Elevated blood cobalt secondary to metal-on-metal (MoM) hip arthroplasties has been shown to be a risk factor for developing cardiovascular complications including cardiomyopathy. Published case reports document cardiomyopathy in patients with blood cobalt levels as low as 13μg/l. Clinical studies have found conflicting evidence of cobalt-induced cardiomyopathy in patients with MoM hips. The extent of cardiovascular injury, measured by global longitudinal strain (GLS), in patients with elevated blood cobalt levels has not previously been examined.

Sixteen patients with documented blood cobalt ion levels above 13μg/l were identified and matched with eight patients awaiting hip arthroplasty with no history of cobalt implants. Patients underwent echocardiogram assessment including GLS.

Patients with MoM hip arthroplasties had a mean blood cobalt level of 29μg/l compared to 0.01μg/l in the control group. There was no difference or correlation in EF, left ventricular (LV) end systolic dimension, LV end diastolic dimension, fractional shortening, ventricular wall thickness or E/e’ ratio. However, GLS was significantly reduced in patients with MoM hip arthroplasties compared to those without (-15.2% v -18%, (MoM v control) p= 0.0125). Pearson correlation demonstrated that GLS is significantly correlated with blood cobalt level (r= 0.8742, p=0.0009).

This study has demonstrated reduced cardiac function in the presence of normal EF as assessed by GLS in patients with elevated cobalt above 13μg/l. As GLS is a more sensitive measure of systolic function than EF, routine echocardiogram assessment including GLS should be performed in all patients with MoM hip arthroplasties and elevated blood cobalt.

Further studies will be needed to identify the redox sensitive molecular pathways, that are altered by Glrx overexpression in the maternal cardiovascular system.

**Cardiac function is compromised in patients with elevated blood cobalt levels secondary to metal-on-metal hip implants**

1,2Mark Jenkinson*, 1Dominic Meek, 1Sandy MacMillan, 1Rothwelle Tate, 1M Helen Grant, 1Susan Currie. 1Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK; 2Department of Trauma and Orthopaedics, Queen Elizabeth University Hospital, Glasgow, UK; 2Department of Biomedical Engineering, University of Strathclyde, Glasgow, UK

10.1136/heartjnl-SCF-2023.11

**GLUTAREDOXIN-OVEREXPRESSION ATTENUATES CHRONIC ANGIOTENSIN-II INDUCED HYPERTENSION AND CHANGES CARDIAC DYNAMICS**

Hollie Whyte*, Yashika Relan, Colin Murdoch. Dundee University, Dundee, UK

Angiotensin-II (AngII) induces hypertension and cardiac hypertrophy and is a potent inductor of oxidative stress, which causes oxidative post-translational modifications (oxPTMs). Glutaredoxin-1 (Glrx) catalyses the removal of an oxPTM, S-glutathionylation, and has been shown to be important in peripheral artery disease. Therefore, we investigated the effect of Glrx overexpression on AngII-pressure overload.

Glrx transgenic (TG) and wild-type (WT) littersmates were implanted with osmotic pumps (Alzet) containing either saline or AngII (1.1mg/kg/day; s.c). After 2 weeks, mice were anaesthetised (2% isoflurane) and a pressure-volume (PV) catheter was inserted retrogradely into the left ventricle (LV).

In WT mice, AngII increased systolic and diastolic BP. However, no significant increase in SBP and DBP were observed in TG mice. Heart rates remained similar between all 4 groups. Although AngII increased BP in WT mice, LV end-diastolic/systolic pressure (EDP/ESP) and end systolic volume (ESV) remained unchanged between the four groups. However, AngII significantly lowered end diastolic volume (EDV) in TG compared to WT. Hence, stroke volume (SV) was also lowered in TG compared to WT. Yet, these changes had no overall effect on LV cardiac output or stroke work. Interestingly, AngII significantly lowered LV contractile state (Powermax) in response to AngII in TG compared to WT mice.

In summary chronic AngII infusion did not increase blood pressure in mice overexpressing Glrx, but lowered pre-load with subsequent lower stroke volume and cardiac contractility. Future studies will investigate which redox sensitive proteins undergo reversal oxPTM to elicit these functional changes.

**Redox regulation of Jagged1 modulates cell cycle, adhesion and ECM pathways in endothelial cells**

Shawn Cottrill*, Colin Murdoch, Iain Phair, Andy Howden. University of Dundee, Dundee, UK

10.1136/heartjnl-SCF-2023.13

Jagged1 (Jag1) has essential roles in angiogenesis and development. Altered function of this transmembrane protein results in congenital birth defects and cancer progression. Redox signalling regulates cardiovascular physiology through Endothelial cells (EC). Proteins sense redox signals through cysteine thiols.