Acute cardiac effects of marathon running

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Trivax JE, Franklin BA, Goldstein JA, Chinnaian KM, Gallagher MJ, deJong AT, Colar JM, Haines DE, McCullough PA. Acute cardiac effects of marathon running. J Appl Physiol 108: 1148–1153, 2010. First published February 11, 2010; doi:10.1152/japplphysiol.01151.2009.—We sought to clarify the significance of cardiac dysfunction and to assess its relationship with elevated biomarkers by using cardiovascular magnetic resonance imaging in healthy, middle-aged subjects immediately after they ran 26.2 miles. Cardiac dysfunction and elevated blood markers of myocardial injury have been reported after prolonged strenuous exercise. From 425 volunteers, 13 women and 12 men were randomly selected, provided medical and training history, and underwent baseline cardiopulmonary exercise testing to exhaustion. Blood biomarkers, cardiovascular magnetic resonance imaging, and 24-h ambulatory electrocardiography were performed 4 wk before and immediately after the race. Participants were 38.7 ± 9.0 yr old, had baseline peak oxygen consumption of 52.9 ± 5.6 ml·kg⁻¹·min⁻¹, and completed the marathon in 256.2 ± 43.5 min. Cardiac troponin I and B-type natriuretic peptide increased following the race (P = 0.001 and P < 0.0001, respectively). Cardiovascular magnetic resonance-determined pre- and postmarathon left ventricular ejection fractions were comparable, 57.7 ± 4.1% and 58.7 ± 4.3%, respectively (P = 0.32). Right atrial volume index increased from 46.7 ± 14.4 to 57.0 ± 14.5 ml/m² (P < 0.0001). Similarly, right ventricular end-systolic volume index increased from 47.4 ± 11.2 to 57.0 ± 14.6 ml/m² (P < 0.0001) whereas the right ventricular ejection fraction dropped from 53.6 ± 7.1 to 45.5 ± 8.5% (P < 0.0001). There were no morphological changes observed in the left atrium or ventricle or evidence of ischemic injury to any chamber by late gadolinium enhancement. There were no significant arrhythmias. Marathon running causes dilation of the right atrium and right ventricle, reduction of right ventricular ejection fraction, and release of cardiac troponin I and B-type natriuretic peptide but does not appear to result in ischemic injury to any chamber.

prolonged strenuous exercise; gadolinium enhancement; biomarkers; right ventricular dysfunction

Acute cardiac effects of marathon running has increased in popularity over the last three decades with participation in the United States rising from 25,000 runners in 1976 to nearly 470,000 in 2008 (36). It is estimated that six to eight marathon runners will die while running each year in the United States due to the combination of myocardial injury and the absence of signs, symptoms, or medical history of heart disease, including coronary artery disease (CAD) or structural heart disease, 25 were randomly selected (concealed in opaque, sealed envelopes) to participate. Additional exclusion criteria included pregnancy and allergy to gadolinium. Written informed consent was obtained from all participants. The study protocol was approved by the Human Investigation Committee at William Beaumont Hospital in Royal Oak, Michigan.

Materials and Methods

Subjects. All enrollees in the 2008 Detroit Free Press/Flagstar Marathon received an e-mail communication after registering for the race that described the study and invited their participation. Responses were received from 428 individuals; after verifying age (>18 yr old) and the absence of signs, symptoms, or medical history of heart disease, including coronary artery disease (CAD) or structural heart disease, 25 were randomly selected (concealed in opaque, sealed envelopes) to participate. Additional exclusion criteria included pregnancy and allergy to gadolinium. Written informed consent was obtained from all participants. The study protocol was approved by the Human Investigation Committee at William Beaumont Hospital in Royal Oak, Michigan.

