Ventricular Structure and Function

Myocardial Adaptations to Recreational Marathon Training Among Middle-Aged Men

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Background—Myocardial adaptations to exercise have been well documented among competitive athletes. To what degree cardiac remodeling occurs among recreational exercisers is unknown. We sought to evaluate the effect of recreational marathon training on myocardial structure and function comprehensively.

Methods and Results—Male runners (n=45; age, 48±7 years; 64% with ≥1 cardiovascular risk factor) participated in a structured marathon-training program. Echocardiography, cardiopulmonary exercise testing, and laboratory evaluation were performed pre and post training to quantify changes in myocardial structure and function, cardiorespiratory fitness, and traditional cardiac risk parameters. Completion of an 18-week running program (25±9 miles/wk) led to increased cardiorespiratory fitness (peak oxygen consumption, 44.6±5.2 versus 46.3±5.4 mL/kg per minute; *P*<0.001). In this setting, there was a significant structural cardiac remodeling characterized by dilation of the left ventricle (end-diastolic volume, 156±26 versus 172±28 mL, *P*<0.001), right ventricle (end-diastolic area=27.0±4.8 versus 28.6±4.3 cm²; *P*=0.02), and left atrium (end-diastolic volume, 65±19 versus 72±19; *P*=0.02). Functional adaptations included increases in both early (E=12.4±2.5 versus 13.2±2.0 cm/s; *P*=0.007) and late (A=11.5±1.9 versus 12.2±2.1 cm/s; *P*=0.02) left ventricular diastolic velocities. Myocardial remodeling was accompanied by beneficial changes in cardiovascular risk factors, including body mass index (27.0±2.7 versus 26.7±2.6 kg/m²; *P*<0.001), total cholesterol (199±33 versus 192±29 mg/dL; *P*<0.01), low-density lipoprotein (120±29 versus 114±26 mg/dL; *P*<0.01), and triglycerides (100±52 versus 85±36 mg/dL; *P*<0.01).

Conclusions—Among middle-aged men, recreational marathon training is associated with biventricular dilation, enhanced left ventricular diastolic function, and favorable changes in nonmyocardial determinants of cardiovascular risk. Recreational marathon training may, therefore, serve as an effective strategy for decreasing incident cardiovascular disease. (Circ Cardiovasc Imaging. 2015;8:e002487. DOI: 10.1161/CIRCIMAGING.114.002487.)

Key Words: echocardiography ■ exercise ■ risk factors

Exercise-induced cardiac remodeling is the process of structural and functional myocardial adaptation that occurs in response to exercise training. Cross-sectional studies of competitive athletes have documented a high prevalence of cardiac chamber enlargement1–4 and increased wall thickness5,6 and more recently, longitudinal studies have begun to clarify the causal relationship between exercise training and myocardial adaptation.7–9 Recreational athletes, a growing population that is commonly encountered in clinical practice, perform far less exercise volume and do so at lower training intensities than elite athletes. To what degree the moderate intensity exercise training typically practiced by recreational athletes stimulates exercise-induced cardiac remodeling remains largely unknown.

The popularity of marathon (42-km foot race) running has risen steadily over the past decade, in large part, because of increasing popularity among middle-aged runners seeking the reported health benefits of regular physical exercise.10,11 Most recreational marathoners train with a goal of safely completing the race distance and thus typically engage in several months of daily aerobic exercise that meet or exceed current public health recommendations.12 Several recent studies have characterized the myocardial and biochemical responses to a single marathon run.13–15 To date, the effects of the preparatory marathon training on cardiac structure and function have received comparatively little attention.

We hypothesized that recreational runners participating in a structured marathon training program would demonstrate evidence of exercise-induced cardiac remodeling similar to...
that previously documented among more elite competitive athletes. To address this hypothesis, we performed a longitudi-
dinal, repeated measures study designed to examine the effect
of recreational marathon training on cardiac structure, cardiac
function, and relevant biological metrics, including cardiopul-
monary fitness and cardiovascular disease risk factors.

Methods

Study Design Overview

We used a prospective, longitudinal, and repeated measures study
design to examine the effects of marathon training on cardiac mor-
phology and function among recreational athletes. Participants
were assessed before and after an 18-week marathon-training pro-
gram designed to facilitate completion of the 2013 Boston Athletic
Association Boston Marathon. At baseline, a detailed demographic
and clinical profile were collected via a written questionnaire that
included assessment of previous long-term (baseline running mile-
age, number of previous marathons etc.) and recent (miles/wk, as
well as total endurance hours/wk activity and strength training
hours/wk) exercise exposure. Assessment at both time points in-
cluded measurement of height, weight, resting vital signs, fasting
blood sampling, echocardiographic evaluation, and cardiopulmo-
mary exercise testing.

