treated at -3 days and -1 pre-surgery, followed by post-surgery weekly boosting. HLI was achieved by unilateral ligation and excision of the femoral artery of the left hind limb. The right hind limb served as non-ischemic control. Gene expression analysis in the hind limbs 3 days post HLI showed decreased miR29a expression in normal chow fed B6, but elevated miR29a expression in HFD (B6 vs HFD; 0.5730±0.01 vs.1.02 ± 0.06, n=3–4, p= 0.001). Treatment with miR29a inhibitor decreased miR29a expression in HFD and increased ADAM12 expression compared to control untreated HFD mice (miR29a INH vs Control HFD: 0.70±0.06 vs 1.02±0.06, n= 4–5, p= 0.004) ADAM12 expression (miR29A INH vs Control: HFD 208.62±24.52 vs 11.75±4.94, n= 3–4 P<0.01). Although ADAM12 cDNA improved ADAM12 expression, miR29a inhibition increased ADAM12 expression to a greater extent (HFD vs ADAM12 vs miR29aINH; 11.75±4.94 vs 20.71±2.98 vs 208.62±24.52, n3-4, p=< 0.001). Accordingly, miR29a inhibition and ADAM12 augmentation decreased skeletal muscle injury assessed by the number of centralized nuclei/muscle fibre (Control vs ADAM12 vs miR29aINH: 0.252±0.043, vs 0.139±0.041 vs 0.040±0.012 n=4, p= 0.05), and improved skeletal muscle function assessed as maximum muscle contraction (Control vs ADAM12 vs miR29aINH: 0.17±0.06 vs 0.26±0.06, vs 0.54±0.08, n=6–7, p<0.01). It also improved perfusion recovery, (% ischemic to non-ischemic limb, control vs ADAM12 vs miR29aINH: 42.52±5.35, vs 58.45±4.87, vs 97.59±6.14, n= 5–10, p<0.01). Thus, our results show augmentation of ADAM12 and Inhibition of MiR29a improves outcomes in experimental PAD in diabetic mice but inhibiting miR29a is a more effective strategy.
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Insulin Resistance Is Associated With Impaired HDL Function and Atherogenic Modification of LDL in Polycystic Ovarian Syndrome

Jan Hoong Ho, MBChB, MRCP[1], Safwaan Adam, MBChB MRCP[2], Yifen Liu, Dr, PhD[1], Shaishav Dhage, DNB MRCP MRCP ENDOCRINOLOGY[3], Sotirios Tsimikas, MD[4], Handrean Soran, MD[1], James Gibney, MD[5].
[1]University of Manchester, Manchester, United Kingdom, [2]THE CHRISTIE NHS FOUNDATION TRUST, Bolton, United Kingdom, [3]North West Deanery, Bolton, United Kingdom, [4]University of California San Diego, San Diego, CA, USA, [5]Tallaght University Hospital, Dublin, Ireland.

Background and Aims: Polycystic ovarian syndrome (PCOS) is associated with increased risk of cardiovascular disease (CVD). The aim of this study was to assess the association between PCOS and markers of HDL functionality and atherogenic LDL modification. **Methods:** This is a cross-sectional study of 104 women with PCOS [median (IQR); age 29 (24–36) years, and BMI 32.9 (25.7–38.5) kg/m^2] and 103 BMI-matched healthy participants (age 34 (27–37) years, and BMI 31.1 (27.6–35.5) kg/m^2). PCOS was defined using the NIH criteria. Measurement of lipid profile and glycaemic blood parameters were undertaken. Patients with PCOS were divided into tertiles of insulin resistance assessed using the homeostatic model assessment (HOMA-IR). Cholesterol efflux capacity (CEC), and paraoxonase-1 (PON1) activity were measured as markers of HDL functionality. Oxidized LDL (OxLDL), lipoprotein-associated phospholipase A2 (LpPLA2), oxidized phoshopholipids on apolipoprotein B-100 (OxPL-apoB) and apolipoprotein(a) (OxPL-apo(a)), and glycated apoB were used as markers of atherogenic modification of LDL. **Results:** Patients with PCOS in the upper tertile of insulin resistance had impaired HDL functionality compared to the lower tertile and controls, with lower CEC [13.7 (12.4–14.6) vs 14.9 (13.6–17.0), *P*=0.003; and 14.5 (13.0–16.0) %, *P*=0.063 respectively] and PON1 activity [77.2 (48.2–129.2) vs 112.9 (54.0–175.4), *P*=0.043; and 131.6 (89.5–195.1) nmol/ml/min, *P*<0.001 respectively]. Markers of atherogenic modification of LDL were also increased in the upper tertile compared to the lower tertile and controls, with higher levels of OxLDL [91.6 (58.8–120.9) vs 67.2 (20.1–86.3), *P*=0.016; and 74.8 (47.6–89.5) ng/ml, *P*=0.013 respectively], LpPLA2 [1.66 (1.48–1.84) vs 1.48 (1.39–1.60), *P*=0.004; and 1.53 (1.37–1.70) μg/ml, *P*=0.015 respectively], small-dense LDL cholesterol (sdLDL) [24.8 (16.8–35.0) vs 15.3 (11.3–20.1), *P*<0.001; and 20.9 (14.6–29.0) mg/dl, *P*<0.001 respectively], and glycated apoB [4.02 (3.63–4.33) vs 3.51 (3.27–3.70), *P*<0.001; and 3.48 (3.20–3.96), *P*<0.001 respectively]. Both BMI and insulin resistance were associated with adverse lipoprotein modification, correlating positively with OxLDL, LpPLA2, sdLDL, and glycated apoB (Spearman's ρ=0.244–0.325 and Spearman's ρ=0.254–0.377 respectively, all *P*<0.050); and negatively with CEC (Spearman's ρ=-0.244 and
Spearman's ρ=0.254 respectively, both *P*<0.050). OxPL-apoB, OxPL-apo(a), and lipoprotein(a) did not differ between PCOS and controls. **Conclusions:** Insulin resistance is a key determinant of decreased HDL functionality and increased oxidative modification and glycation of LDL in PCOS, which is likely to contribute to the increased CVD risk.

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Interaction Between Wnt/β-catenin and ACTH Signaling Pathways and Paracrine Regulation in Aldosterone Producing Adenoma

Alaa B. Abdellatif, MSc[1], Kelly De Sousa, PhD[1], Isabelle Giscos-Douriez, Ms[1], Tchao Meatchi, MD[2], Laurence Amar, MD, PhD[3], Fabio L. Fernandes Rosa, MD, PhD[1], Sheerazed Boulkroun, PhD[1], Maria-Christina Zennaro, MD, PhD[1].
[1]Université de Paris, PARCC, INSERM, Paris, France, [2]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service d'Anatomie Pathologique, Paris, France, [3]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Unité Hypertension artérielle, Paris, France.

Primary aldosteronism (PA) is the most frequent form of secondary arterial hypertension and is caused in the majority of cases by an aldosterone producing adenoma (APA) or bilateral adrenal hyperplasia. Different somatic mutations have been identified in APA and in other aldosterone producing structures, which can be distinct within the same adrenal, suggesting multiple mechanisms underlying