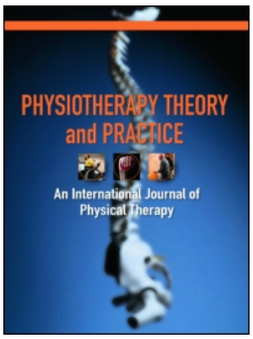

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Measurement of improvement on repeat exercise intolerance testing for suspected dysautonomia in protracted concussion recovery: a retrospective cohort study

Lauren Ziaks PT, DPT, ATC, NCS[a], Jenna Tucker PT, DPT, NCS, CBIS[b], Thomas Koc PT, DPT, PhD, OCS[b], Kristina Hanson PT, DPT[a], and Freya Puxted BS[b]

[a]Rehabilitation Services, Intermountain Healthcare, Park City Hospital, Park City, UT, USA; [b]School of Physical Therapy, Kean University, Union, NJ, USA

ABSTRACT

Background: Research has demonstrated concussion likely causes autonomic dysfunction leading to exercise intolerance.

Objective: To measure improvement in exercise intolerance due to suspected dysautonomia associated with protracted concussion recovery, using objective measurements on a Buffalo Concussion Treadmill Test (BCTT) following participation in a prescribed exercise program.

Methods: This is a retrospective cohort study of 101 patient charts post-concussion. Exercise intolerance was assessed using a BCTT to identify suspected dysautonomia and an exercise prescription was provided using guidelines for treating concussion-associated exercise intolerance. Patients without symptom improvement and/or inability to achieve 80–85% of age-expected maximum heart rate (HR) without symptom exacerbation received a repeat BCTT.

Results: Twelve patient charts met inclusion criteria and were included in data analysis. There were significant improvements from pre-intervention to post-intervention testing in: maximum BCTT stage mean scores ($p = .02$); maximum HR mean scores ($p = .01$); prescription HR (RxHR) mean scores ($p = .01$); and HR delta (HR δ) mean scores ($p = .00$).

Conclusions: Maximum stage, HR threshold, RxHR, and newly identified HR delta (HR δ) are potential objective measurements of progress for dysautonomia treatment post-concussion. Future studies are indicated to create a tailored protocol in the management of protracted concussion-associated dysautonomia.

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Buffalo Concussion Treadmill Test; exercise prescription; reevaluation

Introduction

Concussions are mild traumatic brain injuries that impact millions of individuals, with 10–15% of adults demonstrating symptoms beyond the expected recovery time of two weeks (McCrory et al., 2013). Research has identified concussion-related exercise intolerance as one of these persistent symptoms that is defined as an inability to exercise at or near age-appropriate maximum heart rate (HR) due to exacerbation of concussion-related symptoms (Leddy et al., 2011, 2015). Exercise intolerance is understood to be a result of dysregulation within the Autonomic Nervous System (ANS) control centers, also known as dysautonomia (Kozlowski et al., 2013). The 2020 American Physical Therapy Association Clinical Practice Guidelines outlined clinical profiles for concussion diagnosis and treatment which revealed a knowledge gap in the realm of intervention for concussion-related exercise intolerance (Quatman-Yates et al., 2020).

Disruption of the ANS post-concussion has been reported by multiple studies, with the American Academy of Neurology supporting the concept that "concussion likely causes anomalies within the ANS" (Callaway and Kosofsky, 2019; Gall, Parkhouse, and Goodman, 2004; Pertab et al., 2018). This disorder of the ANS which involves failure of the sympathetic or parasympathetic components and/or overactivity of the ANS, is defined as dysautonomia (National Institute of Neurological Disorders and Stroke, 2019). Research is beginning to demonstrate that elevated sympathetic activity associated with dysautonomia post-concussion can result in varied symptoms, such as mood swings, dizziness, abnormal fatigue, and noise/light sensitivity, as well as a symptom-limited response to exercise (Leddy et al., 2017; Leddy and Willer, 2013; Miranda, Boris, Kouvel, and Stiles, 2018). Graded exertional assessments, which can detect exaggerated sympathetic activity or reduced parasympathetic activity by monitoring the cardiovascular response to exercise, are recommended to assess function of the ANS and assist clinicians in the diagnosis and management of post-

CONTACT Lauren Ziaks ziaks.l@gmail.com Intermountain Healthcare, Park City Hospital, 900 Round Valley Drive, Park City, UT 84049, USA

concussion dysautonomia (Haider, Nowak, Sandhur, and Leddy, 2022; Quatman-Yates et al., 2020).

