

Acute Effects of Prolonged Physical Exercise: Evaluation After a Twenty-Four-Hour Ultramarathon

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Abstract

Background: The consequences and risks of prolonged physical exercise are not well established.

Objective: To evaluate the effects of prolonged physical exercise on the participants of a 24-hour ultramarathon race.

Methods: Twenty male runners were selected for evaluation a day before and immediately after the race, where the athletes had to cover the most distance in 24 hours. Clinical, laboratory and echocardiographic data were obtained at both evaluations.

Results: Mean distance covered was 140.3 ± 18.7 km. Runners showed weight loss ($p < 0.001$) and decrease in systolic ($p < 0.001$) and diastolic ($p = 0.004$) blood pressure. Hematological changes were compatible with the physiological stress. Plasma levels of creatine phosphokinase strikingly increased post-race (163.4 ± 56.8 vs. 2978.4 ± 1921.9 U/L; $p < 0.001$) and was inversely correlated with distance covered: those who covered the longest distances showed the lowest CPK levels (Pearson $r = 0.69$, $p = 0.02$). After the race, 2 runners showed a slight increase in Troponin levels. One of them also had simultaneous decrease in left ventricular ejection fraction (coronary artery disease was subsequently ruled out). Basal echocardiography assessment had shown LV hypertrophy in one and increased left atrial volume in five runners. After the race, there was a decrease in E/A ratio ($p < 0.01$).

Conclusion: Prolonged physical exercise is associated with metabolic and cardiovascular alterations. Cardiac abnormalities found in our study suggest that cardiac fatigue may occur in this specific race modality. The long-term effect of these alterations, while maintaining the routine practice of prolonged strenuous physical activity, is still unknown. (Arq Bras Cardiol. 2013;100(1):21-28)

Keywords: Exercise; physical exertion; running; muscle fatigue.

Introduction

The regular practice of physical exercise is associated with beneficial effects on the control of risk factors and reducing cardiovascular mortality¹. There seems to be a positive association between dose and response to physical training, but the intensity from which there would be harmful effects on the cardiovascular system is still unknown.

Running is an increasingly popular type of sports practice worldwide. Each year, the number of events of this type of sport multiplies and the number of individuals who participate in these events increases significantly. This growing popularity, together with the constant pursuit of humans to overcome their limitations, gives rise to extremely challenging evidence. Consequently, there is increasing concern about the acute effects and possible risks that such activities can bring to the athletes. The very origin of the marathon is associated with the report of a case of sudden death.

The evidence that strenuous exercise can cause alterations in the metabolism and cardiovascular system are derived from several sporting events²⁻⁶. A meta-analysis of 26 studies demonstrated that troponin elevation occurs in approximately half of the participants of endurance tests, and this increase appears to be more common in shorter duration tests⁷. Moreover, the acute effects of continuous and prolonged physical activity remain poorly explored.

The ultramarathon is defined as a race with distance greater than the official marathon (42,195 meters) and may vary according to certain range or time limit. Studies evaluating the cardiovascular effects of different types of this modality are scarce. The aim of this study was to evaluate the metabolic and hematological effects and cardiovascular alterations induced by a 24-hour ultramarathon, of which goal is to travel the longest distance within this time period.

Methods

This study was approved by the research ethics committee (REC) of Pontifícia Universidade Católica do Paraná (PUC – PR) and the free and informed consent form (ICF) was obtained from each participant prior to study inclusion.

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Manuscript received February 21, 2012; revised manuscript August 30, 2012; accepted October 18, 2012.

The study was carried out at the “Ultramaratona 24 h – Corrotododia 2008” sports event, held in Curitiba, state of Parana, Brazil, on 05/17/2008. The broadcasting and initial information about the study were made available on the website of the event, along with the registration form. Runners who had interest in participating in the study were contacted by e-mail and sent an invitation letter and other information. The event had a total of 51 runners (nine women and 42 men).

Inclusion and exclusion criteria

We included only male runners with experience in at least one long-distance competition and no history of cardiopulmonary diseases. Exclusion criteria were: not completing the 24-hour race or not performing blood collection or echocardiogram at any of the two moments (pre-and post-race).

Study protocol

The race was held on an outdoor athletics track with 400 m, and every two hours the race athletes alternated the direction of the race. The alternation is performed for psychological reasons, primarily to avoid monotony and also physical reasons, preventing musculoskeletal unilateral overload. A research station was set up at the site of the event, with all the material needed for data collection. All athletes completed an identification questionnaire with information on health status and history of sports practice.

