Post marathon cardiac troponin T is associated with relative exercise intensity

Running heading: Marathon intensity & Cardiac Troponin

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Abstract

Objectives

This study aimed to investigate whether measures of cardiopulmonary fitness and relative exercise intensity were associated with high sensitivity cardiac troponin T (cTnT) rise after a road marathon.

Methods

Fifty-two marathon runners (age 39 ± 11 yrs, body mass 76.2 ± 12.9 kg, height 1.74 ± 0.09 m) attended the laboratory between 2 and 3 weeks prior to attempting the Brighton Marathon, UK. Running economy at $10\text{km}\cdot\text{hr}^{-1}$ (RE10) and race pace (RERP), ventilatory threshold (VT) and $\dot{V}\text{O}_2\text{max}$ tests were completed. cTnT was measured within 48 hours prior to the marathon and within 10 mins of completing the marathon, using a high sensitivity assay. Heart rates (HR) were recorded throughout the marathon.

Results

Runners demonstrated a significant increase in cTnT over the marathon (pre-race $5.60\pm 3.27\text{ng}\cdot\text{L}^{-1}$, post-race $74.52\pm 30.39\text{ng}\cdot\text{L}^{-1}$, $p<0.001$). Markers of endurance performance such as running economy ($10\text{km}\cdot\text{hr}^{-1}$ $223\pm 18\text{ml}\cdot\text{kg}^{-1}\cdot\text{km}^{-1}$; race pace $225\pm 22\text{ml}\cdot\text{kg}^{-1}\cdot\text{km}^{-1}$), VT ($38.5\pm 6.4\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and $\dot{V}\text{O}_2\text{max}$ ($50.9\pm 7.7\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) were not associated with post-race cTnT. Runners exercise intensity correlated with post-race cTnT (Mean HR %VT $104\pm 5\%$, $r=0.50$; Peak HR %VT $118\pm 8\%$, $r=0.68$; Peak HR % $\dot{V}\text{O}_2\text{max}$ 96 ± 6 , $r=0.60$, $p<0.05$) and was different between the low, medium and high cTnT groups ($p<0.05$).

Conclusions

cTnT increases above reference limits during a marathon. Magnitude of cTnT rise is related to exercise intensity relative to ventilatory threshold and $\dot{V}\text{O}_2\text{max}$, but not individuals' absolute cardiopulmonary fitness, training state or running history.

Keywords: Heart, Endurance, Stress, Cardiopulmonary fitness, Running.

Introduction

With the growing number of people participating in mass endurance events¹ there is an increasing need to understand the impact of undertaking such activity on cardiac health². Cardiac troponin (cTn) is a biomarker released from the myocardium during periods of cardiac stress and injury³. Cardiac troponin T rises above clinically significant values (typically levels greater the 99th percentile of a healthy reference population) after marathon running⁴⁻⁷. Some work has shown marathon times^{4,8,9}, marathons completed¹⁰, training status^{11,12}, body mass¹³ and age^{8,10} to be associated with cardiac troponin rise, yet research on causes of this rise are equivocal.

Shave et al¹³ demonstrated, within a meta-analysis, that cTn values were lower in longer duration endurance events, propounding the importance of exercise intensity in endurance activities. Studies have since attempted to evaluate the influence of exercise intensity during endurance running, showing elevated cTnI with higher intensity work when setting relative intensity¹⁴ or competition intensity¹⁵ over fixed durations of 180mins. Legaz-Arrese et al¹⁵ went on to imply that there may be a critical exercise intensity or threshold at which cTn rise occurs. More recently, Eijssvogels et al¹⁶ demonstrated a positive correlation ($r=0.752$) between exercise intensity and cTnI rise using groups of walkers and runners. Most previous work has either fixed the intensity and duration^{14,15}, or used completion time and heart rate as a percentage of age predicted maximum⁸ as a means of quantifying intensity. In contrast, when measuring cardiopulmonary fitness, Trivax et al¹⁷ found no association between maximal oxygen uptake ($\dot{V}\text{O}_2\text{max}$) markers and the release of cTnI. While Wilhelm et al⁶ did not report any relationship between training state, $\dot{V}\text{O}_2\text{max}$ and cTnT. However, there still

appears to be limited evaluation of cardiopulmonary fitness markers measured prior to marathon running as a means of quantifying relative work intensity during a competitive marathon and relating that to cTnT rise. Much of this previous work has used lower sensitivity cTnT analysis methods or measurement of cTnI. Measurement using high sensitivity cTnT analysis now allows improved accuracy, detection and identification of those above reference limits¹⁸.

