Immediate and 24-h post-marathon cardiac troponin T is associated with relative exercise intensity

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Abstract
Purpose We aimed at exploring whether cardiopulmonary fitness, echocardiographic measures and relative exercise intensity were associated with high-sensitivity cardiac troponin T (hs-TNT) rise and normalization following a marathon.

Methods Ninety-eight participants (83 men, 15 women; 38.72 ± 3.63 years) were subjected to echocardiographic assessment and a cardiopulmonary exercise test (CPET) before the race. hs-TNT was measured before, immediately after and at 24, 48, 96, 144 and 192 h post-race. Speed and mean heart rate (HR) during the race were relativized to CPET values: peak speed (%V\textsubscript{VMAX}), peak HR (HR\textsubscript{MAX}), speed and HR at the second ventilatory threshold (HR\textsubscript{VT2} and %V\textsubscript{VT2}).

Results Hs-TNT increased from pre- to post-race (5.74 ± 5.29 vs. 50.4 ± 57.04 ng/L; \textit{p} < 0.001), seeing values above the Upper Reference Limit (URL) in 95% of the participants. At 24 h post-race, 39% of the runners still exceeded the URL (High hs-TNT group). hs-TNT rise was correlated with marathon speed %V\textsubscript{VT2} (\textit{r} = 0.22; \textit{p} = 0.042), mean HR\textsubscript{VT2} (\textit{r} = 0.30; \textit{p} = 0.007), and mean HR\textsubscript{MAX} (\textit{r} = 0.32; \textit{p} = 0.004). Moreover, the High hs-TNT group performed the marathon at a higher Speed %V\textsubscript{VT2} (88.21 ± 6.53 vs. 83.49 ± 6.54%; \textit{p} = 0.002) and Speed %V\textsubscript{VMAX} (72 ± 4.25 vs. 69.40 ± 5.53%; \textit{p} = 0.009). hs-TNT showed no significant associations with cardiopulmonary fitness and echocardiographic measures, except for a slight correlation with left ventricular end systolic diameter (\textit{r} = 0.26; \textit{p} = 0.018).

Conclusion Post-race hs-TNT was above the URL in barely all runners. Magnitude of hs-TNT rise was correlated with exercise mean HR; whereas, its normalization kept relationship with marathon relative speed.

Keywords Cardiopulmonary fitness · Cardiac stress · Running · Echocardiography · Heart rate

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| hs-TNT       | High-sensitive cardiac troponin T |
| CPET         | Cardiopulmonary exercise test |
| HR           | Heart rate |
| URL          | Upper reference limit |
| BMI          | Body mass index |
| VO\textsubscript{max} | Maximum oxygen uptake |
| RER          | Respiratory exchange ratio |
| VT\textsubscript{2} | Second ventilatory threshold |
| RVEDD        | Right ventricular end diastolic diameter |
| LVEDD        | Left ventricular end diastolic diameter |

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Introduction

The number of recreational/non-elite athletes participating in marathons is increasing yearly. At the same time, it is becoming to be well established that such a strenuous physical effort provokes an acute release of cardiac damage biomarkers (i.e., cardiac troponins), making them rise above clinically significant values (levels greater than the 99th percentile of a healthy reference population, Upper Reference Limit, URL) (Gresslien and Agewall 2016; Regwan et al. 2010; Shave et al. 2007). Although a debate exists about the pathological vs. physiological meaning of such cardiac response to exercise, available evidence majorly supports the latter reasoning (Baker et al. 2019; Dalla Vecchia et al. 2014; Gresslien and Agewall 2016; Kleiven et al. 2019; Vroemen et al. 2019). In fact, specific algorithms have been suggested for managing athletes attending emergency departments with clinical symptoms compatible with a cardiac event after exercise (Baker et al. 2019).

