

## LETTER TO THE EDITOR

### Reply to Greaves et al.

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TO THE EDITOR: We thank Greaves et al. (4) for their Letter and recognizing the challenges of collecting astronaut data, particularly during spaceflight. Both their study (5) and ours (6) report the same direction of pre- to postflight changes in carotid distensibility and stiffness, with different magnitudes. However, we are cautious regarding their approach of extrapolating in- and post-mission cardiovascular health using a model of these parameters developed in a population of 45–84 yr olds (2) that may not be representative of the astronaut corps and not reflective of spaceflight-induced physiological adaptations. Despite studying similarly-aged astronauts drawn from a population with the same flight certification requirements, the model estimates a “vascular age” (2) before flight to be >75 yr old in our astronauts (6) and others (1), but <45 yr old in astronauts studied by Hughson et al. (5). This raises concerns about the applicability of this model to interpret cardiovascular age in astronauts.

Reported changes in carotid stiffness and distensibility have not been consistent. We observed no statistically significant differences from preflight during or after the mission. Arbeille et al. (1) reported decreased distensibility inflight but not post-flight, and Hughson et al. (5) reported decreased distensibility on the day after landing. Our conservative statistical approach (6), combined with the relatively small number of astronauts in each study, may have contributed to different conclusions. Differences in ultrasound data collection (M- versus B-mode) and analysis methods (single-point versus wall-segment), as well as the larger proportion of female astronauts in the cohort studied by Hughson et al. (4/9 versus 3/13) since they reported greater pre- to postflight distensibility changes in women than men, also may contribute to different findings.

Greaves et al. (4) highlight our cautious statements regarding the cardiovascular health risks associated with spaceflight and exploration missions. Risk assessment must consider the preponderance of findings and the limitations of the evidence. For example, we recommend caution when interpreting data collected during the dynamic phase following return to gravity, which includes physical and psychological stress, circadian desynchrony, and motion sickness, unless the outcome of interest is associated specifically with the readaptation period. Near-immediate postflight measurements (5) can be informative, but may not provide clear evidence of health risk during the mission or in long-term recovery. C-reactive protein, a biomarker associated with an increased risk of a cardiovascular event in apparently healthy adults (3), was elevated in our astronauts after landing but neither we nor Hughson et al. (5) observed an increase during spaceflight. Oxidative stress and inflammation

biomarkers are elevated and lipid profiles are altered during spaceflight, but there is no epidemiological evidence that spaceflight results in an increased lifetime cardiovascular disease risk. Accordingly, we, Hughson et al., and others are investigating many of these same cardiovascular parameters during the months and years after landing and plan to make these measures during and after upcoming 1-yr missions. Given that mission durations completed thus far and the amount and characteristics of radiation exposure in low Earth orbit are limited relative to future exploration missions to the Moon and Mars, continued monitoring of acute and long-term health is critical to estimating the cardiovascular disease risk in astronauts.

#### DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

#### AUTHOR CONTRIBUTIONS

S.M.C.L. drafted manuscript; S.M.C.L., S.S.L., B.R.M., S.R.Z., S.M.S., and M.B.S. edited and revised manuscript; S.M.C.L., S.S.L., B.R.M., S.R.Z., S.M.S., and M.B.S. approved final version of manuscript.

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