Based on prior findings, it was hypothesised that relative exercise intensity derived from markers of endurance performance would be related to cTnT rise in amateur runners during a competitive road marathon.

Method

Fifty-two runners (13 females, 39 males) aged 39 ± 11 yrs (mean $\pm$ SD), body mass 76.2 ± 12.9 kg, height 1.74 ± 0.09 m, completed all tests and finished the Brighton marathon (9th April 2017). The study was advertised by email and social media to those who had entered the Brighton marathon, runners then volunteered to take part in the study. Runners provided written informed consent and institutional ethical approval (SSCERC 0217) was issued by the University of Brighton in accordance with the Helsinki declaration 1975 (revised 2013). Thirty-four of the runners had previously completed a marathon. The average number of previous marathons was 3 ± 6 (range 0 to 30). Participants self-reported 3 month training history prior to the marathon was 32.5 ± 13.8 miles per week (range 10 to 80 miles per week) at an average pace of 11.4 ± 1.7 km.hr⁻¹ (range 7 to 15 km.hr⁻¹).

All exercise tests were conducted either 2 or 3 weeks prior to the marathon. Runners were required to complete a run at 10 km.hr⁻¹ for 5 mins (RE10) and a 'race pace' run for a further 5 mins (RERP) to obtain running economy at the different paces. Runners rested for 10 mins and then completed an incremental ventilatory threshold (VT) and maximal oxygen uptake test ($\dot{V}O_{2\max}$). 'Race pace' was estimated from participants self-reported expected pacing, training pace or expected finishing time.

On the two days prior to the marathon, runners were invited to give a resting venous blood sample and complete a training diary. Participants were advised not to undertake any strenuous activity between the pre-race blood sample and the marathon. On the morning of the marathon participants were given a heart rate (HR) monitor to collect heart rate throughout the race. Immediately after the marathon participants were escorted to the medical tent, 80m after the finish line, to give a venous blood sample. Weather conditions over the day of the marathon were unusually hot and sunny for the UK in April (18-23°C, 40-50%RH).

Runners completed a run on a treadmill at 10 km.hr⁻¹, 1% gradient, for 5 mins (RE10) and a 'race pace' run, on 1% gradient, for a further 5 mins (RERP). 'Race pace' was determined by the runners' personal target time for the marathon and training information (11.2 ± 1.9 km.hr⁻¹, range 7.1 to 15.3 km.hr⁻¹). Breath by breath expired gas (Metamax 3B, Cortex, Germany) and HR (Polar A300, Kempele, Finland) was collected throughout. RE10 and RERP were calculated from the average physiological values for the final 30 sec of each stage.

A VT and $\dot{V}O_2$ max test was completed 10 minutes after the RE10 and RERP test. Starting velocities and increments were determined by the runners training status and RERP, to achieve a test which lasted between 8 and 12 mins. Breath by breath expired gas and heart rate was collected throughout using the same equipment as the prior RE10 and RERP tests. Rating of perceived exertion (RPE) was collected immediately upon test completion. VT was determined using 9 panel plots and the v-slope method by two independent researchers¹⁹. $\dot{V}O_2$ max was determined if two of the following three criteria were achieved: a $\dot{V}O_2$ plateau (within $0.2\text{ml.kg}^{-1}.\text{min}^{-1}$) between two incremental stages, an RPE of ≥ 19 and a heart rate within 8bts.min^{-1} of age predicted maximum ($220 - \text{age}$). All runners achieved this $\dot{V}O_2$ max criteria.

