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Original Article

Myocardial fatigue in recreational marathon runners: A speckle-tracking echocardiography study

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ABSTRACT

Background: Prolonged aerobic exercise such as marathon running produces supraphysiological hemodynamic stress that can potentially affect the athlete's cardiac homeostasis. While cardiac structural and functional adaptations in professional athletes are well characterized, only a limited information is available for recreational runners undergoing this supraphysiological stress.

Methods: Premarathon and post-marathon echocardiography was performed in 50 recreational marathon runners [age 40.8 ± 7.5 years, 44 (88%) males; running distance 42.195 km]. All the runners received 4-month training for the marathon. The baseline echocardiogram and N-terminal B-type natriuretic peptide (NT-proBNP) were obtained before training, whereas the post-marathon study was performed within 10 days (7.27 ± 0.92 days) of completion of marathon. Two-dimensional speckle-tracking echocardiography was used for characterizing the changes in myocardial mechanics.

Results: There was a significant reduction in heart rate post-marathon, whereas the levels of NT-proBNP increased significantly (86.0 ± 9.5 pg/ml vs 106.5 ± 24.2 pg/ml, $p = 0.001$). The left ventricular (LV) end-diastolic volume (61.8 ± 16.5 ml vs 72.8 ± 5.1 ml, $p < 0.001$), LV mass (120.2 ± 30.0 gm vs 160.3 ± 43.0 gm, $p < 0.001$), and LV ejection fraction (64.9 ± 5.6% vs 72.0 ± 5.7%, $p < 0.001$) also increased significantly. However, there was a significant attenuation in LV global longitudinal (−19.3 ± 2.71% vs −16.5 ± 4.6%, $p = 0.003$) and circumferential strain (−17.2 ± 2.41% vs −15.2 ± 2.6%, $p = 0.001$) post-marathon. The LV global radial strain showed a nonsignificant reduction.

Conclusion: Recreational marathon runners have reduced longitudinal and circumferential shortening of the left ventricle with elevation of NT-proBNP. However, the LV ejection performance remains maintained because of an increase in the LV end-diastolic volume and mass. These changes suggest the possibility of "myocardial fatigue" occurring in response to supraphysiological hemodynamic stress of marathon running.

1. Introduction

Exercise provides many documented health benefits while physical inactivity is a leading risk factor for cardiovascular morbidity and mortality.[1] The amount of physical activity required to achieve these benefits is relatively modest and is equivalent to jogging at a pace of 15 min per mile for 20–30 min daily. The amateur running events such as marathon and half-marathon are becoming increasingly common nowadays. These events expose the runners to a volume and intensity of exercise that is at least five- to 10-fold greater than the general recommendations for physical activity. Such intense exercises cause supraphysiological hemodynamic stress and can potentially affect the runners' cardiac homeostasis.

There have been an emerging number of reports suggesting that intense exercise may have an adverse impact on an otherwise normal heart.[2] These data are now mostly available for elite athletes.[2,3] Studies have reported biochemical and functional cardiac changes, including elevation in cardiac troponin I and B-type natriuretic peptide (BNP) as well as left ventricular (LV) wall motion abnormalities on echocardiography, soon after completion of endurance races of various sporting disciplines.[3–5] Also, effects of

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acute dysfunction have been recently reported post-marathon in elite runners.[5] A number of case reports and cohort descriptions have shown that supraphysiological exercise causes changes in the left ventricle in elite athletes and may even predispose them to ventricular tachycardia and sudden cardiac death.[6,7] However, there is a paucity of information about the cardiac structural and functional changes in recreational runners who undertake this supraphysiological stress of marathon running.

In the present study, we aimed to describe comprehensively the extent of myocardial injury in recreational runners after a full marathon race. To achieve this, established biochemical measures of myocyte damage and cardiac function [N-terminal proBNP (NT-proBNP)] as well as comprehensive echocardiographic measurements were used.

