


COMMENTARY ON: EXPLORING EXERCISE INTOLERANCE IN ADULT PATIENTS WITH PERSISTENT POST-CONCUSSION SYMPTOMS AFTER MILD TRAUMATIC BRAIN INJURY

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To the Editor,

Valaas and colleagues (1) take on a timely question in rehabilitation: how frequently adults with persistent post-concussion symptoms (PCS) after mild traumatic brain injury (mTBI) show exercise intolerance (EI), and which factors track with it. We welcome this focus. Three analytic choices, however, deserve a closer look because they cloud interpretation and can be remedied without altering the study's aims.

First, the abstract reports the association between higher pre-test heart rate and a higher Buffalo Concussion Treadmill Test (BCTT) symptom threshold with a coefficient of 0.34 and a 95% confidence interval of 0.17 to -0.50 (1). The interval is internally inconsistent; the bounds are reversed and the sign is incompatible with the stated direction. In the main text and Table III, the same effect is reported as 0.17 to 0.50 with $p < 0.001$, which is coherent and indicates a positive association (1). A concise erratum that corrects the abstract and checks for internal agreement across sections would prevent confusion and preserve confidence in the statistical reporting.

Second, time since injury differs between groups yet is omitted from the logistic model relating the Rivermead Post Concussion Symptoms Questionnaire (RPQ) score to EI. Table I indicates a meaningful gap in months since injury (6.95 vs 9.44; $p = 0.010$) between EI and exercise-tolerant participants (1). Because recovery after traumatic brain injury is time dependent, not adjusting for this covariate risks attributing the effect of injury chronicity to symptom burden. The reported odds ratio of 1.07 per RPQ point may therefore be inflated by recovery stage. Including months since injury as a covariate, and verifying the result in stratified or sensitivity analyses, would clarify whether RPQ independently predicts EI.

Third, the linear regression of the BCTT symptom threshold uses only the 81% who were EI and excludes the 19% who completed the test without symptom exacerbation (1). For these exercise-tolerant participants, the threshold lies at or beyond the stopping criterion and is unobserved, which makes the outcome right censored. Discarding them can bias coefficients for predictors such as pre-test heart rate and anxiety and narrows applicability to the full clinic population. A straightforward remedy is to treat the threshold

as a censored outcome and analyse it with Tobit or survival methods, coding those who did not reach a symptom limit as right censored at the test maximum or at 90% of age-predicted heart rate. At minimum, the manuscript should state clearly that inferences from the threshold model apply only to the EI subgroup.

Taken together, these are tractable problems: a corrected confidence interval, a model that respects time since injury, and an analysis that honours censoring would materially improve interpretability. None of these changes alters the clinical message that graded, subthreshold aerobic exercise has growing support in the management of persistent PCS (2–4). Evidence from randomized and systematic work shows that carefully prescribed exercise below the symptom threshold can accelerate recovery and reduce the risk of prolonged symptoms (2, 3). The observation that a large majority of patients in this cohort met criteria for EI underscores the value of rigorous modelling, as these results are used to guide return-to-exercise decisions. Addressing the points mentioned would help the field judge the relation between symptom burden and exercise capacity with greater precision and, ultimately, translate testing into safer, more effective rehabilitation.

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REPLY TO THE COMMENTARY ON: EXPLORING EXERCISE INTOLERANCE IN ADULT PATIENTS WITH PERSISTENT POST-CONCUSSION SYMPTOMS AFTER MILD TRAUMATIC BRAIN INJURY

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Thank you for your interest in our paper and for your reflections. This paper as stated in the title aims to explore exercise intolerance, which we believe is a little understood concept in the clinic, especially for patients with persistent symptoms, and research is warranted.

Thank you for also noticing the incidental extra hyphen.

As reported, we used a logistic model adjusted for sex and age to examine the association between Buffalo Concussion Treadmill Test (BCTT) outcome (exercise intolerant vs exercise tolerant) and symptom burden. This analysis was designed to describe associations rather than establish causality, and future studies are needed to elucidate causal and mediating pathways, including the potential role of time since injury, underlying physiology, appropriate psychological measurements, and exercise capacity - which is very difficult to measure in this patient group.

Furthermore, in a cross-sectional study, time since injury may also reflect selection mechanisms, as subgroups of patients may be referred to hospital at different time points (e.g., directly from emergency department due to injury characteristics or later from general practitioner due to persistent symptoms). Because analyses and interpretation of these factors were beyond the scope of the study, time since injury was not included in this model. That said, including time since injury as a covariate did not substantial change the model (OR: RPQ = 1.056 [p = 0.046], sex [male] = 1.22 [p = 0.722], age = 0.94 [p=0.016], months since injury = 0.88

[p = 0.056], nor the conclusions. However, months since injury in this context should be interpreted with caution, and future studies should examine the temporal development of exercise intolerance in patients with persistent symptoms.

Regarding the linear regression of the BCTT symptom threshold, this analysis was intentionally restricted to participants who met the exercise intolerance criteria. We used the BCTT both to classify patients as exercise tolerant or exercise intolerant, and in the latter group, to assess symptom threshold. As clearly stated in the Methods and Results, only exercise intolerant patients were included, and symptom threshold was observed for all patients in that group. Approaches for right-censored outcomes (e.g., Tobit or time-to-event models) are primarily relevant for a different estimand with the full cohort, where exercise tolerant patients would contribute with censored thresholds. Including exercise tolerant patients in this analysis would therefore change the research question and estimand from identifying associated variables of symptom threshold within exercise intolerance. As stated, we explored exercise intolerance, not exercise capacity.

For these reasons, we do not consider the latter two points to constitute methodological issues within the scope of the stated aims. At the same time, based on our analysis in which level of physical activity level was not a significant variable, we agree that further studies, conducted in other centers and countries would be valuable.