Twenty-five runners chose to wear their own personal recording HR monitor (various models of Polar or Garmin, all beat-to-beat), checked by the research team. The remaining twenty-seven runners were given a Polar A300 (Kempele, Finland) to wear throughout the race. Of the 52 participants, 38(74%) recorded full HR traces, these were downloaded and the time that HR was above VT was analysed. From the 14(26%) monitors that were not capable of downloading, mean and peak HR was obtained directly from the watch. From the files downloaded, peak HR was taken as the highest HR maintained for at least 1 minute during the marathon.

Runners gave a resting pre-race venous blood sample on either of the two days prior to the marathon. Post-race blood samples were taken within 5 min of runners completing the race by escorting the runners into the medical tent (80m after finish line). For both pre and post-race samples, 5ml of blood was extracted from the antecubital vein. Whole blood was then stored in Gel (SST gel) BD vacutainers and analysed within 4 hours of collection. CTnT was analysed using an electrochemiluminescence assay [Roche Modular E170 (fifth generation); Basel, Switzerland]¹⁸. This had a limit of blank of 3ng.L^{-1} , limit of detection (LoD) of 5ng.L^{-1} , upper reference limit (URL) based on the 99th percentile of 14ng.L^{-1} , coefficient of variation at URL of $<8\%$.

Data was assessed for normality and sphericity and adjusted where necessary using the Huynh-Feldt method. Paired t-tests were used to calculate difference in pre to post race cTnT values. Both Pearson's and Spearman correlation were used where appropriate to determine relationship between cardiopulmonary fitness measures, exercise intensity and cTnT change on the whole sample. Additionally, the data set was split into three groups based on absolute post-race cTnT values; lowest third (LcTnT $n=18$), middle third (McTnT, $n=16$) and highest third (HcTnT, $n=18$). Group differences were analysed using ANCOVA, Bonferroni post hoc analysis compared separate groups. All statistical tests were completed using SPSS Statistics 22 (IBM, New York). Significance was accepted at $p<0.05$. Values are reported as mean $\pm$ SD unless otherwise indicated.

Results

Pre-race, thirty-four participants presented with values below the LoD (5ng.L^{-1}), two participants presented with values above the URL (14ng.L^{-1}). CTnT and exercise testing data is shown in Table 1. Pre to post race cTnT increased by $68.92\pm 30.16\text{ng.L}^{-1}$ over the marathon ($p<0.001$). All fifty-two runners presented post-race with cTnT values above the

URL. There was no difference in post-race cTnT between gender groups. The three cTnT groups were not different pre-race, but were by the end of the race ($p<0.001$, Table 1). There was no association between post-race cTnT and self-reported training history [prior 3 month training volume ($r=-0.02$) or average training pace ($r=0.05$)].

Measures taken during RE10 and RERP were not found to be associated with cTnT rise, nor were running economy values different between LcTnT or HcTnT groups. RERP was similar to individual's calculated velocity at VT (Velocity RERP $11.0\pm1.8\%$; Velocity VT $11.1\pm1.9\%$, $r=0.89$, $p<0.01$). Subsequently HR at RERP was $101.1\pm6.9\%$ of VT ($r=0.83$, $p<0.01$).

No absolute measures of VT or $\dot{V}O_2\text{max}$ were related to cTnT rise. VT variables expressed as a percentage of $\dot{V}O_2\text{max}$ (Velocity $68\pm5\%$; $\dot{V}O_2$ $76\pm 8\%$; HR $84\pm4\%$) were also not associated with cTnT. cTnT groups were not different for any markers of cardiopulmonary fitness.

Runners completed the marathon in $262\pm52\text{mins}$ (range 166 to 380mins) at a mean velocity of $10.1\pm2.4\text{km.hr}^{-1}$. This was $23\pm26\text{mins}$ slower than what runners expected to achieve based on self-reported race pace. VT based prediction of race time ($235\pm45\text{mins}$) was also on average $26\pm31\text{mins}$ faster than what runners achieved. Overall marathon time was not associated with cTnT rise, nor was the difference between expected and achieved time.

