Diastolic Dysfunction is Closely Associated with Myocardial Steatosis in Women at Risk for Heart Failure with Preserved Ejection Fraction

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Purpose Women with coronary microvascular dysfunction (CMD) diagnosed by invasive coronary reactivity testing are at increased risk for developing heart failure with preserved left ventricular ejection fraction (HFpEF), yet the mechanism remains unclear. Myocardial ischemia triggers a shift in energy metabolism from free fatty acids to glucose, which may predispose individuals to ectopic fat accumulation in cardiomyocytes. Cardiac steatosis has been linked to diastolic dysfunction in other disease states and thus may represent an important mechanism in the pathogenesis of HFpEF. The purpose of this investigation was to test the hypothesis that women with CMD have increased myocardial triglyceride (TG) content and that the level of cardio-myocyte accumulation is directly associated with diastolic function.

Methods Cardiac proton magnetic resonance spectroscopy (^{1}H MRS) to measure myocardial TG and myocardial tissue tagging to measure myocardial diastolic function were performed on 8 control women and 6 women diagnosed with CMD and evidence of early HFpEF (b-type natriuretic peptide>400 pg/mL or LV end-diastolic pressure ≥12 mmHg). Myocardial TG content was measured by ^{1}H MRS using 3T Siemens Verio MRI system, with cardiac and respiratory motion compensations, using a single voxel spectroscopy, PRESS: 4.2 cc volume of interest in the septum; TE= 40 ms; TR= 4s; with 32 averaged scans triggered at the end of systole. LV diastolic function was evaluated by circumferential strain rate from myocardial tissue tagging in the short-axis orientation for two slices evenly spaced centered around the mid-ventricle using FLASH gradient echo sequence with: 8 mm slice thickness; 0 mm gap between slices; 7 mm grid tags; Te = 1.8 ms; Tr = 4.0 ms; matrix = 224 x 100; flip angle=8°; FOV=300 x 330 mm^2. Tags were applied at end-systole to ensure persistence of tags throughout diastole, and were analyzed with HARP, Diagnosoft, Palo Alto, CA.

Results: The major novel findings are presented in Figure and are two-fold: 1) cardio-myocyte fat accumulation was significantly augmented in patients compared to controls (p=0.016), and 2) cardio-myocyte fat accumulation strongly predicted the rate of circumferential strain in diastole (r = -0.82, p=0.0003).

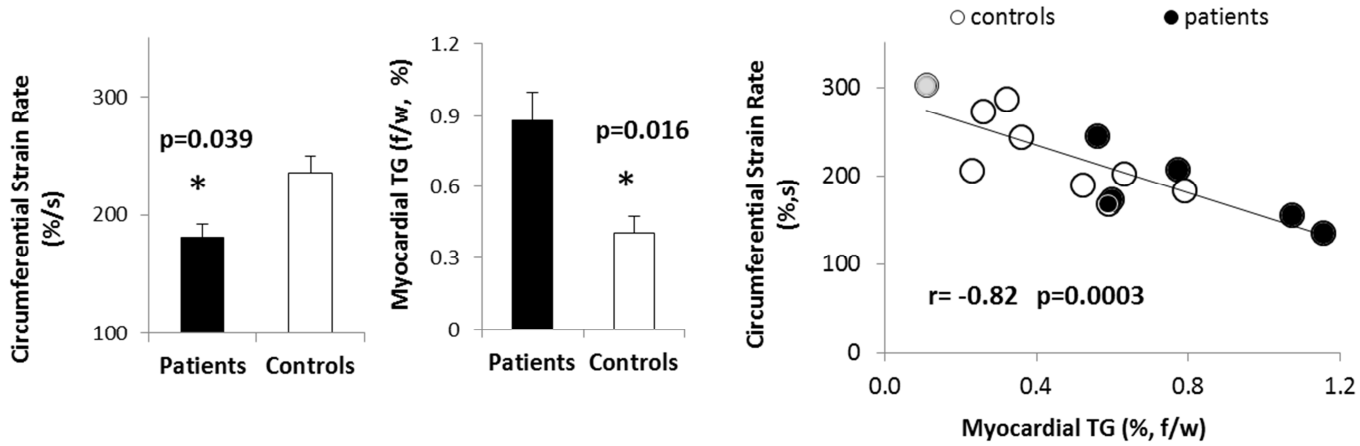

Figure: Myocardial Triglyceride Content and Circumferential Strain Rate in Patients with CMD vs Controls

Conclusion: Our results provide a preliminary support for the hypothesis that myocardial steatosis due to ischemia-triggered shift of myocardial substrate utilization, from free fatty acid to glucose, may predict and promote LV diastolic dysfunction in patients with CMD and early HFpEF.

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