2. Methods

2.1. Study population

This was a prospective study conducted at a tertiary care hospital in central India from September 2013 to January 2014. Fifty recreational runners from the "Orange City Runners Group" who had never participated in any running event volunteered to participate in this study. They were minimally active and never participated in any sport-related activity before the study. They were due to participate in a full marathon (running distance 42.195 km) and were provided 4 months'supervised, structural, physical training before the event. The training involved stretching and aerobic exercises for 1.5 h a day, 5 days a week.

All those who had systemic hypertension, diabetes mellitus, any pre-existing cardiac illness (echocardiographic evidence of regional or global wall abnormalities, atrial fibrillation, valvular heart disease, cardiomyopathy, and so forth), renal disease, chronic obstructive airway disease, and active systemic infection were excluded. Written informed consent was obtained from all the participants, and the study was approved by the institutional ethics committee.

2.2. Study workflow

The study included two visits for the recreational runners. They were evaluated once before the start of 4-month training. The second evaluation was carried out within 10 days (7.27 ± 0.92 days) of completing the full marathon. During each visit, the participants underwent clinical and biochemical evaluation and a comprehensive echocardiographic examination. The clinical evaluation included anthropometric measurements (height, weight, and body surface area), measurement of heart rate and blood pressure (BP), and a general physical examination. Biochemical examination included measurement of NT-proBNP. Venous blood was used to analyze NT-proBNP using a rapid fluorescence immunoassay (Biosite Diagnostics, San Diego, USA). The laboratory lower limit for detection of NT-proBNP was >5 pg/l.

2.3. Echocardiography

At each visit, all participants underwent a comprehensive echocardiographic examination as per recommendations of the American Society of Echocardiography.[8,9] The echocardiographic examination was performed in the left lateral decubitus position, using a commercially available ultrasound transducer and equipment (2.5–4.0 Mhz transducer, Vivid E9; GE Vingmed Ultrasound AS, Horten, Norway). A single experienced operator performed all the image acquisitions.

Basic measurements included LV wall thickness, LV internal diameter, and left atrial (LA) anteroposterior dimension obtained from the parasternal long-axis view. LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) and ejection fraction (EF) were derived from the apical four- and two-chamber views using the biplane Simpson's method. LA volume was estimated by using biplane area-length method and indexed to body surface area. LV mass was calculated using the cubed method recommended by the American Society of Echocardiography.[8]

Conventional pulsed-wave interrogation of transmitral and LV outflow tract was performed according to the existing recommendations.[9] Early (E) and late diastolic (A) mitral inflow velocities were recorded. Pulsed-wave tissue Doppler imaging (TDI) was performed to measure the medial early diastolic mitral annular velocity (e′).

2.4. Speckle-tracking echocardiography

For speckle-tracking echocardiography (STE), standard two-dimensional gray-scale images of the left ventricle were obtained from the apical two-, three-, and four-chamber views as well as the parasternal short-axis views at the basal, mid, and apical level. The images were obtained during end-expiratory breath-hold at a frame rate of 50–80 frames/sec. All the images were transferred to a workstation for further offline analysis.

The offline analysis was performed using the automated EchoPAC PC software, version 112 (GE Healthcare, Chalfont St. Giles, United Kingdom). Longitudinal strain (LS) was derived from the apical two-, three-, and four-chamber views, whereas circumferential strain (CS) and radial strain (RS) were calculated from the three short-axis views. For each view, LV endocardial border was manually traced in the end-systolic frame. The software then automatically divided the entire circumference of the LV into equal segments and generated myocardial strain curves by frame-by-frame tracking of the natural acoustic markers throughout the cardiac cycle. From these curves, peak-systolic strain curves were recorded for each of the myocardial segments and averaged to derive a global value (GLS, GCS, GRS, respectively), which was used for the analysis.

All strain measurements in the present study were performed by a single observer who was blinded to the timing of the study. Intra-observer variability for the same operator for LV strain measurements in healthy volunteers has already been reported previously.[10]

2.5. Statistical analysis

The data on various clinical, conventional echocardiographic, and strain parameters were summarized using mean and standard deviations or as numbers and percentages. Paired *t*-test was used for comparing baseline values with post-marathon values. A *p*-value <0.05 was considered statistically significant. All the analyses were performed using SPSS version 18.0 (IBM SPSS, Inc.) statistical software.