Measurements. One to four weeks before the marathon, during the tapering phase of training, participants provided a detailed medical and training history and blood samples. Cardiac troponin I and BNP (normal range 0–100 pg/ml) were measured using chemiluminescence immunoassays (Bayer Diagnostics, Tarrytown, NY). For cardiac troponin I, the manufacturer reports the minimum detectable concentration 0.03 ng/ml, normal ranges < 0.06 ng/ml, indeterminate range 0.06–1.19 ng/ml, and suggestive of myocardial infarction > 1.2 ng/ml. All subjects underwent 24-h ambulatory electrocardiography (eCardio Diagnostics, Mortara Instrument, Milwaukee, WI) and peak or symptom-limited cardiopulmonary exercise testing, where heart rate and blood pressure were measured at rest, during each 3-min stage of exercise utilizing the Bruce treadmill protocol (4), and throughout a 6-min recovery. The electrocardiogram was monitored continuously throughout exercise and recovery and with recordings at
the end of each stage and at peak exercise. Metabolic data were obtained using Medical Graphics CPX/D Systems (Medical Graphics, Minneapolis, MN) with breath-by-breath analysis via a pneumotachometer and online 15-s calculations of oxygen consumption ($\dot{V}$O$_2$; ml·kg$^{-1}$·min$^{-1}$) or metabolic equivalents (METs; 1 MET = 3.5 ml·kg$^{-1}$·min$^{-1}$)), minute ventilation, carbon dioxide production ($\dot{V}$CO$_2$), and respiratory exchange ratio ($\dot{V}$CO$_2$/\dot{V}$O$_2$) were calculated.

At the finish line, runners provided a blood sample, and a 24-h ambulatory electrocardiography monitor was reapplied. Participants were instructed to follow their usual postrace hydration and nutrition practices. The goal was for each participant to undergo repeat CMR scanning within the time window after the race, the observed parameters. The observed parameters. The observed parameters. The observed parameters. The observed parameters.

Magnetic resonance imaging. Cardiac magnetic resonance imaging was performed using a 1.5-T whole body magnetic resonance imaging scanner (Sonata, Siemens Medical Solutions, Erlangen, Germany) before and after the marathon. Cine bright-blood images in the four-chamber, left-sided two-chamber, right-sided two-chamber, and three-chamber planes were performed using a breath-held balanced steady-state free precession sequence (true fast imaging with steady-state precession; repetition time 70 ms, echo time 1.2 ms, flip angle 72°, slice thickness 8 mm, matrix size 192 × 192). After the initial two- and four-chamber cine images were obtained, first past-perfusion imaging was performed. Gadolinium diethylenetriamine penta-acetic acid (Omniscan, GE Healthcare, Chalfont St. Giles, UK) 0.15 mmol/kg was injected at a rate of 4 ml/s. Multiple images (3 short axis and 1 long axis) were acquired during a single cardiac cycle (turboflash saturation recovery sequencing; inversion time 100 ms, repetition time 172 ms, echo time 1.3 ms, flip angle 72°, slice thickness 8 mm, matrix size 192 × 186). Cine steady-state free precession short-axis images then encompassed the entire RV and LV from the base to the apex (stack of multiple sequential short-axis slices; repetition time 80 ms, echo time 1.2 ms, flip angle 70°, slice thickness 8 mm, slice gap 2 mm, matrix size 256 × 138) to obtain the RV and LV ejection fractions. LGE images were obtained after a minimum of 15 min after the gadolinium injection using an inversion recovery fast low-angle shot technique. Images were acquired sequentially in the short axis, followed by horizontal and vertical long-axis images (inversion time 260–300 ms, repetition time 750 ms, echo time 4.3 ms, slice thickness 8 mm, slice gap 2 mm, matrix size 256 × 199). Quantitative analysis was performed using dedicated computer software (ARGUS; Siemens Medical Solutions). Electrocardiographically gated techniques and standard inversion recovery cine images were obtained in short-axis slices as well as three long axes: horizontal long axis, vertical long axis, and the three-chamber view. End-diastolic short axis images with epicardial and endocardial contours were drawn for the LV, and endocardial contours were drawn for the RV. Left and right ventricular end-systolic and end-diastolic volumes and LV mass were calculated. Right atrial (RA) volume was calculated using the biplane area-length method. All measurements were made by two physicians trained in level III CMR (KC, MG), blinded to the subject’s clinical information and subsequent analysis.

