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Corresponding letter

Managing arterial health in adults with metabolic diseases: Is high-intensity interval exercise the answer? Response to the commentary by Lopes et al.

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Dear editor,

We thank Lopes et al.[1] for their interest in our study and for writing an insightful commentary based on our findings, which were recently published in the *Journal of Sport and Health Science*,[2] and for their work.[3] As noted by the authors, there is consistency in several key findings between our laboratories, and this should serve as a basis for future investigation in this area. We agree that there has been little work examining the effect of high-intensity interval exercise (HIIE) on central arterial stiffness, wave reflections, and hemodynamic responses. However, research is particularly lacking in adults with metabolic diseases, a population with a significantly increased risk of developing cardiovascular disease and cardiovascular mortality. To further the important discussion Lopes et al.[1] have raised in their commentary, our response focuses on raising additional points concerning the responses in central arterial stiffness, wave reflections, and hemodynamics observed following HIIE in adults with metabolic diseases. With this, we hope to shed light on the importance of research in HIIE for this population and their arterial health.

Previous work examining the effect of aerobic exercise in both acute and chronic exercise settings on such arterial health outcomes has been conducted predominately in young, healthy adults.[4] As highlighted in the commentary by Lopes et al.,[1] a transient reduction in wave reflections (as measured by augmentation index at a heart rate of 75 beats/min (AIx@75)) may be intensity dependent, given the findings from each of our respective studies in adults with diabetes[2] or obesity.[3] Both studies observed a significant transient reduction in AIx@75 following a single bout of HIIE; this did not occur after a single bout of moderate-intensity continuous exercise (MICE) or control. Although Lopes et al.[1] highlighted that AIx represents the capacity of the peripheral vessels to dampen the propagation of the forward wave throughout the arterial tree, a recent study has found that AIx also represents cardiac mechanics.[5] Using cardiac computational modeling, Heusinkveld et al.[5] showed that reduced left ventricular shortening velocity was associated with a significantly earlier arrival of wave reflections, which, in turn, increased AIx. This suggests that HIIE may play a role in transiently increasing the left ventricular shortening velocity and improving cardiac mechanics in adults with diabetes or obesity. Additionally, the improvements observed in AIx could also be explained by the biochemical benefits associated with a bout of aerobic exercise, such as increased nitric oxide bioavailability.[6] It is now established that chronic hyperglycemia[7] and increased ectopic fat[8] can contribute to cardiac remodeling and alter cardiac structure and function.[8] For instance, left ventricular hypertrophy,[8,9] worse left ventricular systolic[8] and diastolic function,[9] and reduced ejection fraction[9] have been observed in people with

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diabetes or obesity. Such cardiac remodeling can increase the risk of developing heart failure or cardiomyopathies. Much like improving insulin sensitivity through repeated bouts of exercise, it appears that AIx could be managed through bouts of HIIE. In contrast to the findings from the Lopes' group,[10] we recently showed in adults with obesity and diabetes that 12 weeks of low-volume HIIE (1 × 90% peak volume of oxygen for 4 min, 3 times per week) did not reduce AIx.[11] Although it appears that chronic aerobic exercise appears to decrease AIx in healthy individuals, the effect in people with metabolic diseases remains unclear.

An acute bout of exercise may not improve central arterial stiffness (as measured via carotid-femoral pulse wave velocity (PWV)), but systematic reviews and meta-analyses show that chronic, regular aerobic training may be required to reduce central arterial stiffness in healthy adults[12] and in those with cardiovascular diseases.[13] As highlighted in the commentary by Lopes et al.,[1] it is unlikely that acute exercise provides a sufficient stimulus to promote structural changes in the arteries. However, the effect of chronic, regular HIIE appears to have inconsistent findings. Similar to the Lopes' et al. group,[10] we found a significant reduction in PWV (albeit small) after our 12 weeks of low-volume HIIE intervention in adults with type 2 diabetes and obesity.[11] However, we did not observe a reduction in PWV following MICE.[11] Yet another study conducted by our group found no reduction in PWV following 12 weeks of HIIE in adults with type 1 diabetes (4 × 4 min at 85%−95% peak heart rate (HR_{peak}) interspersed with 3 min of active recovery at 50%−70%HR_{peak}, 3 times per week).[14] This result was surprising, given that we did not find a significant difference in transient responses between adults with type 1 or type 2 diabetes in central arterial stiffness, wave reflections, or hemodynamics following a bout of HIIE.[2] Similarly, Holloway et al.[15] found that 6 weeks of HIIE in young, healthy adults resulted in no change in PWV. It should be noted that the work-to-rest ratio employed in the Holloway study[15] was 1:2; whereas the work of our laboratory and the Lopes' group[10] was based on higher work-to-rest ratios. Given the accelerated cardiovascular pathology observed in metabolic diseases, a more aggressive exercise prescription may be required to provide an adequate stimulus to elicit chronic arterial structural changes. Further research needs to be conducted to determine the effect and underlying mechanisms of HIIE as a potential therapy for improving central arterial stiffness in metabolic diseases.

Sex differences should be more thoroughly evaluated when examining the effect of HIIE on central arterial stiffness, wave reflections, and hemodynamic responses. Important points have been raised in the commentary by Lopes et al.[1] including that females appear to experience a greater reduction in AIx than males following HIIE. We agree, and we recognize that not performing a sex analysis may have attenuated the results observed in AIx in our study. A meta-analysis of 37 prospective trials showed that diabetes led to a profoundly (50%) greater relative risk of fatal coronary heart disease in females when compared to males.[16] The greater cardiovascular burden experienced by females should be accounted for in future studies using larger sample sizes to examine sex differences.

Early evidence suggests that HIIE is effective in eliciting a transient reduction in AIx in individuals with metabolic conditions (such as diabetes and/or obesity), which is not observed with MICE. This suggests that there may be transient improvements in cardiac and vascular function, which play a crucial role in the management of arterial health, similar to the changes observed in insulin sensitivity with acute exercise. Given the cardiovascular burden experienced by individuals with metabolic diseases, it is important that further research be conducted to elucidate the role of exercise intensity, sex, and disease status on acute and chronic exercise-related adaptions to arterial structure and health.

Authors' contributions

KLW conceived the letter of response and drafted the manuscript; AS, ASL, SMT, and NAJ provided critical input for the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

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