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Original Research Article

Cardiac troponin I levels in young healthy athletes and untrained individuals following treadmill exercise

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Abstract: Elevated serum cardiac troponin (cTn) levels are not restricted to acute coronary syndrome (ACS) but has also been frequently observed following exercise in healthy individuals. This study aims to measure and compare the cardiac troponin I (cTnI) levels in young healthy athletes and untrained individuals following a maximal treadmill exercise test. The study population included 100 regularly well trained athletes (age 18-34 years) , from the academy of the Sports Authority of India, Manipur and 100 age-matched untrained healthy individuals, from among the staffs and medical students of our institution, who did not participate in any kind of regular sport activities. The serum levels of cTnI were measured before and within 30 minutes after performing a maximal treadmill exercise (Bruce protocol) in the department of Physiology RIMS, Imphal. Before exercise, all individuals had undetectable cTnI levels. After exercise, cTnI was raised in 48% (n=48) of the trained athletes and only 18% (n=18) of the untrained individuals. The mean post-exercise cTnI level was significantly higher in athletes (0.942±0.42ng/ml; range 0.500-1.800ng/ml) compared to untrained individuals (0.571±0.19ng/ml; range 0.500-1.000ng/ml) (p=0.001). 5(10.42%) athletes had cTnI levels above the myocardial infarction cut-off level (≥1.5ng/ml). The findings suggest that a single bout of a maximal treadmill exercise can cause release of cTnI into the bloodstream of a healthy group of young adults including trained athletes as well as untrained individuals. Athletes ran for a longer time on the treadmill and thus had to face higher exercise intensity (increased speed and gradient). This may be the reason why athletes had a higher incidence of cTnI elevation and a higher cTnI level.
Keywords: Cardiac troponin I, Treadmill exercise, untrained, athletes.

INTRODUCTION:

Cardiac troponins (cTn) are highly specific markers of myocardial cell damage and are central to the diagnosis of acute coronary syndromes (ACS), particularly acute myocardial infarction (AMI) [1, 2]. Many studies have reported that exercise can induce a release of cTnI and cTnT into the bloodstream. It has been shown that 32-100% of athletes demonstrated elevated cTn levels after a range of exercise bouts like marathons[3-5], trianthelons[6], ultra marathon [7], cycling [8,9] and even walking [10]. Few studies have also reported cTn elevation after short duration as well as laboratory based exercises including treadmill run [11, 12], a maximal bicycle exercise test [13] and a maximal rowing test [14] in 37-75% of healthy participants.

Most of the available literature focuses on trained athletes participating in ultra-endurance or prolonged and intense events such as marathon, ultra marathon, triathlons, etc. Limited data is available for shorter duration and laboratory-based exercises. There are also very few studies which have focused on the relationship between training/athletic status of the individual and post-exercise cTn elevations. The present study aims to measure and compare the pre- and post-exercise levels of cTnI in healthy trained athletes and untrained individuals following a maximal treadmill exercise.

MATERIALS AND METHODS:

This cross sectional study was conducted in the Department of Physiology, Regional Institute of Medical Sciences, Imphal, from January 2015 to September 2016. The study population included well

trained athletes of both sexes, in the age group of 18-35 years, from the academy of the Sports Authority of India, Manipur. They were regularly trained (> 5 times a week/ >6 hours a week) for at least one year. Our study also included age-matched untrained healthy subjects, from among the staffs and medical students of our institution, who did not participate in any kind of regular or organized sport activities.

Subjects with pre-existing cardiovascular diseases, pulmonary diseases, autoimmune conditions, renal failure, and history of hypertension, diabetes and peripheral vascular diseases or under any kind of medication were excluded from the study.

Study procedure: After a written informed consent was taken, a brief history of clinical information was recorded and pre-exercise general and systemic examination was done. Anthropometric measurements were taken.

