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Effect of treadmill exercise stress testing on troponin levels in children and adolescents

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Original Article

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Abstract

Background: Chest pain is a common complaint among paediatric patients and cardiac troponin (cTn) level is often part of the initial emergency department evaluation. It is well known that after intense endurance exercise cTn levels can be elevated in patients with otherwise healthy hearts, however the effect shorter duration exercise has on cTn levels in this population is not known. *Objective:* Determine the behaviour of cTn levels in healthy children and adolescent patients after short burst, high-intensity aerobic exercise. *Methods:* Patients without haemodynamically significant heart disease referred for a treadmill exercise stress test (EST) were recruited over a 6-month period. cTn levels were measured prior to exercise and 4 hours after exercise. *Results:* Thirteen patients enrolled. Indications for EST were exertional syncope (six), chest pain (four), and long QT syndrome (three). The median exercise time was 12.9 (9.9–13.7) minutes with an average endurance at the fiftieth percentile for age and maximum heart rate rose to an average of 92 (74–98)% of the predicted peak for age. cTn levels prior to exercise were undetectable in all patients. There was no cTn rise in any patient after exercise. There were no ischaemic changes or arrhythmias on exercise electrocardiograms. *Conclusion:* Serum cTn levels do not rise significantly in healthy children after short duration, high-intensity aerobic exercise. Physicians evaluating paediatric patients with an elevated cTn level after less than prolonged strenuous activity likely cannot attribute this lab value solely to exercise and may need to undertake further cardiac investigation.

Chest pain is a common presenting complaint in the paediatric emergency department.[1] In paediatric patients, chest pain is unlikely to be caused by a cardiac condition, however, since the opposite is true for adults, the initial evaluation for many patients often focuses on cardiac evaluation, including a cardiac troponin (cTn) level.[2–4] An elevated cTn level could signify a serious condition, such as myocardial infarction, myocarditis, or myopericarditis. Regardless of the reason for an abnormal result, an elevated cTn level can lead to hospitalisation, months of activity restrictions, and expensive further testing, so it is important to identify potential confounding factors. Studies have shown that cTn levels increase during strenuous aerobic exercise in adolescent and adult athletes.[5–9] There are currently no studies investigating the effect short burst, high intensity aerobic exercise has on cTn levels in children. We sought to determine the behaviour of cTn levels in healthy children and adolescent patients after short burst, high-intensity aerobic exercise.

Materials and method

Ethical approval for this study was obtained from the Institutional Review Board. Subjects without CHD who were referred by a physician for a treadmill exercise stress test (EST) were recruited. cTn levels were collected prior to exercise and 4 hours post-exercise, which has previously been shown to be the timepoint at which cTn levels peak after exercise.[5,6,8,9] The Siemens Dimension Vista® conventional cTnI assay (Siemens Healthineers, Erlangen, Germany) was used. The lower limit of detection was 0.015– ng/ml and normal values were considered to be less than 0.1 ng/ml. Treadmill EST was conducted according to the standard Bruce protocol.[10] Clinical data collected included age, sex, and diagnosis/reason for referral for testing. EST data included exercise duration, endurance percentile for age, pre-test heart rate, peak heart rate, percentage of age predicted maximal heart achieved, reason for stopping test, and any arrhythmias or exercise electrocardiogram abnormalities. Standard, previously published, normal values were used to assess EST performance, including endurance percentile and predicted maximal heart rate, in paediatric patients.[11]

Prior to subject recruitment, calculation of the proposed sample size was based on the likelihood of measuring a detectable cTn rise after exercise. A planned enrollment of 13 patients was calculated to achieve greater than 80% power to detect a cTn rise using a two-sided alpha level of 0.05 assuming an event rate of 40%. This event rate was selected to increase the sensitivity to

detect cTn rise based on previously published reports of 50% of healthy subjects exhibiting cTn elevation after exercise.[8]

Categorial data are reported as counts and percentages and continuous variables are expressed as medians (interquartile range). Univariable analysis of continuous variables was performed using two sample Student's t-tests. Two-sided p-values <0.05 were considered statistically significant. Analyses were performed with Graphpad Prism version 9.2.0 for Windows (GraphPad Software, San Diego, California).

Results

A total of 13 patients referred for an EST consented to participate in this study (Table 1). None of the 13 subjects had structural heart disease, prior cardiac surgery, or known uncontrolled arrhythmia syndromes. Participants' ages ranged from 9 to 17 years with a median of 15 years and 62% were female. The reason for referral to EST was exertional syncope in six patients, chest pain in four patients, and long QT syndrome (without a history of a sentinel cardiac event) in three patients.

The EST results are summarised in Table 2. The median EST endurance time was 12.9 (9.9–13.7) minutes. The exercise time in the standard Bruce protocol for each participant corresponded to a median endurance percentile, grouped for age and sex, of 50 (25–75). The median pre-test heart rate was 85 (56–99) beats per minute (bpm) with an increase to a median peak heart rate of 190 (154–198) bpm. The group achieved a peak heart rate equal to 92 (74–98) percent of their age-predicted maximal heart rate.