However, whether the magnitude of post-exercise elevation in troponin concentration is related or not with relative intensity at which a marathon is performed is still a relevant and open-to-debate question (Brzezinski et al. 2019; Donaldson et al. 2019). Indeed, several studies have attempted to identify predictors of exercise-induced troponin release (Eijsvogels et al. 2015; Fortescue et al. 2007; Kleiven et al. 2019; Kosowski et al. 2019; Mehta et al. 2012; Neilan et al. 2006; Paana et al. 2019; Richardson et al. 2018), but as far as we are aware, only one investigation included objectively measured marathon relative intensity (i.e., speed and HR as percentages of maximums attained at a cardiopulmonary exercise test) (Richardson et al. 2018). On the other hand, no previous investigations have checked whether the normalization of high-sensitivity cardiac troponin T (hs-TNT) levels is associated with either baseline echocardiographic and fitness variables or relative intensity at which the race has been performed. Compared to the second- and third-generation assays, the accessibility to high-sensitive methods now allows to measure more accurately and to identify values above the reference limits (Giannitsis et al. 2010; Vilela et al. 2014). The hs-TNT peak is usually observed within 3–6 h following a marathon and its concentration normally falls under the URL within 24 h (Baker et al. 2019). Notwithstanding, a percentage of athletes (between 22 and 27%) still display values exceeding the URL at this time point (Baker et al. 2019; Scherr et al. 2011).

Therefore, the aim of this study was twofold. First, we were interested in assessing whether the degree of post-exercise hs-TNT rise was associated with any of the following variables: baseline echocardiographic, cardiovascular fitness and training variables; or relative intensity at which a marathon was performed. Second, we wanted to explore if any of the abovementioned variables were different among those runners who normalize hs-TNT within the initial 24 h post-exercise and those who do not. Our study hypothesis was that relative exercise intensity derived from a cardiopulmonary exercise test would be related to both immediate and 24-h post-race hs-TNT concentration. We also hypothesized that baseline echocardiographic and cardiovascular fitness variables would be associated with the hs-TNT rise and normalization.

Methods

Participants

All participants of the Valencia Fundacion Trinidad Alfonso EDP 2016 Marathon received an invitation email to participate in the study. Two information seminars were organized to fully explain the study design (aims, measurements, etc.) to those individuals who accepted the invitation (N=456). A total of 98 runners (83 men and 15 women) were selected to participate in this study, according to the following inclusion criteria: age between 30 and 45 years; body mass index (BMI) between 16 and 24.99 kg m$^{-2}$; previous marathon experience; having a performance best time in marathon between 3 and 4 h for males and 3:30 and 4:30 h for females; and individuals who were free from cardiac or renal disease and from taking any medication on a regular basis. Participants in the study abstained from competitions during the four weeks prior to the race and the marathon constitute a main competitive goal for all of them. Participant characteristics are presented in Table 1. All individuals included in the current study were fully informed and gave their written consent to participate. The research was conducted according to the Declaration of Helsinki and it was approved by the Research Ethics Committee of the Jaume I University of Castellon. This study is enrolled in the ClinicalTrials.gov database, with the code number NCT03155633 (www.clinicaltrials.gov).

Cardiopulmonary exercise test

Cardiopulmonary exercise tests (CPET) were performed on a treadmill (H/P/cosmos pulsar, H/P/cosmos sports & medical GmbH, Nussdorf-Traunstein, Germany) between 2 and
4 weeks prior to the marathon. Pulmonary VO₂ and VCO₂ were measured breath-by-breath using an automated online system (Oxycon Pro system, Jaeger, Würzburg, Germany). Gas analysis system was calibrated for ambient temperature and humidity, air flow and VO₂ and VCO₂ concentrations (with a 4.96% CO₂—12.10% O₂ gas mixture) before each testing session according to manufacturer instructions (Rietjens et al. 2001). CPET protocol consisted of 3 min warm up at 6 km/h and 1% slope followed by ramp speed increases of 0.25 km/h every 15 s until volitional exhaustion. A 3-min constant speed stage at 11 km/h for women and 12 km/h for men was included in the protocol so as to enable running economy measurements. Maximum oxygen uptake (VO₂max) values were accepted when a plateau (an increase of < 2 mL/kg/min) or a decline in VO₂ was reached despite increasing workloads and a respiratory exchange ratio (RER) above 1.15 was achieved. If this criterion was not met, a VO₂peak value was taken, defined as the highest VO₂ measured over a 30-s period. Second ventilatory threshold (VT₂) was estimated from gas exchange data by two independent researchers following a validated standard methodology as previously described (Lucia et al. 2000).

