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Predictors of cardiac troponin release after a marathon

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ABSTRACT

Objectives: Exercise leads to an increase in cardiac troponin I in healthy, asymptomatic athletes after a marathon. Previous studies revealed single factors to relate to post-race cardiac troponin I levels. Integrating these factors into our study, we aimed to identify independent predictors for the exercise-induced cardiac troponin I release.
Design: Observational study.
Methods: Ninety-two participants participated in a marathon at a self-selected speed. Demographic data, health status, physical activity levels and marathon experience were obtained. Before and immediately after the marathon fluid intake was recorded, body mass changes were measured to determine fluid balance and venous blood was drawn for analysis of high-sensitive cardiac troponin I. Exercise intensity was examined by recording heart rate. We included age, participation in previous marathons, exercise duration, exercise intensity and hydration status (relative weight change) in our model as potential determinants to predict post-exercise cardiac troponin I level.
Results: Cardiac troponin I increased significantly from 14 ± 12 ng/L at baseline to 94 ± 102 ng/L post-race, with 69% of the participants demonstrating cardiac troponin I levels above the clinical cut-off value (40 ng/L) for an acute myocardial infarction. Linear backward regression analysis identified younger age ($\beta = -0.27$) and longer exercise duration ($\beta = 0.23$) as significant predictors of higher post-race cardiac troponin I levels (total $r = 0.31$, $p < 0.05$), but not participation in previous marathons, relative weight change and exercise intensity.
Conclusions: We found that cardiac troponin I levels significantly increased in a large heterogeneous group of athletes after completing a marathon. The magnitude of this response could only be partially explained, with a lower age and longer exercise duration being related to higher post-race cardiac troponin I levels.

1. Introduction

The presence of the cardiac troponin I (cTnI) in blood is a highly sensitive and specific biomarker for cardiac injury and serves as a central marker in the diagnosis of acute coronary syndromes.[1–3] Many studies have demonstrated an increase in cTnI after prolonged endurance exercise, in the absence of clinical symptoms of a myocardial infarction.[4–6] Relatively little is known, however, about factors that may be associated with, and thus potentially predict, the degree of elevation in cTnI after strenuous running exercise. This important information may help clinicians and laboratories with the challenging interpretation of elevated cTnI levels in athletes.

Studies examining factors that relate to the exercise-induced increase in cTnI have predominantly included small and homogeneous groups of athletes. These studies demonstrated that subject characteristics (i.e. age and running experience),[7] exercise characteristics (i.e. exercise duration and intensity),[5,8,9] and hydration status[10] may relate to the exercise-induced increase in cTnI. These studies typically focused on a single factor only, thereby being unable to assess multiple parameters which may relate to post-race cTnI levels. As an exception to this rule, Fortescue et al. studied cardiac troponin responses in >400 Boston marathon runners.[6] Although age and running inexperience were identified as factors contributing to post-exercise increases in cTnT, they did not correct for important confounders, such as exercise intensity.[11,12] Therefore, current studies provide only a limited insight into factors that

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could independently, or in combination, predict the magnitude of the exercise-induced increase in cTnI.

Therefore, the aim of this study was to identify parameters that predict the elevation in cTnI after a marathon in a large and heterogeneous group of athletes, and to explore the interaction of the identified parameters using regression analysis. The novel aspect of our study is that we examined the potential independent predictive capacity of parameters that have previously been related to the exercise-induced cTnI release. We hypothesized that exercise intensity, exercise duration, age, loss of body mass and running experience independently predict post-race cTnI levels.

2. Methods

A total of 92 moderately to highly trained runners (26–71 years of age) of the Eindhoven Marathon 2010 (The Netherlands) were recruited to the study. An advertisement was placed on the Eindhoven Marathons website to recruit participants. Before participation all participants provided written informed consent. The medical ethical committee of the Radboud University Nijmegen Medical Centre approved the study which was conducted in line with the Declaration of Helsinki.

All participants completed an online questionnaire about subject characteristics, including daily physical activity, marathon experience (e.g. previous completed marathons, personal record) and health (e.g. medical history and medication use). On the day of the marathon, participants underwent a series of measurements in our laboratory near the start/finish area. After demographic data were obtained a venous blood sample was taken. Heart rate was monitored continuously during the race using a chest band. Immediately after the marathon (<5 min), all measurements were repeated in the same order. Additionally, participants reported their fluid intake, use of analgesics, physical complaints and rate of perceived exertion.

