Long-distance running events are increasingly popular in all age groups worldwide. In 2012, ≈2.3 million participated in marathon or half marathon races, with a total of 15.5 million finishers in road running events in the United States.1

To maximize training effects, athletes frequently perform high-intensity training sessions. High-intensity interval training is an enhanced form of interval training, alternating periods of short intense aerobic exercise (usually sessions varying from 15 s to 12 minutes) with less-intense recovery periods.2,3

Myocardial adaptation or remodeling in professional athletes has been demonstrated in cross-sectional echocardiographic4,5 and cardiovascular magnetic resonance (CMR) imaging6,7 studies. Longitudinal studies, especially in previously sedentary individuals, are limited. CMR imaging is considered the current reference standard for the evaluation of left ventricular (LV) and right ventricular (RV) cardiac volume and mass, allowing for detection of smaller changes than other imaging modalities.8 Most previous studies focused only on specific aspects of cardiac adaptation, for example, LV or RV hypertrophy,7,9 assessment of myocardial strain,10 or evaluation of cardiac fibrosis with late gadolinium enhancement (LGE).11

There is still controversy whether besides beneficial cardiovascular adaptation12,13 there might be adverse cardiac effects14 of high-intensity endurance training. High rate of LGE in marathon runners11 has been reported, and electrophysiological...
investigations revealed enlargement and reduced contractility of
the RV, which might be associated with ventricular tachycardia.\textsuperscript{15}

The Running Study and Heart (RUSH) trial was designed
to address these issues. Physiological and morphological data
were collected and cardiopulmonary exercise testing with
blood lactate analysis as well as CMR imaging was performed in
a randomized controlled trial.

Methods

Study Population

The study (www.clinicaltrials.gov, NCT01406730) was approved by
the institutional review board and written informed consent was ob-
tained from all subjects. Sample size was determined with G\textsuperscript{*}power
(version 3.1.3; 2009, Faul et al,\textsuperscript{16} Dusseldorf, Germany). We esti-
mated that a sample size of 32 individuals in each group would have
a power of 90\% to detect a between-group difference of 8±10 mL in
end-diastolic volume (EDV) with \( \alpha=0.05 \). Assuming a dropout rate
of 20\%, our goal was to recruit 40 subjects per group. Study sub-
jects were recruited by local newspaper advertisement from January
until March 2011. The study was conducted from April 2011 until
July 2012. Participants were randomly assigned to a training and
recovery group.

Eighty-eight male volunteers, who were either completely seden-
tary or did not engage in any routine (ie, >3 hours per week) physi-
cal training, were enrolled in this study. All participants completed a
medical history and physical activity questionnaire. All subjects de-
ied the use of illicit substances and underwent physical examination,
treadmill testing, rest electrocardiography, and echocardiographic ex-
iminations. After clinical evaluations, 4 subjects were excluded from
the study because of too high a fitness level (n=2), contraindication to
CMR imaging (n=1), or evidence of cardiac disease (n=1). Physical
characteristics at baseline and post-training are shown in Table 1.

Treadmill Testing and Training Procedure

Before and after the intervention, all subjects performed a stepwise
progressive-intensity treadmill test (Technogym, Gambettola, Italy)
at 1\% slope up to a voluntary maximum with continuous assessment
of heart rate and ventilation parameters (Polar RS 400, Kempele,
Finland; Oxicon mobile, Vienna, Conshohocken, PA). Intensity was
increased in steps of 1 km/h (0.62 mph) every 3 minutes, beginning at
7 to 8 km/h (4.35–4.97 mph), depending on the performance capacity
of the subject. Participants provided a blood sample at the end of ev-
every 3-minute stage to determine heart rate at the anaerobic threshold
from the blood lactate concentration.