Statistical analysis. The primary endpoint was the change in cardiac chamber volumes indexed to body surface area calculated from the prerace weight and height. With a sample size of 25, which was the largest feasible number of individuals who could undergo CMR scanning within the time window after the race, the observed power for detecting changes in any one of the cardiac chambers was >99% using the paired t-test, α = 0.01, two-tailed, and assumed SE = 1.90 (derived from RA volume index mean 45 ± 15 ml/m² assuming the correlation between pre- and postmeasures was 0.80 or greater). Univariate statistics were reported with means ± SD or counts with proportions as appropriate. Comparisons were made using the paired two-sample t-test or the paired Wilcoxon rank sum test for variables that were not normally distributed. Pearson correlations were used to evaluate bivariate relationships. A P value < 0.05 was considered statistically significant.

RESULTS

Baseline parameters. A total of 25 runners, 13 women and 12 men, averaging 38.7 ± 9.0 yr of age (range 23–58 yr) participated in the study. Baseline characteristics are reported in Table 1. The average body mass index was 23.0 ± 2.6 kg/m². The mean training mileage over the previous 5 years and over the previous 6 mo was 17.0 ± 11.8 and 30.2 ± 11.4 miles/wk, respectively. Of the 25 subjects, 7 were participating in their first marathon and an additional 7 were participating in their second. The remaining 11 runners had participated in three or more previous marathons. The mean marathon finishing time was 2:56.2 ± 43.5 min, corresponding to an average pace of 9.8 ± 1.7 min per mile. The temperature at the start of the marathon was 33°F (1°C).

Ambulatory electrocardiography and cardiopulmonary exercise testing. Ambulatory electrocardiography was performed in 24 participants for 20.5 ± 4.2 h at baseline; 22 underwent a second recording for 21.5 ± 3.5 h after the marathon. The underlying baseline rhythm was sinus with minimum, average, and maximum heart rates of 44.7 ± 6.0, 71.5 ± 10.3, and 126.2 ± 20.4 beats/min, respectively. Similarly, after the race, sinus rhythm predominated with minimum, average, and maximum heart rates of 46.8 ± 6.5, 72.1 ± 7.6, and 120.9 ± 11.2 beats/min, respectively. Premature atrial complexes were rare, with 0.2 ± 0.2 per hour premarathon and 0.3 ± 0.6 per hour premarathon.

Table 1. Baseline characteristics of the study group (n = 25)

<table>
<thead>
<tr>
<th>Group Characteristics</th>
<th>Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>38.7 ± 9.0</td>
</tr>
<tr>
<td>Male</td>
<td>12 (48%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.0 ± 2.6</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172.5 ± 0.1</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>68.9 ± 13.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Prior smoking</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dl</td>
<td>104.2 ± 25.0</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl</td>
<td>72.4 ± 18.9</td>
</tr>
<tr>
<td>Average training mileage, miles/wk over previous 5 yr</td>
<td>17.0 ± 11.8</td>
</tr>
<tr>
<td>Number prior marathons</td>
<td>2.3 ± 3.0</td>
</tr>
</tbody>
</table>

Cardiopulmonary stress testing results

Baseline heart rate, beats/min 64.3 ± 9.1
Baseline systolic BP, mmHg 121.5 ± 18.6
Baseline diastolic BP, mmHg 76.2 ± 12.1
Peak HR, beats/min 178.0 ± 9.8
Percent predicted maximum HR, % 98.0 ± 4.1
Peak systolic BP, mmHg 192.8 ± 22.8
Peak diastolic BP, mmHg 78.1 ± 9.9
\dot{V}$O$_2$, l/min 3.600 ± 838.0
\dot{V}$CO$_2$, l/min 3.970 ± 984.9
\dot{V}$v$, minute ventilation 110.5 ± 28.2
RER 1.10 ± 0.10
% with RER > 1.10 52.0%

Values are means ± SD. BP, blood pressure; HDL, high-density lipoprotein; HR, heart rate; LDL, low-density lipoprotein; RER, respiratory exchange ratio; \dot{V}$v$, minute ventilation; \dot{V}$CO$_2$, carbon dioxide production; \dot{V}$O$_2$, oxygen consumption.

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postmarathon. Three participants experienced runs of supraventricular tachycardia (2 persons with 3 runs (heart rate during salvos = 100, 151 beats/min), 1 participant with 6 runs (peak heart rate during salvos = 152 beats/min)). The longest run of supraventricular tachycardia was 11 beats. Premature ventricular complexes were also sparsely recorded with 0.1 ± 0.3 and 0.1 ± 0.1 per hour before and after the race. No ventricular arrhythmias were noted after the marathon.

