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MORPHOLOGICAL ORGANIZATION OF THE HEART AND FEATURES OF HYPOXIC CHANGES IN THE MYOCARDIUM UNDER THE INFLUENCE OF CARBON MONOXIDE

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Abstract

The article presents modern data on morphological changes in the heart under the influence of carbon monoxide. Carbon monoxide induces hypoxic damage to the myocardium, accompanied by disturbances in the structural organization of cardiomyocytes and microcirculation. Mitochondrial destruction, sarcoplasmic swelling, myofibril fragmentation, and stromal edema are observed. The degree of morphological disorders correlates with the duration and concentration of carbon monoxide exposure. Experimental and clinical findings provide a basis for further studies of the mechanisms of the toxic cardiomyopathic effect of carbon monoxide.

Keywords: heart, carbon monoxide, morphology, hypoxia, cardiomyocytes.

The heart is the central organ of the circulatory system, providing blood circulation in a closed vascular bed and maintaining the body's homeostasis. It is a hollow muscular organ consisting of four chambers—two atria and two ventricles—separated by a valve apparatus that ensures unidirectional blood flow [5]. In mammals, including humans, the heart has a similar structure, which makes these animal models valuable for experimental morphology and pathophysiology [3]. Morphologically, the heart is covered by the pericardium, which performs protective and fixing functions. The middle layer—the myocardium—consists of specific striated cardiac muscle tissue, which has automaticity, excitability, conductivity, and contractility [1]. Unlike skeletal muscle fibers, cardiomyocytes are connected to each other by intercalated

disks, which provide electrical and mechanical communication between cells. Intercalated discs contain desmosomes, fascioles, and gap junctions (nexuses), allowing the myocardium to function as a single syncytium [2].

An important morphofunctional difference is observed between the working myocardium and the cardiac conduction system. The latter is represented by the sinoatrial node, atrioventricular node, bundle of His, and Purkinje fibers. These structures consist of atypical cardiomyocytes with increased automaticity and reduced contractility [3]. Their morphology is characterized by the presence of light cytoplasm, sparse transverse striations, and a reduced number of myofibrils.

The cardiac microcirculation includes arterioles, precapillaries, capillaries, postcapillaries, and venules, all closely associated with cardiomyocytes. Of particular importance is the high density of the capillary network, which ensures a constant supply of oxygen and metabolites to the myocardium. Normally, there are 1–2 capillaries per cardiomyocyte [4]. The endothelium of cardiac vessels not only regulates vascular tone but also plays a role in maintaining tissue metabolism and repair.

At the ultrastructural level, cardiomyocytes contain a developed sarcoplasmic reticulum and a large number of mitochondria, which make up to 30–40% of the cell volume, reflecting the high energy demands of the myocardium [5]. Intracellular structures—sarcomeres, composed of actin and myosin filaments—provide a contraction mechanism controlled by changes in the concentration of calcium ions in the cytoplasm.

The heart has distinct age- and sex-related morphological characteristics. In men, the myocardium is thicker, which is associated with greater body weight and circulating blood volume, while in women, a slightly thinner wall is observed but with higher resistance to ischemia, which is associated with the influence of estrogens [6]. With age, degenerative changes in myofibrils, the development of interstitial fibrosis, and a decrease in capillary density occur, which reduces the heart's reserve capacity [7].

From a comparative morphological perspective, the structure and functional organization of the hearts of laboratory animals (rats, mice, and rabbits) are similar to that of humans, making them suitable models for studying pathological processes, including carbon monoxide toxicity [8]. In rats, the heart weighs 0.3–0.4% of body weight, and the ratio of the wall thickness of the left and right ventricles is similar to that of humans. Furthermore, the myocardium of animals exhibits structurally similar elements of the conduction system and capillary network.

At the molecular level, the functioning of cardiomyocytes is determined by the coordinated activity of cytoskeletal proteins (desmin, actin, troponin, titin), mitochondrial enzymes, and receptor systems. The protein desmin is an important marker of myofibrillar integrity: it forms intermediate filaments that connect sarcomeres and provide mechanical stability to cardiomyocytes [9]. Disruption of desmin structures is observed during hypoxia, toxic exposure, and ischemic injury, which can serve as an early morphological criterion for myocardial destruction [10].

