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Short-term repeated remote ischemic conditioning effect on post-infarct myocardial function: the importance of neuregulin-1

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Introduction: Adverse left ventricle (LV) remodelling following myocardial infarction plays a significant role in the progression of heart failure (HF). Long-term repeated remote ischemic conditioning (RIC) following MI improved post-infarct cardiac function. However the underlying mechanisms are not completely understood. Clinical trials have shown that neuregulin-1 (NRG-1) administration improves cardiac function in HF patients.

Aims: The present study's aims were to (1) clarify the effect of short period of RIC on cardiac hemodynamic function post MI and to (2) assess the effect of RIC’s correlation to NRG-1 plasma levels

Methods: Male OFA rats were subjected to left coronary artery (LCA) occlusion and allocated to two groups: (1) Myocardial infarction (MI; permanent ligation of LCA; n=7) and (2) MI+RIC; n=5). RIC treatment was performed by 3 cycles of 5 min of bilateral hindlimb ischemia and 5 min of reperfusion once a day for 5 days starting on day 3 post-MI). Functional parameters were assessed by echocardiography and were evaluated on an isolated erythrocyte-perfused working heart model. The expression of plasma levels of NRG-1 was measured by ELISA.

Results: Despite comparable reduction in left ventricle ejection fraction (LVEF; 61±2% vs 62±1%) and the enlargement of left ventricle with an increase in end-diastolic (LVEDD; 8.9±0.2 mm vs 8.8±0.07 mm) and end-systolic (LVESD; 6.2±0.2 mm vs 6.1±0.1 mm) diameters on the 3rd day following MI, short term RIC has slightly improved LVEF (63±1% vs. 58±2%, p=0.074). Furthermore RIC had the tendency to prevent LV enlargement compared to the MI group (LVESD: 5.9±0.06 mm and 6.4±0.2 mm, p=0.064). In addition, both coronary flow (CF) and LVESP was markedly enhanced in rats with RIC in comparison with MI (CF; 4.3±0.2 vs 3.1±0.2 ml/g heart, LVSP: 109±2 mm Hg vs 119±4; p<0.01 and p=0.07, respectively). Of importance, the expression of NRG-1 in plasma was significantly elevated in RIC group (10.6±1.7 µg/ml vs 19.4±3.3 µg/ml, p<0.05).

Conclusion: Short-term RIC improved cardiac function, preserved systolic LV function and coronary flow post-MI. This was associated with a marked increase of NRG-1 plasma levels. Our results indicate that short-term RIC might be a novel, cost-effective approach to improve cardiac function and minimize adverse LV remodelling following myocardial infarction.