Detailed results from baseline exercise testing are reported in Table 1. The average duration of exercise was 15.5 ± 2.0 min on a standard Bruce protocol. The highest achieved heart rate averaged 178.0 ± 9.8 beats/min, corresponding to 98% of the age-predicted maximum value. Peak systolic and diastolic blood pressures were 192.8 ± 22.8 mmHg and 78.1 ± 9.9 mmHg, respectively. The mean maximal oxygen consumption and minute ventilation were 52.9 ± 6.6 ml·kg⁻¹·min⁻¹ (15.2 ± 1.6 METs) and 110.5 ± 28.2 l/min. There were no signs or symptoms of myocardial ischemia or significant exercise-induced arrhythmias observed.

Laboratory data. Laboratory data are shown in Table 2. There was a significant rise in cardiac troponin I from baseline levels to levels immediately after the race (0.03 ± 0.003 to 0.20 ± 0.30 ng/ml), \( P = 0.001 \). Serial changes in cardiac troponin I for each participant are displayed in Fig. 1. Creatine kinase and CK-MB isoenzyme increased from baseline values of 186.4 ± 132.7 and 2.6 ± 1.6 U/l, respectively, to 1,984.8 ± 2,031.0 and 16.4 ± 9.8 U/l (\( P < 0.0001 \) for each paired comparison). Serum aldolase also increased from 5.9 ± 1.7 to 15.2 ± 5.0 U/l immediately after the race (\( P < 0.0001 \)). BNP more than doubled from mean baseline to peak values (15.3 ± 11.3 to 44.8 ± 31.2 pg/ml) (\( P < 0.0001 \)). Serial changes in BNP for each participant are shown in Fig. 1. Blood urea nitrogen and serum creatinine both increased significantly with baseline and peak values of 15.6 ± 3.1 to 24.0 ± 4.8 mg/dl and 0.9 ± 0.1 to 1.2 ± 0.2 mg/dl, respectively (\( P < 0.0001 \)), for each pairwise comparison. Finally, there was a rise in potassium levels immediately after crossing the finish line, 4.3 ± 0.2 to 5.5 ± 0.6 meq/l (\( P < 0.0001 \)).