The Buffalo Concussion Treadmill Test (BCTT) is the gold standard to assess exercise intolerance post-concussion, with the results used to guide appropriate exercise prescription for facilitation of ANS recovery and resolution of symptoms (Leddy et al., 2019, 2018). Current recommendations for treatment of concussion-associated exercise intolerance involves a prescription of cardiovascular exercise beginning at 80% of HR threshold (HRt), defined as the heart rate (HR) at symptom exacerbation on the baseline BCTT (Leddy et al., 2010; Leddy and Willer, 2013). The prescription is increased by 5–10 beats per minute (bpm) every two weeks until the individual is able to exercise at 80–85% of age-expected maximum HR without symptom exacerbation, defined as physiological recovery post-concussion (Leddy et al., 2010; Leddy and Willer, 2013). The literature has demonstrated that prescribed exercise using this protocol can reduce symptoms with protracted recovery (Haider, Nowak, Sandhur, and Leddy, 2022). In a study by Leddy et al. (2010) 12 participants with post-concussion syndrome completed a baseline BCTT between 6 and 40 weeks post injury. They were then provided an exercise prescription using this protocol and were administered follow-up testing every 3 weeks until symptoms were no longer exacerbated on the treadmill. Using measurements of adverse reactions to exercise, reported symptoms, HR, systolic blood pressure, achievement of maximal exertion, and return to work/sport, they concluded that a treatment plan consisting of controlled exercise may improve persistent concussion symptoms. However, there are no specific clinical guidelines on when to repeat the BCTT for reevaluation, and what measurements should be utilized, should individuals demonstrate persistent symptoms consistent with dysautonomia during participation in a prescribed exercise program. The objective of this study is to measure improvement in exercise intolerance due to suspected dysautonomia associated with protracted concussion recovery, using objective measurements on a post-intervention BCTT following participation in a prescribed exercise program.

Methods

Participants

This is a retrospective study of 101 patient charts with a diagnosis of concussion between August 1, 2019 to May 7, 2020, following approval from the Intermountain Healthcare Institutional Review Board. A waiver of consent was obtained, and the patient's rights were protected. The inclusion criteria were patient charts: 1) with a diagnosis of concussion; 2) were administered an initial post-injury BCTT utilizing a Borg Rating of Perceived Exertion Scale; 3) documented signs and/or symptoms of suspected dysautonomia, such as temperature intolerance, visual changes, dizziness, bowel/bladder dysfunction, weight changes, sexual dysfunction, or abnormal fatigue with activities of daily living and exercise; and 4) were administered a post-intervention BCTT (Borg, 1998; Leddy et al., 2011; Leddy and Willer, 2013; Reichgott, 1990). Exclusion criteria included: 1) BCTT was not completed if lost to follow up or deemed inappropriate based on clinic protocol; 2) patients who completed the pre-intervention BCTT per established guidelines, asymptomatically reaching the target HR zone for their estimated HR max; 3) charts with incomplete data collection; 4) utilization of a modified Rating of Perceived Exertion; and 5) charts without a repeat BCTT.

Outcome measures

The BCTT is established as a reliable assessment in the post-concussive population to appraise exercise capacity and determine a safe level of exercise for treatment (Leddy and Willer, 2013). The BCTT Instruction Manual states that the test is terminated upon the presence of one or more of the following criteria: 1) an increase of 3 or more points on the VAS scale from resting VAS score; 2) a Rating of Perceived Exertion (RPE) of >17 without significant symptom exacerbation; 3) a clinical judgment that continuing the test constitutes a significant health risk for the patient; 4) the patient has reached 90% or more of age-expected maximum without any increase in symptoms and still reporting low RPE; or 5) the patient requests to stop for any reason (Ontario Neurotrauma Foundation, 2018).