Members of the intervention group were trained for 16 weeks.
Each subject was provided with an individual training log that pre-
scribed the intensity, volume, and duration of the running exercise
for the following 4 weeks. Frequency of running was progressively
increased from 2 sessions per week during the first month to 2 to 3
sessions per week during the second month, and 3 to 4 sessions per
week during the last 2 months of intervention. At least 1 supervised
training unit per week was performed. In addition to pure high-
intensity interval training,\textsuperscript{7} high-intensity (interval) training (HI(I)
T) in RUSH included a continuous high-intensity running session
performed at the individual anaerobic threshold every fifth session
(range, 25–45 minutes; ≥85\% of maximum heart rate). The high-in-
tensity running intervals (range, 90 s–12 minutes) were performed with
a targeted exercise intensity of 95 to 102.5\% of individually
calculated heart rate at the anaerobic threshold (ie, 80\%–90\% of
maximum heart rate; 73\%–83\% of \( V_{O_{2max}} \) [maximal aerobic capac-
ity]). Bouts of interval runs were alternated with active recovery
(1–3 minutes jogging or fast walking at 65\%–70\% of maximum
heart rate). In total, 25\% of exercise volume was performed at low
exercise intensities (70\%–82.5\% of individually calculated heart
rate at the anaerobic threshold) during warm-up, cool-down, and
the active rest periods (Figure 1). Daily data were recorded on
duration and type of training activities performed during study
period. Subjects were excluded from final data analysis if they had
breaks in training ≥2 weeks during the study period.

CMR Imaging Protocol

CMR imaging was performed on a 1.5-T unit (Magnetom Avanto,
VB 17A; Siemens Healthcare, Erlangen, Germany) using a 6 channel
phased-array surface and spine matrix receiver coil. Four-, 3-, and
2-channel long- and short-axis cine images were acquired by
using breath-hold balanced steady-state free-precession sequences
with retrospective electrocardiographic gating with the following
scan parameters: field of view, 215 to 265×300 to 340 mm; slice
thickness, 6 mm; intersection-gap, 1.5 mm; repetition/echo time,
41.25 to 50.7/1.12 to 1.38 ms; flip angle, 61° to 75°; matrix, 105 to
156×192 to 256; pixel size, 1.5 to 2.8×1.2 to 2.0 mm; number of
reconstructed phases, 25; integrated parallel acquisition techniques
acceleration factor of 2. Myocardial strain was assessed using a
prototype balanced steady-state free-precession–based tagging se-
quence with the following image acquisition parameters: comple-
mentary spatial modulation of magnetization, field of view, 340×340
mm; slice thickness, 6 mm; tag-spacing, 6 mm; repetition/echo time,
32.32/1.23 ms; flip angle, 20°; matrix, 77×256; integrated parallel
acquisition techniques acceleration factor of 2. Ten to 15 minutes
after injection of gadolinium-based contrast medium (0.2 mmol/kg
of body weight; Gadovist, Bayer Healthcare, Leverkusen, Germany)
LGE images were acquired using segmented T1-weighted gradient-
echo inversion-recovery sequence with phase-sensitive reconstruc-
tion in the same views used for cine images.\textsuperscript{8} The inversion time
was individually adapted to optimize the suppression of the signal of
normal myocardium (range: inversion time, 230–290 ms). Sequence
parameters for LGE were as follows: field of view, 276×340 mm;
slice thickness, 8 mm; repetition/echo time, 603 to 912/3.2 ms; flip
angle, 25°; matrix, 156×256; no interslice gap, segments, 20; inte-
grated parallel acquisition techniques acceleration factor of 2.

Image Analysis

Quantitative image analysis was performed using dedicated soft-
ware (Argus, 4.01; Siemens Healthcare). LV and RV functional
analysis was performed by 2 observers with >4 (M.S.) and 11
(M.M.L.) years of experience in CMR imaging. Both readers
evaluated the studies separately in random order and were blinded
to group assignment. Tracing of the endo- and epicardial borders
from base to apex was performed manually at end-diastole and end-
systole with carefully excluding epicardial adipose tissue.

For mass calculations, papillary muscles were excluded and the
interventricular septum was added to the LV. All results were di-
vided by body surface area to minimize differences of myocar-
dium parameters related to weight and height. LV wall thickness
was defined as the average of 6 segment thickness measurements
of the midventricular level at end-diastole (anterior, anterolateral,
anteroseptal, inferior, inferolateral, and inferoseptal). We calcu-
lated the LV and RV remodeling index (myocardial mass/EDV).

An increased remodeling index is consistent with concentric hy-
pertrophy, whereas a reduced remodeling index is indicative of
isolated cavitory dilation.\textsuperscript{9} In addition, the maximum left atrial
(LA) volume was calculated according to the biplane area-length
method and indexed for body surface area.\textsuperscript{18} A total of 55 mL/m\textsuperscript{2}
was defined as the upper limit for LA volume index.\textsuperscript{19} Evaluation of
LGE was performed according to the AHA–17–segment mod-
el.\textsuperscript{20} Presence of LGE was visually determined by using short-
and long-axis views and was defined as present only if detectable
in 2 orthogonal planes.

