MICRORNA PROFILING IN DIASTOLIC DYSFUNCTION

ACC Poster Contributions
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Background: MicroRNAs (miRNAs) are non-coding endogenous small RNAs of 21-25 nucleotides that can regulate the gene expression by pairing with 3’ untranslated regions (UTR) in messenger RNAs (mRNAs) of protein-coding genes. The importance of miRNAs in diastolic dysfunction is associated with their ability to be used as circulating biomarkers. We assessed the hypothesis that miRNAs may leak into circulation and serve as biomarkers of diastolic dysfunction.

Methods: Identification of candidate miRNAs was done by microarray analysis in patients with isolated diastolic dysfunction and preserved systolic function. Selected miRNAs were then individually validated in a cohort of 8 patients with diastolic dysfunction compared with 8 health controls by quantitative real-time PCR.

Results: Circulating levels of miR-454 (50,000-fold, p<0.05), miR-500 (12,553 fold, p<0.05), miR-142-3p (4,832 fold p<0.05) and miR-1224-5p (6 fold, p<0.05) were all downregulated while miR-1246 (40,286 fold, p<0.05) was upregulated in isolated diastolic dysfunction. This was also validated in 25 dilated cardiomyopathy patients with systolic dysfunction and varying degrees of diastolic dysfunction.

Conclusion: Our results suggests that diastolic dysfunction results in sequestering the expression of miR-454, miR-500, miR-142-3p and miR-1224-5p from circulation and induces a detectable release of miR-1246 into the circulation. These differential levels of circulating miRNAs can be used as a biomarker panel in identifying diastolic dysfunction. Further studies are warranted to study the differential target gene expression regulated by these miRNAs in diastolic dysfunction.