

Original Article



Effects of Super-ultramarathon Running on Cardiac Structure and Function in Middle-aged Men

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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

BACKGROUND: It remains unclear whether high-intensity exercises result in deformities and reduced function of cardiac muscle. This study hypothesized that participants in a six-day super-ultramarathon (622 km) with sleep deprivation would show serial changes in cardiac structure and function pre- and post-marathon and during the recovery period.

METHODS: Cardiac structure and function of middle-aged male volunteers were assessed through echocardiography at pre- and post-marathon, and at 2 recovery periods with a three-day interval.

RESULTS: There were no differences in left ventricular end-diastolic and end-systolic dimensions, and end-diastolic volume between pre- and post-marathon. Interventricular septum thickness, left ventricular posterior wall thickness, left ventricular mass, and mass index significantly increased at post-marathon compared to pre-marathon, which decreased during the recovery period. Stroke volume and left ventricular ejection fraction significantly decreased at post-marathon, while both values increased during the recovery period. There were no significant differences in indices for left ventricular relaxation at each assessment period.

CONCLUSIONS: An extreme endurance exercise could induce temporary myocardial hypertrophy and contractility reduction.

Keywords: Ultra-marathon; Cardiac function; Middle-age

INTRODUCTION

Regular physical exercise has positive effects against cardiovascular diseases, while chronic physical exercise, especially in athletes, causes changes in myocardial structure depending on the type of sport. In general, athletes who require endurance training exhibit a more noticeable increase in the diameter of the left ventricle and greater stroke volume (SV), compared to athletes focused on resistance training.¹⁻⁴⁾ In contrast, athletes who focus on resistance training exhibit smaller inner diameter and thicker ventricle wall, compared to athletes focused on endurance training. More specifically, endurance-trained athletes are known to exhibit better diastolic compliance compared to other athletes.⁵⁾ These chronic adaptations of the heart based on exercise type do not result in severe complications.⁶⁾ Nevertheless, even well-trained professional athletes sometimes experience temporary changes in myocardial structure or reduced myocardial function during high-intensity

training. In other words, ultramarathons or triathlons, who are exposed to long-term physical exercise, have been reported to induce reduced contractility and relaxation of left ventricle, along with myocardial expansion and increased SV.^{7,42} Cardiac dysfunction caused by one-time high-intensity training has been introduced as exercise-induced cardiac fatigue, however, no clear mechanism has been described until now.¹³ In a recent study involving long-distance and high-intensity training, cardiac function of the participants in a 330-km mountain ultramarathon event were examined through echocardiography. However, the study did not have detailed assessments of the participants, including the thickness and mass of the myocardium, as well as its recovery period. Moreover, it remains unclear whether high-intensity exercises result in deformities and reduced function of cardiac muscle. In our study, for the first time, we assessed the changes in myocardial structure and function of the participants in a 622-km super-ultramarathon with sleep deprivation. The assessments were made at pre- and post-marathon, as well as during two recovery periods with a three-day interval (days 3 and 6).

METHODS

Subjects and study protocol

Runners aged between 40 and 59 who had previously completed at least one ultramarathon event (200 or 308 km) were eligible for the study. The subjects were required to reach each checkpoint (50 km apart), where they were given water and food, within a given time limit. Exercise habits and medical history of eligible subjects were obtained prior to the study using a survey questionnaire, and cardiopulmonary fitness test were performed prior to study participation.

The method of super-ultramarathon race method in this study is that runners who participated in this study must complete 622 km within 150 hours and can receive food, drinks and massages from volunteers at check points every 50 km, and clothes and necessities from family members. Other meals and drinks in the main course of marathon race should be resolved by themselves. Abandoned midwayers could be contacted by phone to the person closest to the checkpoint area.

Subjects with hypertension, diabetes, cardiovascular disease, stroke, or liver diseases were excluded. Eligible participants underwent the Bruce protocol and echocardiographic examinations. Immediately post-completion and on recovery days three and six, echocardiography was performed again. This study obtained approval from the local Institutional Review Board, and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's Human Research Committee. And all participants provided written informed consent.