3. Results

The baseline clinical and echocardiographic characteristics of the participants before the training for marathon (before marathon) are shown in Table 1. The mean age of the study participants was 40.8 ± 7.5 years and 44 (88%) were males. The average heart rate was 74.6 ± 6.4 beats/min and the average systolic and diastolic BP were 123 ± 10 mmHg and 79 ± 5 mmHg, respectively. The mean body mass index was 26.3 ± 3.6 kg/m^2.

3.1. Clinical and biochemical characteristics before and -after marathon

The clinical and biochemical characteristics of the participants before the training for marathon and -marathon are summarized in

Table 1
Premarathon clinical and echocardiographic characteristics in the study population.

Characteristics	Overall (n = 50)	Men (n = 44)	Women (n = 6)
Age (years)	40.8 ± 7.5	40 ± 6.8	46.3 ± 10.6
Weight (kg)	75.0 ± 10.7	76.8 ± 9.7	62.5 ± 8.6
Height (m)	1.69 ± 0.1	1.71 ± 0.08	1.53 ± 0.09
Body mass index (kg/m^2)	26.3 ± 3.6	26.3 ± 3.6	26.8 ± 4.0
Heart rate (beats/min)	74.6 ± 6.4	74.4 ± 5.8	76.0 ± 10.2
Systolic BP (mmHg)	123 ± 10	124 ± 10	117 ± 10
Diastolic BP (mmHg)	79 ± 5	79 ± 5	78 ± 4
Left atrial volume index (ml/m^2)	22.8 ± 6.4	22.4 ± 6.3	27.7 ± 5.3
IVSd (cm)	0.93 ± 0.15	0.93 ± 0.15	0.92 ± 0.17
LVEDV (ml)	61.4 ± 15.3	63.2 ± 14.4	48.1 ± 16.1
LVESV (ml)	21.8 ± 7.2	22.5 ± 7.0	17.3 ± 7.4
LVEF (%)	64.7 ± 5.9	64.7 ± 6.1	64.7 ± 4.7
LV mass (gm)	118.5 ± 29.7	119.8 ± 29.1	108.9 ± 34.6
Mitral E (m/s)	89.5 ± 16.0	87.4 ± 14.7	104.0 ± 18.0
Mitral A (m/s)	59.7 ± 16.0	58.0 ± 15.5	71.3 ± 16.0
Mitral E/A	1.57 ± 0.39	1.59 ± 0.40	1.49 ± 0.26
Mitral annular e′ (cm/s)	10.5 ± 2.3	10.4 ± 2.2	11.0 ± 2.5
E/e′ ratio	9.0 ± 2.2	8.8 ± 2.0	10.0 ± 3.2

All values are expressed as mean ± standard deviation.
A, late diastolic mitral inflow velocity; BP, blood pressure; E, early diastolic mitral inflow velocity; e′, early diastolic mitral annular velocity; E/A, ratio of early to late diastolic mitral inflow velocity; E/e′, ratio of early diastolic mitral inflow to mitral annular velocity; IVSd, diastolic interventricular septum thickness; LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume.

Table 2. The heart rate significantly decreased from baseline to post-marathon (74.1 ± 6.4 beats/min vs 64.5 ± 7.6 beats/min, $p < 0.001$), but there was no significant change in BP. There was a significant rise in NT-proBNP levels from premarathon to post-marathon period (86.0 ± 9.5 pg/ml vs 106.5 ± 24.2 pg/ml, $p = 0.001$) (normal range for the laboratory 0–125 pg/ml).

