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SIMULATED MICROGRAVITY INHIBITS VINCULIN EXPRESSION, INTENSIFYING MYOCARDIAL REMODELING AND HEART FAILURE

Abstract

Currently, the effect of microgravity on the extracellular matrix (ECM) of the myocardium has not been sufficiently studied. In order to determine the role of simulated microgravity, we conducted a study to assess the state of a number of structural and contractile proteins that bind ECM to cardiomyocytes (CM). Biopsy tissue was taken from patients suffering from coronary artery disease during coronary artery bypass surgery. The studied samples were subjected to artificial microgravity using the Desktop random positioning machine (RPM) in sealed tubes with Normacor solution in an incubator at 37.0C for three hours. The control samples were in the same conditions in immobility. Cryostatic sections were examined using an indirect immunofluorescence method. Mouse monoclonal antibodies to actin, desmin, vinculin, titin and the second antibodies to mouse immunoglobulin labeled with FITC were used. When assessing the state of actin, desmin and titin, no pronounced changes were noted in any of the samples. In all cases, the proteins were able to be visualized in normal localization: actin – in the area of narrow isotropic discs; desmin - in the area of insertion discs and Z-lines of CM. However, some changes were found in samples exposed to microgravity during the study of the expression of vinculin (a membrane-associated protein that binds cytoskeleton actin to sarcolemma). This protein is expressed in the sarcolemma zone, in the so-called costamers. Hypertrophy of costamers was detected. Normally, with immunofluorescence staining, such expression is represented as a linear reaction along the perimeter of the CM with a cross-section, or in the lateral part of the CM with a longitudinal one. We suggest that the increased expression of vinculin in these areas is a compensatory mechanism in combination with oxidative stress. However, its excessive accumulation can make it difficult to transmit the signal of contraction and relaxation from the ECM cell and back to the costamer region, as well as prevent the release of calcium ions from the T-tubules into the sarcoplasm of the cell, which dramatically reduces the ability of the heart muscle to contract and leads to an increase in the so-called myocardial stiffness. A similar pattern is observed in dilated cardiomyopathy. Our work provides new and important information about understanding the mechanisms of heart failure progression and how it adapts to changes in gravity.