physical activity, were revealed: anomalous left coronary artery from the pulmonary artery, the left artery from the right sinus of Valsalva, both arteries from the right or left sinus of Valsalva. A sharp, incompatible with life violation of the coronary circulation, acute cardiovascular failure, and death occur in abnormal coronary arteries during physical exercise in aortic stenosis.

Small doses of ethanol as a risk factor for the onset of SCD in young people, especially with signs of CTD, have a direct toxic effect on velocity of the conduction system of the heart. In particular, acetaldehyde affects the sinus node and atrioventricular compound, with the subsequent release of noradrenaline, which leads, consequently, to paroxysmal tachycardia, and ultimately, to spontaneous ventricular arrhythmias. In individuals with signs of CTD, hypersympathicotonia is a frequently observed condition, which is in real life accompanied by increased myocardial oxygen consumption, increased energy consumption, which contributes to the development of metabolic disorders in the myocardium and energy-depleted cardiomyocytes, creating a substrate for the development of fatal arrhythmias. In the last 5 years, the growth of SCD due to dilated cardiomyopathy, where the development of fatal arrhythmias is the main link of the onset of death, has been of particular concern. This fact can be explained by an increased consumption of low alcohol products (beer) and consumption in large quantities of energy drinks since adolescence, the development of metabolic injury of the myocardium, dilatation of the heart cavities, and progressive reduction of myocardial contractility with arrhythmias.

Conclusion

SCD from diseases of the cardiovascular system is a global problem being solved in all countries of the world, as its figures reflect economic and social development of a country. Of course, the key in prevention and reduction of SCD is to develop criteria and methods for prevention of CVD, introduction of modern medical technology, a systematic approach to patient management, as well as identification and reduction of such risk factors for SCD as smoking, overweight, and hypertension.

Particular attention in the prevention of SCD should be paid to younger people, aged up to 39 years, where death is due to mainly pathological changes of the cardiovascular system, and the main mechanism of the onset of death is arrhythmic mechanism. Among

the most common causes of pathology of the heart in young people is CTD, where the body's damage has systemic character with the primary lesion of the cardiovascular system. This pathology, which was not diagnosed timely in life, is realised by irreversible terminal conditions, which are fatal when joined by stress factors. The most significant risk factors for SCD in young people are psychoemotional stress, smoking, consumption of alcoholic beverages, physical exercise (in some cases, above limits), and minor injuries. Therefore, it is important for prevention of SCD to determine predictors of SD and foresee the mechanism of terminal symptom complex that most often realised in young people through arrhythmic death.

Conflict of interest: None declared

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