Investigation of Cardiac Function in Insulin Resistant Rats Using Triggered Cine MRI

G. Govindarajan[1], L. Ma[1], T. Hoffman[1], C. Stump[1], S. Cooper[1], Z. Resch[1], J. Sowers[1]
[1]University Of Missouri-columbia and Harry S.Truman VA Hospital, columbia, Missouri, United States

Introduction:

Insulin resistant conditions such as diabetes and the metabolic syndrome are associated with a cardiac dysfunction and remodeling. These maladaptive changes in diabetics are also known as diabetic cardiomyopathy. These changes include cardiac hypertrophy, and diastolic and systolic dysfunction, which often presents clinically as increased incidence of congestive heart failure. Non-invasive studies to measure the physiological correlates for such changes in insulin resistant rodent models may provide us a powerful tool to study the cardiac functions longitudinally–in a controlled setting. Here, we use cine cardiac magnetic resonance imaging (MRI) technique to assess the cardiac function in insulin resistance rat models. Therapy targeted at insulin resistance may ameliorate these remodeling seen in these rodent models.

Methods

Obese insulin resistant rats (Zucker Obese (fa/fa)) were assigned to rosuvastatin (dose) or untreated conditions. All rats were weighed and systolic blood pressure measured by tail cuff method. Thereafter, rats were anaesthetized using 1.5-2.0 % isoflurane in oxygen, fitted with rectal thermometer, and ECG and respiratory sensors. Imaging was performed on a 7T Varian Unity Inova horizontal bore MRI unit with a 63mm quadrature driven birdcage RF coil. Physiological monitoring and gating were performed using a Physiological Monitoring and Gating System (SA Instruments, Inc.). An ECG-triggered and respiration-gated cine gradient echo pulse sequence was used with a slice thickness of 2 mm, flip angle 20° – 40°, and AVE=2 to obtain 12 to 20 frames. The time to echo was 3.1 ms. The R-R interval (150 to 200 ms for 330 to 410 bpm) was divided into 12 to 20 equally spaced time points that led to a repetition time of 9 to 13 ms. The same line of k-space was collected for each of the phases during 1 heart cycle. This was repeated until all the 256 phase-encoding steps were acquired. A FOV of 60X80mm and a matrix size of 256X512 led to an in-plan resolution of 234X156μm. Data were processed and zero-filled by 2 using VnmrJ (Varian, Inc.). The wall thickness, left ventricle volume, heart mass, and ejection volume measurements were done using VnmrJ and ImageJ™.

Results

Left ventricular ejection fraction (EF) was calculated using the formula (EDV-ESV/EDV) X 100, where EDV is the end diastolic volume; ESV is the end systolic volume. Left ventricular (LV) volume was assessed on a single two chamber long axis plane. LV volume was calculated using the formula $8(A_{(t)})^2 / 3L_{(t)}$, where A is area of the LV in long axis, L is the half distance between the root of aorta and the apex and $_{(t)}$ the cardiac cycle at 12 (to 20) different equally spaced time points between R-R interval. The lowest volume obtained was considered as the ESV and largest volume obtained the EDV. In Zucker obese-untreated, the EF was calculated as 63.10 ±3.28 %. EF for the rosuvastatin treated group was 71.89 ±4.55 percent. Wall Thickness was measured from the single transverse axial image, showing the heart at the widest point obtained at 0 millisecond delay after R wave. Wall thickness in the Zucker obese-untreated was 1.464 ±0.119 mm, treated group was 1.200±0.084 mm.

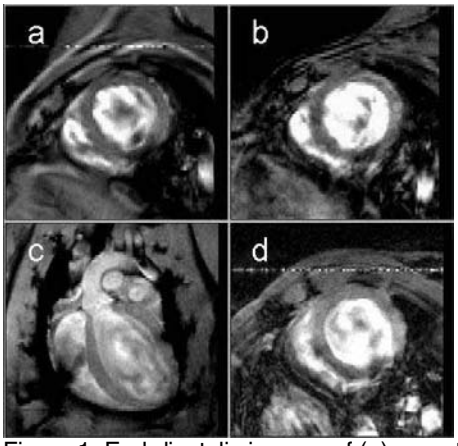

Figure 1. End-diastolic images of (a) an untreated and (b) a rosuvastatin treated Zucker rat heart in midventricular short-axis views; and a normal rat heart (c) long-axis view and (d) short-axis view.

Discussion:

This study used cine cardiac MRI to detect and quantify changes in LV anatomy and function in insulin resistant rodent model. The EF was improved in rosuvastatin treated animals which was associated with decreased LV wall thickness when compared to untreated animals. This experiment demonstrates the usefulness of the non-invasive cardiac MRI technique to study obese insulin resistant rodents. This technology should provide future opportunities to study cardiovascular function in rodents in longitudinal studies before and after specific interventions.

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