CMR imaging. The postmarathon CMR was performed an average of 242.5 ± 97.4 (range 50 to 421) min after crossing the finish line in 24 participants. One additional participant was imaged 24.5 h after completing the race and included in the final data set. The imaging findings are summarized in Table 3. Pre-marathon LV ejection fraction, end-diastolic volume index, end-systolic volume index, and stroke volume CMR were 57.7 ± 4.1%, 79.1 ± 13.7 ml/m², 33.5 ± 6.7 ml/m², and 83.2 ± 22.2 ml, respectively. The mean LV mass index was 63.8 ± 14.4 g/m². Six subjects (4 men, 2 women) had LV mass above the normal range by CMR (1). No significant differences between the pre- and post-CMRs were seen regarding LV ejection fraction or volumes. Overall, resting cardiac output, which is dependent on the heart rate, increased after the marathon (6.3 ± 1.7 vs. 5.4 ± 1.8 l/min premarathon). The baseline left atrial volume index was elevated 48.0 ± 9.4 ml/m² at baseline and remained unchanged after the race. RV ejection fraction decreased from 53.6 ± 7.1% to 45.5 ± 8.5% (\( P < 0.0001 \)) (Fig. 2), signifying a 5–10% reduction in 7 subjects (28%) and >10% in 10 (40%). RV end-systolic volume index also increased significantly from 47.4 ± 11.2 to 57.0 ± 14.5 ml/m², representing a relative increase of 16.8% (\( P < 0.0001 \)) (Fig. 2). RA volume index increased significantly after the marathon from 46.7 ± 14.4 to 57.0 ± 14.5 ml/m² with a relative change in volume index of 18.1% (\( P < 0.0001 \)). No LGE was detected in any chamber.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Immediately Postmarathon</th>
<th>24 h Postmarathon</th>
<th>Greatest Change in Value</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP, pg/ml</td>
<td>15.3 ± 11.3</td>
<td>18.7 ± 15.8</td>
<td>44.8 ± 31.2</td>
<td>28.5 ± 35.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>15.6 ± 3.1</td>
<td>24.0 ± 4.8</td>
<td>17.0 ± 3.3</td>
<td>8.4 ± 5.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>0.9 ± 0.1</td>
<td>1.2 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.3 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum sodium, meq/l</td>
<td>140.9 ± 3.4</td>
<td>141.3 ± 3.3</td>
<td>141.2 ± 2.2</td>
<td>0.4 ± 4.3</td>
<td>0.69</td>
</tr>
<tr>
<td>Serum potassium, meq/l</td>
<td>4.3 ± 0.2</td>
<td>5.5 ± 0.6</td>
<td>4.3 ± 0.4</td>
<td>1.3 ± 0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood glucose, mg/dl</td>
<td>91.9 ± 11.7</td>
<td>108.9 ± 26.9</td>
<td>91.3 ± 16.7</td>
<td>17.0 ± 24.5</td>
<td>0.004</td>
</tr>
<tr>
<td>CK, U/l</td>
<td>186.4 ± 132.7</td>
<td>675.3 ± 497.7</td>
<td>1,984.8 ± 2,031.0</td>
<td>1,802.0 ± 1,976.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CK-MB, U/l</td>
<td>2.6 ± 1.6</td>
<td>10.1 ± 5.1</td>
<td>16.4 ± 9.8</td>
<td>13.8 ± 9.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac troponin I, ng/ml</td>
<td>0.03 ± 0.003</td>
<td>0.2 ± 0.3</td>
<td>0.1 ± 0.2</td>
<td>0.2 ± 0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Aldolase, U/l</td>
<td>5.9 ± 1.7</td>
<td>15.2 ± 5.0</td>
<td>13.4 ± 7.5</td>
<td>9.3 ± 4.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are means ± SD. BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CK, creatinine kinase; CK-MB, creatine kinase MB isoenzyme.
Table 3. Cardiovascular magnetic resonance imaging data before and after marathon

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Postmarathon</th>
<th>Change in Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %</td>
<td>57.7 ± 4.1</td>
<td>58.7 ± 4.3</td>
<td>1.0 ± 4.9</td>
<td>0.32</td>
</tr>
<tr>
<td>LVESV index, ml/m²</td>
<td>79.1 ± 13.7</td>
<td>78.8 ± 11.5</td>
<td>0.3 ± 1.7</td>
<td>0.88</td>
</tr>
<tr>
<td>LVEDV index, ml/m²</td>
<td>33.5 ± 6.7</td>
<td>32.6 ± 6.0</td>
<td>0.9 ± 1.0</td>
<td>0.36</td>
</tr>
<tr>
<td>LA volume index, ml/m²</td>
<td>48.0 ± 9.4</td>
<td>49.8 ± 9.8</td>
<td>1.8 ± 10.2</td>
<td>0.38</td>
</tr>
<tr>
<td>RVEF, %</td>
<td>53.6 ± 7.1</td>
<td>45.5 ± 8.5</td>
<td>8.1 ± 7.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RVESV index, ml/m²</td>
<td>101.7 ± 17.8</td>
<td>104.2 ± 19.7</td>
<td>2.5 ± 14.3</td>
<td>0.40</td>
</tr>
<tr>
<td>RA volume index, ml/m²</td>
<td>47.4 ± 11.2</td>
<td>57.0 ± 14.5</td>
<td>9.6 ± 11.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV volume index, ml/m²</td>
<td>46.7 ± 14.4</td>
<td>57.0 ± 14.5</td>
<td>10.3 ± 11.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are means ± SD. LA, left atrium; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-systolic volume; RA, right atrium; RVESV, right ventricular end-diastolic volume; RVEF, right ventricular ejection fraction; RVESV, right ventricular end-systolic volume.

