More than 60% of US astronauts participating in Mir and early International Space Station missions (>5 months) were unable to complete a 10-min 80° head-up tilt test on landing day. This high incidence of post-spaceflight orthostatic intolerance may be related to limitations of the inflight exercise hardware that prevented high intensity training. **PURPOSE:** This study sought to determine if a countermeasure program that included intense lower-body resistive and rowing exercises designed to prevent cardiovascular and musculoskeletal deconditioning during 70 d of 6° head-down tilt bed rest (BR), a spaceflight analog, also would protect against post-BR orthostatic intolerance. **METHODS:** Sixteen males participated in this study and performed no exercise (Control, n=10) or performed an intense supine exercise protocol with resistive and aerobic components (Exercise, n=6). On 3 d/wk, exercise subjects performed lower body resistive exercise and a 30-min continuous bout of rowing (≥75% max heart rate). On 3 other d/wk, subjects performed only high-intensity, interval-style rowing. Orthostatic intolerance was assessed using a 15-min 80° head-up tilt test performed 2 d (BR-2) before and on the last day of BR (BR70). Plasma volume was measured using a carbon monoxide rebreathing technique on BR-3 and before rising on the first recovery day (BR+0). **RESULTS:** Following 70 d of BR, tilt tolerance time decreased significantly in both the Control (BR-2: 15.0±0.0, BR70: 9.9±4.6 min, mean ±SD) and Exercise (BR-2: 12.2±4.7, BR70: 4.9±1.9 min) subjects, but the decreased tilt tolerance time was not different between groups (Control: -34±31, Exercise: -56±16%). Plasma volume also decreased (Control: -0.56±0.40, Exercise: -0.48±0.33 L) from pre to post-BR, with no differences between groups (Control: -18±11%, Exerciser: -15±10%). **CONCLUSIONS:** These findings confirm previous reports in shorter BR studies that the performance of an exercise countermeasure protocol by itself during BR does not prevent orthostatic intolerance or plasma volume loss. This suggests that protection against orthostatic intolerance in astronauts following long-duration spaceflight will require an additional intervention, such as periodic orthostatic stress, fluid repletion, and/or lower-body compression garments.