Graded exercise testing

The Bruce protocol was used for the exercise load testing. For the actual event, a treadmill (Medtrack ST 55, Quinton Instrument Co., Boston, MA, USA), a respiratory gas analyzer (QMC, Quinton Instrument Co.), a real-time 12-channel ECG monitoring system (Q4500, Quinton Instrument Co.), and an automatic blood pressure and pulse analyzer (Model 412, Quinton Instrument Co.) were used. At rest and maximum exercising, hemodynamic parameters including heart rate and blood pressure were measured. Respiratory gas analysis was performed to measure oxygen consumption and respiratory exchange ratio. In

addition, the rating of perceived exertion was recorded based on Borg's scale, indicating the degree of fatigue. The completion standard of the examination was based on the ACC/AHA guidelines.¹⁴⁾

Echocardiographic measurements

Echocardiography was performed pre- and immediately post-marathon, as well as during the recovery period on days three and six, by an expert echocardiographer. Measurement at a stable condition before the start was performed five minutes after stabilization, and post-marathon measurements were made after 20 minutes of adequate stabilization. To measure the myocardial structure and function under stable conditions, the Sequoia 256 (Acuson, Mountainview, CA, USA) cardiac ultrasound machine and 5-MHz transducer were used. Myocardial structure and function were assessed using an M-mode echocardiogram, whereas the measurements of left ventricular end-diastolic dimension (LVEDD), posterior wall thickness (LVPW), interventricular septum thickness (IVS), left ventricular end-diastolic volume (LVEDV), ejection fraction (LVEF), SV, and cardiac output were taken according to the American Society of Echocardiography guidelines. Left ventricular mass (LVM) was calculated with a corrected American Society of Echocardiography method using a cube formula. LVM index (LVMI) was calculated after dividing by the body surface area. To measure cardiac relaxation, pulsed Doppler tissue imaging was used to measure peak velocities of early filling (E) and atrial filling (A), deceleration time (DT), early diastolic annulus velocity (E'), and late diastolic annulus velocity (A').

Statistical analysis

All data were represented using mean and standard deviations, and statistical analysis was performed using the S-Link statistical analysis package. To assess the differences among the four repeated measurements, a Friedman test (non-parametric version of one-way repeated measures ANOVA) was performed. For post-hoc analysis of the difference in measurement data between pre- and post-marathon or between time points, the matched samples Wilcoxon signed-rank test was performed. Given that there were four different time points (pre-marathon, post-marathon, and days three and six of the recovery period), the assessment was performed eight times. To correct for errors from the post-hoc analysis differences, Bonferroni correction was performed. All statistical analyses were conducted using SPSS statistical software, version 19.0 (IBM Corp., Armonk, NY, USA), and statistical significance was set at $p < 0.05$ (two-sided).

RESULTS

Among 15 patients who completed 622-km super-ultramarathon and pre- and post-marathon echocardiographic assessment, 8 underwent additional echocardiography during recovery period (**Figure 1**). A mean age was 51.7 years, and the other demographics and cardiorespiratory fitness characteristics are summarized in **Table 1**.

In the assessment of left ventricular structure, LVEDD, left ventricular end-systolic dimension (LVESD), and LVEDV did not exhibit differences at different time points. However, IVS, LVM, and LVMI were significantly higher at post-marathon than pre-marathon, whereas those values were significantly reduced on days three and six of the recovery period compared to the post-marathon (**Table 2** and **Figure 2** and **3**). For the indices of left ventricular contractility, SV and LVEF were significantly lower in the post-marathon assessment compared to the

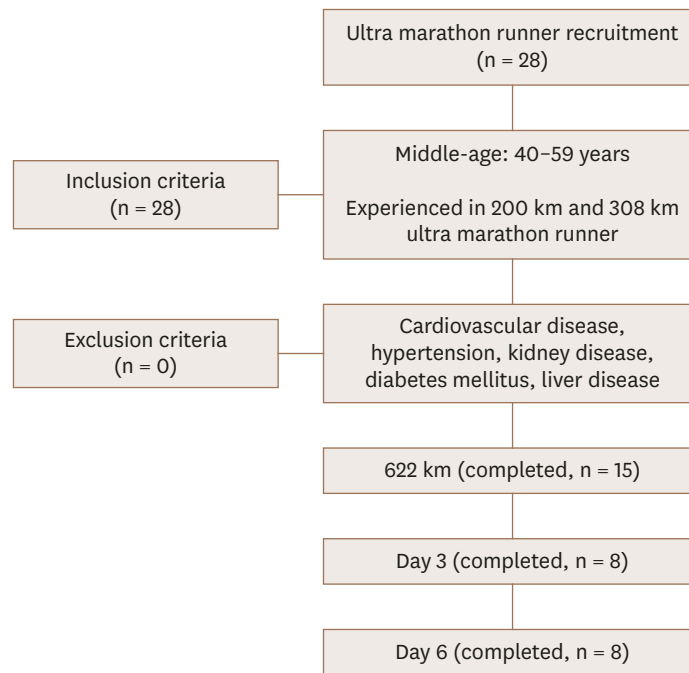


Figure 1. Flow chart of the study population.

