This is a peer-reviewed, author's accepted manuscript of the following meeting abstract: Olatunji, Z. O., MacMillan, S., Cameron-Ruiz, M., Bosakhar, Z. Y., MacKenzie, G., Grant, M. H., Tate, R., MacQuaide, N., & Currie, S. (2023). Effects of acute and chronic cobalt treatment on adult rat cardiomyocyte calcium handling. *Heart* , *109*(Supplement 2). https://doi.org/10.1136/heartjnl-SCF-2023.18

Patients with cobalt-chromium hip arthroplasties display increased cobalt levels in circulation. Elevated cobalt has been linked to cardiomyopathy, yet the mechanisms underlying cobalt-induced pathology remain unknown. Here, we have examined the effects of acute (

Cardiomyocytes were isolated enzymatically from adult male rats (n=9) and treated acutely for 5min, 1h and 24h with 1, 10 and 100µM $CoCl_2$. After loading with Cal520 AM, calcium transients were measured during electrical pacing at 1Hz and sparks were recorded using confocal microscopy. Chronic cobalt effects were measured in cardiac preparations taken from adult male rats (n=8) injected daily with $CoCl_2$(1mg/kg) for 28 days.

A concentration and time-dependent decrease in Ca^{2+} transient amplitude was evident in cobalt-treated cells compared to controls, with 10µM $CoCl_2$ inducing an amplitude reduction of 15.1±5.4% and 30.0±7.2% at 5min and 1h respectively and 100µM resulting in 25.6±0.05% and 58.8±0.09% reduction at 5min and 1h. Spark frequency was increased with 100µM cobalt relative to control, resulting in 55.4±0.9% and 76.8±1.4% increase at 5min and 1h. RyR2 expression in chronic cobalt-treated ventricular tissue was similar to controls, suggesting RyR2 post-translational modification may account for altered spark frequency.

This study demonstrates reduced Ca^{2+} release and increased RyR2 activation in cardiomyocytes treated acutely with $CoCl_2$. Indications suggest RyR2 phosphorylation may be involved in the negative inotropic effects observed.