Patient Population

Individuals enrolled in the 2013 Boston Marathon Dana-Farber
Marathon Challenge charity were recruited by email invitation.
Charity runners were chosen for this study because they are more
representative of typical middle-aged recreational marathon run-
ners than the faster qualifying athletes that comprise the majority
of the Boston Marathon field. Men ranging from 35 to 65 years
were considered eligible for participation. Individuals were ex-
cluded if they had been previously diagnosed with any of the fol-
lowing conditions (1) coronary artery disease, (2) left ventricular
(LV) dysfunction, (3) known genetic cardiomyopathy, or (4) val-
vular heart disease characterized by moderate or greater stenosis
or regurgitation in any valve. To examine interactions between
previous marathon running experience, baseline characteristics,
and cardiovascular disease risk factors. Participants

Marathon Training Program

Participants were provided with a structured online training program
that contained daily instructions detailing running mileage goals. Each
week consisted of 3 to 4 basic training runs (4–8 miles [6.4–12.9 km])
and 1 longer run that increased in distance throughout the 18-week
calendar (maximal long-run distance, 20–22 miles [32.2–35.4 km],
week 15). Optimal running effort (scale: 1 [easy] through 5 [maxi-
imal sustainable pace]) was specified for each run. Each participant
was supervised throughout the study period by a single coach with
>20 years of experience coaching marathoners. A training log was
provided to each participant in which running volume (distance/wk,
hours/wk) and injuries or adverse events were recorded. Individuals
were excluded from the final analysis for training absences >2 weeks
for any reason.

Cardiopulmonary Exercise Testing

Cardiopulmonary exercise testing was performed using a maximal
effort-limited protocol with continuous electrocardiography and
measurement of metabolic gas exchange. Participants abstained
from all exercise for 24 hours before testing. A single exercise
physiologist and study physician performed all testing. The cardio-
pulmonary exercise testing protocol consisted of a graded maximal
effort test on a treadmill (Trackmaster TMX425C; Full Vision,
Newton, KS). Specifically, after a 3-minute period of rest to fa-
cilitate ventilatory equilibration, participants ran at a 1% grade (to
simulate air resistance) at a speed of 5 miles/h (8.0 km/h) for 10
minutes to facilitate musculoskeletal warm-up. After the 10-min-
ute warm-up period, speed was maintained at a constant 5 mph
(8.0 kph), whereas the incline increased by 0.5% every 15 s until
exhaustion. Gas exchange data were measured breath-by-breath
using a commercially available metabolic cart (Ultima CardiO2;
Medgraphics, St. Paul, MN). Peak oxygen consumption (Vo2) was
defined as the highest O2 uptake, averaged over a period of 30 s, dur-
ing the last minute of symptom-limited exercise.14 The ventilatory
threshold was determined by the modified V-slope method.15 Heart
rate was continuously recorded during exercise using a wireless 12-
lead ECG system (Mortara X12+ Transmitter; Mortara Instruments,
Milwaukee, WI). Blood pressures were determined by auscultation
using a manual sphygmomanometer before exercise, at 3-minute
intervals during exercise, immediately after peak exercise, and at
3-minute intervals during recovery.

Echocardiography

Cardiac structure and function were assessed via transthoracic
echocardiography (Vivid-1, GE Healthcare, Milwaukee, WI). A
single experienced sonographer performed standard 2-dimensional
(2D) and Doppler imaging at both study time points. A single expe-
rienced investigator who was blinded to study time point performed
analysis of echocardiographic data. LV volumes, ejection fraction,
and left atrial volume were calculated using the modified biplane
 technique.18 LV mass was calculated using the area-length method,
and LV geometry was assessed using relative wall thickness.19 Right
ventricular (RV) end-diastolic area, end-systolic area, and fractional
area change were measured from RV-optimized apical 4-chamber
views. Myocardial tissue velocities were measured off-line from 2D
color-coded tissue Doppler images and reported as the average of 3
consecutive cardiac cycles. Strain imaging was performed by speck-
led tracking analysis (EchoPac, version 6.5; GE Healthcare). The
presence and severity of LV diastolic dysfunction were assessed
in accordance with current recommendations.19 Body surface area
was calculated using the Mosteller formula.20 Measurements are
presented as raw data and after body surface area indexing when
appropriate.

