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Short Communication

Elevation of cardiac troponins measured after recreational resistance training

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ABSTRACT

Background: Whereas elevated cardiac troponin (cTn) concentrations i.e. above the 99th percentile of healthy reference population (recommended cutoff for the diagnosis of myocardial infarction) are well-documented in healthy individuals after prolonged and/or intensive exercises such as marathons, data on less-strenuous sports are scarce. Therefore, our aim was to investigate cTnI and cTnT release in response to recreational resistance training, here a single-bout of 1-h kettlebell workout.

Methods: Serum samples were collected from 11 apparently healthy volunteers the previous day (pre-exercise), three hours after the kettlebell class (post-exercise), the next day and three days later. The aliquoted samples were analyzed with Abbott Laboratories' Architect high-sensitivity (hs)-cTnI assay (limit of detection, LoD = 2 ng/L), our 3 + 1-type cTnI assay free from cTn-specific autoantibody interference (LoD = 3 ng/L) and Roche Diagnostics' hs-cTnT assay (LoD = 5 ng/L).

Results: The post-exercise cTn concentrations were significantly higher than the pre-exercise values (median 5.5–9.6 ng/L vs. <LoD, $P < 0.05$ for all) and they correlated strongly between the three assays (Spearman r = 0.881–0.960, $P < 0.001$ for all). Furthermore, a few post-exercise concentrations even exceeded the 99th percentile of Architect hs-cTnI (>26 ng/L, n = 2) and/or hs-cTnT (>14 ng/L, n = 4). The cTn concentrations returned to baseline during the three days of follow-up.

Conclusions: Our study demonstrates abnormally elevated cTns with well-validated sensitive cTn assays after resistance training. This confirms that different kinds of recreational physical activity are yet another confounder that may affect the determination and use of 99th percentile reference values. Therefore, exercise-associated changes should be carefully addressed as part of the evaluation what is "normal cTn".

1. Introduction

Cardiac troponin (cTn) I and T are the recommended biomarkers for the diagnosis and risk stratification of patients with suspected acute coronary syndrome (ACS). They are conventionally believed to indicate irreversible myocardial damage albeit reversible cTn release mechanisms have also been proposed [1,2]. High-sensitivity (hs) assays have recently emerged enabling reliable measurement of cTn values in healthy individuals and thus, the detection of ever-smaller myocardial injuries. These assays have also demonstrated that elevated cTn concentrations i.e. above the 99th percentile of healthy reference population (recommended cutoff for the diagnosis of myocardial infarction) are relatively frequently found in a variety of acute and chronic medical conditions other than ACS [3] but also in healthy subjects after prolonged and/or intensive exercise bouts, such as marathons, long-distance cycling and triathlons [4,5]. Although available data have suggested that duration and intensity are important determinants of post-exercise cTn levels [6,7], data on less-strenuous sports commonly performed by non-elite athletes are scarce. Therefore, our aim in this small-scale preliminary study was to investigate both cTnI and cTnT release in response to recreational resistance training, here a single-bout of interval-based kettlebell workout that combines aerobic and anaerobic exercises.

2. Materials and methods

Serum samples were collected from 11 apparently healthy non-obese volunteers [mean (SD) age: 31 (6) years; 64% women] at the Department of Biotechnology, University of Turku in 2014 as follows: the previous day (pre-exercise), three hours after the 1-h kettlebell class (post-exercise), the next day and three days later. The instructor-led

Abbreviations: cTn, cardiac troponin; ACS, acute coronary syndrome; hs, high-sensitivity; cTnAAb, cardiac troponin specific autoantibody; LoD, limit of detection; skTn, skeletal troponin.

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interval training consisted of weight lifting and jogging/running and was intended for beginners. The intensity of exercise, which naturally varies with each individual, was not monitored. None of the test subjects had history of earlier cardiovascular events and they were instructed to exercise as usual during this study (exercise diary from the previous week and from the time of blood collection). Although some participants exercise several times a week, no one did anything but incidental exercise in addition to the kettlebell between the first two blood sampling points. The study was approved by the local ethics committee. Informed consent was obtained from all volunteers and the study was compiled with the Declaration of Helsinki.

The aliquoted samples (stored at −70 °C) were analyzed with our cTn-specific autoantibody (cTnAAb) assay [8], Abbott Laboratories' (Abbott Park, IL, USA) Architect hs-cTnI assay (limit of detection, LoD: 2 ng/L; 99th percentile: 26 ng/L; sex-specific 99th percentiles: 34 ng/L for men and 16 ng/L for women; 10% CV at 5 ng/L), our 3 + 1-type cTnI assay free from cTnAAb interference (LoD: 3 ng/L; 99th percentile: not determined; 20% CV at ~10 ng/L) [9], Roche Diagnostics' (Mannheim, Germany) hs-cTnT assay (LoD: 5 ng/L; 99th percentile: 14 ng/L; 10% CV at 13 ng/L), and our novel sandwich-type skeletal troponin (skTn) I assay [analytical sensitivity (3SD of blank): 657 ng/L; unpublished assay using HyTest's (Turku, Finland) Mabs 12F10 and 7G2 that is calibrated with HyTest's human skTnI]. Architect hs-cTnI and hs-cTnT were analyzed as a single run on an Architect 8000 (Abbott Laboratories) and Cobas 6000 (Roche Diagnostics) instruments, respectively, while our investigational assays as two sequential runs on 96-well plates. The skTn cross-reactivity of cTn assays was evaluated by spiking 50,000 or 500,000 ng/L human skTnI or skTnT into Tris-buffered saline with atzide (50 mmol/L Tris–HCl, pH 7.75, 150 mmol/L NaCl and 0.5 g/L NaN_3) containing 75 g/L BSA or serum samples, and by interpreting skTn-derived signals as apparent cTn concentrations. IBM SPSS Statistic 22 (IBM, Armonk, NY, USA) was used for nonparametric testing (Wilcoxon signed-rank test, Spearman r) and two-sided P values < 0.05 were considered statistically significant.

