The Summary

The coexistence of stress/depression with cardiovascular diseases has been known for a long time. However, while the role of cardiovascular diseases in the development of depression is quite well documented, the knowledge of cardiotoxicity caused by stress/depression is mainly based on epidemiological studies. The collected literature from the few experimental studies confirms this thesis. Some studies point to an increase in cortisol level under stress/depression, others the possibility of cortisol's impact on glucocorticoid and mineralocorticoid receptors in cardiomyocyte and the pathological consequences of such hyperactivation in the myocardium. Other studies suggest that changes in the myocardium occurring as a result of stress/depression may be dependent on the activation of adrenergic receptors through indirect (adrenal medulla) and direct (heart) activation of the sympathetic nervous system. Unfortunately, the available literature lacks studies showing the dependence of changes in the heart muscle on stress/depression in a direct way.

Therefore, the aim of the study involved the assessment of the direct impact of stress/depression on changes in the myocardium and the comprehensive assessment of the prevalence of these changes at the molecular, biochemical and tissue levels.

The experiment was performed using male Wistar rats. The rodents were randomly divided into two groups, each consisted of 10 rats. The rats of the control group had been kept undisturbed in their colony cages, while those of the study group had been subjected to various stressors for 40 days. The rats were sacrificed by decapitation at 24 h following the last stressor. The exprerimental material was obtained from the left ventricle and taken for histopathological examination, the rest of the heart tissue was frozen at -80 °C. The blood was collected for following biochemical analyses: glucose and lactate levels. Other biochemical parameters related to metabolism, redox balance and oxidative stress were performed in homogenates of rat hearts. Therby, the concentration of free amino acids, NAD +, NADH, NADP +, NADPH were determined. Among studies at the molecular level, the determination of 44 genes divided into panels associated with glycolysis, anabolism, catabolism and lipid trnasport, as well as oxidative stress and heart remodeling was carried out. In addition, LDHA, LDHB and NT-proBNP protein levels were determined using the immunoenzymatic method. Histological assessment of the myocardium was carried out using H+E, van Gieson, PAS and PAS with diastase stainings.

On the basis of the conducted studies the following conclusions were drawn: (1) The significant increase in blood glucose concentration in rats exposed to chronic mild stress is consistent with the thesis statement based on the previous behavioral and molecular studies in the hippocampus that under our experimental conditions there are changes characteristic of human depression, which confirms the choice of the used model; (2) In rats exposed to stress there was no change in blood lactate concentration, what indicates a lack of hypoxia in the myocardium; (3) In rats exposed to stress, an increase in the transcription signal for anabolism, catabolism and lipid transport and the gluconeogenesis pathways with accompanying glycogen storage have been demonstrated, suggesting an increase in ATP uptake based on lipid metabolism pathawy rather than glucose metabolism; (4) Changes in the expression of genes related to myocardial remodeling and the simultaneous increase in NT-ProBNP may indicate the process of heart remodeling in stressed rats; (5) Further research requires determining whether the observed features of necrosis in the hearts of rats exposed to stress are caused by oxidative stress; (6) In the hearts of rats exposed to stress, the redox imbalance and the oxidative stress were found, as evidenced probably by the adaptive increase in NADPH concentration and superoxide dismutase gene activity and an increased oxidative DNA damage; (7) The conducted studies provided the direct evidence on the dependence of changes in the myocardium on the molecular, biochemical and tissue levels, and stress/depression.