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Heart Failure and Cardiomyopathies

CIRCULATING FREE AND EXOSOMAL MICRORNAS AS BIOMARKERS OF SYSTEMIC RESPONSE TO HEART FAILURE

Moderated Poster Contributions
Heart Failure and Cardiomyopathies Moderated Poster Theater, Poster Hall, Hall C
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Session Title: Put Your Codon! Genetic Insights Into Heart Failure
Abstract Category: 12. Heart Failure and Cardiomyopathies: Basic
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Background: Mir-486 and mir-146a are cardiomyocyte-enriched microRNAs that target proteins in cell signaling, survival, and self-regulation of inflammation. These microRNAs are released into circulation and can be detected in plasma or in circulating exosomes. Studies show that plasma miR-486 and miR-146a are dysregulated in myocardial infarction, coronary heart disease or peripartum cardiomyopathy, indicating their roles as biomarkers and therapeutic targets. However, little is known about their levels in circulating exosomes in heart failure. The aim of this study was to determine the levels of these two microRNAs in plasma and exosomes of patients with heart failure.

Method: microRNAs from plasma or exosomes isolated from the 200 μl of plasma of 40 heart failure patients (ejection fraction less than 35% or NYHA class III or IV) and 20 healthy controls were prepared using the miRVana Kit. Most patients were on guideline directed therapy. qRT-PCR was used to quantify levels of miR-486, miR-146a, and miR-16. Spiked c-ele-mir39 was used as technical control. The expression levels of miR-486 and miR-146a were normalized to miR-16 by $2^{-\Delta\Delta Ct}$ method.

Results: Heart failure did not significantly affect plasma miR-486 and miR-146a although miR-146a showed a trend of elevated expression (2.3±0.79, p=0.27). By contrast, circulating exosomal miR-146a was elevated in heart failure patients compared to control (2.46±0.51, p=0.05). Similar trend was noted with miR-486 (3.0±0.95, p=0.14) in heart failure patients. Thus, heart failure may be associated with changes in microRNA content of circulating exosomes.

Conclusions: miR-146a is induced in response to inflammation as a negative feedback loop to attenuate inflammation. Since exosomes serve as cargos that transfer biological materials to distant organs, elevated levels miR-146a may indicate systemic efforts to attenuate heart failure-induced inflammation. Future studies with additional samples are needed to develop miR-146a as a biomarker of systemic response to heart failure. Furthermore, circulating exosomal rather than plasma microRNAs are likely specific biomarkers of heart failure, an important consideration for clinical translation.