During the competition they had free access to fluids (water, soft drinks and sports drink beverages) and carbohydrate-rich food (fruits, noodles, mashed potatoes and sandwiches) available in support tents along the track.

Likewise, they were allowed to rest during the race for as long as necessary. However, the athletes had to complete the 24-hour race.

Clinical and laboratory assessment

The runners were submitted to clinical evaluation to obtain anthropometric data before and after the race. After weighing, at both moments, bioelectrical impedance was carried out in a tetrapolar device Maltron BF 906. For that purpose, the athlete was placed in the supine position on a stretcher, with the right foot and hand slightly away from the trunk. The distal electrodes of the feet were placed at the base of the middle toe, and the proximal ones between the medial and lateral malleoli. In the hands, the distal electrodes were placed at the base of the middle finger, with the proximal electrodes coinciding with the styloid process.

Venous blood samples were obtained the day before the race and immediately after. At each phase, 20 ml of blood were collected. The samples were immediately stored on ice and protected from light. In the laboratory, the blood plasma was separated by centrifugation at 3000 rpm for 15 minutes and stored in a freezer at - 20 °C until the analysis was performed. Each sample underwent complete blood count and analysis of urea, creatinine, creatine phosphokinase (CPK), creatine kinase-MB (CK-MB), potassium and cardiac troponin T (cTnT).

Echocardiography

Complete echocardiographic study (including two-dimensional, M-mode and Doppler) was performed the night before the race and immediately after it, at the same place where the event was held. The device used was an Agilent Sonos 5500, Philips, equipped with a 2.5 MHz transducer. All images were obtained by the same echocardiographer (SHB) and analyzed during runtime.

The following linear measurements were obtained by the M mode: interventricular septum thickness in diastole, left ventricular systolic and diastolic diameter (LVSD and LVDD), and left ventricular (LV) posterior wall thickness in diastole.

The LV mass was calculated according to the equation of the American Society of Echocardiography and indexed by body surface, diagnosing LV hypertrophy when the indexed mass was $> 115 \text{ g/m}^2$. LV systolic function was assessed by ejection fraction (EF), which was calculated by the Teichholz method. The mitral inflow velocities in pulsed Doppler were recorded at the apical four-chamber view with the sample volume positioned at the extremities of the mitral valve leaflets during calm and controlled breathing. Early rapid filling (E) wave velocity, atrial contraction (A) wave velocity and E / A ratio were estimated in accordance with the recommendations of the American Society of Echocardiography.

The early (E') and late (A') diastolic mitral annular velocities at tissue Doppler and their ratio (E'/A') were recorded in the apical four-chamber view with a sample volume of 1 mm at the junction between the LV lateral wall with the annulus. The left atrium (LA) size was calculated by estimating the left atrial volume (LAV), which was determined by biplane Simpson's method at the two-dimensional echocardiography and indexed by body surface. All measurements represent the mean of three cardiac cycles.

The intraobserver variability for echocardiographic variables evaluated in this study has been previously published by our group^{8,9}.

Statistical Analysis

Results are expressed as mean, median, minimum and maximum values and standard deviations. To assess the impact of the race on the data obtained in the two predetermined moments (pre- and post-race), the Student's *t* test was used for paired samples. The variables' normality was analyzed by the Shapiro-Wilks test. P values < 0.05 were considered statistically significant.

Results

A total of 20 athletes were included in the study. Twelve completed the 24-hour race and participated in all stages of the study. Of the eight eliminated, three did not complete the race due to physical problems and five did not participate in some stage of the evaluation. The mean age of the 12 participants was 43.3 ± 9.9 years. The mean distance covered during the race was 140.32 km, ranging from 111.60 km and 169.60 km. The temperature during the 24 hours ranged from 9-21 °C.

Clinical, anthropometric and laboratory data

In relation to the pre-race moment, runners had weight reduction, with a mean loss of 3.2% of the initial weight. Data from bioimpedance analysis showed no change in body composition of water. Despite this finding, there was a significant reduction in systolic (120.8 ± 6.7 in pre- vs. 103.3 ± 8.9 in post-race, $p < 0.001$) and diastolic blood pressure (83.3 ± 10.7 vs. 73.3 ± 8.9 , $p = 0.003$). The clinical and anthropometric data are summarized in Table 1.