Mean HR during the marathon ($157\pm14\text{bts.min}^{-1}$) was $102\pm5\%$ of that performed at VT ($154\pm13\text{bts.min}^{-1}$) during exercise testing and correlated strongly ($r=0.87$, $p<0.01$). Yet average velocity was slower during the marathon (Marathon $10.1\pm1.9\text{ km.hr}^{-1}$; VT $11.1\pm1.9\text{ km.hr}^{-1}$). Mean HR was $86\pm4\%$ of max HR achieved at $\dot{V}O_2\text{max}$ and $87\pm5\%$ of age predicted HR max. Peak HR during the marathon ($178\pm14\text{bts.min}^{-1}$) was $115\pm8\%$ of that performed at VT ($r=0.68$, $p<0.01$), $97\pm7\%$ of max HR achieved at $\dot{V}O_2\text{max}$ and $98\pm6\%$ of age predicted HR max.

Both mean HR ($r=0.50$, $p<0.05$) and peak HR ($r=0.68$, $p<0.01$) expressed as a percentage of VT were found to be strong correlates of post-race cTnT (Figure 1). Additionally, both variables were greater in the HcTnT group ($p<0.05$) (Table 1). Total time spent above VT was weakly correlated with post-race cTnT ($r=0.28$, $p<0.05$). Peak HR expressed as a percentage of max HR achieved during $\dot{V}O_2\text{max}$ was also strongly associated with cTnT ($r=0.60$, $p<0.01$) and was greater in the HcTnT group ($p<0.05$) compared to both LcTnT and McTnT groups.

Discussion

The study measured markers of endurance performance and cTnT in fifty-two runners undertaking the Brighton marathon. The findings demonstrated that post-race cTnT is associated with working at a greater relative exercise intensity during the marathon. Further, post-race cTnT rise was not associated with any absolute markers of cardiopulmonary fitness, endurance performance, marathon time or prior experience and training.

Comparison of absolute cTn values to others work must consider sensitivity improvements in cTn analysis and thus expect a less dynamic range. There are excellent reviews available on marathon running and cTn rise ^{5,13}, however these were written prior to analytical developments. To our knowledge only a small number of papers have used fifth generation cTnT assay analysis post marathon ^{4,6,7}. Work by Scherr et al ⁷, noted slightly lower values

[31.07 (IQR 19.25 - 46.86) ng.L⁻¹] of post-race cTnT. While Roca et al ⁴, shows similar [46.9 (IQR 24.1 - 91.1)ng.L⁻¹] cTnT rise to that seen in the current study [50.12 (IQR 28.3 - 67.9)ng.L⁻¹].

The potentially damaging effects of excessive endurance exercise on the heart are well discussed elsewhere ²⁰. The measurement of cTnT related to these deleterious effects and the clinical significance of raised cTnT values has yet to be established. Wilhelm et al ⁶ evaluated structural and functional cardiac assessment in response to a marathon in combination with cTnT (fifth generation) measurements. Wilhelm et al ⁶ and others ^{7,21} suggest short duration cTn release seems to be as a result of membrane leakage induced by altered myocyte metabolism, as opposed to permanent cardiomyocyte necrosis. Our study only evaluated the biomarker cTnT and not the underlying inflammatory mechanisms. Work by others ^{6,7,22,23} offer greater explanation for the cardiac stress, whether this is in response to exercise induced inflammatory processes is equivocal.

Relative exercise intensity during the marathon was found to induce rise in cTnT. The findings support the previous work of others ^{14,15} who used fixed duration and intensity trials to demonstrate that greater intensity, long duration (180min) exercise induces rise in cTn. This work builds upon the fixed nature of these trials to demonstrate this response in a competitive 'self-paced' marathon. Eijssvogels group ^{8,16,24} has produced much work attempting to evaluate the role of exercise intensity in self-paced long duration exercise. To demonstrate this relationship across a wide intensity range Eijssvogels et al ²⁴ used groups of twenty-three walkers and runners, completing 40.6-42km, to show strong correlation between %HRmax and cTnI ($r=0.752$, $p<0.001$). Later ¹⁶, Eijssvogels found no association between exercise intensity and cTnI in ninety-two competitive marathon runners. Age predicted HRmax attained ($91\pm5\%$) suggested similar exercise intensities between runners, which authors used to explain why longer duration rather than higher intensity exercise correlated with cTnI. Our group showed slightly higher age predicted HRmax values ($98.5\pm6.4\%$) during the marathon, with only a weak correlation ($r=0.3$) to cTnT. Using a similar method, Scherr et al ⁷ found no relationship between mean exercise intensity (%HRmax), finishing time, training history and cTnT rise. In the only other study to measure cardiopulmonary fitness markers and HR during a marathon, Trivax et al ¹⁷ found no association between variables at $\dot{V}O_2$ max and cTnI rise. However, the lack of analytical comparison between cardiopulmonary fitness measures and HR recorded during the race, in addition to the reduced sensitivity of the cTnI assay and small sample size ($n=25$), possibly prevented similar findings to that presented here. Many of the studies above have used peak HR attained against age predicted HRmax, however this is unlikely to provide an effective spread of data to identify reasons for those with elevated cTn. More importantly, it is not an accurate representation of, or relative to, the individual's physiological thresholds and limits. When using peak HR attained in the marathon against HR achieved at $\dot{V}O_2$ max ($r=0.60$) or at VT ($r=0.68$), our work showed much stronger correlation with cTnT values, than when using age predicted max ($r=0.3$).

