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MORPHOLOGICAL AND MORPHOMETRIC CHANGES IN THE THYROID GLAND IN SUDDEN CARDIAC DEATH

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Annotation: dysfunctional morphological and morphometric changes in the thyroid gland in sudden cardiac death at the age of 20-60 years and older were studied, and an inverse relationship between SCD and the morphofunctional state of the thyroid gland was revealed. In the presence of IHD, there is a decrease in activity in the thyroid nodule - a hypofunctional state; as the node thickens and increases in size, these changes intensify and run parallel to metabolic changes in the myocardium. These conditions limit the adaptive capabilities of the thyroid gland, which can be observed in hypothyroidism and cause an unpleasant course of cardiovascular diseases.

Key words: morphology, morphometry, thyroid gland, sudden cardiac death

Relevance. The functional state of the thyroid gland is of great importance in the course of coronary artery disease. A number of studies [1, 3, 5 7, 8, 10] have proven the significance of manifest, subclinical hypothyroidism as an independent and important risk factor for the development of acute forms of coronary heart disease.

In sudden cardiac death, sudden cardiac arrest is associated with the development of ventricular fibrillation in 78.9%, asystole in 20.3%, and electromechanical dissociation in 0.8% [4].

In ventricular fibrillation, cardiac and extracardial trigger factors are actively involved. The leading role of the extracardiac factor belongs to the dysfunction of the glands of the internal system, which control the activity of internal organs (hypothalamic-pituitary-adrenal system, thyroid gland, etc.) [6, 9, 12].

Numerous studies have been conducted on the causes and pathogenesis of sudden death, sudden cardiac death, and thyroid dysfunction, however, when analyzing literature, the functional changes of the thyroid gland in endemic goiter as a cause of sudden cardiac death have not been sufficiently studied [14, 15]. It remains one of the main causes of late diagnosis and increased mortality from sudden cardiac death, which requires further improvement of morphological diagnostics.

Decreased contractility of the left ventricular myocardium due to sclerotic changes and conduction disorders are considered the main risk factor for SCD development. An important role in the occurrence of SCD (substrate+trigger factor) is played by the disruption of rhythm, weakening of the heart muscle, as well as the action of trigger factors (metabolic, ischemic, mechanical influences).

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Purpose of the study: to study the dysfunctional morphological and morphometric changes of the thyroid gland in sudden cardiac death.

The study used archival materials from the pathoanatomical department and forensic medical examination of persons who died from sudden cardiac death. The deceased were aged 20-60 years and older, in each age group (control group, study group (diffuse and nodular colloid macro-microfollicular goiter) 10 subjects of the study were taken. The control group for the study included 25 patients. In the control group, myocardium and thyroid tissue were obtained from individuals who died not from sudden cardiac death and thyroid pathology, but from those who died from other causes: damage to large vessels, internal bleeding. A total of 75 autopsy protocols, clinical and anatomical conclusions, and histological examination of autopsy materials were obtained.

Research methods: organometry (weighing, volume measurement), general morphological examination (staining with hematoxylin and eosin), morphometry (measuring cardiomyocyte and thyroid parameters), macro-microscopy, statistical processing of the obtained data.

The myocardial and thyroid tissue pieces were cut separately, measuring 1x1 cm, and fixed in 4% neutral formalin prepared on a phosphate buffer solution. For histological examination, sections were taken from the anterior and posterior walls of the left ventricle, 2 cm above the apex, 2 cm below the fibrous ring of the mitral valve, and the interventricular septum. After dehydration in alcohol and chloroform, the cuttings were poured into paraffin blocks. 5-8 μm thick tissue cuts were stained with hematoxylin and eosin [11].

To assess the morphofunctional state of the heart and thyroid gland, their absolute mass was measured. Colored sections of myocardial and thyroid tissue were examined under a light microscope, and the left ventricular contractile coefficient, the number of cardiomyocytes with wave defects, and cardiomyocytes with dissociation signs were comprehensively studied in the myocardium.

Thyroid morphometry was performed using a MOF-15 eyepiece micrometer. The average values for 100 observations were measured and calculated - follicle diameter, diameter and height of follicular epithelium and their nuclei, stroma and interfollicular thickness. Attention was also paid to the presence of colloid, changes in the follicular-cellular index Brown index [2], desquamation of the follicular epithelium. Desquamation of the follicular epithelium was considered a morphological sign of a high degree of thyroid functional tension. The morphofunctional state of the thyroid gland was determined and assessed according to the recommendation of O. Khmelnitsky [13].

