SECONDARY INSULIN RESISTANCE DEFINES A SUBSET OF PEDIATRIC HEART FAILURE PATIENTS

Poster Contributions
Poster Sessions, Expo North
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Session Title: Role of Comorbidities in Heart Failure: From Diabetes, Pulmonary Disease, Hypertension to Atrial Fibrillation
Abstract Category: 15. Heart Failure: Clinical
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Background: Secondary insulin resistance (IR) occurs in adult heart failure (HF) patients. Biomarkers of IR, including inflammatory cytokines and adipocytokines, have been found to be abnormal in adult patients. Secondary IR and biomarkers of IR have not been studied in the pediatric HF population.

Methods: Thirty-two children aged 1-18 years (median 5.8 years) with symptomatic HF due to systolic dysfunction and 123 healthy, age-, sex-, BMI-, and pubertal stage-matched controls were enrolled. All subjects had normal BMI. Fasting glucose, insulin, homeostasis model assessment of insulin resistance (HOMA-IR) and several biomarkers were assessed. IR was defined as HOMA-IR>95th %ile. Severity of HF was assessed by NYHA class, serum BNP, and echocardiography.

Results: HF patients had lower fasting glucose levels compared to controls (85.4 ± 1.92 vs. 92.4 ± 0.94 mg/dl, p=0.001), though both groups were normoglycemic. A higher proportion of HF subjects were hyperinsulinenic (9% vs. 0%, p=0.008) and insulin resistant (16% vs. 4%, p=0.03) compared to controls. HF patients were at higher risk of IR compared to controls (OR 4.4; 95% CI 1.2-16.2, p=0.03). Among HF patients, HOMA-IR correlated with age (r=0.343, p<0.001), but not with NYHA class, BNP or echocardiographic indices of ventricular function. There was no difference in serum IL-6, TNF-α, leptin, resistin, adiponectin, MCP-1, GLP-1 or ghrelin levels, but there was a trend toward higher TNF-α levels in HF patients (5.7 vs. 4.4 pg/mL, p=0.057). IL-6 was higher in insulin resistant HF subjects vs. insulin resistant controls (9.53 vs. 4.69 pg/mL, p=0.014). In a multivariate stepwise logistic regression model with all biomarkers in all subjects and in HF subjects alone, leptin was the only independent predictor of IR (all subjects p<0.001, R2=0.193; HF patients p=0.014, R2=0.66). After adjusting for age, both leptin and IL-6 significantly predicted IR (p<0.001, R2=0.66) in HF subjects.

Conclusions: Our study is the first to demonstrate secondary IR in pediatric HF patients. IR tends to be seen in older patients but does not correlate with degree of HF. IL-6 may play a specific role in secondary IR. These findings suggest novel targets for research and therapy.