Application of Clinical Cut Points

Values defining the limits of normal cardiac structure and function
were adopted from the American Society of Echocardiography/
European Association of Echocardiography chamber quantification
and diastolic function recommendations.5,13,15 Normal cut point values
applied for these analyses included LV end-diastolic volume index
(>29 mL/m2), RV end-diastolic area (<29.0 cm²), LV wall thickness
(>11.0 mm), LA volume index (<29 mL/m2), LV ejection fraction
(<55%), RV fractional area change (<32%), septal E (<8.0 cm/s), and
lateral E' (<10.0 cm/s).

Biochemical Studies

Fasting (>12 hours) venous blood samples were collected at both
study time points before exercise testing. Samples were taken 24
hours after the last bout of exercise. Blood was collected into stan-
dard anticoagulant Ethylenediaminetetraacetic acid–treated vacutain-
er tubes and into serum separator tubes and processed immediately.
Testing for all of the assays was done in a random batch order, test-
ing personnel were unaware of the clinical status of participants,
and all testing was performed in a Clinical Laboratory Improvement
Amendments certified laboratory. Laboratory parameters assessed
included a complete chemistry profile, complete blood count, iron
studies, endocrine profile (thyroid stimulating hormone, free serum
metabolite, and lipid profile (total cholesterol, low-density lipoprotein, high-density lipoprotein, and
triglycerides), and additional biomarkers of cardiovascular risk (hemoglobin A1C, high-sensitivity C-reactive protein, lipoprotein-(a), and N-terminal fragment of B-type natriuretic peptide).

Statistical Analysis
Normality of distribution for all variables was assessed using the Shapiro–Wilk test. Continuous variables are reported as mean±SD and categorical variables as ratios. Baseline variables characterizing more experienced and less experienced runners were compared using 1-sample t tests or the Mann–Whitney test for continuous variables, as appropriate for data distribution, and Fisher Exact test for proportions. Before and after training variables in the total cohort were compared using paired t testing or the Wilcoxon matched pairs test as appropriate for data distribution. The percentages of participants that fell outside conventional limits of normal before and after training were compared using Fisher exact test. ANOVA and linear regression analyses were used to examine the relationships between exercise exposure (weekly running mileage at baseline, number of previous marathons completed, previous personal best marathon time, and number of miles run during the study period) and changes in key outcome variables. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (SPSS Inc, Chicago, IL). A 2-sided P value of <0.05 was considered significant.

Results
Baseline Characteristics
Forty-five of 49 enrolled participants (92% completion rate) completed the training period and were included in the final analyses. All subject attrition (n=4) was because of musculoskeletal injuries, and there were no adverse cardiovascular events during the study period. Baseline demographics, anthropometric data, vital signs, cardiac history, medication use, and exercise history are detailed in Table 1. The mean age was 48±7 years, and the majority of participants were white (40/45; 89%). Established cardiovascular conditions included previous syncope (13/45; 29%), dyslipidemia (19/45; 42%), hypertension (13/45; 29%), LV diastolic dysfunction (7/45; 16%), and previous palpitations (6/45; 13%). No individuals started or discontinued any prescription medications during the study period. Compared with less experienced runners (n=23; 1.1±1.1 previous marathons), more experienced marathoners (n=22; 8.8±10.2 previous marathons) were older, shorter, lighter, and reported more weekly alcohol consumption but were otherwise similar at baseline. More experienced