LV analysis of myocardial strain was performed using semiauto-
matic software (InTag, CREATIS, Lyon, France).

Statistical Analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS,
Chicago, IL). Baseline and follow-up data are expressed as means±SD.
Normal distribution of the data was statistically (Shapiro–Wilk
test) and graphically determined. Differences within groups were
consistently analyzed by paired $t$ tests. ANOVA with repeated measurements consequently adjusted on baseline values was performed to check time-related intergroup statistics. Adjustments for multiple comparisons were made using Bonferroni corrections. A 2-sided $P$ < 0.05 was considered statistically significant. For comparison of proportions, we used the $\chi^2$ test. Degree of correlation between variables was calculated using Pearson correlation. For quantitative evaluation of images interobserver reliability was assessed using Cohen $\kappa$ statistics.

**Results**

At baseline study, subjects were equally distributed to the HI(I)T group (n=42) or control group (n=42). During the training program there were several dropouts in the HI(I)T group (injuries, n=2; illness, n=6; training protocol violations, n=2) and in the control group (training protocol violations, n=3).

Resting heart rate did not differ significantly at baseline and follow-up between intervention and control group (Table 1). In HI(I)T group, a decrease in resting heart rate from 70 bpm pre- to 66 bpm post-training was found ($P$=0.10). In both groups, electrocardiographic patterns did not change during the study period. LV ejection fraction was similar in the training and control group at baseline and post-training (Table 2). Except 2 subjects in the control group, none of the participants had an LV ejection fraction <50%. All RV ejection fraction pre- and post-training were within the normal range (47%–74%).

Diagnostic image quality was obtained in all examinations. Close interobserver agreement for image analysis was found ($\kappa$=0.93). All data showed normal distribution. Indexed LV and RV EDVs were significantly higher after the training period (8.8% and 7.6%) compared with controls (Figure 2), resulting in greater LV and RV stroke volumes (9.6% and 8.3%) with larger end-systolic volumes (8.3%, 6.3%). LV and RV EDVs, except in 3 controls (100, 101, and 110 mL), were within normal ranges for healthy, male, nonathletic subjects (LV, 47–92 mL/m²; RV, 55–105 mL/m²). Indexed LV and RV parameters are detailed in Table 2.

### Table 1. Baseline and Post-Training Physical Characteristics of HI(I)T and Control Group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls</th>
<th>HI(I)T</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>42.4±5.5</td>
<td>44.2±4.8</td>
<td>0.16</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.82±0.6</td>
<td>1.81±0.4</td>
<td>0.71</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>89.5±14.9</td>
<td>89.6±14.2</td>
<td>0.39</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.0±4.1</td>
<td>27.1±4.0</td>
<td>0.23</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>2.12±0.2</td>
<td>2.15±0.2</td>
<td>0.49</td>
</tr>
<tr>
<td>Resting heart rate, bpm</td>
<td>72.1±12.6</td>
<td>77.2±11.6</td>
<td>0.09</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, n (%)</td>
<td>9 (21)</td>
<td>11 (25)</td>
<td>0.48</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>4 (10)</td>
<td>4 (10)</td>
<td>0.97</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>2 (5)</td>
<td>2 (5)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Past medical history</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>β-blockers, n (%)</td>
<td>5 (12)</td>
<td>6 (15)</td>
<td>0.61</td>
</tr>
<tr>
<td>Furosemide, n (%)</td>
<td>4 (10)</td>
<td>3 (7)</td>
<td>0.71</td>
</tr>
<tr>
<td>ACEi/ARBs, n (%)</td>
<td>6 (14)</td>
<td>4 (10)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Data for physical characteristics are given as mean±SD. Values for risk factors and past medical history are indicated as numbers and percentages. $P$ values refer to intergroup differences at baseline. There was a balanced distribution of cardiac risk factors and medications between the 2 groups. ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II inhibitor; BSA, body surface area; HI(I)T, high-intensity (interval) training; and na, not applicable.

