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Chronic Renal Failure Leads to Adverse Cardiac Remodeling after MI Via Upregulation of Gp130-STAT3 Pathway

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Introduction:

Uremia is significant risk factor for cardiovascular mortality. In patients with MI, CRF contributes to poor clinical outcome; however the exact mechanism is unknown. We sought to evaluate the impact of uremia on LV remodeling following MI.

Methods:

SD rats were divided into two groups: control group (n=12) fed with a regular diet and renal failure group (n=15) fed with uremia induced diet by high adenine phosphate regimen. Two weeks later adenine diet feeding, control and renal failure groups were subjected to LAD ligation. Echocardiography, histology, gene and inflammatory markers expression analysis were performed.

Results:

Prior MI, LV dimensions following two weeks high adenine diet consumption were significantly enlarged compared to baseline (LVEDd=0.74±0.05 mm vs. 0.67±0.05mm, LVESd=0.44±0.06 mm vs. 0.37±0.07 mm, $p<0.05$). In RF animals LV end- diastolic (0.87±0.07mm vs. 0.75±0.06mm, $p<0.05$) and end- systolic diameters (0.61±0.11 vs. 0.50±0.09, $p<0.05$) continuously increased one week post MI. However, fractional shortening and MI size show no difference.

Monocyte (12.8±3.6% vs. 8.38±1.2 %, $p<0.05$) and granulocyte blood levels (27.1±10.5% vs. 11.09±2.3, $p<0.05$) were significantly elevated in renal failure group compared to baseline. Furthermore, 2 weeks after MI monocyte (17.9±4.7% vs. 11.7±1.6%, $p<0.05$) and granulocyte (49.9±3.8% vs. 28.7±14.0%, $p<0.05$) blood levels in RF animals continue to be significantly higher compared to control. However, macrophages infiltration to the remote zone two weeks post MI was similar.

Among the three main pathways activated by GP130 through IL-6 cytokines family, expression of JAK/STAT3 axis was significantly upregulated in the RF group ($p=0.01$), while expression of PI3K/AKT and RAF/ERK pathways remained unchanged.

Conclusions:

We demonstrated that CRF is associated with progressive impairment of LV function and severe dilatation. GP130/STAT3 pathway might play an important role in mediating adverse remodeling process. In summary, our results provide a novel perspective to clinical outcome in patients with CRF.