Table 1. Baseline Demographics for the Total Cohort and for the Subgroups of Less Experienced Marathon Runners (≤5 Previous Marathons) and More Experienced Marathoners (>5 Previous Marathons)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort (n=45)</th>
<th>Less Experienced Marathoners (n=23)</th>
<th>More Experienced Marathoners (n=22)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>47.7±7.4</td>
<td>44.8±7.4</td>
<td>50.8±6.2</td>
<td>0.005*</td>
</tr>
<tr>
<td>Anthropometric data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, in</td>
<td>70.0±2.8</td>
<td>71.5±3.0</td>
<td>68.9±2.2</td>
<td>0.01*</td>
</tr>
<tr>
<td>Weight, lb</td>
<td>188.4±25.2</td>
<td>194.0±28.8</td>
<td>182.5±19.7</td>
<td>0.13</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.0±2.7</td>
<td>27.0±2.4</td>
<td>27.0±3.0</td>
<td>0.91</td>
</tr>
<tr>
<td>Vital signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>59±7</td>
<td>60±8</td>
<td>59±8</td>
<td>0.62</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>121±11</td>
<td>121±11</td>
<td>121±12</td>
<td>0.92</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>79±5</td>
<td>79±4</td>
<td>79±6</td>
<td>0.77</td>
</tr>
<tr>
<td>Cardiovascular conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13/45 (29%)</td>
<td>6/23 (26%)</td>
<td>7/22 (32%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>19/45 (42%)</td>
<td>12/23 (52%)</td>
<td>7/22 (32%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Previous syncope</td>
<td>13/45 (29%)</td>
<td>7/23 (30%)</td>
<td>6/22 (27%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Previous palpitations</td>
<td>6/45 (13%)</td>
<td>3/23 (13%)</td>
<td>3/22 (14%)</td>
<td>1.0</td>
</tr>
<tr>
<td>LV diastolic dysfunction</td>
<td>7/45 (16%)</td>
<td>4/23 (17%)</td>
<td>3/22 (14%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Medication use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any prescription</td>
<td>14/45 (31%)</td>
<td>6/23 (26%)</td>
<td>8/22 (36%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Lifestyle factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous smoking</td>
<td>14/45 (31%)</td>
<td>6/23 (26%)</td>
<td>5/22 (23%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Alcohol use, drinks/wk</td>
<td>5.3±5.9</td>
<td>3.0±2.7</td>
<td>7.7±7.3</td>
<td>0.008*</td>
</tr>
<tr>
<td>Exercise history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Running distance, miles/wk</td>
<td>13.6±8.6</td>
<td>13.4±7.6</td>
<td>14.0±7.5</td>
<td>0.48</td>
</tr>
<tr>
<td>Previous marathons</td>
<td>8.8±10.2</td>
<td>1.1±1.1</td>
<td>13.9±10.5</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Age at first marathon, y</td>
<td>33.1±11.0</td>
<td>36.8±13.0</td>
<td>30.2±8.3</td>
<td>0.06</td>
</tr>
<tr>
<td>Fastest marathon finish, hh:mm</td>
<td>3:57±0:45</td>
<td>4:16±0:52</td>
<td>3:43±0:36</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%). Hypertension and dyslipidemia were self-reported by participants. P values reflect comparisons of less experienced marathon runners to more experienced marathon runners. BMI indicates body mass index; and LV, left ventricle.

*P value <0.05 compared to less experienced marathon runners.
and less experienced marathoners were similar at baseline with respect to exercise testing data, echocardiographic data, and laboratory testing values.

Exercise Training
During the 2 months before enrollment, participants ran 13.6±11.5 miles/wk (21.9±18.5 km/wk; Table 1) and participated in no organized road races. Baseline training volume during this prestudy period was similar among less experienced (13.4±7.6 miles/wk [21.6±12.2 km/wk]) and more experienced marathoners (14.0±7.5 miles/wk [22.5±12.1 km/wk]), P=0.79. During the training study period, participants ran 24.2±11.9 miles/wk (38.9±19.2 km/wk), which required 4.0±2.2 hours/wk (P<0.001 for both distance and hours/wk compared with prestudy baseline running) and demonstrated a progressive increase in weekly running distance until the 3 weeks before race day during which training volume decreased to facilitate a taper for optimal recovery and race day performance (Figure 1).

Exercise Physiology
Exercise physiology parameters before and after training are shown in Table 2. Indices characterizing maximal exercise capacity including peak V\(_{\text{O}}\)\(_{\text{2}}\) (44.6±5.2 versus 46.3±5.4 mL/kg per minute; P<0.001), total exercise duration, and peak O\(_{2}\) pulse were significantly higher after marathon training. There were also significant improvements in submaximal exercise performance as reflected by increases in V\(_{\text{O}}\)\(_{\text{2}}\) (35.8±3.7 versus 38.9±3.7 mL/kg per minute; P<0.001) and treadmill incline at the ventilatory threshold. No participants demonstrated ischemic electrocardiographic changes or clinically relevant arrhythmias at either time point. There were no statistically significant relationships between previous marathon running experience, intrastudy training volume, and either baseline or post-training exercise physiology parameters.

Cardiac Structure
Cardiac structural indices are detailed in Table 3. Before training, more experienced runners and less experienced marathon runners were similar across all structural parameters with the exception of LV length, which was higher in the more experienced group. Marathon training was associated with statistically significant increases in LV size as measured by end-diastolic volume, end-systolic volume, longitudinal length, and LV mass index (78.1±14.8 versus 89.3±9.7 g/m²; P<0.001). Similarly, there were significant increases in RV size and left atrial volume. There were no statistically significant relationships between previous marathon running experience, intrastudy training volume, and changes in cardiac structure.