### Echocardiography

Transthoracic echocardiography was performed at baseline with a Philips HD5 Diagnostic Ultrasound System (Philips Ultrasound, Bothell, Washington USA 98,021). All two-dimensional images were acquired from standard parasternal and apical windows by the same experienced echocardiographer following the international recommendations for chambers quantification (Mitchell et al. 2019). The study included the following two-dimensional measures: Right Ventricular End Diastolic Diameter (RVEDD), Left Ventricular End Diastolic Diameter (LVEDD), Left Ventricular End Systolic Diameter (LVESD), Interventricular Septum at the end of diastole (IVS) and Posterior Wall at the end of diastole (PW). Left Ventricular Ejection Fraction (LVEF) was assessed according to the Teichholz Method. Finally, Left Ventricular Mass was calculated using the Devereux modified method and Penn modified method.

### Blood sampling and analysis

Blood samples were collected at baseline (the day before the race), after finishing the marathon and at 24, 48, 96, 144 h and 192 h post-race. Samples were collected from antecubital veins by venipuncture using BD Vacutainer PST II tubes, centrifuged at 3500 rpm for ten minutes and transported at 4 °C within 2 h after their extraction to the Vithas 9 de Octubre Hospital (Valencia), as previously published (Bernat-Adell et al. 2019). hs-TNT was measured quantitatively with the new high-sensitive enzyme immunoassay based on electrochemiluminescence technology (ECLIA), using a Cobas e411 analyzer (Roche Diagnostics, Penzberg, Germany). Detailed descriptions of this assay have been previously published (Giannitsis et al. 2010). The Limit of the Blank (LoB) of this assay is 3 ng/L and the URL, defined as the 99th percentile of a healthy population, 14 ng/L. The approximate hs-TNT equivalent to the upper limit of 30 ng/L for the 4th generation cardiac troponin T assay is 50 ng/L (Giannitsis et al. 2010). For the blood sample obtained immediately after the race, values were corrected due to changes in plasma volume and the hemoconcentration caused by dehydration using Dill and Costill formula (Dill and Costill 1974).
Exercise intensity monitoring

On the morning of the marathon, participants were given a Polar M400 HR monitor (Kempele, Finland) and a GENEActiv accelerometer (Activinsights, Ltd., Cambridgeshire, United Kingdom). Mean and peak HR (highest HR maintained for at least 1 min) during the marathon (both in absolute values and expressed as percentage of HR at VT2 and maximum HR reached at the CPET) were retained for statistical analyses. Time above HR at VT2 and time at extremely vigorous intensity derived from accelerometer data were also considered (Hernando et al. 2018). Finally, marathon finish time was obtained using the ChampionChip time registration (ChampionChip®, MYLAPS, The Netherlands), out of which mean running speed was calculated (both in absolute values and expressed as a percentage of the speed at VT2 and the peak speed reached at the CPET) and retained for statistical analyses.

Statistical analysis

Statistical analyses were carried out using the Statistical Package for the Social Sciences software (IBM SPSS Statistics for Windows, version 22.0, IBM Corp., Armonk, NY). Normal distribution of the variables was a priori verified through the Kolmogorov Smirnov test, obtaining values of \( p < 0.05 \) for all Troponin-related variables. This result motivated the usage of nonparametric tests. Friedman and Wilcoxon tests were used to assess the differences in hs-TNT between pre-race and post-race values (finishing line, 24, 48, 96 and 144 and 192 h post-race). Spearman correlations were employed to analyze the possible relationships between baseline echocardiographic and cardiopulmonary test variables (i.e., VO2max, peak speed and speed attained at VT2), training-related variables, exercise intensity and post-race change in hs-TNT. For this purpose, post-race hs-TNT values for each subject were related to the individual baseline level (values below the LoB were set to 3 ng/L) to calculate delta scores (Δ): Δ (fold increase) = (post-race value−pre-race value)/pre-race value.