Ten milliliters of blood was drawn from an antecubital vein before and immediately after the race. Whole venous blood was collected in serum-gel vacutainer tubes and allowed to clot for ~45 min. After centrifugation, serum was aliquoted, frozen, and stored at −80 °C for later analysis. Analysis was performed on a single day using the same calibration and set-up to minimize variation. cTnI was analyzed using a high-sensitive cTnI assay (Centaur TnI-Ultra, Siemens Healthcare Diagnostics, Breda, The Netherlands). The assay imprecision was 5.3% at 80 ng/L and 3.0% at 27,200 ng/L, with a detection limit of 6 ng/L. A cTnI value of 40 ng/L was used as the clinical cut-off value for an acute myocardial infarction.[13]

Heart rate during the marathon was measured in 70 athletes by using a 2-channel ECG chest band system (Polar Electro Oy, Kempele, Finland). Mean heart rate (HRmean) was determined as the average heart rate between the start and finish of the marathon. Maximal predicted heart rate (HRmax = 208–0.7 * age) and exercise intensity (Exercise intensity = 100 * HRmean/HRmax) were calculated subsequently.[14]

Finish time (exercise duration) was obtained using the ChampionChip time registration (ChampionChip®, MYLAPS, The Netherlands), out of which mean running speed was calculated (Speed = 42.195/exercise duration).

After the marathon, participants completed a questionnaire indicating analgesic use and physical complaints. A visual analogue scale (0 – no effort; 10 – maximal effort) was used to measure rate of perceived exertion.

Participants were allowed to drink ad libitum during the race, whereas they registered the time and amount (standard sized cups, bottles, etc.) of their individual fluid intake after the finish.

Baseline and post-exercise body mass were assessed (Seca 888 Scale, Seca, Hamburg, Germany) to detect changes in hydration status. The relative change in body mass (in %) between the measurements was calculated, while dehydration was defined as a body mass loss of 2% or more.[15,16]

An additional 2 mL of blood was drawn at baseline and directly after finishing to determine plasma levels of sodium, hematocrit and haemoglobin (RapidLab® 1265, Siemens Healthcare Diagnostics Inc., Tarrytown, New York, USA). Hyponatraemia was defined as a sodium concentration ≤135 mmol/L, whereas hypernatraemia was defined as a sodium concentration ≥145 mmol/L.[17,18]

All data were reported as mean ± SD [range] unless stated otherwise and statistical significance was assumed at a p-value <0.05. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). The normality of the data distribution was examined by the Kolmogorov–Smirnov test. When data demonstrated a non-Gaussian distribution, natural logarithmic transformation was applied. Differences between pre- and post-race levels for continuously distributed data were tested for significance with a paired Student's t-test. A backward stepwise linear regression analysis was used to identify factors that significantly relate to post-exercise cTnI-levels. Based on our hypothesis, we have included age, participation in previous marathons, exercise duration, exercise intensity and hydration status in our model as potential determinants to predict post-exercise cTnI level. All predictors with a p-value <0.1 were retained in our final regression model.

3. Results

During the race mean wet bulb globe temperature (WBGT) was 18.8 °C, with a relative humidity of 52%. Of the 92 participants who started the race, 9 participants did not finish the race, because of exhaustion (n = 2), acute knee problems (n = 1), heat (n = 1), dyspnoea (n = 1), hip problems (n = 1), headache (n = 1) or another sport-related injury (n = 2) and were therefore not included in the analysis. One participant was excluded afterwards because of missing multiple data-points. Therefore, 82 participants were included in the data analysis (17 females and 65 males). Demographic characteristics and the medical history of participants are presented in Table 1. On average, participants exercised 8.4 ± 3.4 [3–18] hours per week and had completed 8 ± 16 [0–102] marathons in the past, with a mean personal record (marathon PR) of 210 ± 22 [166–256] minutes.

Post-race blood withdrawal failed in 2 participants. Ln-transformation was applied to the cTnI data set, as a non-Gaussian distribution was found. A significant exercise-induced increase in cTnI was observed, from 14 ± 12 [0–49] ng/L at baseline to 94 ± 102 [3–530] ng/L immediately after the finish (Fig. 1, p < 0.001). In total, 96% of the participants demonstrated an increase in cTnI levels, with 55 participants (69%) exceeding the clinical cut-off value of 40 ng/L after completing the marathon (Table 2).

The average finish time of the marathon was 227 ± 28 [169–307] min with a mean speed of 11.3 ± 1.4 [8.2–15.0] km/h. Participants demonstrated an mean heart rate of 161 ± 9 [136–178] beats per minute, which is comparable to an exercise intensity of 91 ± 5 [76–100] % of the maximal predicted heart rate. Participants scored the post-race rate of perceived exertion with 7 ± 2 [1–10] (Table 2).

Between 12.00 PM and the start of the marathon (i.e. 11.00 AM), participants consumed 1311 ± 848 [125–5330] mL fluid. During the race a total of 2406 ± 1597 [300–6750] mL was consumed (Table 2), which is equal to 644 ± 430 [70–1852] mL/h. As a measure of hydration status, changes in body mass were determined.