3.2. Conventional echocardiographic measurements before and post-marathon

The LVEDV (61.8 ± 16.5 ml vs 72.8 ± 5.1 ml, $p < 0.001$), LV mass (120.2 ± 30.0 gm vs 160.3 ± 43.0 gm, $p < 0.001$), and LVEF (64.9 ± 5.6% vs 72.0 ± 5.7%, $p < 0.001$) increased significantly -marathon, although there was no significant change in LVESV (Table 2). As compared to baseline, there was a reduction in early diastolic mitral E velocity after marathon (89.8 ± 17.1 cm/sec vs 80.1 ± 17.0 cm/sec, $p = 0.001$). However, there was no significant difference in the ratio of mitral E to e′, suggesting that LV filling pressures did not increase post-marathon. LA volume index decreased from 23.2 ± 6.1 ml/m^2 at baseline to 19.0 ± 6.5 ml/m^2 post-marathon.

Table 2
Clinical, biochemical, and conventional echocardiographic measurements before and -after marathon.

Parameter	Premarathon (n = 50)	Post-marathon (n = 50)	*p* value
Heart rate (beats/minute)	74.1 ± 6.4	64.5 ± 7.6	**<0.001**
Systolic BP (mmHg)	123 ± 11	120 ± 9	0.214
Diastolic BP (mmHg)	79 ± 5	79 ± 5	0.675
N-terminal probrain natriuretic peptide (pg/ml)	86.0 ± 9.5	106.5 ± 24.2	**0.001**
IVSd (cm)	0.94 ± 0.16	1.03 ± 0.20	**0.005**
LV mass (gm)	120.2 ± 30.0	160.3 ± 43.0	**<0.001**
LVEDV (ml)	61.8 ± 16.5	72.8 ± 5.1	**<0.001**
LVESV (ml)	21.9 ± 7.5	20.3 ± 3.7	0.191
LVEF (%)	64.9 ± 5.6	72.0 ± 5.7	**<0.001**
Mitral E (cm/s)	89.8 ± 17.1	80.1 ± 17.0	**0.001**
Mitral annular e′ (cm/s)	10.4 ± 2.1	10.1 ± 2.2	0.638
Mitral E/e′	9.1 ± 2.4	8.3 ± 2.7	0.227
Left atrial volume index (ml/m^2)	23.2 ± 6.1	19.0 ± 6.5	**0.01**

Bold values signify that STE revealed a reduction in both GLS and GCS from the baseline.
All values are expressed as mean ± standard deviation.
BP, blood pressure; E, early diastolic mitral inflow velocity; e′, early diastolic mitral annular velocity; E/e′, ratio of early diastolic mitral inflow to mitral annular velocity; IVSd, diastolic interventricular septum thickness; LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume.

3.3. LV myocardial mechanics before and post-marathon

Although the LVEF significantly improved at post-marathon stage, STE revealed a reduction in both GLS and GCS from the baseline (GLS: −19.3 ± 2.71% vs −16.5 ± 4.6%, $p = 0.003$ and GCS: −17.2 ± 2.41% vs −15.2 ± 2.6%, $p = 0.001$, respectively) (Table 3) (Fig. 1). However, there was no significant change in GRS (31.9 ± 7.4% at baseline vs 30.9 ± 1.3% post-marathon, $p = 0.422$).

4. Discussion

This study was designed to understand the impact of training and running a long-distance marathon on LV myocardial function in recreational runners. The major findings of our study were (1) intense and prolonged exercise in recreational runners results in an increase in NT-proBNP, LVEDV, and LV mass; (2) LV longitudinal and circumferential shortening is compromised; and (3) LVEF remains preserved despite impairment of myocardial mechanics, likely due to the increase in LVEDV. These findings extend the previous observations suggesting the possibility of “myocardial fatigue” occurring in response to supraphysiological hemodynamic stress of marathon running, even though overall LV ejection performance is maintained by a concomitant increase in LVEDV. This is the first study from Indian subcontinent looking at LV function in amateur runners.

Myocardial remodeling in response to exercise has been well documented among elite, competitive endurance athletes. Eccentric LV remodeling, right ventricular dilation, biatrial dilation, and supranormal diastolic function are well-recognized attributes of the endurance athletes' hearts.[11–14] To what degree these adaptations occur in recreational runners also, who typically perform far less exercise than elite competitors, has not been well documented till now.