Additionally, 24-h post-race hs-TNT data set was splitted into two groups based on the URL for this biomarker (High hs-TNT and Low hs-TNT groups) and possible differences in baseline echocardiographic and cardiopulmonary test variables, training-related variables and exercise intensity variables were assessed using a Mann–Whitney U test. The meaningfulness of the significant outcomes was estimated through Cohen’s \( d \) effect size: a \( d < 0.5 \) was considered small; between 0.5 and 0.8, moderate; and greater than 0.8, large (Thomas et al. 2005). Likewise, correlations > 0.5 were considered strong; 0.3–0.5, moderate; and < 0.3, small. The significance level was set at \( p < 0.05 \) and data are presented as means and standard deviations (± SD).

Results

From the initial sample of 98 participants, 88 runners finished the marathon. Two athletes failed to undergo post-race blood drawing and nine athletes were excluded from the analysis because of an excessive number of artifacts or missing data in their race HR recording. Therefore, we could obtain whole data from 77 athletes, 64 men (83%) and 13 women (17%), who constitute the final sample set of the study. Their average finishing time was 3 h: 35 min ± 20 min, ranging from 2 h: 58 min to 4 h:35 min. No signs of ischemia were detected in any athlete in the exercise electrocardiogram performed during the CPET.

A significant and large increase of hs-TNT after the marathon was observed compared to pre-race values (5.74 ± 5.29 vs. 50.4 ± 57.04 ng/L; \( p < 0.001; \ d = 1.08 \) (see Fig. 1). hs-TNT dropped significantly from
immediately post-race to 24 h post-race (50.4 ± 57.04 ng/L vs. 15.55 ± 14.29; p < 0.001; d = 0.84), and from 24 h post-race to 48 h post-race (15.55 ± 14.29 vs. 11.49 ± 14.12; p < 0.001; d = 0.29). However, hs-TNT remained largely elevated at 24 h (p < 0.001; d = 0.86) and moderately elevated at 48 h post-race (p < 0.001; d = 0.52) compared to pre-race values. At 96 h post-race, hs-TNT dropped significantly again compared to the 48-h post-race measurement (5.02 ± 4.53 vs. 11.49 ± 14.12; p < 0.001; d = 0.63) and the difference with pre-race values disappeared (p = 0.347).

At baseline, concentration of hs-TNT was negative (i.e., below the LoB) in 15 participants (19%) and only four runners (5%) displayed a value above the URL. After the race, all athletes showed measurable values of hs-TNT; 73 of those runners (95%) displayed values exceeding the URL and 25 participants (32%) surpassed the threshold for suspicion of myocardial injury. The post-race range of hs-TNT concentrations varied from 9.3 to 431.3 ng/L. At the 24-h post-race measurement, 30 runners (39%) still displayed values exceeding the URL but only 3 out of 88 participants (4%) presented a hs-TNT concentration above the threshold for suspicion of myocardial injury. The 24-h post-race range of concentrations varied from <3 to 92.8 ng/L.