Regarding laboratory findings, there was a marked increase in CPK levels, a sensitive marker of muscle injury. This increase was accompanied by increased urea, serum creatinine and decreased kalemia. At the hematological analysis, we observed significant leukocytosis, predominantly by neutrophilia. Laboratory data are shown in Table 2. As shown in Figure 1, CPK levels after the race had an inverse correlation with the distance covered during the marathon.

Markers of myocardial necrosis

There was a marked increase in CK-MB levels. However, such alteration occurred in parallel to the elevation in CPK levels (Table 2).

Regarding troponin T, the values found in the pre-race measurement were below the threshold of detection (0.010 ng/mL). After the race, two athletes showed increased values (0.015 and 0.018 ng/mL), but below the reference value for the detection of myocardial injury.

Echocardiographic findings

In the pre-race assessment, all athletes had normal ventricular systolic and diastolic function. Left ventricular hypertrophy was found in one and left atrial volume increase in five runners.

The mean LVDD decreased significantly ($p < 0.01$), while the LVSD and EF remained unchanged after the race.

Regarding LV diastolic function, we observed a decrease in E/A ratio after the race ($p = 0.001$). This change was mainly due to an increase in the values of A ($p < 0.001$), with no

changes in the value of E. In parallel, we observed decrease in E' velocity and increase in A' velocity, which, although not significant, led to a threshold variation of E'/A' ($p = 0.05$). Finally, there was no change in LAV. The echocardiographic findings are described in Table 3.

Cardiac fatigue

One athlete, the oldest to complete the marathon (63 years), showed a significant decrease in LVEF: 70% pre- and 51% post-test. The dysfunction was global, with no change in segmental contraction. Clinically, there was also marked tachydyspnea upon arrival. This athlete was subsequently assessed with myocardial perfusion imaging and coronary CT angiography, which ruled coronary disease or other structural heart disease. Please note that this was one of two athletes to show troponin elevation, although below the reference value for the diagnosis of myocardial injury.

Discussion

Although the beneficial effects of exercise on overall health have been demonstrated long ago, the acute effects of prolonged aerobic training remain unclear, especially on the heart. Prolonged athletic competitions such as ultramarathons and other competitions involving multiple sports (such as Ironman and Ultraman) become unique opportunities for this type of assessment. As there are few athletes qualified to perform such tests, studies in this area generally comprise a small number of individuals. Therefore, the results of this study are added to others, previously published ones, in order to assess whether physical exercise is always beneficial or if its excess can endanger health.

Many of the alterations observed in our study confirm the results of previous investigations in prolonged endurance events. It is known that CPK levels increase after great physiological stress¹⁰⁻¹⁷, indicating intense catabolic state of skeletal muscle. The intensity and duration of physical exercise are commonly associated with CPK increase and there seems to be a predominant effect of duration¹⁶. Although rare, severe rhabdomyolysis can occur, albeit more commonly in less-trained individuals subjected to strenuous

Table 1 – Anthropometric and clinical data before and after the ultramarathon

Variables	Pre	Post	p
Weight (kg)	72,9 ± 9,73	70,3 ± 9,92	< 0,001
BMI	26 ± 2,6	25,1 ± 2,44	< 0,001
% BF	8,95 ± 4,66	6,61 ± 4,22	Ns
BMR	1738,22 ± 205,09	1748,9 ± 184,96	Ns
% Lean mass	91,04 ± 4,66	93,39 ± 4,22	Ns
% H ₂ O	66,65 ± 3,41	68,35 ± 3,08	Ns
% H ₂ O Variation		1,17 ± 7	
HR (bpm)	63,66 ± 5,77	71,72 ± 7,45	0,008
SBP (mmHg)	120,83 ± 6,68	103,33 ± 8,87	< 0,001
DBP (mmHg)	83,33 ± 10,73	73,33 ± 8,87	0,003

BMI: body mass index; BMR: basal metabolism rate; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2 - Biochemical data before and after the ultramarathon

