Adiposity of the Lipodystrophic Heart

Michael D Nelson¹, Vinaya Simha², Edward Szczepaniak¹, Ronald G Victor¹, Abhimanyu Garg², and Lidia S Szczepaniak¹

¹Cedars-Sinai Medical Center, Los Angeles, California, United States, ²UT Southwestern Medical Center, Dallas, Texas, United States

Introduction

Obesity is associated with ectopic accumulation of fat in organs such as the heart, skeletal muscle and the liver (termed organs steatosis). Seminal basic research suggests that excessive accumulation of fat in non-adipocytes triggers adverse signaling pathways (termed lipotoxicity), ultimately leading to organ dysfunction. Translating this work into the clinical population however, has been less advanced and limited to correlation studies in individuals with a wide range of BMI and presence of obesity associated co-morbidities. Lipodystrophies are rare disorders characterized by absence/loss of body fat and predisposition to metabolic abnormalities, including insulin resistance, diabetes, hypertriglyceridemia and hepatic steatosis. Patients with generalized lipodystrophies have near total lack of body fat and provide the unique opportunity to study the effects of ectopic myocardial fat deposition in the absence of obesity. Importantly, cardiomyopathy is a frequent finding in these patients, yet the exact mechanism remains unclear (1).

Study Population and Experimental Design

Five individuals with Generalized Lipodystrophy (4 with congenital and 1 with acquired lipodystrophy) were recruited. For a cross-sectional baseline comparison, 5 healthy control subjects (matched for age, gender and BMI) were selected from an existing data pool of controls without metabolic diseases, studied by our laboratory in the past. Patients and controls underwent cardiac magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) examinations performed with a 1.5-T Gyroscan INTERA. Cardiac MRS and MRI were used to measure myocardial steatosis and left ventricular (LV) end-diastolic and end-systolic volumes, respectively. Localized ¹H MR Spectroscopy for the quantification of triglyceride droplets in the cytosol of cardiomyocytes was performed with the following parameters: Tr=4s, Te= 40 ms, 1,024 data points over a 1,000-kHz spectral width. Volume of interest was centered in intra-ventricular septum and data acquisition was triggered at exhalation and at the end systole. Standard long-axis and short axis cine images spanning the entire LV were obtained using prospective ECG-triggering for the quantification of LV volumes. LV mass was computed as the product of end-diastolic LV volume and myocardial density (1.05 g/mL). Left ventricular concentricity was calculated as a ratio between LV mass and LV end-diastolic volume.

Results and Discussion

Intra-myocardial triglyceride levels were elevated in Lipodystrophy patients compared to controls (panel A, p< 0.05). The Lipodystrophy patients had elevated LV mass (panel B) and LV concentricity index (panel C) compared to controls (P < 0.05).

![Graphs showing myocardial steatosis, LV mass, and myocardial concentricity](https://via.placeholder.com/150)

We propose that myocardial steatosis and associated lipotoxicity may be one of the mechanisms contributing to cardiomyopathy in patients with generalized lipodystrophy.

References:


Support: NIH RO1DK081524 (LSS), NIH R01-DK54387(AG), Heart and Stroke Foundation of Canada (MDN)