Impact of marathon running on cardiac structure and function in recreational runners

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A B S T R A C T

The present study examined the relationship between LV (left ventricular) function, markers of cardiac-specific damage and markers of oxidative stress in recreational runners following a marathon. Runners (n = 52; 43 male and nine female; age, 35 ± 10 years; height, 1.74 ± 0.08 m; body mass, 75.9 ± 8.9 kg) were assessed pre- and immediately post-marathon. LV function was assessed using standard M-mode two-dimensional Doppler echocardiography and TDI (tissue-Doppler imaging) echocardiography. Serum was analysed for cTnT (cardiac troponin-T), TEAC (Trolox equivalent antioxidant capacity; a measure of total antioxidant capacity), MDA (malondialdehyde) and 4-HNE (4-hydroxynonenal). A strong relationship was observed between standard and TDI echocardiography for all functional measures. Diastolic function was altered post-marathon characterized by a reduction in $E$ (peak early diastolic filling: 0.79 ± 0.11 compared with 0.64 ± 0.16 cm/s; $P < 0.001$), an increase in $A$ (peak late diastolic filling: 0.48 ± 0.11 compared with 0.60 ± 0.12 cm/s; $P < 0.001$) and a resultant decrease in $E/A$ (ratio of $E$ to $A$; 1.71 ± 0.48 compared with 1.10 ± 0.31; $P < 0.001$). Ejection fraction remained unchanged post-marathon. Thirty-two runners presented with cTnT values above the lower limit of detection for the assay (0.01 µg/l), and 20 runners presented post-marathon with cTnT values above the acute myocardial infarction cut-off value (0.05 µg/l). No significant correlations were observed between cTnT and any functional measurements. MDA (2.90 ± 1.58 compared with 3.59 ± 1.47 µmol/l) and TEAC (1.80 ± 0.12 compared with 1.89 ± 0.21 mmol/l) were significantly increased post-marathon, but were unrelated to changes in function or cTnT. In conclusion, the present study demonstrated a reduction in diastolic function and widespread evidence of minimal cardiac damage following a marathon in recreational runners. The mechanism(s) underpinning the altered function and appearance of cTnT appear unrelated to reactive oxygen species.

Key words: cardiac troponin T, echocardiography, marathon, tissue Doppler imaging, reactive oxygen species.

Abbreviations: 2D, two-dimensional; 4-HNE, 4-hydroxynonenal; $A$, peak late diastolic filling; ABTS, 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid); ABTS**, ABTS radical cation; AMI, acute myocardial infarction; BM, body mass; cTnT, cardiac troponin-T; dBP, diastolic blood pressure; $E$, peak early diastolic filling; $E/A$, ratio of $E$ to $A$; EF, ejection fraction; EICD, exercise-induced cardiac damage; EICF, exercise-induced cardiac failure; FS, fractional shortening; HR, heart rate; LV, left ventricular; LVIDd, LV internal diameter during diastole; LVIDs, LV internal diameter during systole; LVMWS, LV meridionial wall stress; LVPWd, LV posterior free wall during diastole; LVPWs, LV posterior free wall during systole; MDA, malondialdehyde; ROS, reactive oxygen species; sBP, systolic blood pressure; SV, stroke volume; TDI, tissue-Doppler imaging; $A′$, TDI-derived peak late diastolic filling; $E′$, TDI-derived peak early diastolic filling; $E′/A′$, TDI-derived $E′$ to $A′$ ratio; TEAC, Trolox equivalent antioxidant capacity.

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INTRODUCTION

Studying the effects of prolonged intense endurance exercise upon the heart is, in part, based upon the concern that such extreme levels of exercise may be deleterious to the heart. It has been suggested that repetitive bouts of arduous exercise may result in pathological changes in the heart, including myocardial fibrosis [1], heart failure [2] and wall motion abnormalities [3,4], in highly trained individuals. Recent studies appear to support this contention reporting a reduction in cardiac function and evidence of minimal cardiac damage following prolonged endurance exercise in highly trained athletes [5–10].