Variables	Pre	Post	p
Urea	44.66 ± 12.82	64.08 ± 11.58	0.002
Creatinine	1.00 ± 0.21	1.19 ± 0.24	0.04
Potassium	4.51 ± 0.26	4.03 ± 0.46	0.009
CPK	163.41 ± 56.78	2978.41 ± 1921.93	< 0.001
CK-MB	21.76 ± 4.74	780.25 ± 957.39	0.01
Erythrocytes	5.07 ± 0.65	5.02 ± 0.63	Ns
Hemoglobin	15.45 ± 0.71	14.97 1.02	Ns
Hematocrit	45.91 ± 2.09	45.28 ± 2.83	Ns
Leukocytes	8400 ± 2696.79	13291.66 ± 3672.36	< 0.001
Lymphocytes	1867.66 ± 574.71	2397.66 ± 715.88	0.02
Rod cells	632.58 ± 303.40	1352.41 ± 561.91	< 0.001
Segmented	5419.25 ± 2141.37	8828.5 ± 2820.37	< 0.001
Neutrophils	6051.83 ± 2360.03	10180.91 ± 3170.27	< 0.001
Platelets	270.25 ± 55.18	281.25 ± 74.98	Ns

CPK: creatine phosphokinase; CK-MB: creatine kinase-MB

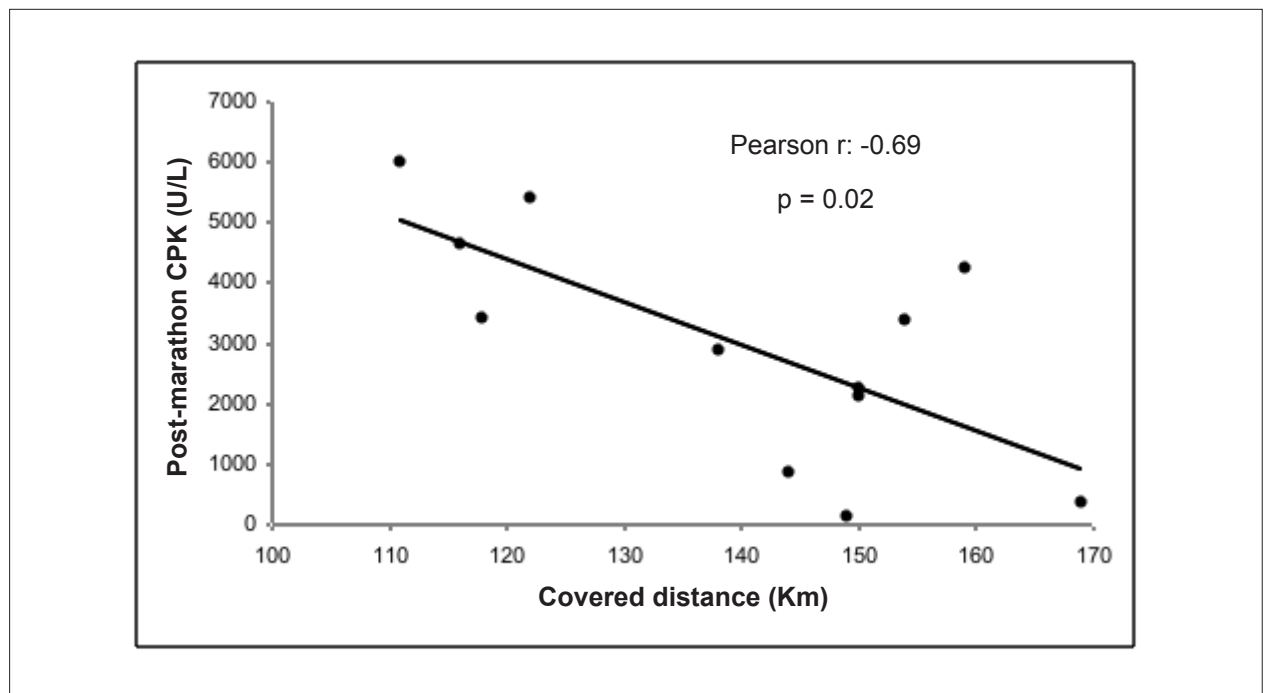


Figure 1 - Correlation between the distance covered in 24 hours (miles) and plasma levels of CPK (U / L) at the collection after the race.

exercise at high temperatures¹⁸. It is noteworthy in our study the close inverse association observed between CPK levels and the covered distance. Athletes who covered the greatest distances had lower levels of CPK, showing that the volume of the effort is not necessarily the major determinant of the increase. One can assume that the best physical fitness, which led athletes to cover longer distances, also prevented major muscle catabolism.

