Cardiac troponin increases among marathon runners in the Perth Marathon: the Troponin in Marathons (TRIM) study

Kelley M Hubble, Daniel M Fatovich, Jonathon M Grasko and Samuel D Vasikaran

ABSTRACT

Objective: To determine the prevalence of elevated troponin levels after a marathon, and test for an association with reduced renal clearance.

Design, setting and participants: Prospective observational study of entrants running the full (42 km) 2007 Perth Marathon, Western Australia.

Main outcome measures: Elevated troponin levels (⩾0.1 μg/L) after the race; pre- and post-race survey data, and biochemical parameters.

Results: 27% of runners (92/346) enrolled in the study, of whom 88 (96%) completed it. Most were men (71%; 65/92); mean age was 43.1 years (SD, 9.8 years; range, 25–64 years) and mean body mass index (BMI) was 24.1 kg/m^2. Raised troponin levels were seen in 32% of participants (28/88), the highest being 1.4 μg/L. The strongest predictor for developing elevated troponin levels was a decrease in weight (odds ratio [OR], 2.15; 95% CI, 1.27–3.65). Creatinine increase was also associated with elevated troponin levels (OR, 1.03; 95% CI, 1.01–1.06), but pre-race estimated glomerular filtration rate, age, sex, BMI, training factors, marathon experience and race time were not. Most runners (99%; 87/88) had elevated levels of ischaemia-modified albumin after the race.

Conclusions: Troponin level increases were common among marathon finishers. The strongest predictors were weight loss and an increase in creatinine levels, suggesting that reduced renal clearance is an associated factor. Further study is needed to determine the clinical significance of these findings, and to understand the mechanism.

MJA 2009; 190: 91–93

Running a marathon (and taking part in many other endurance sports) can be associated with increased serum cardiac troponin levels,[1] in some cases reaching the range seen in acute myocardial infarction.[1-5] The reason for this increase is unclear; however, it appears to be well tolerated and is not associated with significant morbidity or mortality.[1]

In a study of runners in the 2002 Boston Marathon, 68% of 482 study participants had a rise in troponin levels, and 11% had levels that would be diagnostic of acute myocardial infarction.[1]

The purpose of our study was to replicate and extend the Boston study. We aimed to determine whether reduced renal clearance is an associated factor for a raised troponin level.

METHODS

Runners participating in the 2007 Perth Marathon were recruited 0–2 days before the race, with the assistance of the Western Australian Marathon Club. Written informed consent was obtained from all participants. This study was approved by the Royal Perth Hospital Ethics Committee.

Runners were eligible for inclusion in the study if they were running the full marathon (42 km), were over the age of 18 years, and were officially registered in the marathon. They were excluded if they could not read or speak English, or if they did not complete the marathon.

The research team was conveniently located in the club rooms, about 20 m from the start and finish line. Before the race, participants completed a survey (comprising a combination of tickbox and open-ended questions on demographic data, training schedule and relevant medical history), their weights and heights were measured, and blood samples were taken. Participants were instructed to re-present after the race to complete the post-race surveys, detailing symptoms experienced during the race, and to repeat their weight measurements and blood tests.

Blood samples were taken from the antecubital fossa by volunteer medical and nursing staff from the Royal Perth Hospital Emergency Department. Laboratory staff centrifuged and refrigerated samples on site before transporting them to the hospital's Department of Core Clinical Pathology and Biochemistry, where they were frozen at –80°C until analysed.

Biochemical studies

We analysed pre- and post-race blood samples for a range of biochemical parameters.

We used the TnI-Ultra troponin I assay (Siemens Healthcare Diagnostics Inc, Tarrytown, NY, USA). A troponin level ⩾ 0.1 μg/L was considered elevated, based on the recommended 10% analytical coefficient of variation and the 99th percentile of a healthy sample of the local population.[6]

We measured ischaemia-modified albumin (IMA) after the race only. IMA is a non-selective marker of ischaemia, and is potentially useful as an early indicator of myocardial ischaemia.[7] A serum level >85 U/L was considered positive, but this value has not been independently evaluated. IMA was assayed with the ACB (Albumin Cobalt Binding) test (Inverness Medical Innovations, Brisbane, Qld) on a Cobas Mira analyser (Roche Diagnostics, Indianapolis, Ind, USA).

The estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease (MDRD) study formula,[8] based on the participant's age, sex, and plasma creatinine levels, which were measured by an isotope dilution mass spectrometry (IDMS) traceable Jaffe kinetic assay for creatinine on a Hitachi 917 analyser (Roche Diagnostics).

Statistical analysis

For most parameters, the difference between levels before and after the race (post-race levels minus pre-race levels or vice versa [to avoid negative calculations]) were calculated. Paired Student's *t* tests were used to determine if these differences were significant. Logistic regression analysis was used to determine whether any variables (including medical and training history and differences between pre- and post-race biochemical parameters) were predictive for raised troponin levels. Principal component analysis was used to reduce the effect of multicollinearity in model building. Model diagnostics were used to identify influential observations. A backward stepwise (conditional) approach was used to eliminate variables in

1 Baseline (pre-race) characteristics of 92 participants in the Perth Marathon, 2007

Demographics	
Male, no. (%)	65 (71%)
Mean age, years (SD)	43.4 (9.8)
Mean weight, kg (SD)	72.1 (10.3)
Mean body mass index, kg/m^2 (SD)	24.1 (2.3)
Previous marathon experience	
Median marathons completed (interquartile range)	3 (1–8)
Mean training, km/week (SD)	60.1 (20.5)
Mean training, days/week (SD)	4.5 (1.1)
Medical history	
Cardiac history,* no. (%)	2 (2%)
Hypertension, no. (%)	8 (9%)
High cholesterol, no. (%)	4 (4%)
Smoking, no. (%)	4 (4%)
Renal disease, no. (%)	1 (1%)
Medication, no. (%)	11 (12%)

* That is, a history of ischaemic heart disease. ◆

2 Biochemistry results of 88 participants in the Perth Marathon, 2007

Parameter	Pre-race, mean (SD)	Post-race, mean (SD)	Reference range
Sodium, mmol/L	140 (2)	141 (3)	134–146
Potassium, mmol/L	4.3 (0.3)	4.6 (0.5)	3.4–5.0
Bicarbonate, mmol/L	24 (2)	21 (2)*	22–32
Urea, mmol/L	5.7 (1.1)	7.0 (1.6)*	3.0–8.0
Creatinine, μmol/L			
Men	87 (10)	128 (24)*	60–110
Women	74 (12)	109 (36)*	45–90
Albumin, g/L	47 (3)	49 (3)*	35–50
Creatine kinase, U/L			
Men	159 (95)	527 (344)*	30–190
Women	102 (37)	581 (689)*	30–170
Troponin I, μg/L	0.01 (0.01)	0.14 (0.23)*	< 0.1
Estimated glomerular filtration rate, mL/min/1.73m^2	87 (14)	59 (15)*	> 60
Ischaemia-modified albumin, U/L	Not measured	104 (13), range, 78–196	> 85

* Pre-race and post-race values were significantly different (P for t test, < 0.0001). ◆

order of least significance. Statistical significance was set at $P < 0.05$.

Data were recorded and analysed using SPSS, version 16 (SPSS Inc, Chicago, Ill, USA).

RESULTS

Of the 346 entrants in the Perth Marathon, 92 (27%) enrolled in the study. Of these, 88 (96%) completed the pre- and post-race surveys and blood tests, in most cases within 15–30 minutes of race completion. Of the four runners who enrolled but did not complete the post-race survey, two did not finish the marathon.

Baseline demographic data, medical history and training characteristics of the study group are shown in Box 1. Most participants (71%; 65/92) were men.

Participants trained on a mean of 4.5 days per week (mean, 60 km/week) in the 3 months preceding the marathon. Participants had previously completed a mean of 9.5 marathons (median, 3; interquartile range, 1–8). One participant was running his 100th marathon, and 26% (24/92) of runners were competing in their first marathon.

Few runners had a past history of cardiac disease or risk factors for cardiac disease. One runner had a history of renal disease (nephrotic syndrome as a child) but was fully recovered. Eleven runners were taking regular medications, seven for hypertension and four for hypercholesterolaemia.

