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Biological Sex Differences in Exercise-Mediated Femoral Blood Flow and Associations with Intima-Media Thickness

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Peripheral blood flow increases during exercise due to vasodilation. This hyperemic response is considered anti-atherosclerotic and a stimulus for favorable vascular remodeling. As women have a larger vasodilatory response to physiological and pharmacological stimuli compared to men, it is possible that biological sex may also impact the extent of exercise-induced vasodilation. **PURPOSE:** To explore potential biological sex differences in peripheral blood flow in response to moderate-intensity exercise and subsequent associations with arterial wall intima-media thickness (IMT) as a measure of subclinical atherosclerosis risk. **METHODS:** Left superficial femoral artery (SFA) diameter, blood velocity, and IMT were measured by Doppler ultrasound in 20 men (23.85 ± 5.74 years, body mass index [BMI] = 26.00 ± 3.30 kg/m²) and 18 women (22.89 ± 6.53 years, BMI = 25.24 ± 3.81 kg/m²) before, five minutes after, and 25 minutes after 30 minutes of stationary cycling at 65-75% of age-predicted maximum heart rate. SFA diameter and mean blood velocity were used to calculate leg blood flow (LBF), which was expressed in absolute terms and relative to left leg lean mass. Left leg lean mass was estimated via regional bioelectric impedance analysis. Two-way ANOVA with repeated measures was used to analyze biological sex differences. One-tailed Spearman's rank correlation was used to determine the association between IMT and change in LBF from rest to five minutes post-exercise. **RESULTS:** There was a significant biological sex \times time interaction in absolute LBF (men = 66.69 ± 31.21 ml/min, 152.01 ± 71.12 ml/min, and 104.13 ± 52.43 ml/min, respectively; women = 80.63 ± 48.87 ml/min, 130.65 ± 39.18 ml/min, and 83.45 ± 29.90 ml/min, respectively; $p = 0.04$). There was not a significant biological sex \times time interaction in relative LBF (men = 6.85 ± 3.15 ml/min/kg, 15.45 ± 6.83 ml/min/kg, and 10.67 ± 5.60 ml/min/kg, respectively; women = 10.82 ± 5.95 ml/min/kg, 17.97 ± 4.91 ml/min/kg, and 11.44 ± 3.74 ml/min/kg, respectively; $p = 0.20$). There was a significant negative association between IMT and change in relative LBF from pre-exercise to post-exercise in women ($\rho = -0.56$, $p = 0.01$), but not in men ($\rho = 0.02$, $p = 0.47$). **CONCLUSION:** Women had lower absolute post-exercise SFA flow than men, but there were no biological sex differences present when SFA flow was expressed relative to leg lean mass. Greater increases in SFA LBF with exercise was associated with lower SFA IMT in women. **SIGNIFICANCE/NOVELTY:** These results suggest that the absolute hyperemic response to moderate-intensity exercise is lower in young, healthy women compared to men, though sex-specific differences disappear when considered relative to lean tissue mass. Additionally, negative associations between arterial wall thickness and change in peripheral blood flow reveal that a robust vasodilative response to exercise is athero-protective in women.