Procedure

Serial examinations to assess each of the concussion clinical profiles is crucial for comprehensive concussion management. In protracted recovery, patients often present with mixed clinical profiles and determining the primary versus secondary drivers allows the clinician to prioritize treatments for involvement of the various profiles (e.g. vestibulo-oculomotor and cervical-musculoskeletal). Upon implementation of this new clinic protocol (Figure 1), patients meeting inclusion criteria were screened with a BCTT to determine autonomic domain involvement. This clinic's protocol utilized the BCTT pre-intervention and post-intervention to assess signs and symptoms of suspected dysautonomia in patients with

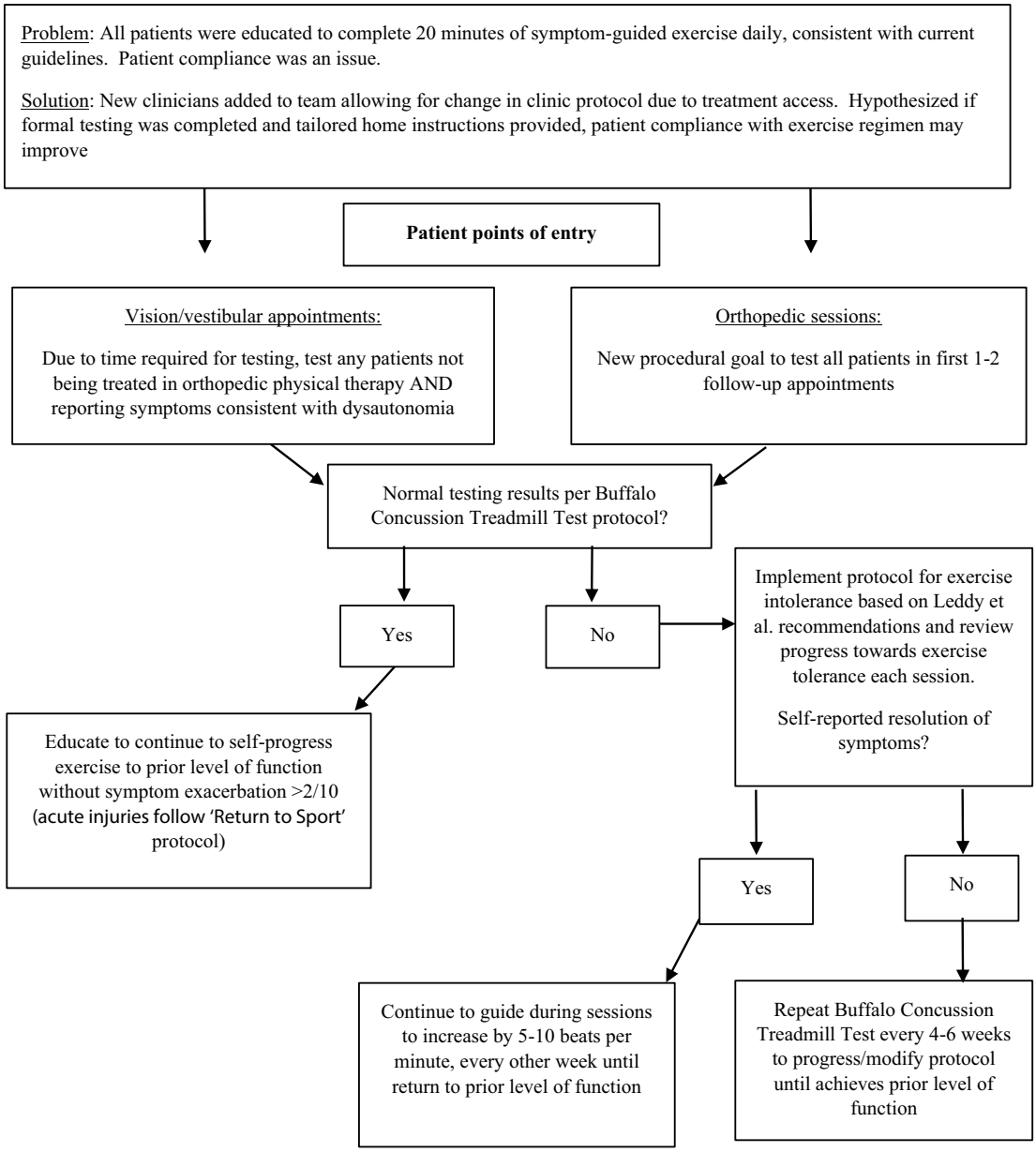

Figure 1. Clinic protocol: domain-based evaluation decision-making tree.

protracted concussion recovery, defined as greater than three weeks (Iverson, Brooks, Collins, and Lovell, 2006). Prior to implementation of the new clinical protocol, clinical staff underwent an initial training session and completed monthly meetings to maintain reliability of test administration. Baseline HR, oxygen saturation, and severity ranking of each symptom using a 0–10 visual analogue scale (VAS) were recorded before beginning the BCTT. Per the BCTT instruction manual, all patients began walking on the treadmill with 0° incline; speed was set to 3.2 mph–3.6 mph depending on patient height (Leddy et al., 2018). They then progressed through each stage by increasing the incline by 1 degree each minute for the first 15 minutes, followed by increasing the speed by 0.4 mph each minute thereafter. Recordings were completed every 60 seconds for heart rate (HR) and oxygen saturation using a medical digit pulse oximetry, as well as RPE, subjective reports of concussion rebound symptoms during recovery, observation of ANS responses, and ranking of symptom severity using a 0–10 VAS. Although these parameters are not commonly recorded during the BCTT protocol, a 2022 study proposed that exacerbation of concussion symptoms, ANS response, rebound symptoms, and desaturation of 90% or below were potential indicators for test termination in individuals with dysautonomia, and therefore included in data collection (Ziaks et al., 2022). Pulse oximetry is an accepted and standardized method of data collection