Our study demonstrated a significant rise in NT-proBNP levels after running the marathon in recreational runners. A similar rise in NT-proBNP has been reported by various authors in earlier studies.[15–18] In a systematic review regarding the pattern of BNP and NT-proBNP rise in runners, Vilela et al[18] reported that the post-running values exceeded the upper reference limit in up to a third of runners. The rise in natriuretic peptides has been reported in other forms of recreational endurance activities also, such as cycling.[19] Furthermore, it has been shown that the amount of rise of cardiac biomarkers is directly related to the distance of marathon run.[20] The elevation in NT-proBNP levels after running persists for a few days. Frassl et al[21] reported elevated levels of NT-proBNP in female amateur marathoners up to 3 days after the marathon. In comparison, we found that the elevation in NT-proBNP levels could be detected until even 10 days after running the marathon. Various mechanisms have been postulated for this rise in natriuretic peptides. These include stimulation of integrins related to mechanical myocardial stretch, insult to the sarcolemmal membrane due to free radicals, altered pH, or the formation of membranous blebs secondary to myocardial ischemia.[22,23]

The effect of running on diastolic function in recreational runners has been reported in several previous studies.[16,24–27] These studies have consistently demonstrated an impairment in LV

Table 3
Speckle-tracking echocardiography–based left ventricular myocardial strain measurements before and after -marathon.

Parameter	Premarathon (n = 50)	Post-marathon (n = 50)	*p* value
Left ventricular global longitudinal strain (%)	−19.3 ± 2.71	−16.5 ± 4.6	**0.003**
Left ventricular global circumferential strain (%)	−17.2 ± 2.41	−15.2 ± 2.6	**0.001**
Left ventricular global radial strain (%)	31.9 ± 7.4	30.9 ± 1.3	0.422

Bold values signify that STE revealed a reduction in both GLS and GCS from the baseline.

