A060 Reduced Hypertrophic Cardiac Remodeling and Preserved Diastolic Function in T Cell-Deficient Mice in a Novel Mouse Model of Heart Failure with Preserved Ejection Fraction

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Introduction: Heart Failure with Preserved Ejection Fraction (HFpEF) is a highly diverse and widespread cardiovascular disease characterized by diastolic dysfunction, the impaired ability of the heart to relax during each beat, despite contracting efficiently. While the prevalence of HFpEF is increasing in the United States, there is no cure or specific treatment for HFpEF, and existing options are limited to symptom management. Obesity and hypertension, both independently associated with inflammation, have been shown to be two major comorbidities for HFpEF. However, how the immune responses to these risk factors coordinate to specifically drive diastolic dysfunction, remains unclear. We hypothesize that systemic inflammation induced by these combined risk factors of HFpEF results in a multi-phasic systemic and cardiac inflammation that results in diastolic dysfunction. **Methods:** C57/BL6 (wild-type, WT) or T-cell-deficient (*Tcr*$^{-/-}$) male mice were fed a high-fat diet (HFD) in combination with L-NAME-treated water to induce HFpEF. HFD-only and standard diet (STD) treated mice were used as controls. After 5 weeks of treatment, diastolic and systolic function were assessed with invasive hemodynamic analyses, and cardiac and systemic inflammation were characterized using flow cytometry in the heart, the spleen, the inguinal and the mediastinal lymph nodes. **Results:** WT HFD+L-NAME mice developed left ventricle hypertrophy and increased passive chamber stiffness (a higher end-diastolic pressure volume relationship, EDPVR), and showed preserved ejection fraction when compared to WT STD mice. Concomitantly, there was a trend to increased cardiac infiltration of CD4+ T-cells and CD11b+ monocytes/macrophages compared to STD controls. There was no significant expansion of CD4+ T-cells compared to controls in the mediastinal or inguinal lymph nodes, nor the spleen. In contrast to WT mice, *Tcr*$^{-/-}$ mice treated with HFD/L-NAME did not develop cardiac hypertrophy or diastolic dysfunction. **Conclusions:** We thereby conclude that T-cells contribute to the development of cardiac hypertrophy and diastolic dysfunction induced by HFD/L-NAME, though T-cell activation is not observed in the cardiac draining lymph nodes or in the spleen. Further studies will interrogate other possible reservoirs of T-cell activation in HFpEF and identify the specific T-cell-dependent mechanisms modulating diastolic function and how the combination of HFD+L-NAME modulates T-cell cardiac infiltration.