In shorter duration activity, Fu et al ²⁵ showed that cTnT was significantly elevated when running at 100%VT in comparison to 80%VT for both 45 and 90 min trials. Authors ²⁵ concluded that duration and intensity were important to cTnT rise, but intensity induced a more pronounced increase. Other work, has looked at higher intensity intermittent exercise with various results. Carranza-Garcia et al ²⁶ showed no increase in cTnT after heavy resistance training or a football match. Yet in a smaller study Nie et al ²⁷ demonstrated

increases in cTnT and cTnI in adolescent basketball players. Clearly further consideration of cTnT and sustained exercise intensity activity is warranted.

Unlike work by others ^{4,8,9}, exercise duration was not related to cTnT in this study. As mentioned by Eijssvogels et al ¹⁶ the relationship between duration and intensity is difficult to derive and in some instances should be viewed as a 'load'. Otherwise the study design should either fix intensity or duration, as approached by the Legaz-Arresse and Serrano-Ostariz group ^{14,15}. Jassal et al ⁹ demonstrated that cTnT increase was greater ($r=0.40$) with exercise time. However, this was collated using both half and full marathons and a large proportion of runners had no detectable cTnT rise. In our study design the measurement of prior cardiopulmonary fitness parameters to derive relative values and sensitivity of cTnT allows clearer interpretation.

The HcTnT group presented a significantly lower HR at VT during exercise testing, yet velocity and $\dot{V}O_2$ at VT were the same for both groups (Table 1). This means there is a greater oxygen pulse ($\text{ml}\cdot\text{b}\cdot\text{t}^{-1}$) at VT in the HcTnT group, indicating a greater stroke volume during submaximal activity. However, there were no differences seen by $\dot{V}O_{2\text{max}}$, nor were there differences in absolute HR requirements during the race. It is therefore possible that individuals more reliant on greater stroke volume to maintain cardiac output induce potentially greater cardiac strain, which over long duration endurance activity is not sustainable, especially exacerbated by potential dehydration and declining venous return. This could subsequently induce greater cardiomyocyte membrane leakage. This links to the work by Feng et al ²⁸ whom demonstrated a relationship between left ventricular end diastolic pressure and cTnI rise. While McNeil et al ²⁹ showed greater mechanical stretch in skeletal muscle caused cell wounds and troponin leakage. These preliminary findings here justify further research.

No marathon performance, cardiopulmonary fitness or running economy measures were associated with cTnT, which is supported by most prior work ^{6,8,17}. Velocity during the marathon ($10.1\pm1.8\text{km}\cdot\text{hr}^{-1}$) was slower than both the RERP ($11.0\pm1.8\text{km}\cdot\text{hr}^{-1}$) and velocity at VT ($11.1\pm1.9\text{km}\cdot\text{hr}^{-1}$). The similarity between RERP and VT demonstrates individuals were not able to pace at their expected velocity for the whole race. It appears as though this is related to experience and training as the difference in actual and expected time was associated with previous marathon number ($r=0.52$) and marathon time ($r=0.55$) but no physiological or performance variables. Other work¹⁰⁻¹² using training reports or running history, have suggested training status to be a factor, yet in our work self-reported training pace ($r=0.05$) or training volume ($r=-0.02$) showed no association with cTnT. Clearly, self-reported methods have limitations but these findings would corroborate that cTn rise cannot be predicted by an individual's prior fitness, experience, training or economy.