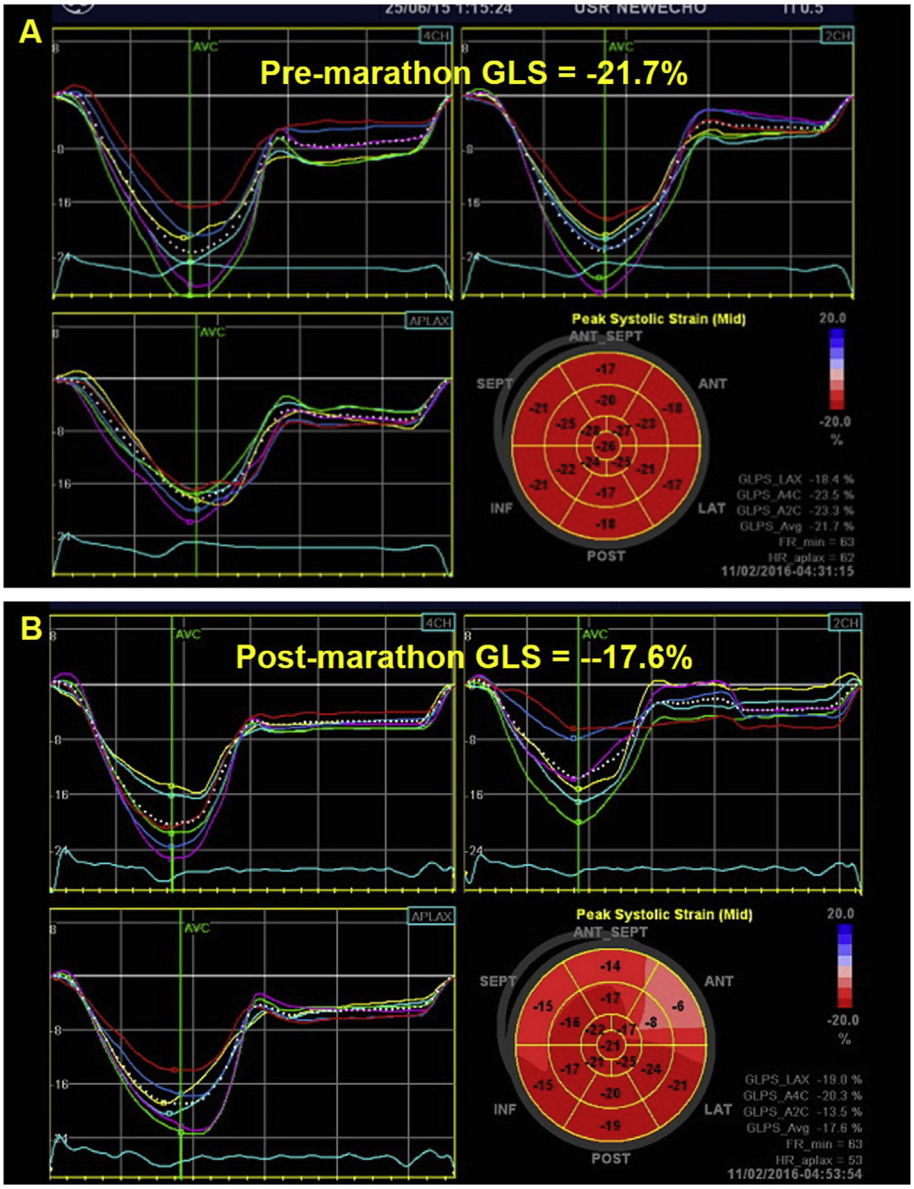

Fig. 1. An illustrative case demonstrating a reduction in global longitudinal strain at post-marathon stage. (A) Before marathon; (B) -after marathon. GLS, global longitudinal strain.

diastolic function after prolonged exercise of more than 2 h, manifesting in the form of a variable combination of reduced mitral E velocity, increased A velocity and E/A ratio, and unchanged or reduced e′ velocity. In our study also, we found a reduction in mitral E velocity, although there was no significant change in e′ velocity. It has been suggested that reduced LV preload contributes to the lower E velocity after prolonged exercise. Other mechanism to explain this can be that due to decrease in heart rate, there is an increase in diastolic interval time. This causes the same amount of LV filling to occur over a longer period of time, resulting in lower blood flow velocity. However, other investigators have shown that the altered loading conditions alone do not fully explain the impairment of LV diastolic function in this setting and myocardial dysfunction seems to play an important role.[28–30] Given the importance of circumferential LV myocardial relaxation in the generation of intraventricular suction gradients during the early LV filling, it is likely that the impaired muscle mechanics underlie the attenuation of transmittal filling, as seen in our subjects also. The LA volume decreased in our study, which is contrary to what one would have expected in view of the impairment of LV diastolic

function. However, it is likely that the reduction in LA volume was mediated by increased LV stroke volume resulting in better LA unloading.

The impact of amateur endurance exercise on LV systolic function has also been assessed in several previous studies.[15,17,24,25,31–38] However, the results have been less consistent as compared with the findings about LV diastolic function. The marked heterogeneity among various studies, with differences in the study population; the nature, intensity, and duration of exercise; and the parameters used for assessment of LV systolic function, seems to contribute to this inconsistency in the observations.

Most of the previous studies evaluating the impact of running on LV systolic function have used LVEF as the measure of LV systolic function,[15,31,32] with the more recent studies using tissue velocity and strain imaging also. Overall, these studies have shown that the LVEF is not significantly altered immediately after a bout of running. George et al[31] studied 35 runners participating in London marathon and found no change in LVEF following the race. Similar findings were noted in another study which included 22 marathoners.[32] In comparison, Knebel et al studied 89 female runners of the Berlin Marathon and found improvement in LVEF immediately after the marathon. In our study also, we found an increase in LVEF post-marathon.[15]

The studies evaluating the impact of different intensities of endurance exercise have shown that while relatively short duration of exercise does not impair LV systolic function, more prolonged exercise does cause a reduction in LV systolic function.[24,33] The impact is more marked in less trained individuals. Middleton et al[24] performed a meta-analysis of 23 such studies evaluating the impact of different levels of exercise. It was found that the reduction in LVEF occurred only in response to ultraduration exercise or among untrained individuals participating in moderate-duration exercise.

