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P-099 - DIASTOLIC HEART DYSFUNCTION IS ACCOMPANIED BY CARDIAC STEATOSIS AND ELEVATIONS OF MYOCARDIAL AND CIRCULATING CERAMIDE 18:0 IN DB/DB MICE

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Resumen

Introduction: Specific plasma ceramides are associated with stress-induced cardiomyocyte damage. However, it is currently uncertain whether plasma ceramides are also associated with cardiac steatosis and myocardial dysfunction in a mouse model of diabesity (db/db) mice.

Material and methods: Non-obese, db/+ mice (on a C57BL/6J genetic background) were bred to mice both homozygous (db/db) and heterozygous (db/+) for $Lepr^{db}$ (db/+). Gross parameters, biochemistry, lipidomic analysis, and functional and structural of the myocardium were determined at the end of the study.

Results: Plasma levels of glucose were significantly elevated (~4-fold, $p < 0.05$) in db/db mice compared with db/+ mice. The db/db mice displayed a mixed dyslipemia, mainly due to increased non-HDL cholesterol (~ 1.5-fold, $p < 0.05$) and triglycerides (~ 1.4-fold, $p < 0.05$), and increased levels of free fatty acids (~ +11%, $p < 0.05$). This phenotype was accompanied by an exacerbated hepatic (liver triglycerides: .5-fold, $p < 0.05$) and adiposity (.10-fold $p < 0.05$). Cardiac steatosis was also elevated in db/db mice (myocardial trilglycerides: .3-fold, $p < 0.05$) compared with non-diabetic mice, but it was not accompanied by a concomitant altered heart weight. Despite this, the E/A ratio was significantly altered (.1.2-fold, $p < 0.05$) in db/db mice, suggesting a diastolic dysfunction. Interestingly, this phenotype was accompanied by a relative increase in the ceramide (Cer) Cer18:0 species in both myocardial and plasma of diabesic mice.

Conclusions: Severe diastolic dysfunction was associated with a restrictive pattern and enhanced myocardial steatosis and accompanied by plasma elevations of Cer 18:0 in db/db mice.