Table 1. Demographics and cardiorespiratory fitness characteristics

Variables	Mean ± SD
Age (years)	51.7 ± 4.9
Gender (male, %)	100
Height (cm)	170.7 ± 4.2
Weight (kg)	71.1 ± 5.4
Body mass index (kg/m ²)	24.3 ± 1.5
Marathon experience (months)	98.7 ± 24.1
No. of participated marathons	57.8 ± 17.0
Race completion time (minutes)	7,958.1 ± 1,430.0
VO _{2max} (mL/kg/min)	50.7 ± 7.6
Heart rate _{rest} (beats per minute)	63.1 ± 9.6
SBP _{rest} (mmHg)	125.8 ± 12.0
DBP _{rest} (mmHg)	81.2 ± 5.8
Heart rate _{max} (beats per minute)	175.8 ± 6.8
SBP _{max} (mmHg)	218.7 ± 17.8
DBP _{max} (mmHg)	73.7 ± 10.2

pre-marathon. SV increased significantly on the day six of the recovery period, while LVEF showed significant increase earlier on the day three of the recovery period. Values indicating left ventricular relaxation, including DT, E, A, E/A ratio, E', A', E'/A' ratio, and E/E' ratio, did not exhibit significant differences among the different time points (**Table 2**). The changes in each variable between pre- and post-marathon were as follows: IVS, LVPW, LVM, and LVMI increased by 27.7%, 19.2%, 32.1%, and 35.0%, respectively, whereas SV and EF decreased by 19.9% and 16.5%, respectively (**Figure 4**).

Table 2. Echocardiographic measurements at each assessment period

	Pre-marathon (n = 15)	Post-marathon (n = 15)	Recovery day 3 (n = 8)	Recovery day 6 (n = 8)
LVEDD (mm)	50.9 ± 3.8	50.7 ± 4.7	51.4 ± 3.8	51.6 ± 3.7
LVESD (mm)	32.9 ± 3.3	32.9 ± 6.3	31.8 ± 3.4	31.7 ± 3.4
IVS (mm)	9.5 ± 1.1	12.1 ± 1.1*	10.1 ± 1.0†	9.6 ± 1.0†
LVPW (mm)	10.1 ± 1.3	12.0 ± 1.1*	10.4 ± 0.8†	9.7 ± 0.9†
LVEDV (mL)	124.9 ± 22.4	123.6 ± 26.4	127.2 ± 22.1	128.3 ± 20.4
SV (mL)	90.3 ± 11.5	71.6 ± 9.6*	85.9 ± 14.2	87.4 ± 13.1†
LVEF (%)	70.4 ± 5.6	58.8 ± 7.3*	67.1 ± 4.4†	68.3 ± 5.1†
DT	213.6 ± 24.0	179.0 ± 52.4	219.3 ± 54.1	197.7 ± 32.3
E-velocity (cm/s)	68.8 ± 21.6	56.8 ± 9.2	67.0 ± 17.6	53.6 ± 12.0
A-velocity (cm/s)	59.4 ± 20.9	62.7 ± 22.6	67.6 ± 21.7	64.8 ± 15.6
E/A ratio	1.1 ± 0.2	0.9 ± 0.3	0.9 ± 0.2	0.8 ± 0.2
E'-velocity (cm/s)	8.7 ± 1.9	8.2 ± 1.5	9.1 ± 3.0	9.1 ± 2.2
A'-velocity (cm/s)	8.9 ± 1.2	9.0 ± 1.1	9.6 ± 2.3	10.2 ± 1.3
E'/A' ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.8 ± 0.1
E/E' ratio	8.1 ± 3.2	7.0 ± 1.6	7.7 ± 3.1	6.2 ± 1.4

Values are presented as mean ± SD.

A: peak velocity of atrial filling, A': late diastolic annulus velocity, DT: deceleration time, E: peak velocity of early filling, E': early diastolic annulus velocity, IVS: left ventricular septum thickness, LVEDD: left ventricular end-diastolic dimension, LVEDV: left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction, LVESD: left ventricular end-systolic dimension, LVPW: left ventricular posterior wall thickness end-diastolic, SV: stroke volume.