The Pearson correlation between baseline cardiorespiratory fitness [maximal oxygen consumption (V̇O₂ max)] and reduction in RV ejection fraction was r = 0.35, P = 0.09. The correlations between V̇O₂ max and change in cardiac troponin I and BNP were r = 0.04, P = 0.87, and r = −0.07, P = 0.73, respectively. Stepwise multiple regression was performed to evaluate absolute and percent change in RA volume index and absolute and percent change in RV end-systolic volume index. There were no statistically significant variables for changes in these outcomes, including V̇O₂ max, metabolic equivalents achieved during premarathon stress testing, percent increase in troponin (baseline to peak), percent increase in BNP (baseline to recovery), number of marathons completed, finishing time of marathon, the time interval from crossing finishing line to CMR imaging, or any other baseline variable.

DISCUSSION

In this study, two-thirds of healthy, well-trained runners had evidence of right heart dysfunction with significant dilation of the RA and RV and hypokinesis of the RV immediately after completing a marathon irrespective of age, sex, cardiorespiratory fitness, or previous marathon experience. In addition, most subjects demonstrated a significant reduction in RV ejection fraction and biochemical evidence of cardiac myonecrosis, including a transient, small rise in cardiac troponin I that did not follow the excursion or time course consistent with acute myocardial infarction (21). Moreover, there was no evidence of LGE in any chamber to suggest myocardial infarction nor any significant arrhythmias observed.

To date, our study is the first to comprehensively evaluate the acute cardiovascular effects of marathon running using multiple diagnostic modalities: premarathon cardiopulmonary exercise stress testing, blood biomarkers, ambulatory electrocardiography, and CMR. Our data support the smaller (n = 14) study by Mousavi and colleagues (26) who also found right-sided chamber dilation but no LV LGE by MRI in runners after a marathon. Recently, Wilson and colleagues (34) demonstrated changes in LV diastolic function by MRI that did not correlate with blood biomarkers (troponin I, NH₂-terminal pro-B-type natriuretic peptide) after marathon running. However, this group did not evaluate changes in right-sided chamber function (34). Using echocardiography, Douglas et al. (7) evaluated 41 Ironman triathletes before the event, immediately after the race, and 1–2 days later and reported significant, transient RV dilation. Neilan and associates (30) evaluated 60 nonelite marathon runners using similar methodology during consecutive Boston Marathons (2004 and 2005) and documented transient increases in echocardiographically estimated pulmonary artery pressure, RV dilation, and RV dysfunction. Le Gerche et al. (20) studied 27 athletes participating in the 2004 Australian Ironman and found ephemeral impairment in RV function, signified by postrace reductions in RV fractional area. Thus our data are consistent with prior studies in the finding that approximately one-third of marathon runners experience transient dilation of the RA, RV, and a reduction in RV ejection fraction.

The findings in our study of right heart overload and a modest rise in biomarkers can be explained by both increased preload and afterload. Contrary to previous reports that stroke volume plateaus during exercise at 40% of V̇O₂ max, recent studies have shown that in endurance athletes, stroke volume increases to >75% of V̇O₂ max secondary to enhanced diastolic filling and ventricular emptying (12, 18, 32). While increased stroke volume is an effective means to increase cardiac output,
the RV may be overwhelmed with excessive, prolonged volume overload resulting in RV dysfunction. In addition, with prolonged strenuous exercise, pulmonary artery pressures may increase by as much as 70% over baseline values and likely remain elevated throughout a marathon (2, 7). The RV responds differently to prolonged strenuous exercise than the LV, with increased RV dimensions and greater dependence on atrial systole. RV work load increases 3.6- to 5.2-fold, whereas the same exercise results in a 2.1- to 2.8-fold increase in the LV work load (7, 13). Thus the RV is differentially overworked compared with the LV and is susceptible to fatigue and exhaustion in the setting of marathon running and probably other comparable aerobic endurance challenges.