within the clinic setting, however, 2 or 3 monitors were used to confirm data during abnormal testing results. Peak HR was recorded at the workload of concussion symptom exacerbation, representing the individual's HRt and subsequently used to determine appropriate parameters for exercise prescription. The delta (δ) difference of 80% of HRt compared to 80% of age-expected HR max for each individual's test was also collected (HR δ).

Using the results from their pre-intervention BCTT, patients were instructed to exercise at the specified prescribed exercise HR (RxHR) defined as 80% of HRt, for 20 minutes once per day, 5 out of every 7 days at minimum, via a safe modality of their choice (e.g. stationary bike or treadmill). Patients were educated on the use of a heart rate monitor, or instructed in manually taking their HR if they did not have a device. If working at HRt provoked symptom exacerbation by >2/10 on the VAS, patients were educated to reduce their workload to a tolerable level and complete the 20 minutes versus terminating exercise when able (Leddy et al., 2010; Leddy and Willer, 2013). Patients' self-reported compliance with their exercise program was tracked weekly by the treating clinician. Once they were able to tolerate 20 consecutive minutes at their RxHR without symptom exacerbation during or after exercise, they were instructed to gradually progress their RxHR by 5–10 bpm biweekly (Baker et al., 2012). Simultaneously, patients received interventions for vestibular, cervical and visual involvement as indicated by individual impairment and determined pragmatically by the trained concussion clinic treatment specialist (Ziaks, Brown, and Iversen, 2021). Patients who self-reported symptoms consistent with dysautonomia received a repeat BCTT to evaluate progress and determine if a change in exercise prescription was warranted. Examples of dysautonomia symptoms reported include: ongoing limitations in exercise capacity; nausea; dizziness; poor concentration; light/noise sensitivity; excessive fatigue; and mood changes.

