DIET-INDUCED HYPERCHOLESTEROLEMIA LEADS TO CARDIAC DYSFUNCTION AND ALTERATIONS IN THE MYOCARDIAL PROTEOME

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High blood cholesterol is a major risk factor for coronary heart disease. Moreover, direct effects on the myocardium also contribute to the adverse effects of hypercholesterolemia. In the present study, we aimed to investigate the global proteome changes in the left ventricle of hypercholesterolemic rats in order to clarify the underlying protein expression changes associated with the direct cardiac effects of hypercholesterolemia. Male Wistar rats were fed with a laboratory rodent chow supplemented with 2% cholesterol and 0.25% sodium-cholate hydrate for 8 weeks to induce hypercholesterolemia. Proteomic characterization of left ventricular samples from normo- and hypercholesterolemic animals was performed with liquid chromatography-mass spectrometry analysis. The significantly altered proteins from the proteomic data were subjected to gene ontology and protein interaction analyses. Additionally, similar expression patterns were explored through the whole unfiltered proteome data. Elevated circulating cholesterol level was accompanied by mild diastolic dysfunction in cholesterol-fed animals. Proteomic characterization of left ventricular samples revealed altered level of 45 proteins due to hypercholesterolemia. Based on our gene ontology and protein interaction analysis results, hypercholesterolemia was associated with disturbed expression of cytoskeletal and contractile proteins. Beta-actin was downregulated in the hypercholesterolemic myocardium and established a prominent hub of the revealed network. Deeper GSEA analysis of the unfiltered dataset revealed concordant downregulated expression patterns in proteins associated with the arrangement of contractile and cytoskeletal system, and in protein subunits of the mitochondrial respiratory chain system. We conclude that disturbed expression of proteins associated with the contractile apparatus as well as with the mitochondrial respiratory chain due to hypercholesterolemia may play a role in the cardiac diastolic dysfunction in the myocardium of cholesterol-fed animals.

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