*Significantly different from the pre-marathon measurement at $p < 0.05$; †Significantly different from the post-marathon measurement at $p < 0.05$.

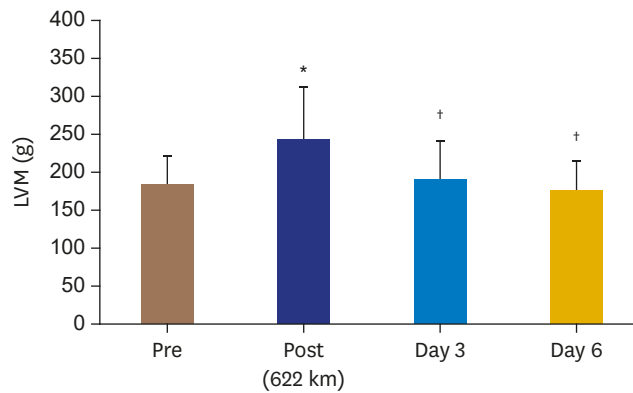


Figure 2. Left ventricular mass (LVM) at pre-, post-marathon, recovery day 3, and recovery day 6.

*Significantly different from the pre-marathon measurement at $p < 0.05$; †Significantly different from the post-marathon measurement at $p < 0.05$.

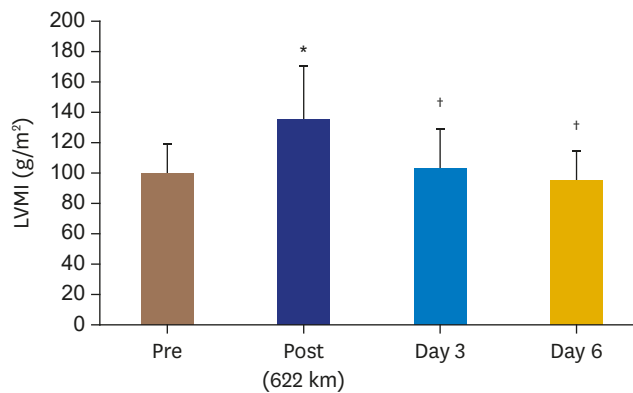


Figure 3. Left ventricular mass index (LVMI) at pre-, post-marathon, recovery day 3, and recovery day 6.

*Significantly different from the pre-marathon measurement at $p < 0.05$; †Significantly different from the post-marathon measurement at $p < 0.05$.

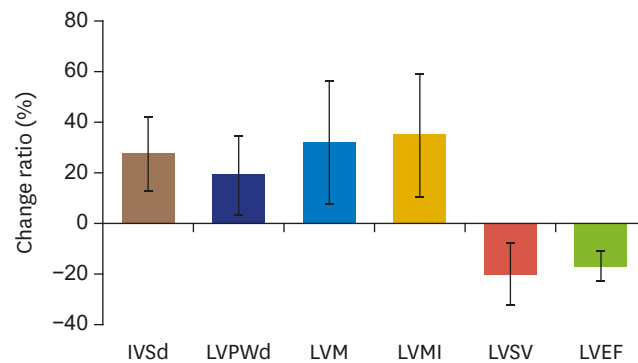


Figure 4. Changes in indices for left ventricular structure and contractility. IVSd: left ventricular septal thickness at end-diastole, LVEF: left ventricular ejection fraction, LVM: left ventricular mass, LVMI: left ventricular mass index, LVPWd: left ventricular posterobasal free wall thickness at end-diastole, LVSV: left ventricular stroke volume.

DISCUSSION

This study assessed changes in myocardial structure and function after the 622-km super-ultramarathon performed under high temperature and humidity and with sleep deprivation.

It is generally known that athletes who do resistance training have concentric hypertrophy with thicker LV, whereas athletes who focus on endurance training have eccentric hypertrophy with a greater inner diameter of the LV.^{5,6)} These phenomena are results of chronic adaptation to the physical training. More specifically, athletes with endurance training develop eccentric hypertrophy due to volume overload caused by moderately increased blood pressure and persistent systemic circulation.⁴⁾ The athletes who participated in this study are long-distance running experts, and the inner diameters of their ventricles in the systolic and diastolic phases immediately post-marathon were not significantly different from those pre-marathon. However, the thickness of the middle and posterior wall of the ventricle increased significantly immediately post-marathon, but returned to the normal range during the recovery period. The increased ventricular wall thickness resulted in a significantly increased ventricular mass. Although the evidence for ventricular hypertrophy caused by long-term, chronic training has been consistent,^{4,5,6,12)} acute studies on echocardiography have focused strictly on the ventricular function^{10,15,16)}; thus, unfortunately, it was difficult to compare our results to the outcomes of other studies.