Cardiac magnetic resonance imaging allowed us to explore ischemia and microinfarction as a possible mechanism by which the RA and RV sustain transient injury. Prior studies have established that CMR cannot only identify large, transmural infarctions with characteristic findings of LGE and microvascular obstruction, but also smaller, subendocardial infarctions with a high specificity at 24 or more hours after the event (33, 35). Moreover, CMR techniques using LGE can diagnose RV infarction with good interobserver reliability, high sensitivity (19), and high negative predictive value (5). Our findings suggest that RA or RV ischemia and or infarction is not the mechanism of injury. We found an absence of LGE in all subjects, effectively ruling out infarction of myocardial tissue as an explanation for the changes in cardiac imaging and blood biomarkers seen in our data and prior studies (6, 7, 20, 29, 31). We believe the sustained increase in cardiac output over ~4 h leads to increases in RA and RV wall tension, and, in susceptible individuals, dilation of those chambers secondary to myocyte changes and possibly due to slippage of myocytes within cardiac tissue. Loss of integrity of the intercellular junctions may lead to chronic changes in activity of pericytes and myofibroblasts that participate in cardiac fibrosis. Recently, Brueckmann and colleagues (3) demonstrated chronic patterns of LV LGE in 12 and 4% of male marathon runners and normal controls, respectively, some of which were clearly not related to CAD or prior infarction. These data, in aggregate, suggest that repetitive transient chamber dilatation with extreme exhaustion may lead to cardiac fibrosis and thus be the etiology of nonischemic sudden arrhythmic death in marathon runners (3).

Our observations provide additional clarity on the issue of training effect. In two prior studies, exercise-induced RV changes were inversely related to self-reported training mileage and marathon experience (10, 29). Neither study measured baseline cardiorespiratory fitness. We found that measured baseline cardiorespiratory fitness, i.e., peak VO₂ (and training mileage), was not related to the frequency or severity of right-sided chamber dilatation nor elevation of cardiac biomarkers. Thus we believe that inherent susceptibility to chamber dilatation and biomarker release is a more plausible explanation for our findings than variation in adaptive fitness.

Our postrace period of cardiac monitoring did not demonstrate an increase in any form of arrhythmia. However, we acknowledge this observation cannot be applied to possible arrhythmias that occurred during the race itself. Right-sided chamber enlargement and dysfunction after prolonged endurance exercise may be the substrate for arrhythmias (9, 16, 17, 24). In a longitudinal prospective study, the incidence of atrial fibrillation was 5.3% in endurance athletes vs. 0.9% among control subjects (17). In addition, in a 10-yr follow-up of participants in the Barcelona Marathon, runners were found to have a fourfold increased incidence of atrial fibrillation when compared with sedentary healthy individuals (24). The suggested substrates for atrial arrhythmias in endurance athletes include pressure and volume overload, atrial stretch, and myocyte alterations from repetitive atrial dilation, inflammation, and fibrosis (25). Despite our demonstration of postexercise RA and RV dilation substantiating these earlier investigations, no significant arrhythmias were observed in our cohort.

We recognize several limitations to this small observational study, including the lack of a control group. The temporal relationships to the race suggest it was the marathon effort itself that induced the evidence of myocardial dysfunction and elevation in cardiac biomarkers that we observed. We recognize that marathon runners are very different from healthy controls, and both biomarkers and CMR findings in part may have reflected long-term changes in skeletal and myocyte adaptive changes (e.g., relatively larger CK-MB fractions). We did not measure right-sided pressures and could not evaluate pressure overload as a possible mechanism. Echocardiography was not performed on our subjects and we therefore do not have measures of diastolic function. Cardiac magnetic resonance imaging has not been validated in the assessment of diastolic dysfunction. In addition, while we have indirect measurement of postmarathon dehydration with measurement of blood urea nitrogen and serum creatinine, we do not have indirect measure of plasma volume loss, measurements of body weight, or postrace hydration or nutrition. We did not adjust for the time range during which the postrace CMR was performed, nor did we perform serial postrace CMR to identify the time course of resolution of chamber dilatation. While we did not present long-term follow-up data for either variable, several studies have shown the exercise-induced cardiac dysfunction to be transient with systolic and diastolic abnormalities resolving within 48 h and 1 mo, respectively (8, 30). Finally, our results cannot be extrapolated to individuals participating in shorter or longer distance races or nonrunning events.

Marathon running causes acute dilation of the RA and RV, reduces RV ejection fraction, but does not appear to result in ischemic injury to any chamber. We postulate that increased wall tension, dilation of the right-sided chambers, or both, account for the elevation in cardiac biomarkers associated with prolonged endurance running, rather than of ischemic damage or infarction. Future research is needed to clarify the long-term sequelae: possibly cardiac fibrosis in susceptible individuals, and the risks of arrhythmias and sudden death.

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