Abnormal liver metabolism and pro-inflammatory responses as modulators of cardiac cachexia in a rat model of heart failure

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Backgrounds

- Cachexia, namely body wasting, is a common complication in cases of congestive heart failure (CHF).

Methods

- Animal: Inbred male Dahl salt-sensitive (DS) rats were fed an 8% NaCl (high-salt; HS) diet which shows a distinct transition from compensated left ventricular hypertrophy to CHF (Figure 2). DS rats fed only the low-salt diet (low-salt; LS) were used as controls.

- Sampling of hepatic tissue: To obtain liver tissues for biochemical analyses, 11-week-old LS (n=6), 11-week-old HS (n=8), and 17-week-old HS (n=6) rats were sacrificed by decapitation without fasting.

- Analyses: Blood chemicals and inflammatory cytokines, metabolome analysis of liver tissue, hepatic levels of glycogen and triglycerides, gene expression used by quantitative RT-PCR, Western blotting, and hepatic uptake of 18FDG and 125I-9MPA were performed.

Hypothesis

We assessed the hypothesis that the liver is important in the pathogenesis of cardiac cachexia, since the liver plays a critical role in systemic metabolic regulation.

Results

CHF rats ate less than control rats. CHF rats showed a failure to grow.

Blood sugar and insulin levels were decreased, and triglyceride and cholesterol levels were increased in CHF rats.

Metabolic remodeling in CHF

(Kato et al. Circulation: Heart Failure, 2010)

The Dahl salt-sensitive rat can be used as a model of cardiac cachexia.

Question: What is the upstream signal of enhancing lipogenesis and cachexia?

Analyses of metabolites, mRNA, and protein expression showed lipogenesis was increased, and gluconeogenesis was decreased.

Clinical implications

- SREBPs increased in association with the amount of TNF-α mRNA and protein in this study. CHF-associated pro-inflammatory responses may be a mechanism of abnormal lipid metabolism in CHF rats.

- The response appears to be maladaptive, when the body is losing weight and peripheral tissues need more substrates to maintain tissue homeostasis.

- Although this study is an observational one, the findings indicate the abnormal liver metabolism to be a maladaptive process and worsen the CHF.