Previous studies have shown that exercise training actually reduces the release of CPK in the same individual¹⁹.

The increase of urea and creatinine is another common finding in strenuous physical training tests, but its meaning is less clear. While it may reflect large degradation of muscle creatine, we found no correlation between creatinine variation and CPK increase (data not shown). Other mechanisms may be associated

Table 3 - Echocardiographic findings before and after the ultramarathon

Variables	Pre	Post	p
LVDD (mm)	51.70 ± 3.86	50 ± 3.83	0.007
LVSD (mm)	32.25 ± 3.27	32.58 ± 3.17	ns
EF (%)	66.91 ± 4.29	64 ± 5.62	ns
LAV (ml/m ²)	49.25 ± 8.09	46.75 ± 9.47	ns
LAVi	27.08 ± 4.49	25.07 ± 4.05	ns
E (cm/s)	70 ± 14.22	70.5 ± 17.43	ns
A (cm/s)	37.16 ± 6.89	55.16 ± 9.57	< 0.001
E/A	1.96 ± 0.6	1.3 ± 0.37	0.001
E' (cm/s)	11.71 ± 2.1	11.01 ± 2.95	ns
A' (cm/s)	9.54 ± 2.64	10.18 ± 1.73	ns
E'/A'	1.35 ± 0.55	1.12 ± 0.42	0.05
E/E'	6.08 ± 1.33	6.56 ± 1.58	ns

LVDD: left ventricular diastolic diameter; LVSD: left ventricular systolic diameter; EF: ejection fraction; LAV: left atrial volume; LAVi: left atrial volume index; E: early mitral inflow filling velocity; A: atrial contraction mitral inflow velocity; E': early diastolic velocity of the mitral annulus; A': late diastolic velocity of the mitral annulus.

with these elevations, such as decrease in renal blood flow and glomerular filtration rate. Mild, but persistent kidney injury has been demonstrated in some high-performance athletes²⁰. The hypovolemia itself may be one of the causes of increased creatinine¹⁵. Increased urea can be explained by the increased catabolic state.

Among the metabolic alterations we observed a slight kalemia decrease in the runners. This finding is opposed to what is described in the literature regarding the alterations in this electrolyte levels due to exercise practice¹¹. The possibility of adequate nutrition and hydration during the race possibly contributed to the lack of more significant electrolyte alterations.

The absence of alterations in the bioimpedance should be interpreted with caution, as its performance immediately after intense physical exercise can reduce its accuracy for the measurement of total body water. Hemodynamic alterations, such as increased cardiac output and skeletal muscle perfusion, and the process of heat dissipation, with cutaneous vasodilation, increased skin temperature and sweating, reduce the body impedance, affecting the results. This could have limited the bioimpedance analysis to detect dehydration inferred by body weight measurement. Fluid intake was free and at the discretion of the athlete in this study in order to evaluate the effects of prolonged exercise in the conditions under which this type of test is usually performed. We observed that the mean weight reduction was 3.2%, which is within the range of significant dehydration according to the National Athletic Trainer's Association²¹.

However, the estimate of the degree of dehydration based on changes in weight has been questioned. Recently, Knechtle et al²² found a mean reduction of 2.5% in the weight of athletes after a 100-km ultramarathon, which can not be totally explained by the reduction in total body water, suggesting that the loss resulted from solid mass loss (muscle mass and fat).

There was no change in hematocrit or hemoglobin levels similar to what was found in previous studies with ultramarathon

runners²³. The increased activity of vasopressin and plasma aldosterone, promoting the maintenance or increasing plasma volume is a possible explanation for this finding. The leukocyte alterations were in accordance with what is expected in stress situations. There was significant leukocytosis with marked formation of neutrophils. Lymphocyte alterations showed more divergent results, although some studies corroborate our findings on lymphocytosis¹¹.

Regarding the assessment of myocardial injury in athletes, it is essential to correctly interpret laboratory test results. As the skeletal injury also alters markers that are commonly used in myocardial assessment, sensitive and specific markers such as cardiac troponins I and T, should be used. The assessment of CPK and CKMB fails to differentiate myocardial injury from the one that occurs in skeletal muscle. Several studies, such as ours, showed no elevation in TnT, even with significant increases in CKMB²⁴⁻²⁸. Others showed an increase of this marker in a heterogeneous group of athletes²⁹⁻³³, although it is not known whether this increase really reflects myocardial damage and what the determinants of alteration are in just some athletes.