Cardiac Function
Parameters defining cardiac function before and after marathon training are detailed in Table 3. Before training, more experienced runners and less experienced marathon runners were similar across all functional parameters. LV diastolic function, as assessed both by early diastolic relaxation velocity (E′=12.4±2.5 versus 13.2±2.0 cm/s; P=0.007) and late diastolic relaxation velocity (A′=11.5±1.9 versus 12.2±2.1 cm/s; P=0.03), was enhanced after marathon training. Complementary indices of LV and RV systolic function (ejection fraction, RV fractional area change, basal LV and RV S′, global LV longitudinal strain, and tricuspid annular plane systolic excursion) were not significantly affected by marathon training. There were no statistically significant relationships between previous marathon running experience, intrastudy training volume, and changes in cardiac function. Application of Clinical Cut Points
The application of established clinical cut points for measurements of cardiac structure and function for selected metrics is shown in Figure 2. At the completion of marathon training, indices defining cardiac structure, including LV end-diastolic

![Figure 1. Running mileage performed during an 18-week structure marathon-training program.](http://circimaging.ahajournals.org/)

<table>
<thead>
<tr>
<th>Table 2. Cardiopulmonary Exercise Testing Data</th>
</tr>
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<tbody>
<tr>
<td>Pretraining</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Treadmill time, min*</td>
</tr>
<tr>
<td>Treadmill incline, %</td>
</tr>
<tr>
<td>Respiratory exchange ratio</td>
</tr>
<tr>
<td>V(<em>{\text{O}})(</em>{\text{2}}), L/min</td>
</tr>
<tr>
<td>V(<em>{\text{O}})(</em>{\text{2}}), mL/kg per minute</td>
</tr>
<tr>
<td>V(<em>{\text{O}})(</em>{\text{2}}), % predicted</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
</tr>
<tr>
<td>Breathing reserve, %</td>
</tr>
<tr>
<td>Respiratory rate, bpm</td>
</tr>
<tr>
<td>VE/V(<em>{\text{CO}})(</em>{2}), L/mL CO(_{2})</td>
</tr>
</tbody>
</table>

DBP indicates diastolic blood pressure; SBP, systolic blood pressure; VE/V\(_{\text{CO}}\)\(_{2}\), ventilatory equivalent ratio for carbon dioxide; and V\(_{\text{O}}\)\(_{\text{2}}\), peak oxygen consumption.

*Treadmill time includes a 10-minute warm-up period as described in the Methods section of this article.

†P value <0.05 comparing pretraining values to posttraining values.
Table 3. Effects of Marathon Training on Cardiac Structure and Function

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pretraining</th>
<th>Post-training</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac structure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV wall thickness, mm</td>
<td>10.3±0.2</td>
<td>10.8±0.2</td>
<td>0.002*</td>
</tr>
<tr>
<td>LV length, mm</td>
<td>45.9±4.0</td>
<td>48.2±3.5</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>156±26</td>
<td>172±28</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LV mass/BSA, g/m²</td>
<td>78±15</td>
<td>89±10</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LAEDV, mL</td>
<td>65±19</td>
<td>72±19</td>
<td>0.02*</td>
</tr>
<tr>
<td>RVAd, mm²</td>
<td>4.5±0.5</td>
<td>4.7±0.6</td>
<td>0.012*</td>
</tr>
<tr>
<td>RVAd, mm³</td>
<td>27.0±4.8</td>
<td>28.6±4.3</td>
<td>0.02*</td>
</tr>
<tr>
<td><strong>Cardiac function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systole: left ventricle Ejection fraction, %</td>
<td>60±2.0</td>
<td>58±2.6</td>
<td>0.18</td>
</tr>
<tr>
<td>Basal S', cm/s</td>
<td>10.3±2.0</td>
<td>10.6±1.7</td>
<td>0.18</td>
</tr>
<tr>
<td>Longitudinal strain, %</td>
<td>−18.4±2.6</td>
<td>−18.3±2.3</td>
<td>0.74</td>
</tr>
<tr>
<td>Diastole: left ventricle LV basal E', cm/s</td>
<td>12.4±2.5</td>
<td>13.2±2.0</td>
<td>0.007*</td>
</tr>
<tr>
<td>LV basal A', cm/s</td>
<td>11.5±1.9</td>
<td>12.2±2.1</td>
<td>0.03*</td>
</tr>
<tr>
<td>Transmitral E-wave, cm/s</td>
<td>75±15</td>
<td>73±15</td>
<td>0.34</td>
</tr>
<tr>
<td>Transmitral A-wave, cm/s</td>
<td>59±11</td>
<td>61±11</td>
<td>0.09</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.3±0.3</td>
<td>1.2±0.2</td>
<td>0.01*</td>
</tr>
<tr>
<td>Systole: right ventricle RVFAC, %</td>
<td>39±8</td>
<td>41±12</td>
<td>0.53</td>
</tr>
<tr>
<td>Basal S', cm/s</td>
<td>17.5±2.9</td>
<td>17.4±3.1</td>
<td>0.60</td>
</tr>
<tr>
<td>TAPSE, mm²</td>
<td>32±5</td>
<td>31±5</td>
<td>0.53</td>
</tr>
</tbody>
</table>

*P value <0.05 comparing pretraining values to posttraining values.