Participants took a mean of 4 hours and 5 minutes to complete the marathon. Weight difference (pre-race minus post-race) ranged from a loss of 5.1 kg to a gain of 1.3 kg (mean loss, 1.37 kg; SD, 1.16 kg). Six (7%) of the 88 runners who completed the study reported chest symptoms: chest pain (4/88), palpitations (1/88) or both (1/88) during the race.

All pre-race blood test results were within laboratory reference limits, except for two runners with elevated creatinine levels and one with reduced eGFR (Box 2). Elevated troponin I levels were found in 28/88 (32%; 95% CI, 23%–43%) on post-race testing. The highest troponin I level observed was 1.4 μg/L. When measured to three decimal places, every runner showed a rise in their troponin level. However, before the race, 15 had levels less than the manufacturer's reported detection limit of 0.006 μg/L. The lowest post-race troponin level was 0.019 μg/L. The 28 runners with elevated troponin levels had a mean age of 42.0 years, and 17 (61%) were men. Five of the six participants who experienced symptoms during the race had raised troponin levels. The significantly different biochemical parameters are highlighted in Box 2. After the race, all participants except one had elevated IMA levels.

Principal component analysis indicated that eGFR difference, urea difference, bicarbonate difference, albumin difference and creatine kinase difference were collinear, and they were excluded from the logistic regression analysis. Thus, the model contained the following variables: age, sex, body mass index, km/week trained, days/week trained, marathons, race time, weight loss and creatinine difference. One participant was excluded from the model as an outlier. After further analysis, only two independent variables made a unique statistically significant contribution to the model — weight loss and creatinine difference.

After adjusting for the covariates listed above, weight loss and creatinine difference remained significant. The strongest predictor for an elevated troponin level after a marathon was weight loss (odds ratio [OR], 2.15; 95% CI, 1.27–3.65; $P = 0.004$). This indicated that the greater the weight loss, the more likely there was to be a troponin increase above the upper reference limit. Creatinine difference was also associated with elevated troponin levels (OR, 1.03; 95% CI, 1.01–1.06; $P = 0.01$), meaning that the greater the increase in post-race creatinine levels, the more likely there was to be a troponin increase. Pre-race eGFR was not a predictor of increased troponin levels ($P = 0.45$). Serum albumin difference was correlated with weight loss (Pearson correlation, 0.47; $P < 0.01$).

DISCUSSION

We found that an increase in troponin level was common after completion of the marathon. This was associated with weight loss and increased serum creatinine levels, suggesting that reduced renal clearance may be involved. However, such an association does not prove causation.

Previous studies have found that troponin elevation after endurance events correlates with transient cardiac dysfunction, and may represent subtle cardiac damage.[9-12] However, in studies that repeated post-race troponin measurements, all athletes with initially positive results had normal troponin levels within 24 hours.[5,13-15] Although there is compelling evidence for the cardiovascular benefits of regular exercise, the mechanism and clinical significance of this troponin effect is unknown and requires further investigation, including quantitative measures of myocardial function.[1,16] Nevertheless, this phenomenon appears to be well tolerated.[2]

During a marathon, a 1%–2% decrease in bodyweight typically occurs without a change in total body water.[17] Although some participants in our study lost a substantial amount of weight, the mean weight loss of 1.37 kg (1.9% of the pre-race weight) suggests that the runners were generally effective at maintaining euvolaemia. However, the correlation of a rise in serum albumin levels with weight loss suggests that dehydration is an associated factor in the observed effects.

Our study had limitations. The sample size was relatively small. Also, the runners used an unknown volume and range of drinks to maintain their hydration. However, overhydration is unlikely to have occurred because there was no exercise-associated hyponatraemia, apart from one runner with a post-race sodium level of 133 mmol/L.[17]

In summary, troponin increases were common among the competitors in the Perth Marathon. The strongest predictors for this were weight loss and increased creatinine levels, indicating an association with renal clearance. Clinicians should be aware of this phenomenon, but further research is required to understand the mechanism.

ACKNOWLEDGEMENTS

We thank the staff from the Royal Perth Hospital Emergency Department and Department of Core Clinical Pathology and Biochemistry who volunteered their assistance. We also thank Ian Rogers, Associate Professor of Emergency Medicine, University of Western Australia, for his helpful comments and Michael Phillips, Biostatistician, Western Australian Institute for Medical Research, for his assistance with the statistical analysis.