Previous studies reporting a reduction in LV (left ventricular) diastolic and systolic function following prolonged exercise have employed standard M-mode, 2D (two-dimensional) and Doppler echocardiography. The assessment of LV function using standard echocardiography following prolonged exercise has been questioned [5]. Changes in loading conditions may affect indices of LV diastolic and systolic function independent of prior exercise. Pre-load may be altered following prolonged exercise for a number of reasons, including a reduced blood volume, concomitant to whole body dehydration, redistribution of blood flow to peripheral non-working tissue associated with thermoregulation, and increased heart rate. Furthermore, the assessment of systolic LV function by way of M-mode-derived measurements [e.g. EF (ejection fraction)] makes specific assumptions about the geometry of the left ventricle that may introduce error into the data [10].

TDI (tissue Doppler imaging) is an ultrasound technology that allows a relatively preload-independent assessment of regional myocardial function [11,12]. Due to the unique ability of TDI to detect subtle functional changes at a regional (segmental) level, it may be more sensitive and accurate than standard echocardiography in the identification of alterations in cardiac function following prolonged exercise. To date, however, TDI has not been employed in the assessment of LV function following prolonged exercise.

The observation of blood-borne markers of cardiac damage has led to the suggestion that prolonged exercise may induce some level of EICD (exercise-induced cardiac damage) in a small number of highly trained individuals [4,5,7,8]. A recent study [13], however, reported a large number of cTnT (cardiac troponin T)-positive cases in recreational runners following a marathon. These data, however, are yet to be corroborated in other studies examining the impact of prolonged exercise in recreational participants. Despite evidence for the presence of a reduction in LV function and EICD following prolonged endurance exercise, few studies have examined the relationship between the two phenomena. Those studies that have examined the link have reported limited evidence for a cause and affect relationship. These studies, however, have employed small cohorts of participants with a limited number of EICD-positive cases. Further work is required examining the relationship between EICD and the altered LV function observed following prolonged exercise.

A number of mechanisms have been proposed for the observed reduction in LV function and EICD following prolonged exercise, including ROS (reactive oxygen species) [14]. The production of free radicals and associated ROS increases markedly during sustained endurance exercise [15]. These ROS have the potential to trigger the cytotoxic process of lipid cell membrane peroxidation resulting in the formation of MDA (malondialdehyde). Lipid peroxidation may result in myocyte cell membrane dysfunction and damage. It may be suggested, therefore, that ROS may contribute to the reduction in LV function and EICD observed following prolonged endurance exercise. To date, however, no studies have examined the role of ROS in the reduction in LV function and EICD in humans.

Accordingly, the purpose of the present study was to examine the role of TDI in the assessment of LV function and cTnT in the assessment of EICD following a marathon in recreational runners. Furthermore, the relationship between LV function and EICD and the role of ROS in the generation of these phenomena was examined.

METHODS

Participants and design

Following approval by the local Research Ethics Committee, 52 runners [43 male and nine female; age, 35 ± 10 years (range, 18–63 years); height, 1.74 ± 0.08 m; BM (body mass), 75.9 ± 8.9 kg; values are means ± S.D.] participating in the Flora London Marathon 2003 (distance 42.2 km) volunteered for the study and provided written informed consent. Exclusion criteria for the study included any history of cardiopulmonary disease. The London Marathon course is considered relatively flat, and the ambient conditions were seasonally warm with a maximal temperature of 14 °C and approx. 50 % relative humidity.

Participants were initially assessed approx. 24 h prior to the completion of the race. Participants were instructed to attend the testing area as soon as possible following race completion. All test procedures, apart from a general health questionnaire, were administered on both occasions. Participants were advised to abstain from hard training during the 48-h period prior to pre-testing. Subjects were also advised to drink water ad libitum before, during and after assessment in order to maintain hydration status.