![Figure 1. Total exercise volume of high-intensity (interval) training (HI(I)T) group in different intensity levels. HI(I)T focused on interval training with a prescribed exercise intensity around (95%–102.5%) or above (>102.5) individually calculated heart rate at the anaerobic threshold. Twenty-five percentage of total exercise volume was performed at low exercise intensities (70–82.5% of individually calculated heart rate at the anaerobic threshold) during warm-up, cool-down, and the active rest periods. HR indicates heart rate; and IAS, individual anaerobic threshold.](http://circimaging.ahajournals.org/).
There was a strong positive correlation between EDV and myocardial mass of the LV (Pearson correlation, 0.66; \( P < 0.001 \)) and RV (Pearson correlation, 0.68; \( P < 0.001 \)). In addition, changes in LV EDV and myocardial mass in the HI(I)T group were significantly correlated with changes in absolute and relative VO\(_{2\text{max}}\) (Pearson correlation, 0.61 and 0.59; \( P < 0.001 \); Figure 3). In the HI(I)T group, increase of indexed ventricular volume was significantly correlated with a decrease in blood lactate concentration at the anaerobic threshold (Pearson correlation, −0.36; \( P < 0.05 \)), whereas changes in indexed myocardial mass were not (Pearson correlation, −0.07; \( P = 0.69 \)).

The LV and RV remodeling indices in the HI(I)T group were similar before (LV, 0.76±0.09; RV, 0.19±0.02 g/mL) and after (LV, 0.76±0.1; RV, 0.19±0.02 g/mL; \( P = 0.97 \) and \( P = 0.72 \)) the training period, which indicates balanced adaptation of the heart. Furthermore, LV/RV ratios in the running group for EDV and myocardial mass were comparable before and after training (EDV, 1.05 versus 1.04; \( P = 0.21 \) and myocardial mass, 3.94 versus 3.93; \( P = 0.008 \)).

In the HI(I)T group, the mean value for indexed maximum LA volume at end systole increased by 12.9% from 41.0±8.2 to 46.3±9.0 mL/m\(^2\) (\( P = 0.001 \)). The ratio of indexed end-systolic LA volume to end-diastolic LV volume at baseline was similar in the HI(I)T group and controls (0.53 versus 0.52, respectively; \( P = 0.38 \)). Post-training ratio of end-systolic LA volume to end-diastolic LV volume had slightly increased with HI(I)T (0.56; \( P = 0.042 \)).

Peak systolic circumferential strain before and after training ranged between −10% to −25% in the control and HI(I)T group without significant intergroup differences (Table 3). Intragroup analysis showed a postinterventional decrease of myocardial shortening for circumferential strain in HI(I)T members within all 6 basal segments, reaching statistical significance in the anteroseptal \( (P = 0.01) \) and the anterolateral segment \( (P < 0.001) \); Figure 4). No statistically significant differences between pre- and post-training were found within the 3 LV levels for radial and for longitudinal strain. No areas of LGE indicative of structural myocardial damage in any of the participants, neither before nor after the training program, were found.

### Table 2. LV and RV Morphological and Functional Parameters of HI(I)T and Control Group at Baseline and Post-Training

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls Baseline (n=42)</th>
<th>Controls Follow-Up (n=39)</th>
<th>HI(I)T Baseline (n=42)</th>
<th>HI(I)T Post-Training (n=32)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic volume index, mL/m(^2)</td>
<td>84.6±12.7</td>
<td>84.0±12.3</td>
<td>77.1±8.5</td>
<td>83.9±8.6</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>End-systolic volume index, mL/m(^2)</td>
<td>35.4±8.4</td>
<td>34.5±7.8</td>
<td>31.3±4.6</td>
<td>33.9±6.1</td>
<td>0.002*</td>
</tr>
<tr>
<td>Stroke volume index, mL/m(^2)</td>
<td>49.2±7.2</td>
<td>49.5±6.9</td>
<td>45.9±6.7</td>
<td>50.3±6.7</td>
<td>0.002*</td>
</tr>
<tr>
<td>Mass index at end-diastole, g/m(^2)</td>
<td>55.8±5.6</td>
<td>55.4±5.5</td>
<td>58.2±6.4</td>
<td>63.4±8.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Wall thickness, mm</td>
<td>7.9±0.8</td>
<td>7.8±0.8</td>
<td>8.5±0.8</td>
<td>8.8±1.0</td>
<td>0.001*</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>58.4±5.2</td>
<td>59.1±4.8</td>
<td>59.4±4.7</td>
<td>59.7±5.3</td>
<td>1.000</td>
</tr>
<tr>
<td>RV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic volume index, mL/m(^2)</td>
<td>86.8±12.4</td>
<td>85.9±12.2</td>
<td>80.5±8.5</td>
<td>86.6±8.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>End-systolic volume index, mL/m(^2)</td>
<td>37.4±8.3</td>
<td>36.4±7.9</td>
<td>34.7±4.8</td>
<td>36.9±5.8</td>
<td>0.001*</td>
</tr>
<tr>
<td>Stroke volume index, mL/m(^2)</td>
<td>49.4±7.1</td>
<td>49.5±7.1</td>
<td>45.8±6.6</td>
<td>49.6±6.2</td>
<td>0.005*</td>
</tr>
<tr>
<td>Mass index at end-diastole, g/m(^2)</td>
<td>14.2±1.5</td>
<td>14.1±1.4</td>
<td>14.8±1.7</td>
<td>16.1±2.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>57.1±5.2</td>
<td>57.8±4.9</td>
<td>56.8±4.6</td>
<td>57.4±5.0</td>
<td>1.000</td>
</tr>
<tr>
<td>Cardiac index, L/(min·m(^2))</td>
<td>3.5±0.6</td>
<td>3.5±0.6</td>
<td>3.5±0.7</td>
<td>3.7±0.7</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Data are given as mean±SD. \( P \) values compare differences from baseline to follow-up for controls vs HI(I)T. Ejection fraction=(stroke volume/end-diastolic volume)×100. HI(I)T indicates high-intensity (interval) training; LV, left ventricle; and RV, right ventricle.

