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Effects of Nutritional disorders impairing the one-carbon cycle on diabetic cardiomyopathy remodeling: Experimental data and clinical perspectives

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Statement of the problem: Choline is recognized as an essential nutrient for public health with crucial role in the pathway of one-carbon metabolism through its implication in the methionine-homocysteine cycle. Its deficiency setting is an established experimental model of non-alcoholic steatohepatitis (NAFLD), which is associated with insulin resistance, increased oxidative stress, abnormal fat metabolism and increased morbidity due to cardiovascular disease; NAFLD might be predisposed by diabetes and vice versa, while diabetic cardiomyopathy is characterized by increased fibrosis, stiffness and diastolic dysfunction.

The purpose of this study was to evaluate the cardiac mechanical properties and remodeling process in the case of concomitant conditions of choline deficiency and diabetes.

Methodology and Theoretical Orientation: Wistar Albino rats (about 3 months old) were divided randomly into rats fed with standard (C) or choline deficient diet (CDD) and diabetic rats receiving standard (DM) or choline deficient diet (CDD+DM). Diabetes was experimentally induced by intraperitoneal injection of streptozotocin. After five weeks of dietary intervention cardiac function was evaluated by echocardiography followed by a histopathology and immunohistochemistry evaluation in order to investigate the architecture of the myocardium

Findings: Echocardiography evaluation revealed dilation of the left atrium in the CDD+DM group accompanied by a decrease of the left ventricular wall thickness ($p=0.041$ vs DM, $p=0.009$ vs CDD and $p=0.015$ vs C) with preserved ejection fraction. Histological examination showed inflammatory and fibrotic lesions in the choline-deprived diabetic rats that were more extended in comparison to the diabetic or choline-deprived only rats ($p<0.001$).

Conclusion & Significance: Choline deficiency impairs heart mechanical properties and induces extracellular matrix dysregulation leading to a restrictive pattern with diastolic dysfunction. On a diabetic substrate, the induced choline-deprived cardiomyopathy follows an intriguing pattern with restrictive and dilated features at the same time, implying that in this case the cardiac reserve is exhausted and cardiac dysfunction might establish more easily.

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