The results from correlational analyses are presented in Tables 2 and 3. No relationship was found between post-race levels of hs-TNT and self-reported training history. Similarly, the hs-TNT rise was uncorrelated with cardiopulmonary test variables. Regarding the baseline echocardiographic measures, only LVESD showed a significant, but small, association with post-race values of hs-TNT (r = −0.26; p = 0.018). However, the rise in hs-TNT was moderately correlated with marathon mean HR (r = 0.41; p < 0.001), marathon mean HR%VT2 (r = 0.30; p = 0.007) and marathon mean HR%MAX (r = 0.32; p = 0.004). The increase in hs-TNT also displayed a significant, but small, association with marathon speed %VVT2 (r = 0.22; p = 0.042). On the contrary, no relationships were found between post-race levels of hs-TNT and marathon peak HR, time spent above HRVT2 and time at extremely vigorous intensity level of physical activity measured by accelerometry. The results from Mann–Whitney U test revealed no differences in baseline echocardiographic and cardiopulmonary exercise test variables, as well as in the self-reported training history, between High and Low hs-TNT groups. Conversely, marathon speed, either relativized by VT2 or maximum attained at the cardiopulmonary exercise test, was significantly and moderately greater in the High hs-TNT group compared to

| Table 2 | Correlational results and differences between High hs-TNT and Low hs-TNT groups regarding baseline echocardiographic and cardiopulmonary exercise test variables and self-reported training history |
|---------|-------------------------------------------------------------|
|         | All sample Mean ± SD (n = 77)                               | Correlation with post-race Δ hs-TNT (r/p) | High hs-TNT group Mean ± SD (n = 30) | Low hs-TNT group Mean ± SD (n = 47) |
| RVEDD (cm) | 2.11 ± 0.38                                    | 0.041/0.718                                | 2.15 ± 0.36                          | 2.09 ± 0.39                        |
| IVS (cm)    | 1.06 ± 0.11                                     | −0.132/0.237                               | 1.05 ± 0.1                           | 1.05 ± 0.11                        |
| LVEDD (cm)  | 4.96 ± 0.52                                     | −0.208/0.061                               | 4.87 ± 0.53                          | 5 ± 0.51                           |
| LVESD (cm)  | 3.05 ± 0.41                                     | −0.261/0.018*                              | 2.98 ± 0.45                          | 3.08 ± 0.38                        |
| PW (cm)     | 1 ± 0.12                                        | −0.140/0.211                               | 1 ± 0.11                            | 1 ± 0.12                           |
| LVEF (%)    | 67.8 ± 8.45                                     | 0.069/0.54                                 | 67.99 ± 9.68                         | 67.79 ± 7.71                       |
| LVMass_devereux (g) | 104.72 ± 21.15 | −0.197/0.076 | 102.78 ± 20.77 | 105.02 ± 21.11 |
| LVMass_penn (g) | 120.32 ± 26.12 | −0.195/0.079 | 117.89 ± 25.65 | 120.72 ± 26.07 |
| VVT1 (km/h) | 11.42 ± 0.85                                     | −0.039/0.724                               | 11.42 ± 0.93                          | 11.38 ± 0.81                        |
| VVT2 (km/h) | 13.99 ± 0.91                                     | −0.142/0.193                               | 13.81 ± 1.14                          | 14.02 ± 0.81                        |
| VO2peak (mL O2/kg/min) | 53.9 ± 5.27 | −0.086/0.432 | 53.97 ± 5.35 | 53.39 ± 5.28 |
| VMAX (km/h) | 16.95 ± 1.19                                    | −0.074/0.497                               | 16.93 ± 1.5                           | 16.88 ± 1.05                        |
| RE (mL O2/kg/km) | 211.25 ± 14.61 | −0.01/0.931 | 213.03 ± 14.82 | 209.95 ± 14.56 |
| RE (kcal/kg/km) | 1.06 ± 0.07 | −0.035/0.753 | 1.06 ± 0.07 | 1.05 ± 0.07 |
| Number of years running | 6.66 ± 3.13 | 0.008/0.939 | 6.91 ± 3.07 | 6.4 ± 3.09 |
| Number of previous marathons | 3.49 ± 3.18 | 0.016/0.888 | 3.41 ± 3.35 | 3.62 ± 3.1 |
| Weekly training days | 4.89 ± 0.85 | −0.073/0.51 | 4.88 ± 0.81 | 4.87 ± 0.82 |
| Weekly running volume (km) | 62.52 ± 13.53 | −0.019/0.86 | 61.62 ± 13.24 | 63.83 ± 12.9 |
| Weekly training hours | 7.32 ± 2.44 | −0.081/0.471 | 6.79 ± 1.82 | 7.66 ± 2.73 |