*Statistically significant values.
Discussion

This longitudinal study shows that 16 weeks of HI(I)T in previously untrained male individuals lead to significant morphological changes of the LV and RV, which correlate with improvements in maximal aerobic capacity ($\text{VO}_{2\text{max}}$). Morphological cardiac adaptation is characterized by a balanced increase in end-diastolic ventricular volumes associated with a similar increase of myocardial masses. Pre- and post-training indexed LV and RV myocardial masses in our study were below previously reported mean values for healthy subjects (LV, 69–112 g/m² and RV, 16–36 g/m², respectively).21–23 This is most likely because of a larger body surface area in our study population as compared with previous studies. None of our study subjects exceeded upper limits for indexed LV and RV myocardial mass. This is relevant because previous studies showed that values above these limits are associated with an increase in cardiovascular mortality.24 The combined mean value for LV wall thickness of HI(I)T and control group at baseline (8.1 mm) is below that of previously reported reference values (8.8 mm).3 This difference might be related to the selection of older subjects in our study (30–50 years). Post-training LV wall thickness in our HI(I)T group was lower than that reported in cross-sectional studies in elite athletes,25 reflecting the different fitness level.

In this study, we did not find statistically significant differences in the LV/RV ratios for volume and mass indices, indicating balanced cardiac adaptation with regulative enlargement of all chambers. Previous cross-sectional studies in elite athletes proposed 2 types of ventricular remodeling5,26: either volume load in endurance training associated with thickening of the ventricular wall and cavity dilation (eccentric hypertrophy) or pressure load in resistance training inducing concentric hypertrophy characterized by increased myocardial mass and wall thickness without substantial change in cavity size.27 In contrast, the findings of similar remodeling indices of subjects in our intervention group pre- and post-training are indicative of cardiac adaptation without preponderance of 1 specific remodeling mechanism. The discrepancy between results found in our study and previous investigations15,28 might predominantly be explained by different effects of type, intensity, and duration of training, as our study population consisted of previously untrained subjects with relatively more potential for cardiac remodeling than active sportsmen.

Furthermore, our data suggest that in HI(I)T ventricular remodeling is accompanied by LA dilation. However, the percentage of individuals with LA enlargement in our study (13%) was lower than that observed in long-term elite athletes (≤62%).25

Table 3. Mean Peak Systolic LV Circumferential Strain of HI(I)T and Control Group at Baseline and Follow-Up

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (n=42)</th>
<th>Follow-Up (n=32)</th>
<th>P Value (Intergroup)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>HI(I)T</td>
<td>Controls</td>
<td>HI(I)T</td>
</tr>
<tr>
<td>LVES Ecc apikal</td>
<td>−19.5±4.4</td>
<td>−19.0±3.2</td>
<td>0.66</td>
</tr>
<tr>
<td>LVES Ecc basal</td>
<td>−13.2±5.4</td>
<td>−14.5±3.8*</td>
<td>0.26</td>
</tr>
<tr>
<td>LVES Ecc medial</td>
<td>−22.2±2.4</td>
<td>−21.5±2.7</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Data are given as mean in percentage shortening of circumferential strain at LVES±SD. There were no statistical significant intergroup differences at the 3 short-axis levels at baseline and follow-up. The only statistical significant difference was between pre- and post-training basal circumferential myocardial shortening in the HI(I)T group (P<0.001). HI(I)T indicates high-intensity (interval) training; and LVES, left ventricular end-systole.