Procedures

Participants completed a general health questionnaire to determine personal and family history of heart disease as
well as to identify current use of medication. Participants were then assessed for BMI and stature, wearing only running shorts and vest, on standard portable scales and a stadiometer. Participants were then instructed to lay supine and, after a 15 min resting period, duplicate brachial artery sBP and dBP (systolic and diastolic blood pressure respectively) were assessed by standard auscultation, and resting HR (heart rate) was recorded by ECG within the echocardiography system. Participants then underwent standard echocardiographic assessment and TDI, and a venous blood sample collected following the methods outlined below.

**Echocardiography**

**Standard M-mode, 2D and Doppler echocardiography**

Each participant underwent a standard 2D, M-mode and Doppler echocardiographic examination in the left lateral decubitus position using a commercially available echocardiographic device (Acuson Sequoia, Siemens, Mountain View, CA, U.S.A.). Using a 2.5 MHz transducer, standard 2D-guided M-mode echocardiography was used to evaluate LV structures according to ASE (American Society of Echocardiography) guidelines [16]. Measurements obtained included: LVPWd (LV posterior free wall during diastole; peak R-wave) and LVPWs (LV posterior free wall during systole; maximum thickening), LVIDd (LV internal diameter during diastole) and LVIDs (LV internal diameter during systole; minimum separation of septum and LV). EF, velocity of FS (fractional shortening) and SV (stroke volume) were derived from M-mode data using the following formulae [16a]:

\[ EF(\%) = \frac{[(LVId^3 - LVIds^3) \times 100]}{LVId^3} \]

\[ FS(\%) = \frac{[(LVId - LVIds)/LVId] \times 100}{100} \]

\[ SV(ml) = LVId^3 - LVIds^3 \]

LVMWS (LV meridional wall stress) was derived from the formula

\[ LVMWS(g/cm^2) = (sBP \times LVIds \times 1.33))/[4 \times (LVPWs \times (1 + LVPWs/LVIds))] \]

and was calculated as a surrogate for afterload [17].

Doppler echocardiography was employed to assess diastolic function. An apical four-chamber view was imaged, taking care to maximize the diameter of the mitral valve annulus. Pulsed-wave Doppler interrogation of mitral valve inflow velocities was then performed with alignment of the sample volume cursor parallel to flow at the level of the mitral annulus, minor transducer adjustments were made to obtain optimal spectral display (highest velocity with least spectral dispersion). The Doppler velocity curves of three to five consecutive cardiac cycles were digitized through the darkest grey scale, and the measurements obtained were averaged. E (peak early diastolic filling) and A (peak late diastolic filling) were measured and E/A (ratio of E/A) was calculated.

**TDI**

Tissue Doppler echocardiography was performed on 29 (26 male and three female) participants as an addition to the standard echocardiography protocol. All TDI recordings were performed using a commercially available echocardiographic device (Acuson Sequoia, Siemens). Two experienced sonographers were used for all examinations. Longitudinal TDI of the mitral and tricuspid annuluses were obtained from an apical window using a 5 mm sample gate. Myocardial velocities were obtained from five different sites of the mitral annulus of the left ventricle (septal, lateral, inferior, anterior and posterior). Circumferential TDI was obtained from a parasternal window using a 5 mm sample gate, located at the basal anteroseptum and basal posterior wall of the left ventricle. The 2D image was optimized so that the movement of the annulus was at the smallest angle to the ultrasound beam. To display tissue velocities, the high-pass filter was bypassed. Gains and filters were adjusted to optimize the spectral display, allowing for a clear tissue signal with minimal background noise. All TDI recordings were acquired during normal respiration. The following measurements were made from the pulsed-wave TDI recordings: E′ (TDI-derived peak early diastolic filling), A′ (TDI-derived peak late diastolic filling) and E′/A′ (ratio of E′ to A′). An average value was obtained from recordings of three consecutive cardiac cycles with simultaneous ECG. The mean E′ and A′ from all five LV annular sites were calculated to provide a measurement of global LV velocities and were used for analysis in the present study.