V02peak peak oxygen uptake, VMAX peak speed reached at the CPET, VVT1 speed associated with the first ventilatory threshold in the CPET, VVT2 speed associated with the second ventilatory threshold in the CPET, RE running economy, RVEDD right ventricular end diastolic diameter, IVS interventricular septum at the end of diastole, LVEDD left ventricular end diastolic diameter, LVESD left ventricular end systolic diameter, PW posterior wall at the end of diastole, LVEF left ventricular ejection fraction LVMass left ventricular mass
Table 3 Correlational results and differences between High hs-TNT and Low hs-TNT groups regarding exercise intensity variables

|                                | All sample Mean ± SD (n = 77) | Correlation with post-race Δ hs-TNT (r/p) | High hs-TNT group Mean ± SD (n = 30) | Low hs-TNT group Mean ± SD (n = 47) |
|--------------------------------|--------------------------------|------------------------------------------|------------------------------------|------------------------------------|
| Marathon speed (km/h)          | 11.91 ± 1.13                   | 0.039/0.724                              | 12.17 ± 1.14                       | 11.71 ± 1.1                        |
| Marathon speed %V\text{VT2} (%) | 85.21 ± 6.87                   | 0.22/0.042*                              | 88.21 ± 6.53*                      | 83.49 ± 6.54                       |
| Marathon mean HR (bpm)         | 70.33 ± 5.18                   | 0.207/0.056                              | 72 ± 4.25*                         | 69.40 ± 5.53                       |
| Marathon mean HR%\text{VT2} (%)| 161.56 ± 8.5                   | 0.414/0.001**                            | 163.26 ± 6.35                      | 160.82 ± 9.68                      |
| Marathon mean HR%\text{MAX} (%)| 96.68 ± 4.66                   | 0.298/0.007**                            | 97.27 ± 4.49                       | 96.41 ± 4.78                       |
| Marathon mean HR%\text{MAX} (%)| 89.94 ± 3.82                   | 0.318/0.004**                            | 90.09 ± 3.50                       | 89.67 ± 4.01                       |
| Marathon peak HR (bpm)         | 177.89 ± 12.47                 | 0.212/0.058                              | 181.76 ± 14.95                     | 176.41 ± 11.35                     |
| Marathon peak HR%\text{VT2} (%)| 106.44 ± 7.43                  | 0.137/0.223                              | 108.33 ± 9                         | 105.71 ± 6.68                      |
| Marathon peak HR%\text{MAX} (%)| 98.95 ± 7.07                   | 0.104/0.357                              | 100.3 ± 8.48                       | 98.41 ± 6.27                       |
| Time at EV intensity (min)     | 119.51 ± 82.27                 | -0.039/0.719                             | 121.44 ± 81.05                     | 118.26 ± 85.43                     |
| Time above HR\text{VT2} (min)  | 56.62 ± 67.2                   | 0.168/0.135                              | 58.42 ± 70.83                      | 58.67 ± 65.22                      |

Marathon speed %\text{VT2} marathon speed as a percentage of the velocity at \text{VT2} in the CPET, marathon speed %\text{MAX} marathon speed as a percentage of the peak velocity in the CPET, marathon mean HR%\text{VT2} marathon mean HR as a percentage of the HR at \text{VT2} in the CPET, marathon mean HR%\text{MAX} marathon mean HR as a percentage of the peak HR in the CPET, marathon peak HR%\text{VT2} marathon peak HR as a percentage of the peak HR in the CPET, time at EV intensity, time at extremely vigorous intensity measured by accelerometry, time above HR\text{VT2} time at a HR above the HR corresponding to \text{VT2} in the CPET.

*p < 0.05, **p < 0.01, *Significantly different from Low hs-TNT group (p < 0.01)

the Low hs-TNT group (p = 0.002 and p = 0.009, respectively; \(d = 0.73\) and \(d = 0.52\), respectively).