Statistical analysis

Data was transferred from Qualtrics to SPSS Statistics Version 27 (IBM Corporation, Armonk, NY) for statistical analysis. Descriptive statistics were generated for demographic characteristics. Data was analyzed for normality using the Shapiro–Wilk test. Statistical significance was set at $p < .05$ for all analyses. Paired-sample t-tests analyzed the pre-intervention and post-intervention changes in maximum-stage mean, maximum HR mean, RxHR mean, and HR δ mean scores (Faul, Erdfelder, Lang, and Buchner, 2007).

Results

Of the 101 patient charts with concussion screened for this study, 12 patient charts met all inclusion criteria and were included in data analysis (Figure 2). The sample included seven females (58.3%) and five males (41.7%), with a mean age of 24.08 years (SD ± 12.14). There was an average of 29.67 (± 21.33) days from injury to pre-intervention BCTT and an average of 37.75 days from pre-intervention BCTT to post-intervention BCTT. Demographic characteristics are reported in Table 1.

The reported symptoms consistent with dysautonomia that resulted in discontinuation of the post-intervention BCTT included reports of maximal effort indicated by a rating of 19/20 on the Borg (n = 11), exacerbation of concussion symptoms including nausea or headache (n = 6), drop in HR (n = 3), and autonomic symptoms, such as emotional changes (n = 2).

The maximum stage mean scores significantly improved from pre-intervention BCTT to post-intervention BCTT, $t(11) = -2.63$, $p = .02$. Each stage is equivalent to one minute of the BCTT protocol completed. The HRt mean scores significantly improved from pre-intervention BCTT to post-intervention BCTT, $t(11) = -3.10$, $p = .01$. The RxHR mean scores significantly improved from pre-intervention BCTT to post-intervention BCTT, $t(11) = -3.10$, $p = .01$. The newly proposed HR δ mean scores significantly improved from pre-intervention BCTT to post-intervention BCTT, $t(11) = 9.48$, $p = .00$ (Table 2).

Discussion

This is the first study to measure maximum stage mean scores, mean HRt, mean RxHR and newly identified HR δ mean scores on a post-intervention BCTT to assess improvement in exercise intolerance following participation in a prescribed exercise intervention for dysautonomia with protracted concussion recovery. In this study, improvements were identified within all four constructs measured during the post-intervention BCTT, indicating some degree of physiological improvement despite incomplete resolution of dysautonomia symptoms. This is believed to indicate increased activity tolerance on the BCTT despite not yet achieving full symptom resolution or complete physiological recovery.

Although the patients in our study had a higher average age, the low pre-intervention HRt average is consistent with the results from a 2018 randomized controlled trial in acutely concussed adolescents, which reported that a HRt < 135 bpm was significantly associated with prolonged concussion recovery (Leddy et al., 2018). Early exercise intolerance with symptom exacerbation