Depending on the morphofunctional state of the thyroid gland, the material was divided into 3 groups: 1st group - control (thyroid gland and its histological structure have normal mass), 2nd group - hypofunction (diffuse macr follicular colloid, diffuse nodular colloid macr follicular and

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endemic goiter, "diffuse sclerotic goiter"), 3rd group - hyperfunction (nodular colloid-microf follicular and diffuse colloid-microf follicular goiter).

During the statistical analysis of the materials, the arithmetic mean (M), the errors of the arithmetic mean (m) were calculated, statistically processed, and the differences in indicators were calculated using the statistical method according to Student's t-test (t) and considered significant ($p<0.05$).

Research results. In the main group of SCD, pathomorphological changes in the heart represent macroscopic signs of myocardial ischemia, small foci of sclerosis, about 10% of lipid spots and fibrous plaques in the vessel intium, microscopic venous swelling, perivascular sclerosis, ischemia, hypercontactile state of cardiomyocytes, wavyness, fuchsinophilia, fragmentation (Table. 1).

Heart morphometric parameters

Indicator	Control group	Main group
Heart weight	280,4 ± 3,2 g	330 ± 1,1 g
Heart length	9,5± 0,1 cm	10,1± 0,1 cm
Heart width	9± 0,1 cm	9,4± 0,1 cm
Heart thickness	4,8± 0,1 cm	5,2± 0,1 cm
Right ventricular wall thickness	0,4± 0,02 cm	0,6± 0,02 cm
Left ventricular wall thickness	1,3± 0,03 cm	1,6± 0,04 cm
Number of left ventricular contractures	64,5 ± 1,7 %	5 4,6 ± 0,7 %
Quantitative determination of cardiomyocytes with signs of wave-like deformation	57,3 ± 1,02 % ,	44,6 ± 1,6 %
Quantitative determination of cardiomyocytes with dissociation signs	64,9 ± 0,7 %	5 7 , 3 ± 1,2 %
Contracture damage to cardiomyocytes	3 degrees	2-3 degrees

When studying the wave size of cardiomyocytes depending on age, it was noted that the indicators in the main group were lower than in the control group.

When studying the degree of cardiomyocyte dissociation depending on age, it was found that the

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indicators in the main group were somewhat lower than in the control group.

When studying the contractile coefficient of left ventricular cardiomyocytes depending on age, it was noted that the indicators in the control group were significantly higher than the indicators in the main group (Table. 2-3, Fig. 1).

