In vivo and ex vivo longitudinal follow-up of resveratrol supplementation or restauration of a normal diet in female rat hearts submitted to high-fat-high-sucrose diet

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to follow the evolution of cardiac function for 28 days after in vivo myocardial infarction in control or PNOF mice.
Method C57BL/6 male mice were raised in litter adjusted to 9 or 3 pups for control and PNOF group respectively. After weaning, mice of both groups had free access to standard diet and water. At 4 months, they were subjected to permanent ligation of the left anterior descending artery (LAD) to induce myocardial infarction or to sham surgery. Echocardiographic measurements were acquired at baseline and 1, 7, 15 and 28 days after surgery for cardiac function evaluation. Twenty-eight days after surgery, the left ventricle (LV) and lungs were weighed and infarct size was assessed.
Results At basal state, no difference of cardiac function was observed between the 4 groups. In both control and PNOF mice subjected to LAD ligation, the fractional area change (FAC) was significantly decreased 24 h after surgery and the systolic/diastolic LV area was significantly increased 7 d after surgery, and both remained stable until 28 d. However, no differences neither in LV contractile function nor in infarct size were noticed between control and PNOF mice, except for an increased LV mass in PNOF mice.
Conclusion While all groups of mice subjected to myocardial infarction developed heart failure, as demonstrated by decreased LV contractility and dilation, there were no differences between control and PNOF groups. Further measures will be done in order to assess circulating biomarkers as cardiac troponin I (cTnI), brain natriuretic peptide (BNP) and growth differentiation factor-15 (GDF-15).
Disclosure of interest The authors declare that they have no competing interest.

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168

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Introduction Prediabetic women are at greater risk of cardiovascular diseases than men, investigating new sex dependent strategic therapies is then essential to limit cardiovascular complications in prediabetic women.
Objective We aimed to evaluate the effects of resveratrol supplementation (RSV) or restauration of a standard diet on the heart of prediabetic female rats submitted to high-fat-high-sucrose diet (HFS).
Methods Wistar female rats were divided in 4 groups fed for 5 months with: normal or HFS diet (CTRL/HFS), HFS with RSV (1 mg/kg/day) during the last 2 months or HFS for 3 months and 2 months of standard diet (RSD). We performed a longitudinal in vivo study of cardiac function, morphology and perfusion by MRI, then rats underwent an IPGTT. Ex vivo experiments on isolated perfused hearts were realized to study cardiac function [rate pressure product (RPP), end diastolic pressure (EDP)] and energy metabolism with ^{31}P magnetic resonance spectroscopy during an ischemia-reperfusion injury (IR). Tissues were collected for analyzes.
Results Five months of HFS diet-induced glucose intolerance ($P < 0.05$), increased heart perfusion and heart/tibia length ratio (HTLR) ($P < 0.01$ vs. CTRL). HFS also induced altered myocardial tolerance to IR, characterized by impaired RPP and EDP ($P < 0.001$) associated with lower ATP and PCr levels during reperfusion ($P < 0.001$, $P < 0.05$ vs. CTRL). RSV had no effect on glucose tolerance and heart perfusion ($P < 0.01$ vs. CTRL) but normalized HTLR to CTRL level. Interestingly, RSV diminished EDP during reperfusion ($P < 0.05$ vs. HFS). RSD normalized glucose tolerance without effect on heart perfusion and HTLR ($P < 0.01$ and $P < 0.05$ vs. CTRL). RSD improved tolerance to IR with increased RPP ($P < 0.05$ vs. HFS), ATP and PCr levels during reperfusion ($P < 0.01$, $P < 0.001$ vs. HFS).
Conclusion The two approaches have distinct effects on cardiac function and energy metabolism of prediabetic female rats. Further studies are on the go to explore the mechanisms involved.
Disclosure of interest The authors declare that they have no competing interest.

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133

Postnatal overfeeding induces a higher cardiac sensitivity to in vivo ischemia-reperfusion injury at all ages in male mice, but only in young females

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Introduction Nutritional disturbances during the postnatal period may be responsible for a predisposition in adulthood to increased cardio-metabolic risk and a greater myocardial vulnerability to ischemia. However, these data have mainly been obtained in young male mice, but less is known for females and for older animals.
Objective Evaluate the impact of postnatal overfeeding on:
— cardiac sensitivity after in vivo ischemia-reperfusion (I-R) on both sexes;
— in young (4 months), adult (6 months) and mature (12 months) mice.
Methods PNOF was induced by reduction of litter size of C57/BL6 mice immediately after birth: normally-fed group (NF) litters were composed of 9 pups/mother and overfed group litters (OF) of 3 pups/mother. The in vivo ischemia was induced by a 45 min ligation of the left anterior interventricular artery, followed by 24 hours of reperfusion, in hearts from 4-, 6- and 12-months aged male and female mice. The area at risk (AAR) was determined by Evans blue coloration and the infarct size by TTC staining.
Results PNOF induced an early and permanent increase in body weight in OF group, for males (4 months: +13%; 6 months: +23%; 12 months: +23%) and female mice (4 months: +23%; 6 months: +27%; 12 months: +15%). A significant increase of infarct size was observed in hearts of overfed male mice aged at all ages (4 months: +37%, 6 months: +32% and 12 months: +38% of AAR), but for females, infarct size was significant increased at 4 months (+34%), but not at 6 and 12 months. However, in all female groups (NF and OF) we observed a higher post-surgical mortality and a greater data variability as compared to males.
Conclusion Nutritional programming through short-term PNOF induced a higher susceptibility to myocardial I-R injury in vivo at all ages in male mice, but only in young females. The mechanism of this sexual dimorphism in our model is not well understood, but could involve distinct levels of cardioprotective pathways expression, related to hormonal status.
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