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**THE INHIBITORY EFFECT OF REMOTE ISCHAEMIC
CONDITIONING ON A CELLULAR MODEL OF CARDIAC
HYPERTROPHY**

doi:10.1136/heartjnl-2012-303148a.13

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Remote ischaemic conditioning (RIC) protects against ischaemia-reperfusion injury, but it is unclear whether it could also attenuate adverse cardiac remodelling post-MI. We hypothesised that RIC

generates a blood born signal capable of reducing the hypertrophic response by modulating gene expression associated with remodelling.

Superfusate was collected from ischaemic conditioned Langendorff perfused rat hearts (RIC-superfusate). Blood was taken from healthy volunteers after three cycles of upper arm conditioning (RIC-serum). The RIC-superfusate/serum was applied to H9c2 cardiomyoblasts in culture treated with endothelin-1 (ET-1) to stimulate hypertrophy. Immunofluorescence was used to determine cell area. Expression of four genes associated with cardiac remodelling: BNP, α -actin, β MHC and ms^{-1} were determined using qRT-PCR. Response was compared to saline/unconditioned serum.

ET-1 (100 ng/ml) caused a significant degree of cellular hypertrophy after 48 h: 22.8 ± 1.1 vs $16.4 \pm 0.7 \text{ mm}^2$ in untreated cells ($n=300$ $p<0.01$). Pre-treatment with RIC-superfusate/RIC-serum significantly reduced ET-1 induced hypertrophy from 19.8 ± 0.8 to $14.7 \pm 0.6 \text{ mm}^2$ and 23.6 ± 1.5 to $16.1 \pm 1.1 \text{ mm}^2$ respectively ($n=300$ $p<0.01$). RIC-superfusate caused a significant decrease in ET-1 induced expression of α -actin (fold-change 8.0 ± 0.4 to 1.7 ± 0.1 , $n=4$ $p<0.01$), β MHC (6.5 ± 0.5 to 2.5 ± 0.3 , $n=4$ $p<0.01$), BNP (1.3 ± 0.3 to 0.4 ± 0.2 , $n=4$ $p<0.05$) and ms^{-1} (31.6 ± 2.7 to 13.0 ± 1.4 , $n=4$ $p<0.01$) after 48 h. RIC-serum significantly reduced ET-1 induced expression of β MHC (7.7 ± 1.0 to 3.9 ± 0.5 , $n=4$ $p<0.05$) and ms^{-1} (15.4 ± 2.7 to 7.0 ± 0.7 , $n=4$ $p<0.05$) after 48 h.

Our data supports the hypothesis that RIC initiated humoral signalling may attenuate the deleterious process of cardiac remodelling. The findings identify a new therapeutic approach that may be beneficial in reducing adverse ventricular hypertrophy post-MI.