Impact of chronic heart failure on adipose tissue functional plasticity – a role for fatty acids?

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Introduction

Chronic heart failure (HF) is a major cause of morbidity and mortality in humans and domestic animals. HF is a systemic condition characterised by chronic inflammation and functional changes in non-cardiovascular tissues; obesity is also associated with low level chronic inflammation, with adipose tissue (AT) exhibiting infiltration of macrophages and alterations in fatty acid (FA) profiles(1).

Our **hypothesis** was that AT from animals with HF will display greater expression of inflammatory mediators and a fatty acid profile consistent with an inflammatory state.

Therefore the **aim** of this project was to investigate expression of regulators of lipid metabolism and inflammation and fatty acid profiles in AT from a rodent model of HF.

Methods

Rats with HF post myocardial infarction were compared with age matched non-failing controls. Intra-abdominal (IA) and subcutaneous (SC) adipose tissue depots were sampled after humane euthanasia, and then processed for analysis.

Adult male Sprague-Dawley rats (N=6) underwent proximal coronary ligation to induce chronic myocardial infarction. Sham ligation was used as control (N=6). Sixteen weeks later assessment of cardiac function completed and rat humanely euthanased and adipose tissue removed and stored at -80°C.

RNA extracted, reverse transcribed and subjected to QPCR. Rat specific primers for several inflammatory mediators and metabolic markers included stearoyl-CoA desaturase-1 (SCD1), interleukin 1 (IL1) and phosphoenolpyruvate carboxykinase (PCK1)

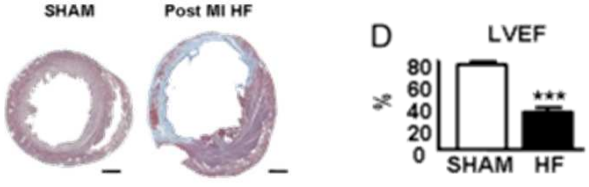
Lipid extracted (Folch method(2)); triglycerides (TAG) measured colourometrically, fatty acid profiles assessed using gas chromatography.

Statistical significance was assessed using ANOVA with post hoc Tukey tests

Results

Triglycerides - Greater storage of TAG observed in HF intra-abdominal AT.
Gene Expression - Reduced expression of SCD1 (enzyme that catalyses desaturation to mono-unsaturates) in HF intra-abdominal AT.
Fatty Acids - FA analysis identified differences in several species; including reductions in C10, C15 and C17 in HF-SC. However, most interesting was a reduction of both C20:5n3 (EPA) and C22:6n3 (DHA) in HF-SC.

Figure 1: Confirmation of heart failure in rats (HF)(3)



SHAM = sham ligation (control group)
MI HF = myocardial infarction heart failure
LVEF = left ventricular ejection fraction

Figure 2: Selected fatty acid profiles in adipose tissue

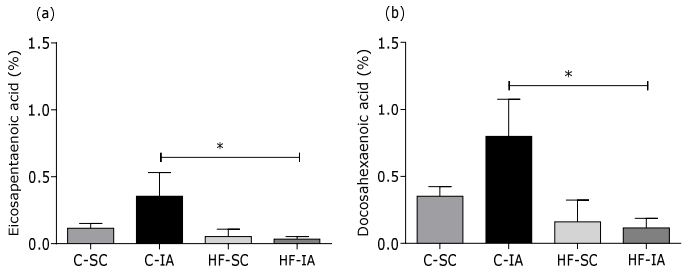


Figure 3: SCD1 expression in adipose tissue

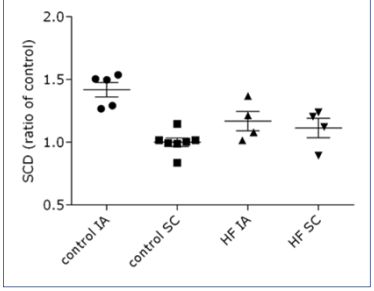


Figure 4: Adipose tissue TAG content

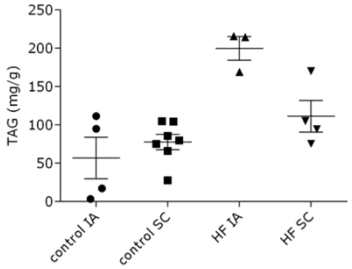
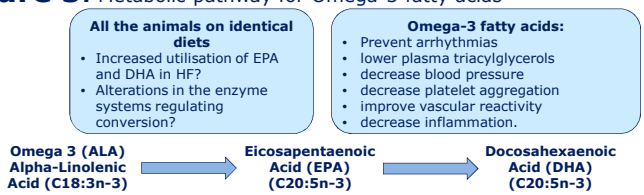


Figure 5: Metabolic pathway for Omega-3 fatty acids



Conclusions

Despite a reduction in SCD1 expression, we did not detect any difference in mono-unsaturated FA species in the HF rats.

EPA and DHA are omega 3 FAs with recognised anti-inflammatory and cardio-protective effects; a reduction in HF suggests altered uptake and metabolism in these animals.

Future Research

Possible areas for further research are:

- To investigate the impact of SERCA2 gene therapy and whether it can ameliorate the effects of HF on adipose tissue.
- To assess the impact of HF on brown adipose depots given. the emerging roles of BAT in adult mammals.
- To determine whether the FAs act as biomarkers of HF.
- Nutritional intervention

Reference

(1) Cinti S, et al. J Lipid Res. 2005;46.
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(3) Lyon, A. R., et al. (2009) Proceedings of the National Academy of Sciences **106**(16): 6854-6859.

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