Discussion

This study was designed to examine the effect of marathon training on cardiac structure and function, cardiorespiratory fitness, and laboratory determinants of cardiovascular disease risk among middle-aged men. Our findings are summarized as follows. First, our data demonstrate that an 18-week recreational running program leads to structural myocardial remodeling characterized by LV dilation, RV dilation, and left atrial dilation that commonly results in chamber sizes that exceed clinical cut points for normality even among recreational athletes. Second, we observed myocardial functional adaptation in the form of enhancement of LV diastolic function. Third, we found that resting biventricular systolic function is mildly reduced among a sizable percentage of otherwise healthy runners with supranormal exercise capacity both before and after training. Finally, myocardial adaptations to recreational marathon training were accompanied by significant increases in maximal exercise capacity (peak V̇O₂), improved exercise performance at submaximal workloads, and favorable changes in several biochemical markers of cardiac disease risk.

Myocardial remodeling in response to exercise training has been well documented among elite level competitive endurance athletes. Eccentric LV remodeling, RV dilation, biatrial dilation, and supranormal diastolic function are well-recognized attributes of the endurance athlete’s heart. To what degree these adaptations occur in recreational athletes who typically perform far less exercise than elite competitors remains uncertain. Our findings suggest that a recreational running program is sufficient to stimulate both the structural and the functional cardiac changes that have previously been documented among elite competitors. The observed structural remodeling in this setting was of sufficient magnitude such that post-training cardiac parameters commonly fell outside the established clinical ranges of normal. Thus, structural characteristics of the athlete’s heart are not confined to elite caliber competitors and are likely to be found among a sizable population of active people. It is also noteworthy that among the 16% of participants with grade 1 LV diastolic dysfunction before training, LV diastolic function normalized in all but in 1 case after training. It is noteworthy that the majority of the individuals (6/7) with pretraining diastolic dysfunction were experienced marathoners, which may reflect the age-associated decline in ventricular relaxation because the experienced marathoners were older than the less experienced marathoners. This beneficial adaptation suggests a key mechanistic link between...
recreational exercise and reduced cardiovascular disease burden. Finally, we observed that a significant minority of recreational athletes, both before and after a period of structured training, demonstrated mildly reduced resting left and RV systolic function coupled with well-above normal exercise capacity. This observation suggests, as previously
The popular notion that marathon training may confer potential health benefits is substantiated by a study that demonstrated that marathon training can improve cardiovascular health. The study, which involved a 18-week training program, observed significant reductions in body mass, increases in peak aerobic capacity, and improvements in serum lipids. Data presented here may enable clinicians to provide quantitative expectations about the effect of marathon training on modifiable cardiac disease risk factors better (Figure 3). Our data demonstrate that marathon training can facilitate reversal of left ventricular dysfunction as was observed in the majority of our participants with this condition before training. This finding substantiates important previous work, which demonstrated that aerobic exercise can prevent or mitigate age-associated decline in LV relaxation.