*Statistically significance.
Besides the beneficial cardiovascular effects of regular endurance exercise training, there is still uncertainty whether excessive endurance training is associated with increased risk of myocardial inflammation and fibrosis, being responsible for arrhythmia and sudden cardiac death. Postmortem investigations in athletes having sudden cardiac death have shown myocardial interstitial fibrosis and animal studies have demonstrated that intensive endurance exercise can trigger the development of myocardial inflammation and fibrosis in rats. CMR imaging after intravenous gadolinium application is the current reference standard modality to detect myocardial LGE in 12% of healthy male marathon runners. In our trial (age range, 30–50 years; no history of cardiac disease; no competitive sports), which is in accordance to a recently published study by Breuckmann et al showing myocardial LGE in 12% of healthy male marathon runners (n=102) aged 50 to 72 years and 4% in the age-matched control group could be explained by the selection of participants in our trial (age range, 30–50 years; no history of cardiac disease; no competitive sports), which is in accordance to Karlstedt et al.

LV and RV ejection fraction in our study did not alter with training. This finding corresponds to results of previous echocardiographic and CMR imaging studies that showed that even dramatic changes in training loads do not influence this index of integrated ventricular systolic function at rest. Therefore, we conclude that the increase in stroke volume in the HI(I)T group is attributable to the larger EDV of hypertrophied ventricles, despite higher end-systolic volume.

For the assessment of myocardial deformation, we focused on circumferential strain analysis as radial strain has been shown to be relatively imprecise because only a small number of tags span the myocardial wall. Circumferential strain values at systole in our study ranging from −10% to −25% are in agreement with the results of previous studies in healthy subjects. Postinterventional decrease of Ecc in the HI(I)T group is probably related to a physiological process with transient myocardial adaptation leading to enhanced cardiac structure and function. This is in agreement with previously published cross-sectional studies reporting transient functional cardiac abnormalities on echocardiography and elevation of cardiac biomarkers after completion of intensive endurance races, which resolve within 1 week.

**Limitations**

For a methodical point of view, there might be some selection bias because we did not use the intention-to-treat principle. However, the primary intention of this exercise study was to reproduce a scenario with data of motivated subjects that are able or willing to select this intense and frequent type of intervention to individually improve health and performance.

By selecting volunteers who applied for high-intensity interval training, there might be some overestimation of study results. We performed CMR imaging only at the beginning and end of the training or waiting period, so we do not have information about specific time-dependent effects on cardiac adaptation. Because most of the participants continued running after the training period, reversibility of myocardial adaptation could not be tested. The long-term dynamics of myocardial adaptation need to be addressed in further studies. We did not perform CMR imaging with treadmill or pharmacological stress, which in part may explain the relatively wide range in end-systolic volume. Including only male subjects in our study, sex-specific cardiac changes could not be investigated. Finally, we did not perform a direct comparison to the effects of other types of training (eg, resistance training) to describe differences in cardiac adaptation.

**Conclusions**

A relatively short period of HI(I)T in previously untrained men is associated with significant changes in cardiac atrial and ventricular morphological characteristics and function, as measured with CMR imaging. These findings correlate with improvements in parameters of endurance capacity without pathological features of cardiac adaptation.

**Acknowledgments**

We thank Andreas Greiser for technical support, Pierre Croisille for providing InTag-software, and Joost Kuijer for providing the prototype tagging sequence.

**Sources of Funding**

The study was supported by a research grant from Bayer Healthcare, Leverkusen.
Disclosures

Drs. Scharf and Lell received a research grant from Bayer-Healthcare, Leverkusen. The other authors report no conflicts.

References


---

**CLINICAL PERSPECTIVE**

A relatively short period of high-intensity (interval) training in previously untrained middle-aged men leads to significant physiological changes in cardiac atrial and ventricular morphology and function, which are closely correlated to improvements in parameters of endurance capacity. No association with training-induced pathological features of cardiac adaptation has been found.
Myocardial Adaptation to High-Intensity (Interval) Training in Previously Untrained Men With a Longitudinal Cardiovascular Magnetic Resonance Imaging Study (Running Study and Heart Trial)


_Circ Cardiovasc Imaging_. 2015;8:
doi: 10.1161/CIRCIMAGING.114.002566

_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/8/4/e002566

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Imaging_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Cardiovascular Imaging_ is online at:
http://circimaging.ahajournals.org/subscriptions/