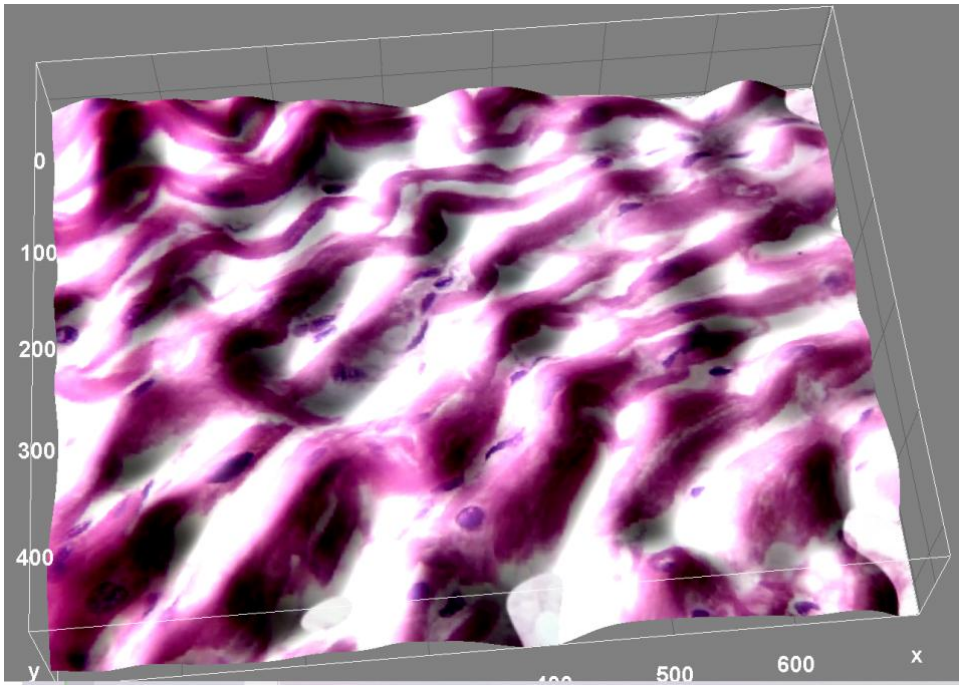

Figure 1. Relative comparative morphogram along the X, Y, Z axes of the confocal-relief uneven surface. NanoZoomer scanned (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS-/431-3196 JAPAN). - was uploaded to QuPath-0.5.0 ImageJ and the spatial form was measured. Contract damage to cardiomyocytes of the 2nd-3rd degree in sudden cardiac death (30-40 years). Staining with gemm-eosin. Magnification 4x40.

Table 2

Morphometric indicators of myocardial composition in acute myocarditis

cardiac death with various nosologies.

№		Diameter of myocardial structures. μm	P

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		Right ventricular anterior surface cardiomyocytes		Cardiomyocytes of the lateral surface of the left ventricle		Cardiomyocytes of the left upper posterior surface		≤
		Typical	Atypical	Typical	Atypical	Typical	Atypical	
1	Myocardium in disgormonal disorders	**36,26±1 .01**	**21,26±0 ,95**	**34,23±0 ,89**	**24,13±0 ,63**	**32,43±0 ,78**	**20,96±0 ,95**	**0,01**
2	Myocardium in coronary heart disease	**41,24±1 .08**	**17,86±1 .05**	**43,26±1 .24**	**16,98±0 ,84**	**44,31±0 ,95**	**15,52±1 .01**	**0,01**
3	Normal myocardium	**24,56±1 .12**	**16,21±0 ,86**	**26.01±0 ,12**	**15,12±0 ,65**	**25,89±0 ,69**	**14,22±0 ,92**	**0,01**

Table 3

Morphometric indicators of myocardial composition in acute myocarditis cardiac death of various nosologies.

№		The structures of the myocardium have an area of 83,000 μm2.						Average indicators of myocardial structural structures		P ≤
		Cardiomyocytes of the anterior surface of the heart		Cardiac myocytes of the lateral surface of the heart		Cardiomyocytes of the posterior surface of the heart				
		Typical	Atypical	Typical	Atypical	Typical	Atypical	Typical	Atypical	
1	Myocardium in disgormonal disorders	**1314,78±31,5**	**35000,96±266,75**	**1171,69±22,89**	**39000,8713±275,26**	**1051,71±2,78**	**37000,97±280,95**	**1179,39±19,05**	**37000,931±274,32**	**0,01**

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2	Myocardium in coronary heart disease	**1701,73±25,5**	**27012,26±321,12**	**1871,69±55,16**	**30113,31±259,13**	**1962,49±39,78**	**27012,26±328,26**	**1845,33±40,14**	**28045,941±302,5**	**0,01**
3	Normal myocardium	**603,13±21,1**	**23457,51±412,46**	**676,52±35,14**	**28457,51±423,11**	**665,64±43,16**	**26175,51±389,51**	**648,43±33,13**	**26030,176±408,36**	**0,01**

65% of those who died from SCD were men aged 30-60 (average 45 years), 21% were women aged 40-60 years, and 15% were men and women over 60 years old. Signs of myocardial ischemia were observed in 1/4 of cases, and angioneurotic changes in 1/5 of cases.

In autopsies, uneven filling was observed in 1/3 of cases as a sign of macroscopic myocardial ischemia. Macroscopically, small sclerotic foci and cardiomyocyte atrophy were observed.

Parallel changes were observed in the myocardium and thyroid tissue during SCD.