### Discussion

The main purposes of the present study were to identify possible predictors of exercise-induced troponin release and explore whether runners who do not normalize hs-TNT within the initial 24 h post-exercise display different values in baseline echocardiographic, cardiovascular fitness and training variables or performed the marathon at a higher relative intensity. As we hypothesized, mean HR during the marathon (both the absolute value and the percentage of the HR in \text{VT2} and the peak HR reached at the CPET) was directly correlated with the post-race rise in hs-TNT; whereas, athletes who still displayed a hs-TNT concentration above the URL 24 h following the race performed the marathon at a significantly higher relative speed (i.e., expressed as a percentage of either the speed at \text{VT2} or the peak speed reached at the CPET). However, contrary to our expectations, baseline echocardiographic and cardiovascular fitness variables were not associated with hs-TNT rise and normalization, except for a small association between LVEF and post-race hs-TNT values, which seems clinically unimportant.

The percentage of runners with post-race hs-TNT values above the URL in our study (95%) falls within the range previously reported following a road marathon (between 86 and 100%) (Mingels et al. 2009; Paana et al. 2019; Richardson et al. 2018; Roca et al. 2017; Scherr et al. 2011). Due to the absence of statistics regarding the percentage of participants who surpassed the threshold for suspicion of myocardial injury (i.e., 50 ng/L) in previous studies, we cannot compare our results at that point. Our finding of a direct relationship between post-exercise rise in hs-TNT and marathon speed %\text{VT2} suggests that runners who performed the marathon at a higher relative intensity released greater amounts of cardiac troponins. Previous studies assessing the relationship between hs-TNT response and exercise intensity in endurance competitions have been conflicting: some studies found a direct correlation (Kleiven et al. 2019; Martinez-Navarro et al. 2019); whereas, others found an inverse correlation (Eijsvogels et al. 2015; Jassal et al. 2009; Roca et al. 2017; Scherr et al. 2011) or an absence of correlation (Bishop et al. 2019; Kosowski et al. 2019; Mingels et al. 2009; Richardson et al. 2018). However, all of these studies considered the absolute speed rather than the relative speed (i.e., expressed as a percentage of peak speed and speed attained at \text{VT2} in a CPET). The above suggestion that greater relative intensity is associated with a larger release of cardiac troponin is reinforced in our study by the relationship between post-race hs-TNT values and marathon mean HR. This association agrees with previous results showed by (Richardson et al. 2018 and Stewart et al. 2014), but contrasts with other previous studies that showed no association between post-exercise hs-TNT levels and mean HR during either a 91-km mountain bike race or a marathon (Kleiven et al. 2019; Kosowski et al. 2019; Scherr et al. 2011). This disagreement may be explained by the fact that participants of these latter studies reported HR data from different personal sport watches (Kleiven et al. 2019; Scherr et al. 2011).
and HR was measured in 1-min intervals (Kosowski et al. 2019). In summary, running the marathon at a higher relative speed and HR appears to increase the release of hs-TNT, probably because sympathetic drive is greater and the heart is subjected to higher strain in those participants (Dalla Vecchia et al. 2014; Richardson et al. 2018; Stewart et al. 2014).

