

## Diastolic Dysfunction Is Temporally Dissociated from Myocardial Steatosis

Michael D Nelson<sup>1</sup>, Laura Smith<sup>1</sup>, Edward W Szczepaniak<sup>1</sup>, Ruchi Mathur<sup>1</sup>, Richard N Bergman<sup>1</sup>, and Lidia S Szczepaniak<sup>1</sup>  
<sup>1</sup>Cedars-Sinai Medical Center, Los Angeles, California, United States

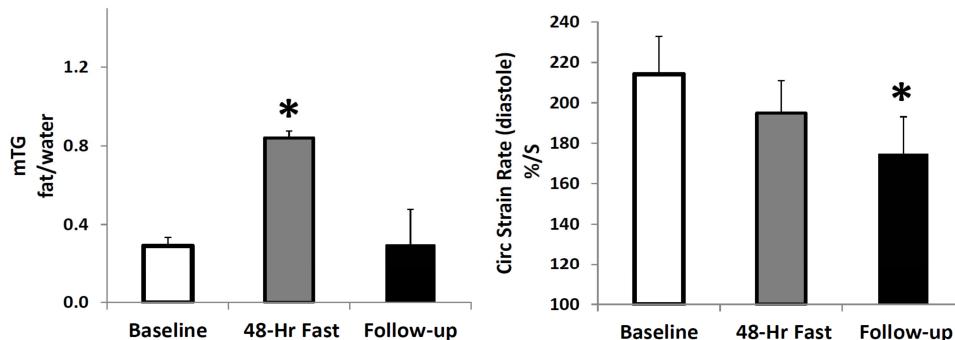
**Target audience** Obesity and type 2 diabetes - mechanisms of cardiomyopathy of obesity/diabetes

**Purpose** The risk for heart failure in obesity and type 2 diabetes is greater than can be accounted for by the traditional antecedent factors of hypertension and coronary artery disease. Altered substrate metabolism is thought to contribute to dysfunction of the diabetic heart. Indeed, with obesity and diabetes, the contribution of glucose oxidation to cardiac energetics is sub-normal, with the reliance on fatty acid metabolism markedly enhanced. Most work in the area of cardiac metabolism has been performed in rodent models, with few studies performed in humans. We present results from a study in which we altered cardiac metabolism by 48 hours fasting in young healthy individuals. Cardiac metabolism was assessed by myocardial triglyceride (mTG) content and diastolic function assessed by myocardial tissue tagging.

**Methods** Five men of age =  $28 \pm 5$  ys; height =  $178.9 \pm 6.6$  cm; and weight =  $82.3 \pm 11.5$  kg were asked to consume only water, at least 3 liters per day, over 2 days. Myocardial triglyceride (mTG) content and left ventricular (LV) diastolic function were evaluated before fasting, immediately after fasting, and one week after resuming a diet ad libitum. Using a 3T Siemens Verio MRI System, we evaluated mTG content by a single voxel spectroscopy, PRESS sequence: 6 cc volume of interest selected in the myocardial septum; TE= 40 ms; TR= 4s; no water suppression during data collection; MRS signal was averaged over 32 scans and collected with a trigger delay at the end of systole. LV diastolic function was evaluated by circumferential strain rate (CSR) from myocardial tissue tagging. In the short-axis orientation, a gradient echo sequence – FLASH (8 mm slice thickness, 0 mm gap between slices, 7 mm grid tags, TE = 1.8 ms, TR = 20.5 ms, matrix =  $224 \times 100$ , flip angle=8°, FOV=300 x 330 mm<sup>2</sup>) was used for two evenly spaced slices centered around the mid-ventricle. Tags were applied at end-systole, defined as the smallest LV cavity area, to ensure persistence of tags throughout diastole, and analyzed with commercially available software (HARP, Diagnosoft, Palo Alto, CA).

**Results and Discussion** Consistent with our previous work, acute starvation caused a significant and transient

elevation in mTG content, increasing nearly 3-fold at 48 hours ( $0.3 \pm 0.03$  to  $0.84 \pm 0.18$  f/w %) and returning to baseline upon follow up ( $0.3 \pm 0.08$  f/w %). Diastolic function declined at 48 hours. However, the significant impairment of diastolic function was recorded one week after resuming normal dietary intake (Figure 1).



**Figure 1.** Changes in myocardial triglyceride content (left) and early circumferential strain rate (right) at baseline, and after 48 hours of fasting in healthy men. Data presented as mean  $\pm$  SE. \*  $P < 0.05$  from baseline.

**Conclusions** The transient changes in mTG content observed during acute fasting highlight the plasticity of human myocardial lipid stores in healthy men. However, the persistence of LV dysfunction after resuming normal nutritional intake and in light of mTG levels returning to baseline is a novel finding that must be further explored especially in populations at risk for cardiomyopathy i.e. obese individuals with impaired glucose tolerance.

**Support** Heart&Stroke Foundation of Canada, NIH R01-DK081524; Lincy Foundation, NIH DK27619, and DK29867