In the control group, the thyroid gland is a thin connective tissue membrane, typically bumpy in structure, the parenchyma consists of rounded or slightly oval follicles, the interfollicular colloid is homogeneous, reddish-pink in color, and a small amount is vacuolated. The thyroid epithelium is a single-row cubic, its height varies depending on age, the cytoplasm consists of uniformly distributed RNA granules, the nucleus is oval-shaped, the cytoplasm of the interfollicular epithelium is pyroninofilous, rounded, the stroma is thin, smooth. It consists of connective tissue, with fibrous structures and vessels observed. Age-related changes - follicle diameter, thickening of interfollicular connective tissue, hyalinosis, rarely focal lymphoid infiltration, development of atherosclerotic changes in arterial vessels, age-related involuntary changes. Along with the changes, there was a decrease in functional cholangitis, colloid deposition, reduction, resorption, and thickening of the interfollicular barrier.

At 30-40 years of age, signs of increased thyroid function (colloid absorption, central and peripheral vacuolization, proliferation of follicular epithelium, and granulation of the cytoplasm) are observed. After 50 years, due to atherosclerotic changes in the walls of arterial vessels, thyroid ischemia, sclerosis, hyalinosis, and, accordingly, a decrease in its functional state are noted. Accordingly, a decrease in morphometric indicators and functional activity was noted.

Pathomorphological changes in the thyroid gland in the main group. Uzbekistan is distinguished by unique geographical and meteorological conditions, ethnic composition of the population, unique character, and prevalence of risk factors for coronary artery disease. In our country, the Fergana Valley is one of the centers of moderate endemic goiter. At the same time, the prevalence of goiter averages 32.4%, functionally, the euthyroid goiter is prone to hypothyroidism ("Fergana goiter") - manifests alongside pathological changes in the nervous,

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cardiovascular, skeletal, and blood-forming systems of the body.

Factors causing goiter and morphological changes in compensatory processes - occur against the backdrop of age-related evolution of thyroid tissue and manifest differently in different age groups.

The mass of the thyroid gland in residents of the Fergana Valley is presented. After 40 years, the thyroid gland increases significantly. After 60 years, the average weight of the gland reaches 40 g, which continues with its age involvement. Age-related changes are associated with compensatory hypertrophy.

Euthyroid goiter, prone to hypothyroidism, accounts for 7.3% of the population under 40 years old and 21.3% of people over 40 years old.

Macroscopically, the nodules have a soft-elastic consistency, on a cross-section, they differ little in color from the surrounding tissue (with a shiny surface, dark brown or reddish in color), the fibrous membrane is distinguished by a liquid color.

Microscopic examination revealed uneven epithelial growth in the thyroid tissue, accumulation of colloid, remodeling of the vascular bed, stromal edema, hyalinosis, interfollicular barrier covered with thin, flattened epithelium, on the surface of small follicles - cubic epithelium, on the surface of large follicles - flattened epithelium filled with saturated colloid, in the foci of proliferation the epithelium is prismatic, Sanderson's cushions are formed, proliferative activity is increased. In the fragments of the gland, active intrafollicular (16%) and extrafollicular (20%) proliferation is observed, and parenchymatous and parenchymatous-follicular structure (12%) is observed (Fig. 2-6).

An indicator of increased thyroid secretory activity during thyroid morphometric studies is the increase in the height of the follicular epithelium. This indicator decreased with age in the control group and in diffuse macr follicular colloid goiter, while in diffuse macr follicular goiter it was high in all ages, and in micro- and macr follicular nodular colloid goiter it increased with age.

The formation of nodules accounts for 51% of euthyroid goiter cases prone to hypothyroidism. Multiple nodular goiter (1-6 cm) is characteristic of the Fergana Valley. Statistics show that 17% have one node, 39% have 4 to 10 nodes, and 28% have more than 10 nodes.

After 40-50 years, with the onset of involuntary processes, the incidence of goiter in endemic foci increases. They are characterized by the presence of multinodular goiter, the frequency of which is 45%.

Active growth and subsequent encapsulation of the nodes leads to dyscirculatory changes in their vessels, difficulty in the mobilization of colloids, and secondary changes appear (fibrosis, petrification, atrophy, sclerosis, necrosis).