For standard echocardiography and TDI, images were recorded to high-quality videotape and analysed off-line by a single experienced technician, who was blinded to the age and finishing time of the subjects. Based on the HR differences pre-post race, it was difficult to blind the technician to this aspect of analysis. A minimum of three consecutive cardiac cycles were measured and averaged.

**Blood sampling**

Following echocardiographic examination, 5 ml of whole blood were drawn from an antecubital vein. This was allowed to clot, centrifuged and the serum drawn off and frozen (−20 °C) for analysis later. Serum samples were assessed for cTnT. Markers of TEAC (Trolox equivalent antioxidant capacity, a measure of total antioxidant capacity; where Trolox is 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) and oxidative damage (MDA) were measured in 25 runners (19 male and six female).

**cTnT**

Serum samples were assessed for cTnT utilizing a validated third generation assay via electrochemiluminescence...
technology employed within the Elecsys 1010 automated batch analyser (Roche Diagnostics, Mannheim, Germany). The coefficients of variation for the cTnT assay were 5.5 % at 0.32 µg/l and 5.4 % at 6.0 µg/l, with a detection limit of 0.01 µg/l (which coincides with the 99th percentile value) and an upper limit of 25 µg/l. Cross-reactivity with human skeletal troponin T was 0.001 %, human cardiac troponin I was 0.002 %, skeletal tropomyosin was 0.001 %, cardiac tropomyosin was 0.1 % and cardiac myosin light chain 1 was 0.003 %.

**TEAC**

Seraum TEAC was determined following an adapted method of an assay described previously [18]. ABTS \(2,\,2'\)-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) radical cation (ABTS\(^{•+}\)) was produced by reacting 14 mmol/l ABTS with an equal volume of 4.9 mmol potassium persulphate (final concentration: 7 mmol/l ABTS in 2.45 mmol/l potassium persulphate). The mixture was incubated in the dark at room temperature for 12–16 h before use. The ABTS\(^{•+}\) solution was diluted with 5.5 mmol/l PBS (pH 7.4) to an absorbency of 0.70 (±0.02) at 734 nm (MRX, Dynatech Laboratories, Billingham, Kent, U.K.) and equilibrated at 30° C. An aliquot of 10 µl of serum or Trolox standard (0–2.5 mmol/l in PBS) was added to 1.0 ml of the diluted ABTS\(^{•+}\) solution and the absorbance was read at 30° C exactly 1 min after the initial mix and up to 6 min after. The percentage inhibition of the blank absorbency (0.70 ± 0.02) was calculated for each Trolox standard and serum sample for the standard reference data and the sample TEAC respectively.

**MDA and 4-HNE (4-hydroxynonenal)**

Prior to use, 3 vols of reagent 1 (10.3 mmol/l N-methyl-2-phenylindole in acetonitrile) were diluted with 1 vol. of 100 % methanol (HPLC grade). MDA [1,1,3,3-tetramethoxypropane in 20 mmol/l Tris/HCl (pH 7.4)] and 4-HNE (4-HNE diethylacetal in acetonitrile) standards were prepared to a final concentration of 0–20 µmol/l. An aliquot of 10 µl of 0.5 mol/l BHT (butylated hydroxytoluene in acetonitrile) was added to 200 µl of serum, MDA standard or 4-HNE standard, followed by 650 µl of diluted reagent 1 or 75 % acetonitrile/25 % methanol for each sample blank. The solution was vortex-mixed gently before adding 150 µl of 15.4 mol/l methanesulphonic acid (reagent 2). The solution was mixed and incubated at 45° C for 45 min. Samples were centrifuged at 15000 g for 10 min, and absorbance of the supernatant was read at 586 nm (Dynatech MRX).

