



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 onset is 10-20 years after that of men – largely due to menopausal estrogen withdrawal
- Along with premenopausal estrogen levels, regular participation in exercise decreases CMD risk in part by increasing capillary density (CD), which enhances insulin sensitivity, oxygen and nutrient delivery, and waste extraction
- We previously found that the beneficial effects of hormone replacement therapy (HRT) on exercise-induced improvements in insulin sensitivity were most prominent among women performing vigorous-intensity exercise
- The effects of exercise on CMD risk are understudied in postmenopausal women, especially with respect to those taking HRT as a method of restoring estrogen to premenopausal levels
- To better understand postmenopausal CMD risk, we examined the impact of sex, HRT, and aerobic exercise varying in amount and intensity on CD
- We hypothesized that compared to women not using HRT and independent of aerobic exercise amount/intensity, women using HRT and men would display greater exercise-induced increases in CD and lesser declines with detraining, mimicking insulin sensitivity's response to aerobic exercise

Methods

- As part of the STRRIDE I randomized controlled trial, previously sedentary adults with overweight or obesity (n=228) were randomized to an inactive control group or one of three six-month exercise groups as follows:

Exercise Intervention Groups
1. Low-amount/moderate-intensity (n=61): 14 kcal/kg/wk at 40-55% VO _{2peak}
2. Low-amount/vigorous-intensity (n=69): 14 kcal/kg/wk at 65-80% VO _{2peak}
3. High-amount/vigorous-intensity (n=70): 23 kcal/kg/wk at 65- 80% VO _{2peak}

- Biopsy-derived skeletal muscle CD was measured at baseline, 24-hours-, 4-days-, and 14-days post-intervention (4- and 14-days represent the “detraining” period)
- Change scores were calculated by subtracting baseline CD from each post-intervention value and analyzed using one-way ANOVA and post-hoc by two-tailed two-sample t-tests
- Linear mixed models assessed the effects of sex, HRT, and exercise group on CD over time

Results

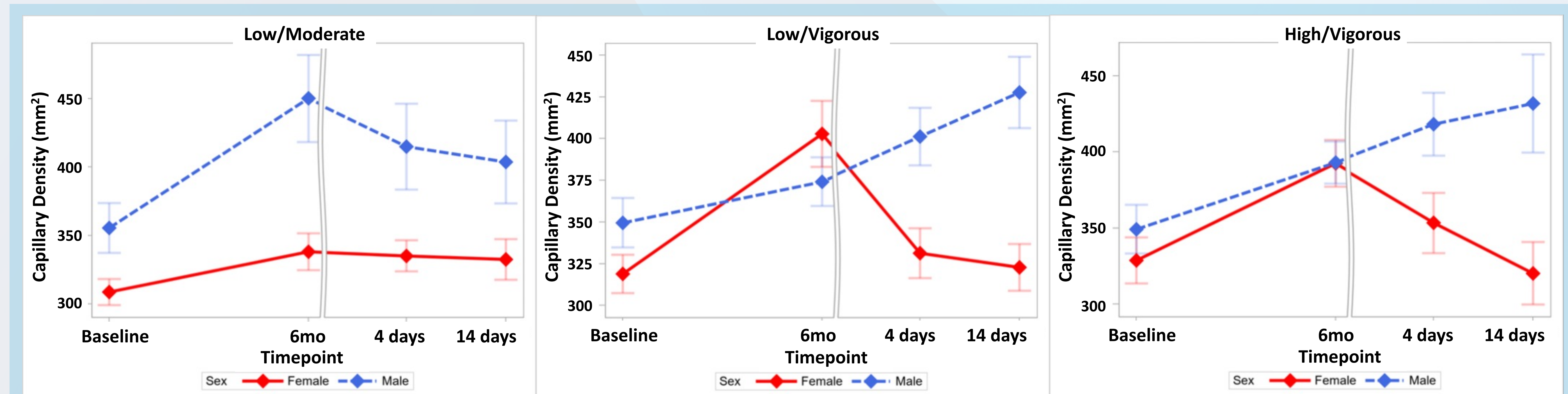


Figure 1. Capillary Density Changes During Exercise and the Detraining Period by Sex and Exercise Amount/Intensity. Error bars represent 95% confidence intervals.

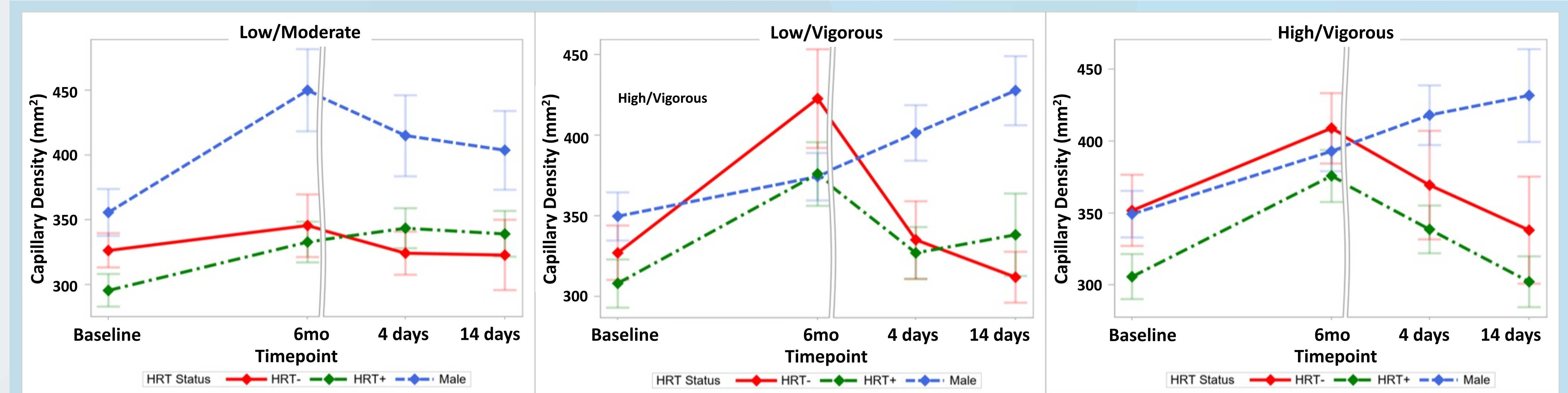


Figure 2. Capillary Density Changes During Exercise and the Detraining Period by Sex, HRT Use, and Exercise Amount/Intensity. Error bars represent 95% confidence intervals.

Discussion

- Sex, HRT use, and aerobic exercise intensity significantly influence CD's response to exercise and detraining
- In general, aerobic exercise training for six months significantly improves CD in both men and women
- Men who perform vigorous-intensity aerobic exercise continue to improve CD for at least 14 days following exercise cessation, while women who perform vigorous-intensity aerobic exercise rapidly return to pre-training CD levels within 4 days of detraining
- Women who take HRT and perform moderate-intensity aerobic exercise training sustain CD improvements throughout 14 days of detraining
- As CD displayed disparate dose-response findings compared to insulin sensitivity in response to exercise, CD and insulin sensitivity may not be directly related as initially hypothesized

Conclusions

- For women taking HRT, compared to vigorous-intensity, moderate-intensity aerobic exercise may be more beneficial to maintain exercise-induced improvements in CD for at least 14 days following exercise cessation
- These findings contribute to expanding knowledge of CMD risk in postmenopausal women taking HRT, and allow for increased ability to personalize exercise prescriptions that treat and minimize CMD risk in this population



Acknowledgments

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