An experimental study by Chen et al³⁴ in rats showed that the extent of myocardial lesions induced by strenuous physical exertion is dependent on the previous physical fitness. If this is an explanation for the discrepant findings in humans, it is still a hypothesis to be tested. However, a small study of marathoners actually showed greater troponin release in less trained runners³⁵. In a meta-analysis, Shave et al³⁶ showed that the release of cTnT induced by exercise is evident in almost half of endurance athletes, with the relatively heavier athletes, competing in long distance events, being more likely to show such release.

While no athlete in this study showed troponin increases above the reference value for the diagnosis of myocardial damage, two runners started to show detectable levels after the race. In a previous study with participants of an Ironman competition, even minor alterations of troponin were associated with echocardiographic abnormalities³⁷. These changes constitute

the picture of cardiac fatigue, an entity described several years ago, but of which etiology remains unclear. It is believed that the stress generated by exercise on the left and right ventricular walls is the origin of these alterations³⁸. The increase in plasma brain natriuretic peptide (BNP) in endurance athletes reinforces this idea³⁹.

In our sample, the only athlete who had a significant decrease in LVEF at the end of the race was exactly the one that showed an increase, albeit slight, of troponin levels. As the possibility of ischemic injury was ruled out by functional (myocardial scintigraphy) and anatomical examination (CT angiography of coronary arteries), the established diagnosis was cardiac fatigue. However, the finding of reduced LVEF in this patient was isolated. The echocardiography showed no decrease in LV systolic function, demonstrating that, in the other runners, exercise intensity was not sufficient to induce significant deterioration in cardiac contractility.

Regarding the diastolic function, the echocardiographic finding of a significant decrease in E/A ratio, commonly interpreted as the onset of diastolic dysfunction has been previously described⁴⁰. Here it is necessary to perform a critical appraisal of the term "diastolic dysfunction" after prolonged exercise. Although this conclusion comes from data derived from conventional Doppler mitral flow (known to be dependent on preload), our study showed only a marginal variation in the E'/A' ratio, this obtained by tissue Doppler and less susceptible to loading status⁹. Thus, on the one hand there may have been an insufficient number of cases to demonstrate significant differences in the E' and A' velocities that would corroborate the hypothesis of actual diastolic dysfunction, but, on the other hand, the decrease in E/A ratio after exercise may simply correlate with preload reduction.

In parallel, we must emphasize that this alteration was secondary to an increase in A wave (atrial contraction phase), with no alteration in the values of E (rapid filling phase). Similarly, as it is reasonable to assume that the decrease in LV diameter was due to the decrease in preload, one may speculate that the increase in A wave may be secondary to concomitant decrease in afterload, with increases in atrial contractility and ventricular compliance. Therefore, the decrease in E/A ratio did not represent actual diastolic dysfunction (except in the aforementioned case of cardiac fatigue), but the complex effect of hemodynamic changes

on the total blood volume and cardiovascular physiology. Future studies should clarify whether strenuous physical exertion promotes actual myocardial relaxation injury.

Our study has some limitations. The number of subjects included in the study was not based on sample-size calculation, but on the total number of individuals who agreed to participate in this research. As it is a strenuous test, the number of participants was small. Still, approximately 50% of the male runners agreed to participate, a higher percentage than in most publications with similar populations. Another limitation was the lack of evaluation of the runners' aerobic capacity. A preliminary assessment of maximal oxygen consumption (VO₂ max) would allow better understanding if certain findings did not reflect, actually, lower cardiorespiratory fitness.

Finally, a single assessment after the marathon does not allow any inference on the temporal evolution of metabolic and cardiovascular alterations found. As most runners were from other cities, further assessment was not feasible.

In conclusion, the ultramarathon race was associated with several metabolic, hematologic and cardiovascular alterations. Regarding skeletal muscle, we observed a lower level of injury in runners who covered greater distances. Slight increase in cTnT was associated with LV systolic dysfunction in one runner, which was compatible with cardiac fatigue. In the others, the finding of a decrease in the E/A ratio on mitral Doppler predominated. The long-term effect of this type of prolonged physical exercise is still unknown.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the master thesis submitted by Daniela G. Passaglia, from Pontificia Universidade Católica do Paraná.

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