Unlike the effect on LVEF, most of the studies have shown a reduction in LV LS after running. In a study involving Boston marathoners, Neilan et al showed that while LVEF was not affected, LV septal strain was found to be reduced in the participants. The reduction persisted for almost 1 month after completion of marathon.[25] This study used TDI-based strain, which has several limitations as compared with two-dimensional strain. However, the more recent studies using STE-based two-dimensional strain and have also shown reduction in LV LS after long-distance running.[17,33,36,37]

A major advantage of STE is that it permits comprehensive assessment of LV myocardial mechanics. However, very few studies have previously explored the effects of recreational running on myocardial mechanics. George et al[38] studied 19 runners participating in Comrades marathon (distance 89 km). It was found that CS and RS significantly decreased after the race. The LS also decreased in some myocardial segments but not globally. In another study, STE was performed in 25 athletes after ultramarathon (distance 160 cm).[17] Peak strain was significantly decreased in all planes, with the largest reduction occurring circumferentially. Similar reduction in all components of LV strain was demonstrated in yet another study involving triathletes.[36] Compared with these studies, we evaluated runners participating in less intense exercise and found a significant reduction in LS and CS with a nonsignificant reduction in RS. These echocardiographic changes in the present study provide functional confirmation of the LV dysfunction in recreational runners suggested by the biochemical abnormalities. The echocardiographic and biochemical results were thus complementary and consistent with each other.

The term “cardiac fatigue” has been coined to describe the impairment of LV myocardial function in response to endurance exercise.[25,34,35,39–41] The potential mechanisms postulated for such postexercise attenuation of cardiac function are alteration in loading conditions, desensitization of beta-adrenoreceptors, oxidative stress, and pulmonary congestion.[33,42,43] These changes are known to recover after a variable period of time, ranging from a few days to 1 month.[4,25,41] Unfortunately, as we could not perform a late follow-up evaluation, we could not determine to what extent the cardiac alternations observed in our study participants were reversible with time.

Another limitation of our study was that the participants underwent cardiac evaluation at only two timepoints, which limited our ability to assess temporality of the cardiac changes observed in this study. As a result, we could not differentiate whether the changes in strains were due to training for marathon or running the marathon or both. More studies, involving imaging immediately before and after the marathon at 30 min, 6 h and 10 days after race, are needed to better understand this phenomenon. Future studies will also have to look at the impact of recreational running on other cardiac chamber (specifically, the right ventricle); the dose-effect relationship between the duration of running and the changes in GLS; and the amount of training required to mitigate the adverse impact of running.

5. Conclusion

Recreational marathon runners have reduced longitudinal and circumferential shortening of the left ventricle with elevation of NT-proBNP. These findings extend the previous observations suggesting the possibility of “myocardial fatigue” occurring in response to supraphysiological hemodynamic stress of marathon running. However, the LV ejection performance remains maintained because of an increase in the LVEDV and LV mass.

6. Perspective

The increasing popularity of recreational marathon running coupled with sporadic incidents of cardiac mishaps during such events has necessitated better delineation of cardiac structural and functional alterations occurring in response to such forms of supraphysiological stress among nonprofessional runners whose cardiovascular system is not well adapted to such stress. Future studies are needed to understand as to how many months training is needed for recreational runners when GLS does not decrease after vigorous exercise. Also, a large study with mixed population of elite and recreational runners is needed to provide more information about the interesting topic of athlete's heart. Our study demonstrated an impairment of LV myocardial mechanics in healthy individuals participating in full marathon, one of the commonest forms of recreational marathon events. Further studies are needed to better define the temporality, underlying mechanisms, and reversibility of such myocardial dysfunction.

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Conflict of interest

All authors have none to declare.

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