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CARDIAC FUNCTION AND HEART FAILURE

INHIBITION OF INTERLEUKIN-1 ACTIVITY IMPROVES SPECKLE TRACKING MYOCARDIAL DEFORMATION BY REDUCING OXIDATIVE STRESS- MEDIATED APOPTOSIS IN RHEUMATOID ARTHRITIS.

ACC Poster Contributions
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Session Title: Myocardial Function/Heart Failure -- Clinical Pharmacologicial Treatment
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Background: Studies have shown that inhibition of Interleukin-1 activity improves myocardial deformation through reduction of nitrooxidative stress and reduces the size of experimental myocardial infarction through reduction of cell apoptosis. We investigated whether inhibition of Il-1 activity reduces apoptosis and thus, improves myocardial deformation in rheumatoid arthritis patients (RA).

Methods: In an acute, double-blind trial, 43 patients with RA were randomized to receive a single injection of anakinra, a recombinant IL-1 receptor antagonist , (150mg s.c.) or placebo and after 48-hours were crossed over to the alternate treatment. At baseline and 3-hours after the single injection, we assessed a) LV longitudinal, circumferential and radial strain and strain rate, using speckle tracking echocardiography and c) Fas, Fas ligand and caspase-9 serum levels, as apoptotic markers and protein carbonyl (PC) as marker of oxidative stress. Patients were reassessed after 30 days of anakinra treatment.

Results: At 3 hours and 30 days after treatment, there was an significant reduction in Fas (541±403 vs. 416±373 vs. 378±200 ng/ml), Fas ligand (median 209 vs. 150 vs. 140 pg/ml), caspase-9 (2.63±2.79 vs. 2.01±1.82 vs. 1.66±1.63 ng/ml) PC (0.16±0.08 vs. 0.12±0.09 vs. 0.11±0.08 nmol/mg protein)), and Longitudinal SR (-1.02±0.23 vs-1.125±0.20 vs -1.25±0.23 l/s) compared to baseline ($p<0.05$ for all comparisons). No changes were observed after placebo. Baseline Fas and Fas ligand predicted the absolute and %change of Longitudinal SR after 3 hours and 30 days post anakinra ($p<0.05$) The percent changes of PC were related with the changes of Fas, Fas ligand and caspace-9 (r=-0.578, r=-0.603, r=-0.523, r=-0.588, $p<0.05$) Additionally the %changes of Fas, Fas ligand and caspase-9, 3 hours post-anakinra were also related to the absolute and %change in Longitudinal SR (r=-0.583, r=-0.555, r=-0.564, r=-0.538, $p<0.05$) Similar association were observed after 30 days of anakinra treatment.

Conclusions: The reduction of apoptosis through reduction of oxidative stress is a potential mechanism for the improvement of myocardial deformation after inhibition of IL-1 activity.