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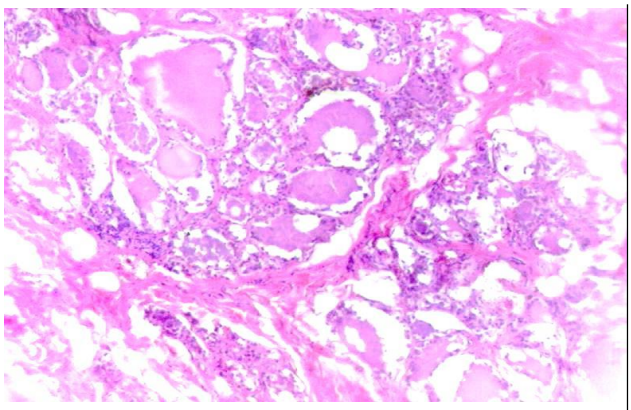

Figure - 2. External appearance of glands in nodes in people aged 20-29 years: colloid saturation, vacuolization, follicles of various sizes, cubic epithelium, growing in individual branches (Sanderson's cushions) with the formation of bumps, swelling in the stroma, hyalinosis. Gemm-eosin staining, magnification 10*12.5.

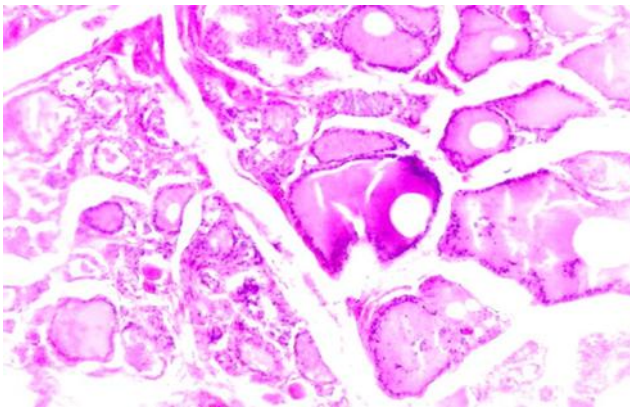

Figure - 3. Appearance of the gland at thyroid nodes in people aged 30-39: colloid saturation, vacuolization, follicles of various sizes, cubic epithelium, swelling in the stroma, hyalinosis. Gemm-eosin, eosin staining, magnification 10*12.5.

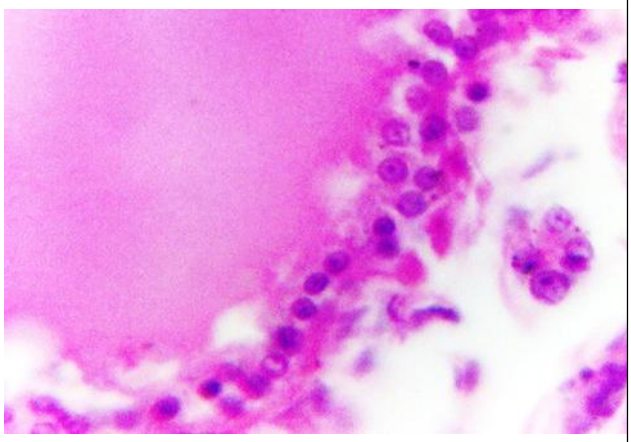

Figure - 4. In 40-49 years of age, colloid saturation, vacuolization, follicles predominantly of large size, cubic, flattened epithelium, swollen stroma, and hyalinosis are observed in the thyroid gland nodes. Gemm-eosin, eosin staining, magnification 40*12.5, 10*12.5.

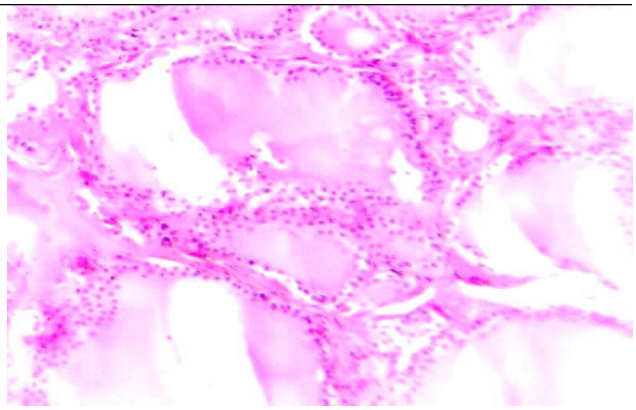

Figure - 5. External appearance of the gland in thyroid nodes in individuals aged 50-59: filled with colloid, follicles predominantly large in size, epithelium flattened, swollen and full in the stroma. Gemm-eosin, coloring by the eosin method, magnification 10*12.5.