In our study, the mean post-marathon ventricular mass was 242.7 g, which was increased by 32.1% compared to the mean pre-marathon ventricular mass of 182.0 g. This indicated mild ventricular hypertrophy compared to the normal range, but it became moderate hypertrophy when calculated using body surface area. Increased severity of ventricular hypertrophy due to long-term exercise is caused by the adaptation of the ventricle to an increased blood flow with a higher pulse rate and chronic exposure to pressure from blood and cardiac volume.⁶⁾ In other words, excessive hemodynamic circulation owing to the long-term marathon increases the production of free radicals, and the body becomes exposed to oxidative stress. This in turn stimulates immune cells to secrete cytokines, signaling myofibroblasts to produce procollagen. Eventually, these are cross-linked to form collagen, resulting in myocardial hypertrophy.^{17,19)} In our study, walking or running over 100 km per day and maintaining high cardiac volume pressure for just six days was sufficient to increase ventricular mass by 32.1%. Cardiac remodeling that occurs in athletes' hearts, such as left ventricular hypertrophy, is evidently an outcome that is observed

even with one week of excessive training. In addition, ventricular contractility of the subjects was characterized by temporary reduction of SV and LVEF caused by persistent left ventricular adjustment and consequent hypertrophy. The effect of high-intensity training on LVEF is thought to decrease after long-distance training, but there is an on-going debate, as other studies suggest no difference is observed.⁷⁾⁹⁾¹¹⁾¹²⁾¹⁵⁾²⁰⁾ In fact, Maufrais et al.¹⁰⁾ reported that SV was increased and EF was unchanged even after a 330-km mountain ultramarathon. In our study, the decreases in SV and LVEF after marathon were 19.9% and 16.5%, respectively, indicating a significant reduction in both measurements. The 622-km marathon is one of the longest distance events that takes place over a six-day time frame, and subjects exhibited extreme cardiac fatigue that was sufficient to cause reduced left ventricular contractility, which was accompanied by myocardial hypertrophy.

Meanwhile, the ventricular relaxation did not exhibit difference at any of the time points. A recent study on 330-km mountain ultramarathon participants also reported that ventricular relaxation did not change after performing strenuous exercises. According to the meta-analysis by Middleton et al.¹¹⁾, high-intensity, long-distance events such as marathons or Ironman tournaments have caused a significant reduction in E/A. Individuals with a certain level of LV hypertrophy often are accompanied with LV relaxation dysfunction,²¹⁾ yet there was no change observed in our study. These differences in relaxation dysfunction may occur because long-distance events over a longer time frame have a relatively low intensity, and thus do not have a significant effect on ventricular relaxation, compared to long-distance events over a short time frame. The subjects who completed a marathon or < 100-km events exhibited clearly increased levels of cardiac markers that indicate myocardial damage and myocardial pressure, whereas the subjects who completed a longer event (308 km) only had an increased level of NT-proBNP.²²⁻²⁴⁾ Longer distance results in lowered training intensity, and this may have different effects on the cardiac muscle. In the future, detailed echocardiography of myocardial structure and function and its association with cardiac markers based on the marathon distance should be analyzed. In addition, an observational study of the meaning and long-term outcome of this recurrent temporary myocardial hypertrophy and dysfunction is underway.

Limitations

A major limitation of our study was that we could not fully control the subjects' environment including meals, drinks, sleep, training intensity, and time limit for marathon completion to be uniform in all subjects. Second, this study included a small number of subjects. However, we believe this number is still valuable considering the extreme distance and low completion rate of the super-ultramarathon.

Conclusion

In this first-ever 622-km marathon event, the subjects exhibited increased interventricular and posterior wall thickness and mass of the left ventricle, along with decreased SV and LVEF. Although myocardial hypertrophy and contractile dysfunction were observed, ventricular relaxation dysfunction was not evident. All the post-marathon responses, including the thickness and mass of LV and reduced contractility, recovered within the six-day recovery period.

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