ZMIANY W METABOLIZMIE ENERGETYCZNYM KOMÓREK SERCA TOWARZYSZĄCE MIAŻDŻYCY

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Background: Hyperlipidemia may lead to the impairment of the mitochondrial function affecting a respiratory chain function, leading to excessive production of reactive oxygen species. However, the exact mechanism of mitochondrial changes in cardiomyocytes exposed to high lipid environment is still unknown.

Objective: The aim of this study was to investigate the activity of respiratory chain complexes in the heart in an experimental model of atherogenic dyslipidemia and to correlate those results with cardiac function.

Methods: Function of isolated cardiac mitochondria was tested in 3-, 6-, and 18 months LDL Receptor and Apolipoprotein E knock-out mice (LA-/-, n=5 in each age group). C57Bl/6J wild types (WT, n=5 in each age group) were used as controls. The analysis was performed using the Seahorse XFp metabolic flux analyzer, by recording the oxygen consumption rate. Function of the heart was measured by echocardiography. To investigate molecular pathways of those changes we evaluated proteins related with mitochondrial biogenesis by using Western Blot and ELISA.

Results: Paradoxically**,** isolated mitochondria from 6-months LA(-/-) mice exhibited increased respiratory rates in comparison to WT. Among the mitochondrial biogenesis proteins, we observed an increased level of phosphorylated AMPK. However, these observations have been reversed in older mice. We revealed decreased activity of cardiac mitochondria and diminished Stroke Volume, Ejection Fraction and Fractional Shortening demonstrated by the echocardiographic examination in older LA(-/-)mice. The observed changes in heart and mitochondrial dysfunction correlated with the reduced level of phosphorylated AMPK.

Conclusion: We established improved cardiac mitochondria function such as an increased respiratory chain function in early stage of atherosclerosis by using LA(-/-) mice. However, we observed an opposite effect in the hearts of mice in advanced stage of atherosclerosis

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