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Resistance exercise does not increase markers of muscle protein degradation in patients with advanced CKD

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Introduction

- Patients with advanced Chronic Kidney Disease (CKD) experience significant muscle wasting that negatively impacts upon quality of life, morbidity and mortality.
- Resistance exercise (RE) is an effective way to increase muscle mass in the general population, but its ability to overcome the catabolic influences associated with pre-dialysis CKD is under investigated.
- Typically, in the presence of nutrients, RE results in an increase in net protein balance. It is not known if this is also the case in patients with advanced CKD, or how protein degradation is regulated in response to RE.

Aim

To investigate two markers of skeletal muscle protein degradation: total protein ubiquitination and accumulation of 14kDa actin fragment, in response to acute RE before and after 8 weeks of RE training in pre-dialysis CKD.

Methods

- PARTICIPANTS
  - 11 patients (Age 59 ± 7years, eGFR 27 ± 7ml/min/1.73m^2) randomised to exercise
  - 7 patients (Age 67 ± 11years, eGFR 20 ± 6ml/min/1.73m^2) randomised to control
- EXERCISE PROGRAMME
  - 3 sets of 10-12 leg extensions at 70% 1-RM performed 3 x week for 8 weeks
  - Controls continued with their usual physical activity
- ASSESSMENTS
  - Rectus femoris cross-sectional area (CSA) was measured by ultrasonography at baseline (BL) and after 8 weeks of RE
  - 3 vastus lateralis muscle biopsies collected under fasting conditions
    1. Baseline → Patients then performed first training session
    2. Untrained → Taken 24h after baseline biopsy
    3. Trained → Taken 24h after final exercise session following 8 weeks of RE
  - Biopsies analysed for total protein ubiquitination and 14kDa actin fragment accumulation by western blot

Results

Rectus femoris CSA

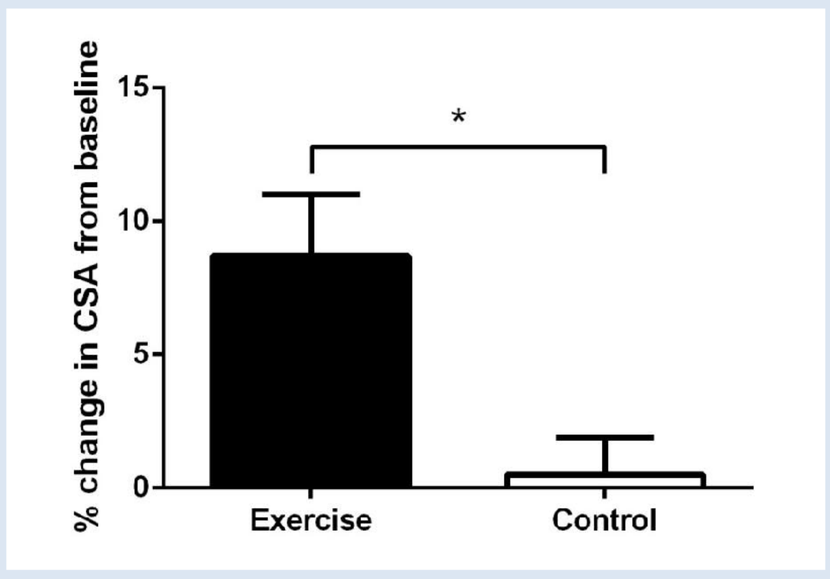

Figure 1. 8 weeks RE resulted in a significant increase in rectus femoris CSA From 5.9 ±2.0cm^2 at BL to 6.4 ±2.2cm^2 (P=0.001).

Results *Continued*

Total Protein Ubiquitination

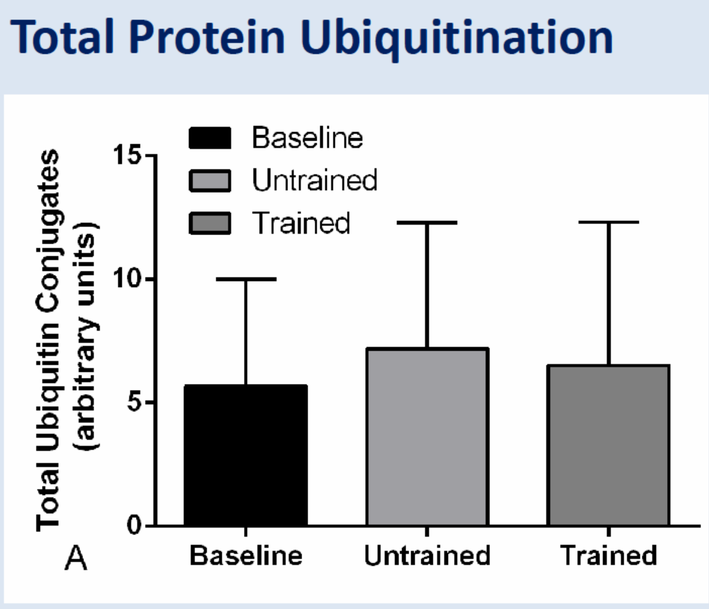

Figure 2. Acute RE did not increase total protein ubiquitination levels either before or after RE training (P=0.55) (A), suggesting muscle protein breakdown was not increased 24h following RE. Representative immunoblot where B= Baseline, U= Untrained and T= Trained (B).

14 kDa Actin Fragment Accumulation

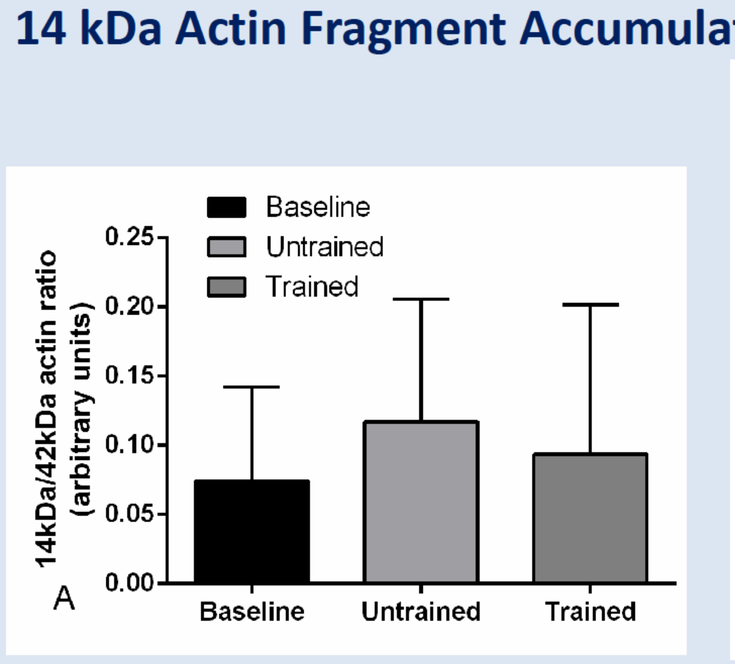

Figure 3. Acute RE did not result in an accumulation of the 14kDa actin fragment (P=0.81) (A), suggesting muscle protein breakdown was not increased 24h following RE. Representative immunoblot where B= Baseline, U= Untrained and T= Trained (B).

Conclusions

- Neither unaccustomed RE (24h post first RE training session), nor accustomed RE (24h post final training session) significantly raised makers of skeletal muscle protein degradation.
- This demonstrates that RE does not appear to negatively affect protein balance in CKD either acutely or in the long-term.
- Furthermore, 8 weeks of RE is effective at stimulating muscle hypertrophy therefore potentially overcoming muscle wasting in pre-dialysis CKD, which has important clinical implications.

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