**Data analysis**

Values are presented as means ± S.D. Pre-post race differences in BM, sBP, dBP, HR, LV loading (LVIDd and LVMWS) and LV systolic and diastolic function for both standard and TDI were analysed using repeated-measures Student’s t test. Post-race cTnT values were analysed descriptively because of the likelihood of no detectable values at baseline. The relationships between indices of LV diastolic and systolic function as well as with post-race cTnT and LV loading were examined via Pearson’s product-moment correlation analysis. The critical α level was set at 0.05, and all analyses were carried out on SPSS software.

**RESULTS**

All 52 runners returned for post-race evaluation having successfully completed the marathon (245.3 ± 46.0 min; range, 181–381 min). Post-marathon testing was commenced within 30 min of race completion in all subjects. BM was significantly reduced post-marathon (75.9 ± 8.9 compared with 73.7 ± 8.9 kg; P < 0.001), whereas HR was significantly increased post-marathon, resulting in a significant reduction in E/A (Table 1). There was no significant reduction in LVIDd, whereas EF was reduced significantly and LVMWS (29.1 dynes/cm; P < 0.001), whereas HR was significantly increased post-marathon, resulting in a significant reduction in E/A (Table 1). EF was set at 0.05, and all analyses were carried out on SPSS software.

| Table 1 | LV function pre- and post-marathon |
|-----------------|-----------------|-----------------|
|                | Pre-marathon    | Post-marathon   | P value |
| E (cm/s)        | 0.79 ± 0.11     | 0.64 ± 0.16     | < 0.001 |
| A (cm/s)        | 0.48 ± 0.11     | 0.60 ± 0.12     | < 0.001 |
| E/A             | 1.74 ± 0.48     | 1.10 ± 0.31     | < 0.001 |
| E′ (cm/s)       | 24.4 ± 5.1      | 19.8 ± 4.3      | < 0.001 |
| A′ (cm/s)       | 16.3 ± 1.9      | 17.9 ± 3.6      | 0.04    |
| E′/A′            | 1.45 ± 0.32     | 1.13 ± 0.37     | < 0.001 |
| SV (ml)         | 112.3 ± 28.7    | 100.5 ± 28.1    | < 0.001 |
| EF (%)          | 75.0 ± 6.1      | 74.4 ± 6.4      | 0.36    |

**Standard echocardiography**

LVIDd was significantly reduced post-marathon (5.28 ± 0.42 compared with 5.09 ± 0.48 cm; P < 0.001) as was LVMWS (119.3 ± 30.6 compared with 105.0 ± 29.1 dynes/cm; P < 0.001). E was reduced significantly and A increased significantly post-marathon, resulting in a significant reduction in E/A (Table 1). EF was unaltered post-marathon; however, SV was reduced significantly post-marathon (Table 1). The reduction in SV can be partially explained by the reduction in LVIDd (r = 0.92, P < 0.05).

**TDI**

Mean E′ was reduced significantly post-marathon. Mean A′ was increased significantly post-marathon, resulting in a significant reduction in E′/A′ (Table 1). There was no
Correlation between standard echocardiography and TDI measures

Doppler-derived measures were correlated with a number of TDI-derived measures, including early LV filling [pre-marathon ($r = 0.62, P < 0.05$); post-marathon ($r = 0.43, P < 0.05$); Δ ($r = 0.53, P < 0.05$)], late LV filling [pre-marathon ($r = 0.52, P < 0.05$); Δ ($r = 0.46, P < 0.05$)] and E/A ratio [pre-marathon ($r = 0.44, P < 0.05$)]. However, no significant correlation was observed between standard and TDI echocardiography for LV filling post-marathon ($r = 0.29, P > 0.05$) and E/A ratio post-marathon ($r = 0.25, P > 0.05$) and Δ ($r = 0.28, P > 0.05$).