3. Results and discussion

As shown on Table 1, the post-exercise cTn concentrations were typically higher than the pre-exercise values (median 5.5–9.6 ng/L vs. <LoD, respectively, P < 0.05 for all three cTn assays). Although there was notable interindividual variability in the post-exercise cTn values, they correlated strongly between the three cTn assays (Spearman r = 0.881–0.960, P < 0.001 for all three assay comparisons). Especially noteworthy is that a few post-exercise concentrations even exceeded the 99th percentile of Architect hs-cTnI (>26 ng/L, n = 2) and/or hs-cTnT (>14 ng/L, n = 4). The number of exceeding values would change slightly if sex-specific 99th percentiles, which tend to be higher for men and lower for women than the generic cut-off value, were applied as recommended. These, however, are not available for hs-cTnT from the manufacturer. The cTn concentrations were again lower on the next day and three days later (Fig. 1). Furthermore, the participants' exercise diaries also describing their physical conditioning did not explain individual cTn increases and other potential exercise-associated cTn increases that could have confused the result interpretation were not seen presumably because of the time between the other exercise bouts and blood sampling points exceeded the time needed for its clearance. Similar, statistically significant, quickly disappearing cTn elevations have previously been reported after other type of recreational exercise, such as spinning [10], floorball [11] and running [12] with Roche Diagnostics' hs-cTnT assay.

On the other hand, biological variation studies have demonstrated that cTns have a low index of individuality and thus, the serial changes detected with hs-cTn assays in an individual patient may be of greater value than the use of population based 99th percentile reference values when attempting to diagnose myocardial infarction. The suggested reference delta change values for different hs-cTn assays are around 50% [13]. Our results unfortunately cannot properly address this aspect as in most of the 11 participants, the pre-exercise cTn concentrations were <LoD and their delta change values could not be calculated. Nevertheless, up to 94% (ID 11, Architect hs-cTnI) delta changes were seen in these subjects.

As expected, the median skTnI concentrations also increased after workout demonstrating concurrent skeletal muscle damage (<LoD, 713.4, <LoD and <LoD ng/L at the day before, after the kettlebell workout, the next day and three days later, respectively). Even though the post-exercise skTnI concentrations did not correlate with the post-exercise cTn values, the cross-reactivity of the three cTn assays was evaluated with human skTnI or skTnT to ensure that cross-reactivity with skTn isoforms would not invalidate the above presented cTn results. The median (range) of apparent cTn concentrations (n = 10) with 50,000 and 500,000 ng/L skTn were 4.2 (0.0–9.0) and 63.0 (45.0–83.0) ng/L with Architect hs-cTnI, 4.5 (3.7–7.6) and 62.8 (37.9–95.2) ng/L with 3 + 1-type cTnI, and 0.7 (0.0–19.6) and 2.4 (0.0–19.1) ng/L with hs-cTnT, respectively. Because at least 50,000 ng/L of skTn was needed for the apparent cTn concentrations to exceed the known 99th percentiles, the cross-reactivity is not likely the cause for the elevated cTns after the kettlebell workout. This is an important confirmation as concerns about the cross-reactivity of hs-cTn assays were recently reraised [14].

Table 1
Summary of the pre- and post-exercise results.

Assay			Architect hs-cTnI (ng/L)			3 + 1-type cTnI (ng/L)			hs-cTnT (ng/L)			skTnI (ng/L)		
LoD			2			3			5			657[a]		
99th percentile			26			Not determined			14			Not determined		
ID	Sex	cTnAAb	Pre-exercise	Post-exercise	P value	Pre-exercise	Post-exercise	P value	Pre-exercise	Post-exercise	P value	Pre-exercise	Post-exercise	P value
1	W	N	4.1	2.2		<LoD	<LoD		<LoD	6.0		<LoD	<LoD	
2	W	N	<LoD	7.2		<LoD	3.2		<LoD	9.6		1149.0	883.6	
3	W	N	<LoD	56.0[b]		<LoD	25.7		<LoD	58.8[b]		<LoD	<LoD	
4	W	P	2.2	5.8		3.1	5.2		<LoD	5.9		<LoD	692.0	
5	W	N	<LoD	2.3		<LoD	<LoD		<LoD	5.3		<LoD	<LoD	
6	W	N	<LoD	9.5		<LoD	5.7		<LoD	13.0		<LoD	<LoD	
7	W	P	<LoD	<LoD		6.9	7.0		<LoD	8.2		7642.8	7497.4	
8	M	N	<LoD	3.1		<LoD	<LoD		<LoD	<LoD		<LoD	719.3	
9	M	N	<LoD	23.0		<LoD	9.6		<LoD	36.2[b]		<LoD	713.4	
10	M	N	2.0	34.1[b]		<LoD	22.1		<LoD	28.1[b]		1057.6	929.3	
11	M	N	4.5	8.2		3.3	5.5		9.9	14.6[b]		<LoD	758.2	
Median			<LoD	7.2	0.012	<LoD	5.5	0.009	<LoD	9.6	0.005	<LoD	713.4	NS

W = woman, M = man, N = negative, P = positive, NS = not significant.
[a] Analytical sensitivity (3SD of blank).
[b] cTn above the 99th percentile.