Modification of cardiac morphology was associated with impaired myocardial sensitivity to ischemia-reperfusion injury in a diet-induced metabolic syndrome model

Natacha Fourny, Carole Lan, Frank Kober, Monique Bernard, Martine Desrois

Fourny N, Lan C, Kober F, Bernard M, Desrois M.

Modification of cardiac morphology was associated with impaired myocardial sensitivity to ischemia-reperfusion injury in a diet-induced metabolic syndrome model.

In: Diabetologia. Vol. 60 Supplement 1. 53rd Annual Meeting of the European Association for the Study of Diabetes (EASD), Lisbon/PT, September 11-15. ; 2017. pp. S547–S547. doi: 10.1007/s00125-017-4350-z.

Background and aims: Metabolic Syndrome (MetS) is defined by multiple risk factors that predict type 2 diabetes and cardiovascular complications, such as myocardial infarction, especially in women. Consequently the aim of this study was to investigate in vivo and ex vivo the effects of a high-fat-high-sucrose diet (HFHSD) on the development of metabolic syndrome (MetS), cardiac morphology and sensitivity to ischemia-reperfusion injury of female Wistar rat.

Materials and methods: Female Wistar rats, subjected to HFHSD (FHFD) or Normal Diet (FND) during 5 months, were explored in vivo every month with multimodal cardiovascular magnetic resonance (CMR). Cine-MRI (Magnetic Resonance Imaging) and arterial spin labeling (ASL-FAIR) techniques were used to determine cardiac morphology, function and perfusion. Triglyceride (TG) content in heart and liver 1was also evaluated with H Magnetic Resonance Spectroscopy (MRS). 1Sub-cutaneous and visceral adipose tissues were measured with H MRI. Then, rats underwent an intraperitoneal glucose tolerance test (IPGTT) to determine glycemic status. Finally, isolated heart were perfused with a physiological buffer containing 0.4 mM palmitate for 24 minutes before switching to 1.2 mM palmitate during 32 minutes low-flow (0.5 mL/min/g wet wt) ischemia. Next, flow was restored with 0.4 mM palmitate buffer for 32 minutes. High-energy phosphates and intracellular pH were measured during the experimental course by P magnetic resonance spectroscopy with simultaneous measurement of contractile function. Coronary flow was measured before and after ischemia. At the end of experiments, hearts were freeze-clamped for biochemical assays.

Results: In FHFD vs. FND, CMR showed an increase of systolic wall thickness over time ($p<0.05$) and diastolic wall thickness at 3 and 5 months 1($p<0.01$); H MRS showed that hepatic TG content was increased ($p<0.01$) at 5 month but myocardial TG content was not different. IPGTT showed a significant glucose intolerance ($p<0.001$) and plasma free fatty acids were increased ($p<0.05$) in FHFD vs. FND. At 5 months, weight was not different between groups but FHFD exhibited an abdominal obesity with increased visceral adipose tissue ($p<0.05$), % fat ($p<0.05$) and % visceral fat ($p<0.05$) compared with FND. Ex vivo myocardial function was impaired in FHFD vs. FND before ($p<0.01$) and after ischemia ($p<0.05$).

Conclusion: HFHSD-induced MetS was characterized by glucose intolerance, abdominal obesity, hepatic fat deposit which were associated with modification

of cardiac morphology and higher myocardial sensitivity to ischemia-reperfusion injury. These results may be related to higher risk of cardiovascular complications among type 2 diabetic obese women. Supported by: Aix-Marseille Univ, CNRS, France Life Imaging Disclosure: N. Fourny: None.