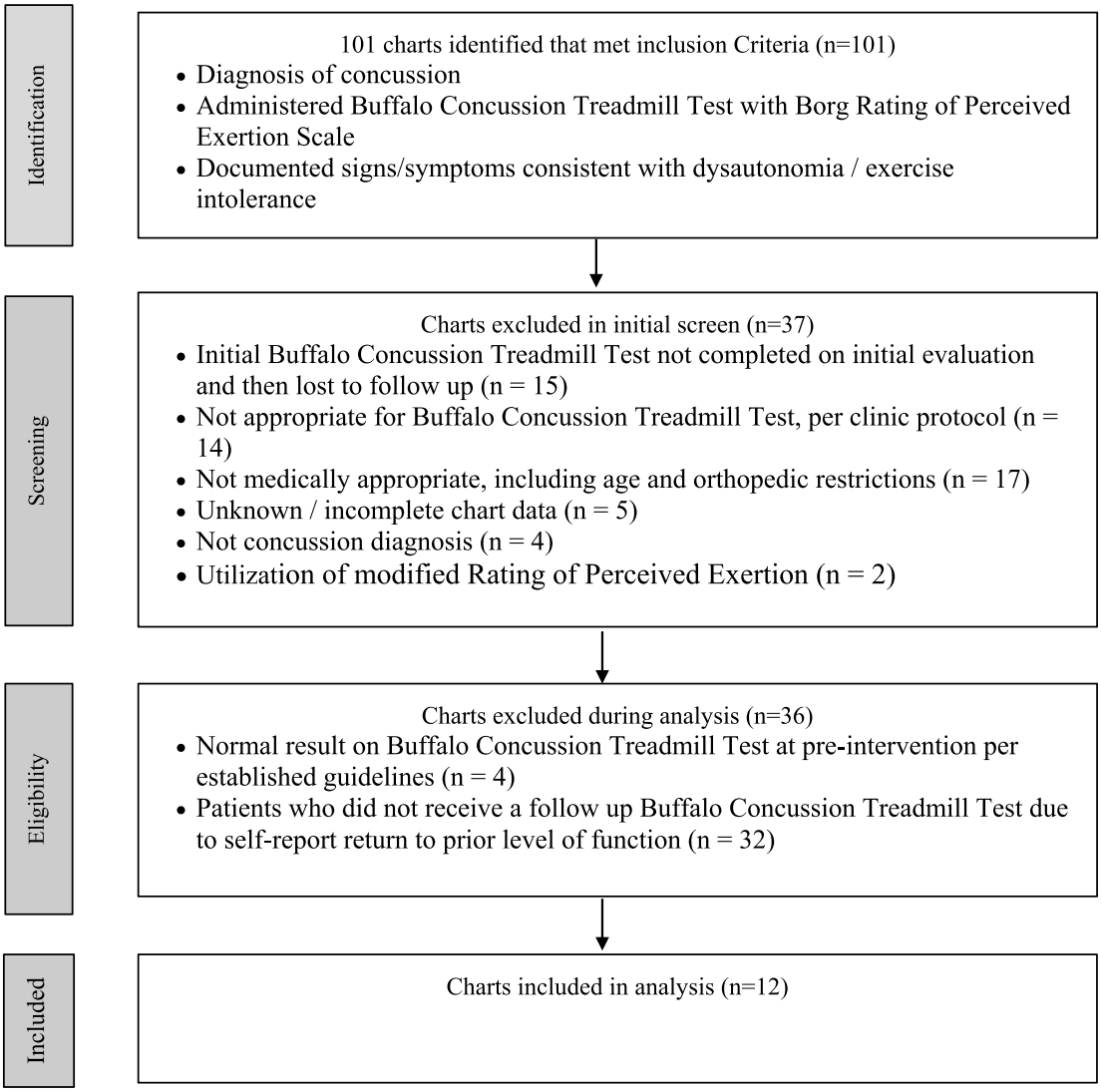

Figure 2. Patient chart screening.

Table 1. Demographic characteristics of the patients (n = 12).

	Frequency (%)	95% CI, Lower	95% CI, Upper
Sex			
Female	7 (58.3%)	33.3	83.3
Male	5 (41.7%)	16.7	66.7
Mechanism of Injury			
Struck by object	3 (25%)	0.0	50.0
Nontraditional sport	4 (33.3%)	8.3	66.7
Sports-related	2 (16.7%)	0.0	41.7
concussion	2 (16.7%)	0.0	41.5
Motor vehicle accident	1 (8.3%)	0.0	25.0
Fall			
History of Concussion			
Yes	4 (33.3%)	8.3	58.3
No	7 (58.3%)	33.3	83.3
Unknown	1 (8.3%)	0.0	25.0

CI: Confidence Interval.

at ≤135 bpm on a baseline BCTT is commonly associated with more severe cases of dysautonomia, likely requiring a longer recovery (Clausen, Pendergast, Willer, and Leddy, 2016). After an average of 37.75 days of treatment, the mean HRt scores for our patients significantly improved from 127.75 bpm to 149.75 bpm. Although individuals did not yet experience complete symptom resolution, the improvement in HRt supports the use of exercise prescription, however, those with persistent dysautonomia symptoms may require a longer duration of prescribed exercise. Research has shown that adults and non-athletes require longer treatment duration than adolescents and athletes, with all individuals requiring anywhere from 13 to 91 days of treatment to achieve full recovery (Cordingley et al., 2016; Lawrence, Richards, Comper, and Hutchison, 2018; Leddy et al., 2019, 2010). Our study was composed primarily of adult non-athletes, which reflects the majority of patients diagnosed with concussion (Peterson, Zhou, Thomas, and Daugherty, 2021). The demographics may explain one possible contribution to

Table 2. Pre-intervention and post-intervention outcomes and significance values.