Table 4. Effects of Marathon Training on Laboratory Values

<table>
<thead>
<tr>
<th>Laboratory parameter</th>
<th>Pretraining</th>
<th>Post-training</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum chemistry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.98±0.13</td>
<td>0.91±0.12</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Cystatin C, mg/L</td>
<td>0.90±0.11</td>
<td>0.88±0.12</td>
<td>0.11</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>91±10</td>
<td>92±11</td>
<td>0.39</td>
</tr>
<tr>
<td>Hemoglobin A1C, %</td>
<td>5.5±0.3</td>
<td>5.5±0.2</td>
<td>0.68</td>
</tr>
<tr>
<td>Iron, µg/dL</td>
<td>95±36</td>
<td>94±32</td>
<td>0.79</td>
</tr>
<tr>
<td>Ferritin, ng/mL</td>
<td>189±141</td>
<td>169±125</td>
<td>0.002*</td>
</tr>
<tr>
<td>Iron-binding capacity, µg/dL</td>
<td>323±41</td>
<td>318±60</td>
<td>0.51</td>
</tr>
<tr>
<td>NT-pro-BNP, pg/mL</td>
<td>29±27</td>
<td>31±28</td>
<td>0.44</td>
</tr>
<tr>
<td>High sensitivity CRP, mg/L</td>
<td>1.9±3.2</td>
<td>1.8±1.8</td>
<td>0.75</td>
</tr>
<tr>
<td>TSH, µU/mL</td>
<td>1.99±1.14</td>
<td>1.96±0.95</td>
<td>0.73</td>
</tr>
<tr>
<td>Testosterone, ng/dL</td>
<td>520±223</td>
<td>537±173</td>
<td>0.62</td>
</tr>
<tr>
<td>Steroid hormone binding Glob., nmol/L</td>
<td>39.2±11.7</td>
<td>43.1±13.0</td>
<td>0.01*</td>
</tr>
<tr>
<td><strong>Serum lipids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>199±33</td>
<td>192±29</td>
<td>0.01*</td>
</tr>
<tr>
<td>Low-density lipoprotein, mg/dL</td>
<td>120±29</td>
<td>114±26</td>
<td>0.01*</td>
</tr>
<tr>
<td>High-density lipoprotein, mg/dL</td>
<td>55±12</td>
<td>55±11</td>
<td>0.81</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>100±52</td>
<td>85±36</td>
<td>0.02*</td>
</tr>
<tr>
<td>Lipoprotein-(a), mg/dL</td>
<td>4.7±3.3</td>
<td>4.8±3.8</td>
<td>0.66</td>
</tr>
<tr>
<td><strong>Hematologic parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell count, ×10^3/µL</td>
<td>5.9±2.2</td>
<td>5.4±2.1</td>
<td>0.01*</td>
</tr>
<tr>
<td>Platelet count, ×10^9/µL</td>
<td>231±49</td>
<td>227±44</td>
<td>0.34</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>15.1±0.9</td>
<td>15.0±0.8</td>
<td>0.78</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>43.8±2.4</td>
<td>44.2±2.3</td>
<td>0.27</td>
</tr>
<tr>
<td>Mean corpuscular volume, fl</td>
<td>88.0±3.5</td>
<td>88.8±3.2</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

CRP indicates C-reactive protein; Glob., globulin; NT-pro-BNP, N-terminal pro-B-type natriuretic peptide; and TSH, thyroid stimulating hormone.

*p Value <0.05 comparing pretraining values to posttraining values.

Proposed that mild depressed resting systolic function in the endurance exercise trained heart may reflect increased contractile reserve rather than an acquired cardiomyopathic condition.

Recreational endurance sports, such as marathon running, have become a popular pastime for many middle-aged people. Growth in marathon popularity has been driven, in part, by the popular notion that marathon training may confer potential health benefits. At present, there are sparse data substantiating this belief. There is, however, a rapidly growing body of literature documenting potentially concerning cardiovascular responses to marathon racing, including cardiac troponin release, subclinical cardiac dysfunction, and myocardial edema. These findings have generated logical concern about the overall health implications of marathon participation. However, observations on transient physiological changes associated with a single intense race, most without apparent clinical relevance, are unlikely to reflect the overall effect of marathon participation on cardiovascular health. Data from the present study, an effort aimed to evaluate the effect of the months of training rather than the hours of the race itself, suggest that the preparatory phase of marathon participation translates into tangible cardiovascular health benefits. To what degree the benefits of training are offset by the proposed dangers of racing and maintenance of these benefits during the offseason remain important questions that will require future work.

There are direct clinical implications of our findings because recreational athletes, specifically long-distance runners, are increasingly encountered in clinical practice. Data defining the expected physiological adaptations to recreational marathon training may serve to reduce unnecessary testing directed at the evaluation of suspected underlying cardiomyopathy in this population. This is particularly relevant given that ventricular dilation coupled with mild reduction in systolic function, a pattern typical of mild cardiomyopathic conditions, was common among the healthy group of athletes studied. In addition to facilitating the differentiation of adaptation from occult disease, clinicians are frequently asked to opine on the potential health risks and benefits of participating in vigorous physical activity. Data presented here may enable clinicians to provide quantitative expectations about the effect of recreational marathon training on modifiable cardiac disease risk factors better (Figure 3). Our data demonstrate that recreational marathon training may facilitate reversal of LV diastolic dysfunction as was observed in the majority of our participants with this condition before training. This finding substantiates important previous work, which demonstrated that aerobic exercise can prevent or mitigate age-associated decline in LV relaxation. The observed reductions in body mass, increases in peak aerobic capacity, and improvements in serum lipids should also translate into improved cardiovascular health. The observed 5% decrease in low-density lipoprotein cholesterol is similar to that afforded by the low saturated fat, low cholesterol American Heart Association Step 2 diet, and by low potency statins. Low-density lipoprotein reduction, even at this magnitude, has been associated with significant reductions in mortality. It is noteworthy that previous cross-sectional work has examined the incidence of atherosclerosis among marathon runners. A case control study...
among men aged ≥50 years demonstrated that marathon runners were more likely to have coronary artery calcium scores ≥100 than age and CV risk factor-matched controls (36.1% versus 21.8%; \( P=0.01 \)). Thus, although our data suggest that marathon training may decrease CV risk factors in the short term, longer term studies adequately powered to evaluate firm morbidity and mortality end points will be needed to delineate the downstream implications of these findings fully.

