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The pathophysiological role of oxidized cholesterols in epicardial fat accumulation and cardiac dysfunction: a study in swine fed a high caloric diet with an inhibitor of intestinal cholesterol absorption, ezetimibe.

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Abstract

Oxidized cholesterols (oxycholesterols) in food have been recognized as strong atherogenic components, but their tissue distributions and roles in cardiovascular diseases remain unclear. To investigate whether accumulation of oxycholesterols is linked to cardiac morphology and function, and whether reduction of oxycholesterols can improve cardiac performance, domestic

male swine were randomized to a control diet (C), high caloric diet (HCD) or HCD+Ezetimibe, an inhibitor of intestinal cholesterol absorption, group (HCD+E) and evaluated for: (1) distribution of oxysterol components in serum and tissues, (2) levels of oxysterol-related enzymes, (3) paracardial and epicardial coronary fat thickness, and (4) cardiac performance. Ezetimibe treatment for 8 weeks attenuated increases in oxysterols in the HCD group almost completely in liver, but reduced only levels of 4 β -hydroxycholesterol in left ventricular (LV) myocardium. Ezetimibe treatment altered the expression of genes for cholesterol and fatty acid metabolism and decreased the expression of CYP3A46, which catabolizes cholesterol to 4 β -hydroxycholesterol, strongly in liver. An increase in epicardial fat thickness and impaired cardiac performance in the HCD group were improved by ezetimibe treatment, and the improvement was closely related to the reduction in levels of 4 β -hydroxycholesterol in LV myocardium. In conclusion, an increase in oxysterols in the HCD group was closely related to cardiac hypertrophy and dysfunction, as well as an increase in epicardial fat thickness. Ezetimibe may directly reduce oxysterol in liver and LV myocardium, and improve cardiac morphology and function.

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