Acute cardiac effects of marathon running

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Trivax JE, Franklin BA, Goldstein JA, Chinnaiyan KM, Gallagher MJ, de Jong 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

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 occult cardiac disease and superimposed physical and/or environmental stresses (36). In 2009, six runners died in the United States while participating in half-marathons, with three of the six dying in the same event (36).

Increased cardiorespiratory fitness and regular exercise are associated with reduced all-cause and cardiovascular mortality (11, 15, 27, 28). However, prolonged exercise has been reported to have adverse cardiovascular consequences. Douglas et al. (6) first described abnormalities in left ventricular (LV) systolic and diastolic function after an ultraendurance race that included a 2.4-mile swim, 112-mile bike ride, and 26.2-mile run. Numerous subsequent studies have shown that endurance exercise evokes abnormal cardiac biomarkers in both elite and recreational athletes, including elevations in creatine kinase (CK), creatine kinase MB isoenzyme, troponin, and B-type natriuretic peptide (BNP) (31). Echocardiographically determined acute and chronic right ventricular (RV) dysfunction has been reported in endurance athletes (30), which are associated with ventricular arrhythmias (9). The shortcomings of echocardiography include limited fields-of-view and effect of loading conditions on Doppler measurements. Cardiovascular magnetic resonance (CMR) imaging has superior capabilities in the evaluation of chamber morphology, function, edema, tissue perfusion, dynamic myocardial contraction, and cardiac blood flow. Moreover, the superb spatial resolution allows for CMR to provide the most accurate evaluation of the RV; thus it is considered the gold standard imaging modality for chamber size and function. Recently, CMR was performed in 14 participants within 3 days of running in a marathon (26). RV systolic dysfunction occurred in all runners without evidence of late gadolinium enhancement (LGE). In our study, we aimed to describe the immediate cardiac biomarker and structural effects of marathon running.

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 detected 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...
Cardiac 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-hold balanced steady-state free precession sequence (true fast imaging with steady-state precession; repetition time 70 ms, echo time 1.2 ms, flip angle 70°, slice thickness 8 mm, matrix size 256 × 126). 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 × 86). 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 256.2 ± 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 cardiorespiratory 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 contractions were rare, with 0.2 ± 0.2 per hour premarathon and 0.3 ± 0.6 per hour postmarathon.
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 ± 5.6 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 ± 2031.0 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. Premarathon 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.

![Fig. 1. Cardiac biomarkers at baseline, peak (immediately after crossing the finish line), and recovery (24 h after marathon). A: cardiac troponin I values for each participant. B: B-type natriuretic peptide values for each participant.](http://jap.physiology.org/)

**Table 2. Biochemical data at baseline, immediately after the marathon, and 24 h later**

<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>Serum creatinine, 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 sodium, meq/l</td>
<td>9.0 ± 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 potassium, 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>BUN, mg/dl</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, creatine kinase; CK-MB, creatine kinase MB isoenzyme.
These outcomes, including VO2 max, metabolic equivalents
There were no statistically significant variables for changes in
evaluate absolute and percent change in RA volume index and
respectively. Stepwise multiple regression was performed to
Table 3.
CMR imaging, or any other baseline variable.
marathon, the time interval from crossing finishing line to
recovery), number of marathons completed, finishing time of
troponin (baseline to peak), percent increase in BNP (baseline
in RV ejection fraction was
in RV end-systolic volume index.
There were no statistically significant variables for changes in
these outcomes, including VO2 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, cardiorespira-
tory 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. 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 electro-
cardiography, and CMR. Our data support the smaller (n = 14)
study by Mousavi and colleagues (26) who also found right-
sided chamber dilatation but no LV LGE by MRI in runners
after a marathon. Recently, Wilson and colleagues (34) dem-
strated transient increases in LV diastolic function by MRI that
did not correlate with blood biomarkers (troponin I, NH2-termi-
pro-B-type natriuretic peptide) after marathon running. How-
ever, this group did not evaluate changes in right-sided cham-
ber 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 docu-
mented transient increases in echocardiographically estimated
pulmonary artery pressure, RV dilation, and RV dysfunction.
La 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 ex-
perience 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 VO2 max, recent
studies have shown that in endurance athletes, stroke volume
increases to >75% of VO2 max secondary to enhanced diastolic
filling and ventricular emptying (12, 18, 32). While increased
stroke volume is an effective means to increase cardiac output,

**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>LV EDDV index, ml/m²</td>
<td>79.7 ± 13.7</td>
<td>78.8 ± 11.5</td>
<td>0.3 ± 1.7</td>
<td>0.88</td>
</tr>
<tr>
<td>LV ESV 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>RV EDDV 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>RV ESV 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>RA 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; LVESV, left ventricular end-systolic volume; RA, right atrium; RV EDDV, right ventricular end-diastolic volume; RVEF, right ventricular ejection fraction; RV ESV, right ventricular end-systolic volume.

The Pearson correlation between baseline cardiorespiratory
fitness [maximal oxygen consumption (VO2 max)] and reduction
in RV ejection fraction was r = 0.35, P = 0.09. The correla-
tions between VO2 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.

Fig. 2. Changes in right ventricular ejection fraction and right heart volumes before and after the marathon. A: mean change in right heart volumes before and after the marathon. RA, right atrium; RV EDDV, right ventricular end-systolic volume.
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 postrace RA and RV dilatation 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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