Outcome	Pre- Intervention (mean ± SD)	Post- Intervention (mean ± SD)	*t-value*	Degrees of Freedom	p-value	95% CI, Lower	95% CI, Upper
Maximal Buffalo Concussion Treadmill Test stage achieved	9.7 ± 7.7	11.8 ± 5.7	−2.63	11	0.02*	−3.98	−.35
Heart Rate Threshold	127.8 bpm ± 24.7	149.8 bpm ± 13.0	−3.10	11	0.01*	−37.63	−6.37
Prescription Heart Rate (80% of Heart Rate threshold)	102.2 bpm ± 19.7	119.8 bpm ± 10.4	−3.10	11	0.01*	−30.10	−5.10
Mean Delta Heart Rate	93.7 bpm ± 26.1	36.9 bpm ± 13.0	9.48	11	0.00*	43.61	69.96

*Significant difference between Pre-Intervention and Post-intervention (paired-sample t test, $p < 0.05$); SD: Standard Deviation; bpm: beats per minute; CI: Confidence Interval.

the increased expected recovery time, which is likely due to the fact that adult non-athletes have a lower baseline fitness on average, putting them at a disadvantage during the recovery process. Another potential contributing factor may be the negative reinforcement of the multiple clinical profiles occurring simultaneously in patients with protracted concussion recovery (Leddy et al., 2021). Although our patients received serial examinations and were undergoing concurrent treatment for mixed clinical profiles per the clinical protocol, involvement of these other systems may have potentially influenced recovery duration (Ziaks, Brown, and Iversen, 2021). For individuals requiring a longer treatment duration, the integration of repeat testing would allow for assessment of physiologic progress, which has the potential to assist clinicians in more accurately assessing progression of ANS recovery and objectively updating exercise prescription for maximal efficacy, specifically in more severe cases of dysautonomia. Future studies are indicated to determine the most appropriate intervals for post-intervention testing and validate the use of specific measurements of exercise tolerance improvement. Concussions often present with impairments reflecting multiple clinical profiles, therefore future research should also attempt to subcategorize patients through a comprehensive evaluation in an effort to control for profile-specific interventions. The nature of protracted concussion recovery and the overlay of clinical profiles continues to be a barrier to controlled research in this clinically complex population.

Prior research has reported prescribed submaximal aerobic exercise resulting in clinical improvement and full recovery. In a study of 41 children and adolescents with post-concussion syndrome, 90.2% demonstrated full physiologic recovery following participation in a prescribed individualized submaximal aerobic exercise based on BCTT performance (Cordingley et al., 2016). Similarly, another study reported that all 12 subjects reached physiologic criterion for treatment success with the ability to exercise at or near to age-predicted HR maximum without symptom exacerbation, demonstrating significant improvements from a mean stage of 9.75 on the pre-intervention BCTT to 18.67 on the post-intervention BCTT (Leddy et al., 2010). However, there have been no studies identifying objective measurements on a post-intervention BCTT to track and assess progress, or lack thereof, for patients' improvement but falling short of full physiologic recovery. The individuals in our study also demonstrated improvements in mean stage achieved, from 9.67 pre-intervention to 11.83 post-intervention indicating improved exercise tolerance, yet did not achieve full symptom resolution or physiologic recovery. Increased duration of exercise time, as indicated by achieving a higher mean BCTT stage, is an indicator of clinical improvement and has been correlated with improvements in maximal exercise HR and systolic blood pressure (Leddy et al., 2010). This objective data suggests that these individuals were making strides toward what is considered physiological recovery, despite persistent symptoms. Prior studies have recommended that exercise training programs should be of sufficient duration to permit regulatory and autoregulatory systems time to adapt to the stress of exercise-induced changes in peripheral physiological variables and should be adjusted at regular intervals to account for a "training effect" on the autoregulatory system (Leddy et al., 2007). Due to resolving but persistent symptoms, it is suspected that these individuals have not yet achieved the adequate level of regulatory/autoregulatory system adaptation, which may explain the rebound symptoms and ANS responses during the BCTT. The authors hypothesize that in protracted recovery, incremental RxHR changes over a treatment protocol that is of longer duration than commonly reported in the current research will allow for this adaptation to occur. Therefore, reassessment of the BCTT at designated intervals during the plan of care has the potential to improve efficacy of treatment by using updated objective measures from repeat testing to adjust parameters of the exercise prescription.