Blood markers
cTnT was undetectable in all subjects pre-marathon. Serum samples from 39 runners were included in the analysis for post-marathon cTnT due to technical difficulties in the analysis of samples. Significant post-marathon increases in cTnT were observed (Table 2). Thirty-two runners presented with cTnT values above the lower limit of detection for the assay (0.01 µg/l; range, 0.01–0.73 µg/l). Twenty runners had values above the AMI (acute myocardial infarction) cut-off of 0.05 µg/l [19]. TEAC and MDA were increased significantly post-marathon. 4-HNE was also elevated post-marathon; however, this failed to reach a significant level (Table 2). Changes in MDA, 4-HNE and TEAC were unrelated to changes in cTnT [MDA ($r = 0.40, P > 0.05$); 4-HNE ($r = 0.39, P > 0.05$); TEAC ($r = 0.10, P > 0.05$)].

Correlation between blood markers and LV function

No significant correlation was observed between cTnT and any diastolic functional measure derived by either standard echocardiography [E ($r = 0.08, P > 0.05$), A ($r = 0.18, P > 0.05$) and E/A ($r = 0.10, P > 0.05$)] or TDI [E′ ($r = 0.12, P > 0.05$), A′ ($r = 0.26, P > 0.05$) and E′/A′ ($r = 0.06, P > 0.05$)]. Similarly, no significant correlation was observed between cTnT and any systolic functional measure derived by standard echocardiography [SV ($r = 0.07, P > 0.05$) and EF ($r = 0.02, P > 0.05$)].

No correlation was observed between TEAC, MDA and 4-HNE and any standard Doppler-derived measure of LV diastolic function [TEAC: E ($r = 0.09, P > 0.05$), A ($r = 0.27, P > 0.05$) and E/A ($r = 0.31, P > 0.05$); MDA: E ($r = 0.15, P > 0.05$), A ($r = 0.21, P > 0.05$) and E/A ($r = 0.32, P > 0.05$); and 4-HNE: E ($r = 0.06, P > 0.05$) and E/A ($r = 0.22, P > 0.05$)]. Similar findings were observed between TEAC, MDA and 4-HNE and TDI-derived measure of LV diastolic function [TEAC: E′ ($r = 0.03, P > 0.05$); A′ ($r = 0.10, P > 0.05$); and E′/A′ ($r = 0.01, P > 0.05$); MDA: E′ ($r = 0.04, P > 0.05$); A′ ($r = 0.41, P > 0.05$); and E′/A′ ($r = 0.37, P > 0.05$); 4-HNE: E′ ($r = 0.09, P > 0.05$) and E′/A′ ($r = 0.32, P > 0.05$)]. However, a change in 4-HNE was correlated significantly with A ($r = 0.33, P < 0.05$) and A′ ($r = 0.49, P < 0.05$).

DISCUSSION

The present study examined the impact of a marathon race on cardiac structure and function in recreationally trained runners. Standard echocardiography and TDI demonstrated a significant reduction in LV diastolic function with no change in systolic function, with the exception of SV, post-marathon. The change in SV reflected a reduced LVIDd in the presence of an unaltered EF, suggesting an altered pre-load rather than an alteration in inotropic contractility. Thirty-two runners presented with cTnT values above the lower detection limit of the assay, with 20 runners demonstrating values above the AMI cut-off value.

