

Exercise-Induced Improvements in Capillary Density are Influenced by Sex, Hormone Replacement Therapy, and Exercise Intensity

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Background While cardiometabolic disease (CMD) is the number one cause of death for women in the US, age at CMD onset is 10-20 years after that of men. This stark difference in CMD incidence is attributed to menopausal estrogen withdrawal. Along with pre-menopausal estrogen, regular exercise decreases CMD risk in part by increasing capillary density (CD). To better understand CMD risk among postmenopausal women, we investigated the impact of sex, hormone replacement therapy (HRT), and exercise amount/intensity on CD. We hypothesized that compared to women not using HRT and independent of exercise amount and intensity, women using HRT and men would display greater exercise-related improvements in CD and lesser declines during a detraining period.

Methods Previously sedentary adults (n=228) with overweight or obesity were randomized to an inactive control group or one of three 6mo exercise groups: 1) low-amount/moderate-intensity: 14 kcal/kg/wk (KKW), 40-55% VO₂peak; 2) low-amount/vigorous-intensity: 14 KKW, 65-80% VO₂peak; or 3) high-amount/vigorous-intensity: 23 KKW, 65-80% VO₂peak. Biopsy-derived skeletal muscle CD was measured at baseline, 24-h post-intervention, and at 4- and 14-days post-intervention (“detraining” period). Change scores were calculated by subtracting baseline from post-intervention CDs and analyzed using one-way ANOVA and post-hoc by two-tailed two-sample t-tests. The effects of sex, HRT, and exercise group on CD over time were assessed by linear mixed models.

Results Exercise significantly increased CD in all groups except women not using HRT who performed low-amount/moderate-intensity exercise and men who performed low-amount/vigorous-intensity exercise. In vigorous-intensity groups, men increased CD through detraining while women rapidly returned to baseline. With low-amount/moderate-intensity exercise, CD in women not using HRT and men returned to baseline with detraining. Women using HRT with moderate-intensity, but not vigorous-intensity exercise, sustained CD improvements through detraining (Figure 1).

Conclusions Sex, HRT, and exercise intensity impacted CD responses to exercise and detraining. Men and women performing vigorous-intensity exercise display strikingly disparate detraining responses, indicating women require continued training to maintain exercise-induced CD improvements. HRT was beneficial in sustaining exercise-induced CD improvements through detraining for women performing moderate- but not vigorous-intensity exercise. These findings influence recommended exercise frequency and intensity by sex and HRT usage to decrease postmenopausal CMD risk.

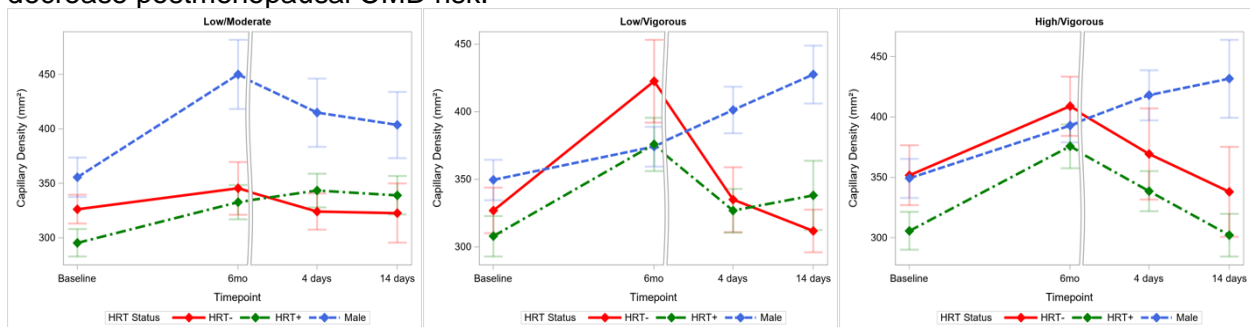


Figure 1. CD changes during exercise and detraining by sex, HRT usage, and exercise amount/intensity. CD by sex, exercise group and HRT status (men in blue, women taking HRT in green, women not taking HRT in red) are shown at baseline, immediately post-intervention (6-mo), and 4- and 14-days following exercise cessation. Error bars show 95% confidence intervals.