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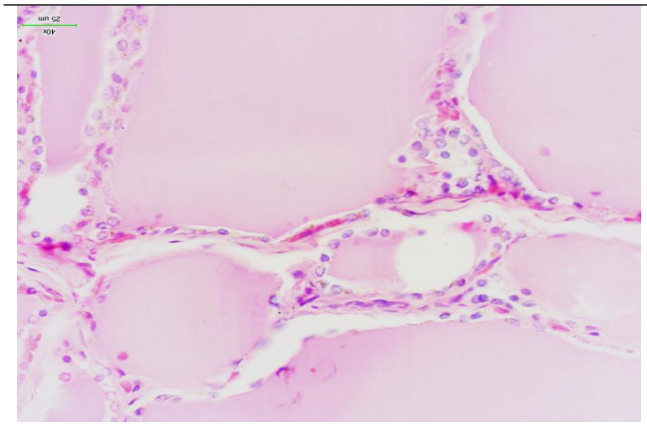

Figure - 6. External appearance of the gland in the thyroid gland nodes in individuals aged 60 and older: filled with colloid, follicles predominantly large in size, cyst enlarged, epithelium flattened, swelling in the stroma, hyalinosis.

Diffuse goiter - 14%, diffuse-nodular goiter - 22%, diffuse small-nodular growth focus - 19%.

After 50 years, nodal and nodal diffuse forms are more common. Such nodes are centers of compensatory-adaptive hypertrophy. Proliferative processes manifest as focal and limited slowing of secretory activity. Focal hypertrophy is an incomplete compensatory reaction that subsequently leads to the formation of multiple nodes characteristic of a colloid goiter.

Diffuse hyperplasia, goiter, and secondary regressive changes affect the growth of the nodes.

In sudden cardiac death, the resorption of hormonal components of the follicular structure in the parenchyma of the thyroid gland is observed: a decrease in the activity of thyrocytes - an increase in the height of the thyroid epithelium, an increase in the number of microfollicles with liquid colloid, the formation of new follicles, a sharp microcirculatory vascular reaction. These indicators differed significantly from the control group.

In the development of the heart, the transition of follicular cells outside the node to increased secretory activity in the thyroid tissue was observed in individuals with nodular colloid macr follicular goiter after 30 years of age in very rare cases compared to individuals who died with signs of myocardial ischemia. Macroscopic and microscopic examination of the heart muscle revealed signs of morphofunctional activity in areas outside the thyroid node in patients with sudden coronary death compared to the control group.

In VTS, thyroid tissue shows activity, a decrease in activity in the node is a hypofunctional state, as the node thickens and increases in size, these changes intensify and parallel metabolic changes are observed in the myocardium.

These conditions limit the adaptation capabilities of the thyroid gland, which can be observed in hypothyroidism and cause an unpleasant course of cardiovascular diseases. Outside the thyroid gland nodes, there is an increase in the resorption of hormonal components of the follicular structure: the activity of thyrocytes is activated (increase in the height of the thyroid epithelium, active colloid resorption), pronounced microcirculatory activity is observed. These indicators

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have a significant difference compared to the control group. With age, sclerosis and thickening are detected in the walls of the thyroid gland vessels, which is observed in organ ischemia.

Morphological characteristics of sudden cardiac death in people living in endemic goiter areas. Changes in the functional activity of the thyroid gland lead to changes in the activity of the cardiovascular system, including systemic vascular resistance, left ventricular blood flow, heart rate, and circulating blood volume.

The results of a morphometric study of the heart in the main group: compared to the control group, the frequency of sudden cardiac death was higher. Histological examination of both ventricles revealed a predominance of 2-3 degree cardiomyocyte contracture damage.

Conclusion: Based on the above, it can be said that there is an inverse relationship between the SCD and the morphofunctional state of the thyroid gland. In the presence of coronary heart disease, thyroid tissue activity is observed, a decrease in activity in the node is a hypofunctional state, as the node thickens and increases in size, these changes intensify and are accompanied by metabolic changes in the myocardium. These conditions limit the adaptation capabilities of the thyroid gland, which can be observed in hypothyroidism and cause a severe course of cardiovascular diseases.

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