A025 Heart Failure Induced Insulin Resistance Is Associated With Decreased Adipokines Production: Role Of Impaired Adipogenesis

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Introduction: The global prevalence of heart failure (HF) has become a crucial medical problem and is a major cause of morbidity and mortality. The presence of HF predicts the development of insulin resistance (IR), which is reported to be 18- 22% higher in HF patients compared to a control patients. Although there is a plethora of evidence that HF affects the heart, kidney, brain, and intestine, the studies addressing the impact of HF on adipose tissue is largely lacking. **Methods:** To investigate how HF affects visceral adipose tissue (VAT), we analyzed omental adipose tissue obtained from deceased patients with myocardial infarction using immunohistochemistry, confocal microscopy and quantitative RT-PCR. To understand the mechanisms of HF-induced insulin resistance, we performed coronary artery ligation in C57BL/6 mice to induce HF. Moreover, we used cardiomyocyte-specific TNF-α transgenic (*Tnfa*^{tg}) mice that develop severe HF and exacerbated glucose intolerance. We further used the 3T3-L1 cell line to understand the effect of inflammation on adipocytes. Serum free fatty acids, glycerol and triglyceride were analyzed by spectrophotometry. ELISA was performed to measure adiponectin and leptin concentrations in serum and 3T3-L1 cell line conditioned medium. **Results:** We observed significantly reduced VAT weight, and adipose cell number and size in C57BL/6 with coronary ligation and *Tnfa*^{tg} HF compared to controls. Furthermore, serum triglycerides, free fatty acids, free glycerol, adiponectin and leptin concentrations were significantly lower in the both mouse models of HF. Consistent with reduced amount of VAT in mice with HF, the expression of the genes responsible for adipogenesis, adipose expansion and fatty acid synthesis was markedly reduced in VAT of patients and mice with HF. Mice deficient of adiponectin had exacerbated glucose intolerance and high insulin levels, suggesting the role of diminished systemic adiponectin levels in HF-associated IR. **Conclusions:** HF reduces adipocyte differentiation and expansion, resulting in reduced VAT weight. This results in reduced adipokines production, resulting in increased systemic glucose intolerance.