In the present study, BM and LVIDd were significantly reduced post-marathon, suggesting a possible reduction in preload. The absence of a correlation between these variables and measures of diastolic function, however, suggests that the depression in diastolic function, evidenced by a shift from early to late diastolic filling, represent a true reduction in LV function. Furthermore, although HR was increased significantly post-marathon, the absence of a significant correlation between HR and any Doppler-derived index of diastolic function offers support for the presence of an alteration in diastolic function. Caution is warranted, however, when interpreting diastolic function measurements using trans-mitral Doppler in light of changes in loading conditions. Results from TDI analysis demonstrated that E′ was reduced significantly and A′ was increased significantly post-marathon, resulting in a significantly reduced E′/A′. The strong agreement observed between TDI and standard Doppler measures of LV diastolic function supports the contention of a load-independent depression in LV diastolic function following a marathon run in recreational runners. Furthermore, these data suggest that standard Doppler is an appropriate tool in the investigation of diastolic function following prolonged exercise, and offers support for previous studies reporting a reduced LV function employing standard Doppler echocardiography following prolonged endurance exercise [7,9,13,20].

Table 2 Biological markers pre- and post-marathon

<table>
<thead>
<tr>
<th></th>
<th>Pre-marathon</th>
<th>Post-marathon</th>
<th>P value</th>
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<tbody>
<tr>
<td>cTnT (µg/l)</td>
<td>&lt; 0.01</td>
<td>0.13 ± 0.22</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TEAC (mmol/l)</td>
<td>1.79 ± 0.13</td>
<td>1.89 ± 0.21</td>
<td>0.03</td>
</tr>
<tr>
<td>MDA (µmol/l)</td>
<td>2.68 ± 1.55</td>
<td>3.56 ± 1.43</td>
<td>0.03</td>
</tr>
<tr>
<td>4-HNE (µmol/l)</td>
<td>1.79 ± 2.21</td>
<td>3.20 ± 2.79</td>
<td>0.06</td>
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</table>
The absence of a change in global systolic function (EF) despite a reduction in afterload (sBP) reported in the present study is similar to that reported elsewhere [7,9,21–23]. Previous studies have suggested that a decreased EF in the presence of a decreased sBP and unaltered LVMWS reflects a depression in the cardiac contractility [24]. These studies, however, have employed exercise of longer duration, suggesting exercise duration may be an important factor in the development of systolic dysfunction [7].

A number of previous studies have reported elevations in biological markers indicative of myocardial damage following prolonged exercise [4,8,25–28]. The majority of these studies have examined highly trained athletes following extreme endurance exercise. Elevated cTnT has been reported in trained athletes following the Hawaii Ironman triathlon [4], the Giro d’Italia [26] and long distance alpine bicycle racing [27,28]. No or limited overall alterations in biological markers of cardiac damage have been reported following a marathon in trained individuals [22,29]. In contrast, EICD has been reported in a small cohort of untrained participants following the Boston marathon [30]. A more recent study examining cTnT following marathon running in recreational runners supports these findings, suggesting EICD may occur following exercise of shorter duration in untrained individuals [13]. Within the present study, 32 runners demonstrated minor elevations in cTnT above the lower detection limit of the assay (0.01 µg/l). Although not evidence for AMI, values exceeding 0.01 µg/l, but lower than 0.05 µg/l, represent minor myocardial injury and, therefore, a cTnT value above the lower detection limit is pathognomonic of myocardial damage [31]. Of greater interest is the present study are the 20 runners presenting with cTnT levels above the AMI cut-off (range, 0.05–0.73 µg/l).

There are a number of non-AMI conditions associated with an elevation in cTnT, including both cardiac disease and interventions and non-cardiac disease [32]. The origin of blood-borne markers of cardiac damage below the AMI cut-off following endurance exercise, however, is unknown. It has been suggested that the low levels of cTnT observed in the present and previous studies represent simple membrane leakage of the cytosolic component of cardiac troponins, rather than a marker of disruption of contractile proteins. With 8% of myocardial cTnT present in the cytosol [33], it has been suggested that the kinetics of cTnT release could be explained by a transient increase in membrane permeability so that cytosolic troponins leak into the circulation [27,28]. It is postulated further that the transitory reversible shift in membrane permeability may be the result of a stress-induced overload of free radicals [27,28].

