Sex-Based Differences in LPS-induced Rapid Myocardial Dysfunction

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Background: Previous studies have indicated better myocardial responses with preserved cardiac function in female animals compared to males after LPS challenge; however, the mechanisms remain incompletely understood. Our published studies have revealed that TNFa substantially increased in heart tissue and serum following LPS. Females experienced less cardiac dysfunction than males during equivalent dose of TNFa infusion. Therefore, sex-related disparities in myocardial impairment could be due to an indirect/secondary outcome from LPS-induced inflammatory cytokines, like TNFa. To dissect the potential mechanism underlying myocardial reactions between males and females, we aim to determine any sex differences in LPS-caused direct effects on cardiac function using coronary infusion of LPS.

Methods: Isolated hearts from aged-matched adult male and female mice were subjected to LPS infusion via Langendorff after >20-min equilibration (Eq), with left ventricular developed pressure (LVDP) continuously recorded. Dose responsive experiments with LPS at 2.5, 5.0, and 7.5 mg/kg of body weight were performed in male hearts. Significant depression of LVDP (>20% drop) after LPS infusion was considered rapid response to LPS. Female estrous cycle was determined via vaginal smear.

Results: Male hearts infused with 5.0 and 7.5 mg/kg of LPS demonstrated significant depression of LV function. Males also experienced worse outcomes of LV function than females following 5.0 mg/kg of LPS infusion. A trend of earlier response to LPS occurred in male hearts compared to females. However, there were no significant differences in cardiac function between female groups in different estrous phases.

Conclusion and Potential Impact: Our data demonstrates that male hearts exhibit higher sensitivity to LPS-induced rapid cardiac dysfunction compared to females, but estrogen may have little influence on LPS-induced rapid functional depression. The insight from our data can be used to better understand the differences between male and female outcomes to cardiac pathologies and insult.