The participants were instructed not to have a heavy meal or caffeine at least 3 hours before the exercise. They first performed a warm-up treadmill run at a speed of 2.7 km/hour and 0% gradient for about 5 minutes or so. When the participants were ready, the treadmill exercise test began, starting with the same speed as in the warm-up (2.7 km/hr) but gradient/inclination increased to 10%. The speed and gradient of treadmill increased every 3 minutes as per the Bruce Protocol [15] given in the table below.

Table 1: Bruce Protocol

Stage	Minutes	% grade	Km/hr	MPH
1	3	10	2.7	1.7
2	6	12	4.0	2.5
3	9	14	5.4	3.4
4	12	16	6.7	4.2
5	15	18	8.0	5.0
6	18	20	8.8	5.5
7	21	22	9.6	6.0

The participants ran on the treadmill until they reached volitional exhaustion after which they were instructed to inform us to stop the protocol, or they could push the emergency stop button on the treadmill. After the exercise protocol was stopped, the speed and gradient of treadmill decrease gradually as a form of cool down exercise, till it comes to a complete halt. The time taken to run was then noted. The Maximal Oxygen uptake (VO_2 Max) was estimated by the Bruce Protocol formula: For Men = $14.8 - (1.379 \times T) + (0.451 \times T^2) - (0.012 \times T^3)$; For Women = $4.38 \times T - 3.9$ where T is the total time taken to run on the treadmill. VO_2 Max value was used to categorize the participants on the cardiorespiratory fitness scale [16].

Sample Collection: The first whole blood sample (3ml) was collected by venipuncture from participant's antecubital vein just before the start of exercise. The second blood sample was collected within 30 minutes after exercise. The blood sample was collected in a plain vial and allowed to clot for a minimum of 30 minutes. Samples which could not be assayed within 24 hours of collection were stored at 2-4ºC or lower. Prior to use, all samples were brought to room temperature.

Diagnostic kit used: Estimation of cTnI was carried out by Enzyme Linked Immunosorbant Assay (ELISA) method using Bio Check Human Cardiac-Specific Troponin-I Enzyme Immunoassay. Bio Check, Inc 323 Vintage Park Dr. Foster City, CA 94404.

Expected values: Normal value was considered to be ≤0.5 ng/ml with the cut off value for AMI patients being 1.5ng/ml.

Statistical analysis:

All the data obtained from the study was statistically analyzed using IBM Statistical Package for Social Sciences (SPSS) Software version 21. Data was expressed in terms of percentages and mean±standard deviation. Independent samples t test and chi square test were done. A p value of <0.05 was considered significant.

Ethical Approval**:** The study was conducted after appropriate approval of the Institutional Ethics Committee.

RESULTS AND DISCUSSION:

There were 42 (42%) females and 58 (58%) males among the athletes (n=100) and there were 41 (41%) females and 59 (59%) males among the untrained subjects(n=100). Athletes consist of boxers, badminton players, hockey players, footballers and basketball players. Table 2 shows the anthropometric measurements and basal parameters of the subjects.

Table 2: Anthropometric and Basal Parameters of the subjects

	Weight (Kgs)	Height (m^2)	BMI (kg/m^2)	Heart rate (beats/min)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Respiratory rate(/min)
Athletes (n=100)	58.76±6.37	1.65±0.74	21.60±1.25	69.12 ± 4.62	118.76 ± 6.56	76.60 ± 5.75	13.62 ± 1.32
Control (n=100)	56.20 ± 6.65	1.60 ± .06	21.75 ± 1.68	78.46 ± 3.89	117.50 ± 6.51	75.34 ± 7.79	13.72 ± 1.49

When the participants are categorized on the fitness scale, 13%, 38% and 49% of the athletes fall on the 'Good', 'Excellent' and 'Superior' level respectively. 14% of the untrained subjects fall on 'Excellent' level but most of them fall on the 'Good' (43%) and 'Fair & below' (43%) levels.

Before the exercise, the cTnI level was below the detection limit (0.5ng/ml) in all of the participants. After exercise cTnI was raised in 48% (n=48) of the trained athletes and only 18% (n=18) of the untrained subjects and the difference is found to be statistically significant ($p<0.0001$). The mean post-exercise cTnI level was significantly higher in athletes (0.942±0.42ng/ml; range 0.500-1.800ng/ml) compared to untrained subjects (0.571±0.19ng/ml; range 0.500-1.000ng/ml) ($p=0.001$) (figure 1).