The clinical significance of elevations in cTnT is not fully understood. It has been suggested that exercise-induced troponin release may require further clinical investigations, including stress testing [34]. In view of the high number of cTnT-positive cases in the present study, however, it is clear that further investigation regarding the clinical significance of such elevations are needed prior to the prophylactic use of stress testing in large cohorts of endurance athletes following prolonged exercise. Previous studies have reported a rapid (24 h) decrease in elevated cTnT levels in highly trained athletes following prolonged exercise [7]. We therefore suggest that follow-up evaluation of positive cTnT subsequent to prolonged exercise be carried out at 6 h post-initial sampling to establish the potential origin of elevated cTnT, in line with previous recommendations [35].

Only a limited number of studies have examined the observed reduction in LV function and EICD concomitantly [4,7,8,22,30,36]. Results from the present study concur with the majority of previous studies suggesting no relationship between the LV function and cTnT. If the observed rise in cTnT in the present and previous studies are associated with the release of the cytosolic component subsequent to an alteration in membrane permeability, this would, theoretically, not alter contractile function. In contrast, Rifai et al. [4] reported greater echocardiographic ‘scores’, indicative of worsening LV function, in those subjects with a significant increase in cTnT compared with those without, suggesting some link between functional decrements and the presence of markers of myocardial damage. The relationship between reduced LV function and EICD remains to be elucidated; however, it appears that they may be two concomitant, but physiologically separate, phenomena.

Evidence for the role of ROS in cardiac dysfunction and cell membrane damage exists in an animal model [14]. Data from the present study represent the first to examine free radical production and its association with LV function following prolonged exercise in humans. The production of free radicals and associated ROS increases markedly during sustained endurance exercise. These ROS have the potential to trigger the cytotoxic process of lipid cell membrane peroxidation and MDA formation. Antioxidant defences may attenuate the deleterious effects of ROS and some free radical scavenging compounds such as uric acid have been found to rise in response to sustained endurance exercise [15,37]. The increase in total antioxidant capacity (TEAC) observed following the marathon in the present study suggests an enhanced ability to scavenge ROS in serum. The rise in serum TEAC, however, was insufficient to prevent exercise-induced lipid peroxidation evidenced by the concomitant elevation of MDA. Similar results have been reported elsewhere following the Helsinki City marathon [37] and a simulated half-marathon [15]. These data suggest that an increased ability to scavenge ROS in serum may have limited biological significance in the prevention of exercise-induced lipid peroxidation. It is unclear whether the extent of lipid peroxidation would have been greater.
had there been no rise in TEAC, suggesting further research is warranted.

Changes in serum TEAC, MDA and 4-HNE were unrelated to cTnT in the present study. These findings suggest that free radical production may be unrelated to the observed minimal cardiac damage following prolonged exercise and, therefore, do not form part of the EICD phenomenon. Furthermore, changes in serum TEAC, MDA and 4-HNE were unrelated to any measure of standard Doppler- and TDI-derived measures of LV diastolic function and standard Doppler-derived systolic function, suggesting that free radical production may be unrelated to alterations in LV function following prolonged exercise. It is important to note, however, that TEAC, MDA and 4-HNE are global biological measures that may not reflect the cellular environment and, specifically, that of the cardiomyocyte. In light of the small number of runners investigated in the present study, further work is warranted.

CONCLUSIONS

Evidence from the present study suggests that diastolic function is reduced immediately post-marathon in recreational runners. In addition, positive cTnT results appear more prevalent in recreational runners compared with previous studies examining highly trained individuals. Of interest were the 20 runners presenting with cTnT concentrations above the AMI cut-off. EICD and EICF (exercise-induced cardiac fatigue) are concomitant but unrelated phenomena, and the underpinning mechanism(s) appear unrelated to ROS. Longitudinal investigations of trained and recreational athletes would assist in defining the underpinning mechanism(s) associated with EICF and EICD and inform as to the long-term clinical implications of repetitive bouts of prolonged, intense endurance exercise.

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