The knowledge gap regarding treatment guidelines for dysautonomia associated with protracted concussion recovery may be filled by identifying key objective measures that can be recorded during the BCTT, which have the potential to assist with developing standardized protocols to design individualized exercise prescriptions.

Despite the improvements in mean stage, HRt, and RxHR these measures do not control for variations in baseline fitness level, and are not immediately transferable across age ranges, which will be of greater importance as research expands beyond the youth sports population. Leddy et al. (2019) utilized the difference between resting HR and HRt as a measure of clinical recovery, in an attempt to accommodate for the individual differences in fitness associated with an absolute HRt cutoff value. Additionally, participation in regular exercise results in decreased resting HR associated with improved cardiorespiratory fitness, making resting HR a moving target relative to general conditioning (Bellenger et al., 2016). Therefore, to accommodate for differences in fitness level and improved resting HR due to conditioning, the authors have proposed mean delta difference (HR δ = 80% age expected max – 80% max HR achieved on BCTT) as another objective measure to assess progress of exercise intolerance treatment in adults. This relative measure may consider differences in age, overall conditioning, and other variables as research expands beyond traditional sports-related concussion in youth athletes. Although we found an improvement in mean HR δ, larger-scale studies are indicated to quantify impairment, which would help establish test–retest criteria. This would also assist clinicians in determining a more accurate prognosis while patients progress through a standardized protocol for exercise prescription.

The retrospective design of this study resulted in a small sample size secondary to a post-intervention BCTT only being administered to those with persistent symptoms, resulting in exclusion of 32 charts. Currently, there is no clinical protocol for BCTT retesting in individuals' post-concussion, however, given the broad demographics and level of impairment for the patients in this study, the clinicians felt retesting was necessary in those individuals with protracted recovery. Patients who exhibited mild deficits and could self-report return to prior level of function were not retested due to time constraints in the clinical setting. In addition, it is understood that physiological recovery is marked by asymptomatically achieving 80%–85% of age-expected HR maximum. Although a direct comparison cannot be drawn, we can infer from established research that these patients were making strides toward what is considered physiological recovery from concussion. A larger-scale prospective study is indicated to include repeat testing for all patients to assess physiological recovery and compare results to those with prolonged recovery. Other limitations include the use of pulse oximetry vs. more specific central monitors and/or a 5-lead electrocardiogram. Clinical data supports use of wearables, rate of perceived exertion, and pulse oximetry for use in the clinic; however, these measures may be unreliable and future studies should utilize more accurate HR monitors during the BCTT and exercise intervention.

Conclusion

The results of this study introduce maximum stage mean scores, maximum HR mean scores, 80% of age-expected HR maximum mean scores and HR δ mean scores as potential objective measurements of progress for exercise intolerance secondary to dysautonomia post-concussion. Future studies are indicated to create an objective tailored protocol to achieve full physiological recovery in the presence of dysautonomia post-concussion.

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ORCID

Lauren Ziaks PT, DPT, ATC, NCS http://orcid.org/0000-0001-6855-8906
Jenna Tucker PT, DPT, NCS, CBIS http://orcid.org/0000-0002-6204-0302

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