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## Ultrastructural Skeletal Muscle Adaptations to Resistance Exercise With or Without Creatine Supplementation in Individuals Treated for Colorectal Cancer

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Background: Colorectal cancer and its treatments accelerate declines in skeletal muscle health, decreasing physical function and increasing vulnerability to morbidity and mortality. While resistance exercise training (RET) is recommended to counter these declines, individuals with cancer may experience a blunted adaptive response. Further, to date RET's impact on skeletal muscle ultrastructure in cancer survivors has yet to be explored. This trial examined the effects of a 10-week RET program with or without creatine supplementation on body composition, physical function, and skeletal muscle ultrastructural changes in individuals treated for colorectal cancer. Methods. Twenty-seven participants were randomized to RET plus creatine (CRE; n=13) or RET plus placebo (PLA; n=14). RET was performed three times per week using a hybrid delivery model. Body composition and physical function [grip strength, chest press, leg extension, Short Physical Performance Battery (sPPB)] were assessed pre- and post-intervention. Vastus lateralis muscle biopsies were analyzed using transmission electron microscopy (TEM) to assess ultrastructural alterations (intramyocellular lipid droplet morphology, mitochondrial organization, and extracellular matrix remodeling). Results: Preliminary analyses revealed no statistically significant between-group differences; however, both CRE and PLA groups demonstrated improvements in lean body mass ( $1.22 \text{ kg} \pm 2.50$ ;  $p=0.023$ ), chest press ( $7.70 \text{ kg} \pm 4.73$ ;  $p<0.001$ ), leg extension ( $12.4 \text{ kg} \pm 7.94$ ;  $p<0.001$ ). TEM analyses showed decreases in intramyocellular lipid droplet number ( $-38\%$ ;  $p=0.031$ ) and increases in mitochondrial area ( $+66\%$ ;  $p=0.006$ ), accompanied by reduced mitochondrial swelling and fragmentation, and no detectable changes in mitochondrial number, indicating improved mitochondrial integrity following RET. Conclusion. Preliminary findings suggest that RET may improve body composition and functional outcomes while eliciting favorable changes in skeletal muscle ultrastructure among individuals treated for colorectal cancer. Although creatine supplementation did not confer additive benefits in this initial analysis, ongoing quantitative TEM analyses will further clarify the extent and significance of exercise-induced muscle remodeling in this population.

### Keywords

cancer survivorship, skeletal muscle remodeling, mitochondria, electron microscopy

### Conflict of Interest & Ethical Approval

yes

### Abstract submitters declaration

yes

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