One limitation is that cTnT values were taken immediately after the race. However, this is not necessarily reflective of the peak cTnT occurring, others work has shown values to peak at various times during and post marathon ²¹, although a peak is likely to be seen within the 3 hours post-race ³⁰.

In the current study mean and peak heart rates were analysed throughout the marathon, while time spent above VT was also assessed on the full HR data sets. However, time above VT may have greater association to cTnT rise than reported here due to sporadic drop out of HR telemetry data and therefore accuracy of time analysis. Further, peak heart rate during

the race may be caused by a number of external factors such as crowd involvement. Therefore taking too much from these parameters could be potentially onerous.

Conclusion

This is the first study to demonstrate that road marathon exercise intensity relative to VT and $\dot{V}O_{2\max}$ is associated with elevated high sensitivity cTnT. Data suggests that exercising at an average heart rate above that of VT or alternatively, achieving a peak HR at a higher percentage of VT or $\dot{V}O_{2\max}$ may induce greater rise in cTnT. The physiological and clinical relevance of this requires elucidation. Future work should consider evaluation of sub-clinical pathology and risk factors of a cardiovascular event.

Practical Implications

- During marathon running the heart undergoes stress that releases a protein called troponin T.
- Those that work at a harder intensity during the marathon, relative to their overall cardiopulmonary fitness, tend to see greater increases in troponin T.
- Marathon runners may consider utilising cardiopulmonary exercising as a means of using relative exercise intensity to pace a race.

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Figure 1: Marathon mean and peak heart rates as a percentage of ventilatory threshold (VT) against post-race high sensitivity cardiac troponin T (cTnT). A: Mean heart rate ($r^2=0.246$, $y=3.2541x-281.04$). B: Peak heart rate ($r^2=0.467$, $y=2.608x-246.15$).

List of Tables

Table 1: Performance measures correlated to post-race cardiac troponin T and comparison of low, medium and high cardiac troponin T groups.

Table 1: Performance measures correlated to post-race cardiac troponin T and comparison of cardiac troponin T groups.