Additionally, our percentage of runners displaying a hs-TNT value above the URL (39%) 24 h post-race was greater than that showed following a road marathon hitherto (between 17 and 27%) (Baker et al. 2019; Mingels et al. 2009; Scherr et al. 2011) and a 91-km mountain bike race (18%) (Kleiven et al. 2019). On the other hand, we are unaware of previous investigations showing that athletes who still displayed a hs-TNT concentration above the URL 24 h following the marathon performed the race at a significantly higher relative speed (i.e., expressed as a percentage of either the speed at VT2 or the peak speed reached at the CPET). It has been stated that in higher-performing endurance athletes resting training-induced bradycardia seems to coexist with an elevated sympathetic activity as an after-effect of the intense training that they regularly undergo (Dalla Vecchia et al. 2019; Furlan et al. 1993). Moreover, these athletes are capable of enhancing their cardiovascular sympathetic drive to the greatest levels (Dalla Vecchia et al. 2019), a condition that may favor the achievement of better performances in competition (Manzi et al. 2009). This sustained increased sympathetic activity, which outlasts race completion (Dalla Vecchia et al. 2014; Furlan et al. 1993; Stewart et al. 2014), may explain why we found that relative marathon speed was higher in the High hs-TNT, as compared with the Low hs-TNT group. In view of these results, athletes who are capable of running the marathon at a greater relative intensity, which has been largely demonstrated to be a key performance factor (di Prampero et al. 1986), are those who sustain greater cardiac strain. Therefore, it becomes crucial for higher-performing athletes to precisely balance training and recovery following strenuous competitions such as a marathon.

The absence of a relationship between post-race hs-TNT levels and self-reported training history was also observed by (Kleiven et al. 2019). However, this observation differs from results of other previous studies (Fortescue et al. 2007; Kosowski et al. 2019; Mehta et al. 2012; Neilan et al. 2006), where cardiac troponin release was inversely associated with training experience and weekly training mileage. Our sample was maybe more homogeneous in relation to training status compared to the previous studies, because of our narrow inclusion criteria. This fact could explain why no relationship was identified between post-race hs-TNT values and self-reported training history. On the other hand, the lack of any association between post-race hs-TNT levels and baseline CPET variables (i.e., VO2max, peak speed and speed attained at VT2) concurs with previous studies (Kosowski et al. 2019; Richardson et al. 2018; Trivax et al. 2010). Similarly, our results also coincide with the preceding investigations, which showed a lack of correlation between echocardiographic measures and hs-TNT release after exercise (Donaldson et al. 2019; Kosowski et al. 2019; Paana et al. 2019).

Conclusions

Runners who performed the marathon at a relative higher mean HR showed a greater post-race hs-TNT rise. Moreover, participants who still displayed values above the URL for this biomarker 24 h post-race ran the marathon at a higher speed relative to their second ventilatory threshold and the peak speed reached at the CPET. Conversely, neither training history nor cardiopulmonary fitness was related to the hs-TNT rise and normalization. These data lead us to suggest that running a marathon closer to each individual’s limits, independent of training background and absolute cardiopulmonary fitness, provokes greater cardiac stress.

Nevertheless, some limitations of the study should be acknowledged. Unfortunately, we could not perform post-race echocardiography; so, further studies are warranted to assess possible relationships between hs-TNT kinetics and echocardiographic changes. Second, we recognize that a single blood drawing immediately post-exercise might not reflect hs-TNT peak concentration, which it is usually observed within 3–6 h following the race (Baker et al. 2019). Finally, participants in our study did not undergo any doping control.

Practical implications

- Running a marathon induces significant cardiac stress. The magnitude of post-race troponin release is correlated with exercise relative intensity.
- A longer post-race recovery time is recommended for those participants who run the marathon at a harder intensity, relative to their cardiopulmonary fitness.
- Performing a CPET before the race and wearing a HR monitor during the marathon, especially those participants with any cardiovascular risk factor, is strongly recommended as a means of better regulate race pace.

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Author contributions Conceived and designed the experiments: IMN JSG DS EC BH NP CH. Performed the experiments: IMN JSG DS EC BH NP CH. Analyzed the data: IMN JSG DS CH. Wrote the manuscript: IMN. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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Data availability Data from the Run, Recovery, Repeat, Always Healthy Project, to whom it belongs results here presented, are stored at the Sports Service of the Jaume I University of Castellon. Applications for data sharing can be made.

Compliance with ethical standards

Conflict of interest Nothing to declare.

Ethical standards Research Ethics Committee of the Jaume I University of Castellon (Expedient number: DOGV 7993, 6/03/2017).

Informed consent All individuals included in the current study were fully informed and gave their written consent to participate and for the data to be published.

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