COMPETING INTERESTS

None identified.

AUTHOR DETAILS

Kelley M Hubble, MB BS, Registrar in Emergency Medicine[1]
Daniel M Fatovich, MB BS, FACEM, Associate Professor of Emergency Medicine[1,2]
Jonathon M Grasko, MB BCh, Registrar in Biochemistry[3]
Samuel D Vasikaran, MD, FRCPA, Medical Biochemist,[3] and Clinical Associate Professor[4]

1 Royal Perth Hospital, Perth, WA.
2 University of Western Australia, Perth, WA.
3 Department of Core Clinical Pathology and Biochemistry, PathWest-Royal Perth Hospital, Perth, WA.
4 School of Pathology and Laboratory Medicine, University of Western Australia, Perth, WA.

Correspondence:
daniel.fatovich@health.wa.gov.au

REFERENCES

1 Fortescue EB, Shin AY, Greenes DS, et al. Cardiac troponin increases among runners in the Boston Marathon. *Ann Emerg Med* 2007; 49: 137-143, 143.e1.
2 Siegel AJ, Lewandrowski EL, Chun KY, et al. Changes in cardiac markers including B-natriuretic peptide in runners after the Boston marathon. *Am J Cardiol* 2001; 88: 920-923.
3 Westermeyer ML, Eilbert WP. Elevation of troponin I in athletes: a case report in a marathon runner. *J Emerg Med* 2008; 34: 175-178.
4 Ortega FB, Ruiz JR, Gutierrez A, Castillo MJ. Extreme mountain bike challenges may induce sub-clinical myocardial damage. *J Sports Med Phys Fitness* 2006; 46: 489-493.
5 Neumayr G, Pfister R, Mitterbauer G, et al. Effect of competitive marathon cycling on plasma N-terminal pro-brain natriuretic peptide and cardiac troponin T in healthy recreational cyclists. *Am J Cardiol* 2005; 96: 732-735.
6 Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *Eur Heart J* 2007; 28: 2525-2538.
7 Apple FS. Clinical and analytical review of ischemia-modified albumin measured by the albumin cobalt binding test. *Adv Clin Chem* 2005; 39: 1-10.
8 Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461-470.
9 Neilan TG, Januzzi JL, Lee-Lewandrowski E, et al. Myocardial injury and ventricular dysfunction related to training levels among nonelite participants in the Boston marathon. *Circulation* 2006; 114: 2325-2333.
10 Rifai N, Douglas PS, O'Toole M, et al. Cardiac troponin T and I, echocardiographic [correction of electrocardiographic] wall motion analyses, and ejection fractions in athletes participating in the Hawaii Ironman Triathlon. *Am J Cardiol* 1999; 83: 1085-1089.
11 Shave R, George KP, Atkinson G, et al. Exercise-induced cardiac troponin T release: a meta-analysis. *Med Sci Sports Exerc* 2007; 39: 2099-2106.
12 Shave RE, Dawson E, Whyte G, et al. Evidence of exercise-induced cardiac dysfunction and elevated cTnT in separate cohorts competing in an ultra-endurance mountain marathon race. *Int J Sports Med* 2002; 23: 489-494.
13 Tian Y, Nie J, Tong TK, et al. Changes in serum cardiac troponins following a 21-km run in junior male runners. *J Sports Med Phys Fitness* 2006; 46: 481-488.
14 Musha H, Nagashima J, Awaya T, et al. Myocardial injury in a 100-km ultramarathon. *Curr Ther Res Clin Exp* 1997; 58: 587-593.
15 Neumayr G, Pfister R, Mitterbauer G, et al. Effect of the "Race Across The Alps" in elite cyclists on plasma cardiac troponins I and T. *Am J Cardiol* 2002; 89: 484-486.
16 Thompson PD, Apple FS, Wu A. Marathoner's heart? *Circulation* 2006; 114: 2306-2308.
17 Hew-Butler T, Ayus JC, Kipps C, et al. Statement of the Second International Exercise-Associated Hyponatremia Consensus Development Conference, New Zealand, 2007. *Clin J Sport Med* 2008; 18: 111-121.

(Received 6 Jun 2008, accepted 8 Sep 2008) ❑