Participants in the present study were not exercise naïve and had a broad range of previous marathon running experience. It is somewhat surprising that we did not detect any significant differences in baseline characteristics between more experienced and less experienced marathon runners. This is best explained by the fact that both groups entered the study in the relatively detrained states and, therefore, suggests that cardiac adaptations associated with exercise training regress after periods of reduced activity. It is further noteworthy that we did not detect any statistically significant dose–response relationships between intrastudy training volume (ie, number of miles per week) and key outcome variables. This is most likely because of the fact that the range of training among our participants was too small to examine this important concept effectively. We are, therefore, unable to comment on whether the adaptations we observed would amplify or diminish with exercise training that falls outside the range of that which we studied. Interestingly, the exercise dose that we studied of ≈25 running miles/wk is in-line with recent observational data, suggesting that moderate, not extreme, amounts of physical exercise promote optimal long-term health. Further study focused on defining both the durability of myocardial adaptations and optimal dose–response relationships between exercise, cardiac remodeling, and cardiovascular disease risk reduction is warranted.

There are several limitations of this study. First, we deliberately chose to study middle-aged, recreational male runners, a population we previously identified as being at highest risk for adverse cardiovascular events during marathon running. Our results, therefore, may not be fully applicable to recreational female runners, more elite caliber athletes, or to individuals with established cardiovascular disease. Second, we made no effort to control diet during this study and thus cannot comment on whether the potential effect of food intake on our observations. It is possible that marathon training coupled with a heart healthy diet would lead to more robust improvements than those observed. Finally, we planned to examine the relationships between final marathon finish time and key outcome variables. This was not however possible because of the bombings that occurred on April 15, 2013, which made finishing the race impossible for a significant portion of our participants.

In summary, this study demonstrates that recreational marathon training facilitates a specific pattern of exercise-induced cardiac remodeling characterized by biventricular dilation, left atrial dilation, and enhanced LV diastolic function. These adaptive myocardial responses seem to be paralleled by numerous beneficial adaptations, including increased cardiorespiratory fitness, decreased body mass, and improved serum lipid profiles. Additional work is necessary to assess the durability of these beneficial adaptations and the cumulative effects longer term training. Yet, these findings suggest that recreational marathon training, a widely accessible and increasingly popular activity, may represent an effective platform for improving cardiovascular health.

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Disclosures

None.

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**CLINICAL PERSPECTIVE**

Exercise-induced cardiac remodeling, which occurs in response to the hemodynamic stresses of exercise training, has been well characterized among elite competitive athletes. At present, there are sparse data defining the effect of real-world exercise participation on exercise-induced cardiac remodeling and on the physiological responses to popular forms of exercise training among recreational athletes. This study examined the effect of recreational marathon training on cardiac structure, cardiac function, and key nonmyocardial determinants of cardiovascular disease risk. Using a prospective, longitudinal study design, we examined anthropometric data, vital signs, cardiac structure/function, exercise capacity, and laboratory parameters before and after an 18-week structured marathon-training program in 45 middle-aged recreational runners. In this study, recreational marathon training among middle-aged men led to a significant exercise-induced cardiac remodeling characterized by dilation of the ventricles and left atrium, as well as increases in early and late left ventricular diastolic velocities. This cardiac remodeling has considerable clinical relevance because it resulted in structural cardiac dimensions that often exceeded clinical cut points for normality and was accompanied by favorable functional changes, including the resolution of diastolic dysfunction. In addition, exercise-induced cardiac remodeling was accompanied by beneficial changes in cardiovascular risk factors, including body mass index, total cholesterol, low-density lipoprotein, and triglycerides. It is further noteworthy that we did not detect any signal of maladaptive change during this period of exercise training. In aggregate, our results suggest that recreational marathon training is a safe and effective platform for enhancing cardiorespiratory health.
Myocardial Adaptations to Recreational Marathon Training Among Middle-Aged Men

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