

Individuals with rheumatoid arthritis (RA) are at greater risk for developing incident heart failure (HF) and HF-associated morbidity and mortality than matched non-RA controls. This increased risk persists even after adjustment for coronary artery disease and conventional cardiovascular (CV) risk factors, indicating that RA associated factors contribute to the increased risk for HF.

Little work has been done, however, to investigate pathophysiological mechanisms underlying myocardial dysfunction in RA. A better understanding of these processes would promote the identification of biomarkers to predict risk for HF, and/or innovative approaches to treat or prevent HF, in RA. Chronic elevations of inflammatory cytokines have been proposed as the primary mechanism of myocardial dysfunction in RA, but this is likely an *oversimplification* of the process. We hypothesize that additional mechanisms related to the overall rheumatoid process including autoantibody responses to citrullinated myocardial proteins, and specific monocyte and/or T cell subsets that can be detected in the periphery, may identify patients with subclinical myocardial pathology that may put them at risk for HF. In a currently enrolling cross-sectional study funded by NIAMS, 150 RA patients without history of clinical CV disease are undergoing cardiac FDG PET-CT scanning to determine the prevalence of subclinical inflammatory myocarditis and microvascular dysfunction. We propose to extend this study to 18 months of followup and to investigate several pathways that may contribute to myocardial dysfunction in RA. Our specific aims are as follows:

Aim 1. To determine the association of imaging biomarkers that are indicative of inflammatory myocarditis and microvascular dysfunction with longitudinal change in measures of LV structure/function over two years in patients with RA.

Aim 2. To identify serum protein and cellular biomarkers associated cross-sectionally with subclinical myocarditis and microvascular dysfunction, and/or predictive of longitudinal change in measures of LV structure/function in patients with RA.

These studies have the potential to significantly advance understanding of the pathogenesis of HF in patients with RA. Understanding pathophysiologic mechanisms that contribute to the increased risk of HF in RA is essential to the development of targeted interventions aimed at reducing CV morbidity and mortality in RA.