The reasons for ending testing were fatigue in eight participants, chest pain in three, and dizziness in two. There were no ischaemic changes on exercise ECG and no patients had an arrhythmia. There was no difference between male and female participants when comparing age and sex-adjusted endurance percentile, 50 (17.5–90) versus 37.5 (13.75–86.25) ($p = 0.77$), or predicted peak heart rate percentage achieved, 93 (89.5–97)% versus 87 (65.25–95)% ($p = 0.14$).

Every participant had an undetectable serum cTn level (<0.015 ng/ml) immediately prior to testing. Additionally, every subject had an undetectable cTn level 4 hours after the completion of their test.

Table 1. Patient demographics

Characteristic	Total
Total participants, n	13
Age, Median (Interquartile range)	15 (12–16)
Female, n (%)	8 (62%)
Reason for exercise test referral	
Exertional syncope, n (%)	6 (46%)
Chest pain, n (%)	4 (31%)
Long QT syndrome, n (%)	3 (23%)

Table 2. Exercise stress test results

Variable	Total
Endurance time (minutes), median (interquartile range, IQR)	12.9 (9.9–13.7)
Endurance percentile, median (IQR)	50 (25–75)
Pretest heart rate (beats per minute), median (IQR)	85 (56–9.5)
Peak heart rate (beats per minute), median (IQR)	190 (154–198)
Percentage of age predicted peak heart rate achieved	92 (74–98)
Reason for ending test	
Fatigue, n (%)	8 (62%)
Chest pain, n (%)	3 (23%)
Dizziness, n (%)	2 (15%)

Discussion

This is the first study to prospectively measure the effects of short burst, high-intensity aerobic exercise on cTn levels in healthy children and adolescents. Multiple studies have demonstrated clear elevations in serum cTn levels in paediatric patients after intense, longer duration, aerobic exercise.[5–8] However, in these studies the amount of exercise ranged from running a half marathon to an hour-long competitive soccer match. The physician asked to assess a paediatric patient with an elevated cTn level after exercise is often seeing an individual who did not adhere to a well-defined, intense exercise regimen prior to presentation. Therefore, it is useful to understand the effects varying levels of exertion have on cTn levels to help guide clinical decision making.

Prior studies have demonstrated that exercise duration, exercise intensity, and amount of prior training correlate with the presence and degree of cTn elevation in adult patients.[12–15] The current data shows that cTn elevation is more likely after longer duration, higher intensity exercise in less-conditioned subjects. Since the paediatric studies to date have only assessed patients after a longer duration of intense exercise, it can be difficult to extrapolate the likelihood of cTn release from adult data since paediatric patients are often not highly trained athletes and often participate in high intensity, short bursts of exercise during routine play.

The underlying mechanisms that cause cTn rise after exercise in otherwise healthy subjects are not completely understood.[9] Most leading theories agree that the rise in cTn in these patients is likely not the result of significant myocardial injury or necrosis.[16–18] Therefore, since the underlying process is thought to be benign, a physician caring for a patient who presents with an elevated cTn level after exercise may wonder if the patient could be spared further cardiac evaluation, intervention, or restriction if the abnormal lab value is indeed secondary to their activity. For patients presenting after intense, long duration aerobic exercise, results of prior studies have suggested that this may in fact be the case.[5–8,18] This pilot project demonstrates that a short burst of high-intensity exercise is not expected to elicit a detectable serum cTn level. Therefore, it would likely be inaccurate to assume these patients have an abnormal lab value attributable to exercise and potential cardiac pathology should be considered.

While this study is strengthened by its prospective approach to evaluation of cTn levels in paediatric patients after exercise, there are limitations. First, while the power analysis presented above was based on prior studies evaluating cTn levels in paediatric patients after exercise, this is the first study to evaluate shorter duration exercise, and therefore, the true event rate of cTn rise in this population was unknown. We attempted to account for this by assuming a lower assumed event rate in the population. Since the subjects recruited were not referred for a cardiopulmonary exercise test with breath-by-breath analysis, the intensity of the exercise performed had to be based on endurance time and peak heart rate achieved rather than Respiratory Quotient (RQ). Thus, subjects

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may have given a more sub-maximal effort than their heart rate and run time would suggest and led to an artificially low troponin value. Finally, a standard cTn level was used in our study and newer, more sensitive cTn assays are currently being developed. Given the typical presentation of paediatric chest pain in the emergency department it would be of interest to conduct a study assessing high sensitivity troponin levels in healthy patients after a variety of activities not currently described in the literature, such as an American football game.

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Conflicts of interest. None.

Ethical standards. This study was approved by the University of Pittsburgh Institutional Review Board. Written consent was obtained from all participants in this study and their parents or legal guardians.

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