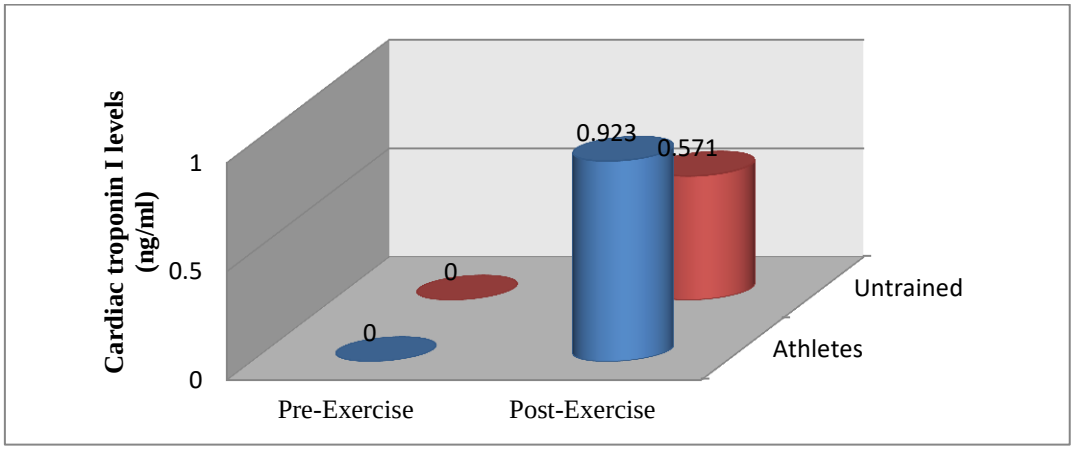

Fig 1: Baseline and Post-exercise mean cTnI levels in athletes and untrained subjects (n=66)

Out of the total 66 subjects that had raised post-exercise cTnI levels, 89.58% of athletes and 100% of untrained subjects had cTnI levels above the detection limit (0.5ng/ml) but below the cut-off for MI (1.5ng/ml). 5 (10.42%) athletes had cTnI levels above the MI cut-off level. (Range: 1.6-1.838 ng/ml).

A significantly higher frequency of cTnI elevation was seen in participants belonging to better cardiorespiratory fitness levels i.e 'Excellent' (55.8%) & 'Superior' (55.1%). No one from the 'Fair and below' level of fitness have elevated cTnI levels. Chi-square test showed an association between cTnI elevation and fitness level of the participants.

Among the 'Excellent' fitness level with elevated cTnI levels (n=29), 18(62%) were athletes and 11 (48%) were untrained subjects and all the subjects in the 'Superior' level with elevated cTnI levels (n=27), were athletes. The mean cTnI level was higher in the fitter subjects in both athletes and untrained subjects (figure 2).

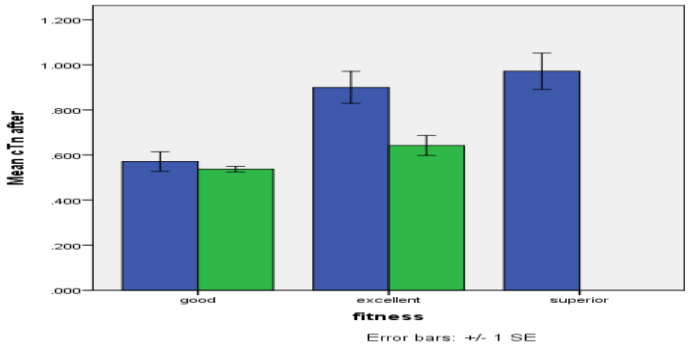

Fig 2: Mean cTnI level in athletes (blue bar) and untrained subjects (green bar) according to fitness level (n=66)

DISCUSSION:

Results from the present study show that a maximal treadmill exercise can cause release of cardiac troponin I into the bloodstream of both healthy trained athletes as well as untrained subjects. Our study agrees with the studies of Shave R *et al.;* [11], Legas-Arrese A *et al.;* [12], Tjora S *et al.;* [13] and Legas-Arrese A *et al.;* [14], which reported cTn elevation after short duration and laboratory based exercises. This show that exercise-induced cTn elevations are seen not only in prolonged strenuous sports events but also in exercises that can be associated with day to day recreational activities like a treadmill run at the gym, cycling, etc. Also, exercise induced cTn elevation is not restricted to athletes alone but can also be seen in healthy untrained individuals, though at lower levels (Tjora S *et al.;* [13], Legas-Arrese A *et al.;* [12,14]). The mechanism for exercise-induced cTn elevation is not understood yet. Irreversible myocardial injury and necrosis as seen in ACS is unlikely because if so, athletes or anyone who regularly exercises should encounter cardiac failure after years of practice and exercise [17]. Some theories have been proposed. One theory is that elevated troponin levels might be due to an increased membrane permeability of cardiomyocytes during exercise allowing unbound cardiac troponins in the cystolic pool to enter the circulation. This increase in membrane permeability can be due to increased mechanical stress on cardiomyocytes, increased production of oxidative radicals or altered acid base balance. Another theory is the stimulation of integrins by myocardial stretch which mediates transport of intact cTn molecules out of the viable myocytes. This release differs from discharge of cTnI from necrotic cardiac myocytes, which is associated with extensive cTnI degradation [15, 18, 19]. It is suggested that the exercise induced cTn elevation is a physiological response rather than a pathological one [20- 22].

Tjora S *et al.;* [13] found that well trained and fitter individuals had a higher frequency (78%) of cTn elevation than untrained and less fit (20%) individuals. Legaz-Arrese A *et al.;* [12] examined the post treadmill exercise cTn levels in subjects before and after they had undergone a training aerobic/endurance exercise program and found that cTn level was higher after they were trained and became fitter. They also found that these trained subjects had higher cTn levels compared to untrained controls. Our study is in agreement with these studies because we also found that the trained athletes had a higher level of post-exercise cTn as well as a higher incidence as compared to untrained subjects. Our findings, however, contradicted the findings of Mingles AM *et al.;* [23] who reported increased cTn values only in untrained subjects after a 5 km recreational run. This could be because of the form of exercise used for the study. Exercise intensity and duration have been found to be important determinants of circulating post-exercise cTn (Shave R *et al.;* [11], Serrano-Ostariz E *et al.;* [9], Eijvogels TM *et al.;* [10, 24]. These studies compared the cTn values of the well trained and untrained groups of population after a 5 km run thereby making them face the same exercise. So, obviously the untrained group will take longer time and with more effort to complete the run as compared to elite runners. In our study we used a maximal exercise where every individual ran on the treadmill till they had reached their own limit. The longer the subject ran, the intensity also increased because the speed and gradient of the treadmill increased with time. So, athletes who ran longer also ran with a higher intensity which could explain our findings of a higher cTn level and incidence in athletes. Also, well trained individuals have a larger cardiac contractile apparatus than those with no training and therefore, they will have larger amounts of troponin in their cytosol and so, more troponin will leak in the circulation during strain [13].

Limitation of our study is that we estimated the post-exercise cTnI level only once i.e immediately after exercise therefore the pattern of cTnI elevation (eg time of peak concentration, time of disappearance) is not known. Our study also included only one age group i.e the healthy young adult group, so we could not assess the association of age with cTn elevation.

CONCLUSION:

The present study showed that cTnI can be released after a maximal treadmill exercise in athletes and also in untrained individuals. It is suggested that these post-exercise cTn releases are not of pathologic nature as in cardiovascular patients, even when clinical AMI cut-off values are exceeded but rather a physiological phenomenon. Clinicians should be aware of exercise as an alternative cause of increased cTn elevation. Thus, when evaluating these biomarkers in an emergency setting, careful information regarding any recent exercise activities should be obtained.

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