

## PRESENTING AUTHOR'S NAME & RESEARCH TITLE

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Circulating Plasma Angiotensin Peptides as Biomarkers of Rheumatoid Arthritis

## PURPOSE/BACKGROUND

The renin-angiotensin system (RAS) controls the cardiovascular system by maintaining arterial blood pressure and balancing body fluids and electrolytes. The RAS is comprised of two opposing arms: i) classical arm, which consists of Angiotensin (Ang) Converting Enzyme (ACE) /Ang II/ Ang II type 1 receptor (AT1R), which modulates a diverse range of biological effects, including vasoconstriction, vascular smooth muscle cell proliferation, and hypertrophy of heart vessel wall, ii) protective arm, consists of ACE2/Ang-(1-7)/Mas receptor (MasR), that acts as the counter-regulatory within the RAS. Chronic imbalances of these two arms of the RAS lead to different pathophysiological conditions in the renal, cardiovascular, and central nervous systems. The circulating plasma level of ACE2 has been associated with various disease conditions such as renal, cardiovascular, and metabolic disease. As a body's defense mechanism, the increased circulating ACE2 degrades Ang II and keeps its status within the normal range. Accordingly, the reduced ACE2 activity due to considerably high levels of circulating anti-ACE2 autoantibody has been associated with disease intensity. We hypothesized that an assessment of circulating ACE2, anti-ACE2, Ang II, and Ang1-7 could provide a sound diagnostic biomarkers panel for patients with different inflammatory diseases.

## MATERIALS & METHODS

This study was conducted based on an approved IRB and using samples of twelve unidentifiable rheumatoid arthritis (RA) patients (five active and seven remission patients), which the Institute of Arthritis Research provided. RA was diagnosed using a RAPID3 questionnaire in tandem with comparing the measured amount of C-reactive protein. Levels of Ang-(1-7) and Ang II peptides were measured using liquid chromatography in tandem with mass spectrometry. Anti-ACE2 autoantibodies were measured using an ELISA method.

## RESULTS

The Mean  $\pm$  SD results of the levels of Ang-(1-7) and Ang II peptides show that Ang-(1-7) status in the active RA group ( $1.29 \pm 0.8$  ng/mL) was significantly lower than in the remission RA group ( $7.63 \pm 2.61$  ng/mL). In contrast to Ang-(1-7), Ang II levels were markedly higher in the active RA patients ( $5.43 \pm 1.82$  ng/mL) when compared with the remission group ( $0.87 \pm 0.16$  ng/mL). The mean ELISA score of anti-ACE2 autoantibodies in patients with active RA was remarkably higher than in patients in remission ( $1.41 \pm 0.11$  vs.  $1.81 \pm 0.11$ ,  $p < 0.05$ ) and was significantly correlated with Ang II levels in the active but not in the remission group.

## DISCUSSION/CONCLUSION

Results indicate that Ang-(1-7) levels were significantly lower in the active RA patients, whereas Ang II levels were markedly higher than patients in remission. Similarly, the mean ELISA score of anti-ACE2 autoantibodies was higher in active RA patients. The soluble ACE2 is responsible for the conversion of Ang II to Ang-(1-7), the lower Ang-(1-7)/Ang II ratio in active RA patients was attributed to the deactivation of ACE2 enzyme by higher anti-ACE2 autoantibodies levels. In conclusion, the findings support the hypothesis that the RAS classical arm is augmented and the protective arm is suppressed in RA. This study suggests that higher systemic and maybe local Ang-(1-7) levels could modulate and put the disease into remission and protect the patient from long-term consequences of RA.