Modern methods of morphological analysis, including light, electron, and confocal microscopy, allow for a detailed study of the cellular and subcellular components of the myocardium. The use of immunohistochemical markers (Desmin, Connexin-43, Troponin I, α-actinin) allows for the identification of functional changes associated with impaired contractile activity and intercellular interactions [11].

The heart possesses significant adaptive plasticity, manifested in its ability to hypertrophy under increased load, as well as partial regeneration through cardiomyocyte proliferation and activation of epicardial stem cells [12]. However, under toxic influences, particularly carbon monoxide (CO), the myocardial compensatory mechanisms are depleted, leading to the development of morphological and functional impairments that require detailed study.

Current understanding of the mechanisms of myocardial damage in carbon monoxide (CO) intoxication is based on data from morphological, biochemical, and molecular studies. As noted previously, the heart is highly sensitive to hypoxic factors due to its intense metabolism and the constant need of cardiomyocytes for oxygen and

energy metabolism substrates. Therefore, exposure to carbon monoxide, which can bind hemoglobin to form carboxyhemoglobin and block oxygen transport, leads to significant impairment of aerobic metabolism and structural destruction of the myocardium [13, 14].

Unlike short-term ischemia, carbon monoxide intoxication is accompanied by persistent tissue hypoxia, mitochondrial dysfunction, and activation of a cascade of molecular reactions leading to cell death. It has been established that even at relatively low CO concentrations (0.05–0.1%), systemic metabolic disturbances develop, affecting the energy and ion homeostasis of cardiomyocytes [15]. The key pathogenetic mechanism of cardiac damage from carbon monoxide exposure is the development of hypoxia. CO has an affinity for hemoglobin approximately 200–250 times higher than oxygen, resulting in the formation of stable carboxyhemoglobin (HbCO), which blocks oxygen transport to tissues [16]. This causes an acute O_2 deficiency in the myocardium and subsequent dysfunction of the mitochondrial oxidative-phosphorylating systems.

Under hypoxic conditions, the formation of adenosine triphosphate (ATP) is disrupted, leading to energy deficiency, decreased activity of Na^+/K^+-ATPase and calcium pumps, disruption of ionic balance, and the development of intracellular edema [17]. This is accompanied by membrane depolarization and dysfunction of intercellular contacts, which contributes to arrhythmogenesis.

Long-term exposure to CO causes not only hypoxic but also histotoxic hypoxia, caused by the direct inhibitory effect of carbon monoxide on the cytochrome oxidase complex IV of the mitochondrial respiratory chain [18]. This leads to decreased oxygen utilization by cells, even when it is present in the blood plasma, exacerbating energy deficiency.

Morphologically, hypoxia manifests itself through the development of degenerative changes in cardiomyocytes, such as granular and vacuolar degeneration, as well as sarcoplasmic edema. In more severe forms of intoxication, coagulative necrosis, fiber fragmentation, destruction of transverse striations, and myofibril discomplexation are observed [19].

Experimental animal studies have shown that within 30–60 minutes after inhalation exposure to 0.1% CO, signs of energy deficiency are observed in the myocardium, manifested by decreased levels of creatine phosphate and adenine nucleotides [20].

Concurrently, anaerobic glycolysis increases and lactic acid accumulates, which contributes to acidosis and impaired contractile function of cardiomyocytes [15]. Electron microscopic studies have shown that early stages of carbon monoxide poisoning are characterized by mitochondrial swelling, decreased cristae density, the appearance of electron-transparent areas in the matrix, and partial destruction of the outer membrane [21]. These changes indicate mitochondrial dysfunction, which underlies impaired energy metabolism and the activation of apoptosis.

Clinical observations of individuals chronically exposed to low doses of CO (e.g., industrial workers) have also described signs of hypoxic cardiomyopathy: dilation of the cardiac chambers, decreased ejection fraction, arrhythmias, and myocardial dysfunction [22]. This confirms the universality of the injury mechanisms identified experimentally.

Thus, hypoxia during carbon monoxide intoxication is a systemic process that includes both hemic and tissue forms of oxygen deficiency. It triggers a cascade of secondary disorders—from energy depletion to structural destruction of the myocardium, which forms the basis for subsequent processes of oxidative stress and cardiomyocyte apoptosis.

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