	Overall (n = 52) Mean $\pm$ SD	Correlation with Post-Race cTnT (r / p)	LcTnT Group (n = 18) Mean $\pm$ SD	McTnT Group (n = 16) Mean $\pm$ SD	HcTnT Group (n = 18) Mean $\pm$ SD
Age (yrs)	39 $\pm$ 11	-0.06 / 0.68	40 $\pm$ 10	40 $\pm$ 14	37 $\pm$ 9
Height (m)	1.74 $\pm$ 0.09	0.13 / 0.37	1.72 $\pm$ 0.08	1.72 $\pm$ 0.09 ‡	1.78 $\pm$ 0.08 #
Weight (kg)	76.2 $\pm$ 12.9	0.09 / .55	75.0 $\pm$ 14.0	74.2 $\pm$ 15.8	79.0 $\pm$ 9.0
VO ₂ @ RE10 (ml.kg ⁻¹ .km ⁻¹)	228 $\pm$ 18	0.04 / 0.81	224 $\pm$ 19	228 $\pm$ 18	225 $\pm$ 18
Velocity @ RERP (km.hr ⁻¹)	11.0 $\pm$ 1.8	-0.13 / 0.36	10.8 $\pm$ 1.7	10.6 $\pm$ 2.4	10.8 $\pm$ 1.6
VO ₂ @ RERP (ml.kg ⁻¹ .km ⁻¹)	225 $\pm$ 22	0.04 / 0.75	224 $\pm$ 24	231 $\pm$ 21	221 $\pm$ 21
Velocity @ VT (km.hr ⁻¹)	11.1 $\pm$ 1.9	-0.17 / 0.23	11.2 $\pm$ 1.7	10.5 $\pm$ 2.3	11.0 $\pm$ 1.8
VO ₂ @ VT (ml.kg ⁻¹ .min ⁻¹)	38.7 $\pm$ 6.4	-0.08 / 0.56	37.7 $\pm$ 6.9	37.8 $\pm$ 7.5	37.9 $\pm$ 5.6
HR @ VT (bts.min ⁻¹)	155 $\pm$ 14	0.27 / 0.053	161 $\pm$ 14	158 $\pm$ 15	152 $\pm$ 12 #
Velocity @ VO ₂ max (km.hr ⁻¹)	16.2 $\pm$ 2.6	-0.08 / 0.58	16.0 $\pm$ 2.3	15.4 $\pm$ 3.3	16.0 $\pm$ 2.4
VO ₂ @ VO ₂ max (ml.kg ⁻¹ .min ⁻¹)	50.8 $\pm$ 7.7	-0.09 / 0.53	49.9 $\pm$ 8.0	49.8 $\pm$ 9.1	50.1 $\pm$ 6.9
HR @ VO ₂ max (bts.min ⁻¹)	184 $\pm$ 15	-0.18 / 0.21	189 $\pm$ 17	185 $\pm$ 17	181 $\pm$ 13
Marathon Time (mins)	265 $\pm$ 52	0.04 / 0.79	263 $\pm$ 45	273 $\pm$ 66	259 $\pm$ 48
Marathon Mean HR (bts.min ⁻¹)	160 $\pm$ 14	-0.02 / 0.88	162 $\pm$ 14	158 $\pm$ 18	160 $\pm$ 12
Marathon Mean HR (% VT)	101.7 $\pm$ 4.6	0.50 / 0.001 *	100.3 $\pm$ 4.0	100.4 $\pm$ 4.3 ‡	105.0 $\pm$ 3.5 #
Marathon Mean HR (%VO ₂ max)	86.4 $\pm$ 4.2	0.26 / 0.064	85.7 $\pm$ 4.1	85.7 $\pm$ 4.7	88.1 $\pm$ 3.4
Marathon Mean HR (% Age Predicted Max)	88.4 $\pm$ 5.3	-0.09 / 0.54	90.0 $\pm$ 5.1	88.0 $\pm$ 6.4	87.3 $\pm$ 4.5
Marathon Time HR > VT (mins)	235 $\pm$ 43 (n=38)	0.28 / 0.045 *	230 $\pm$ 37 (n=13)	235 $\pm$ 49 (n=11)	238 $\pm$ 47 (n=14)
Marathon Peak HR (bts.min ⁻¹)	178 $\pm$ 14	0.28 / 0.045 *	177 $\pm$ 13	175 $\pm$ 18	181 $\pm$ 11
Marathon Peak HR (% VT)	113.6 $\pm$ 8.0	0.68 / 0.001 *	110.1 $\pm$ 5.6	111 $\pm$ 6.8 ‡	119.7 $\pm$ 7.5 #
Marathon Peak HR (%VO ₂ max)	96.4 $\pm$ 6.0	0.60 / 0.001 *	94.0 $\pm$ 5.0	94.7 $\pm$ 5.2 ‡	100.4 $\pm$ 5.8 #
Marathon Peak HR (% Age Predicted Max)	98.5 $\pm$ 6.4	0.30 / 0.029 *	98.7 $\pm$ 5.4	97.2 $\pm$ 7.6	99.5 $\pm$ 6.5
cTnT pre-race (ng.L ⁻¹)	5.60 $\pm$ 3.27	0.12 / 0.41	4.43 $\pm$ 1.89	5.78 $\pm$ 3.89	5.65 $\pm$ 3.85
cTnT post-race (ng.L ⁻¹)	74.52 $\pm$ 30.39	-	22.83 $\pm$ 6.03 †	42.93 $\pm$ 6.20 ‡	84.94 $\pm$ 23.14 #

* denotes significant correlation with post-race cTnT for whole sample. # denotes significant difference between HcTnT and LcTnT groups. ‡ denotes significant difference between McTnT and HcTnT. † denotes significant difference between LcTnT and McTnT. Running economy at 10km.hr⁻¹ (RE10), Running economy at chosen race pace (RERP), Ventilatory Threshold (VT), Heart rate (HR), High sensitivity cardiac troponin T (cTnT), Low cardiac troponin T group (LcTnT), High cardiac troponin T group (HcTnT).