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Post-exertional increase in first-phase ejection fraction in recreational marathon runners

Luca Faconti[1], Iain Parsons[1,2], Bushra Farukh[1], Ryan McNally[1], Lorenzo Nesti[1], Lingyun Fang[1], Michael Stacey[3], Neil Hill[2,3], David Woods[2,4] and Phil Chowienczyk[1]

Abstract

Objectives: Running a marathon has been equivocally associated with acute changes in cardiac performance. First-phase ejection fraction is a novel integrated echocardiographic measure of left ventricular contractility and systo-diastolic coupling which has never been studied in the context of physical activity. The aim of this study was to assess first-phase ejection fraction following recreational marathon running along with standard echocardiographic indices of systolic and diastolic function.

Design and participants: Runners (n = 25, 17 males), age (mean ± standard deviation) 39 ± 9 years, were assessed before and immediately after a marathon race which was completed in 4 h, 10 min ± 47 min.

Main outcome measures: Central hemodynamics were estimated with applanation tonometry; cardiac performance was assessed using standard M-mode two-dimensional Doppler, tissue-doppler imaging and speckle-tracking echocardiography. First-phase ejection fraction was calculated as the percentage change in left ventricular volume from end-diastole to the time of peak aortic blood flow.

Results: Conventional indices of systolic function and cardiac performance were similar pre- and post-race while aortic systolic blood pressure decreased by 9 ± 8 mmHg ($P < 0.001$) and first-phase ejection fraction increased by approximately 48% from 16.3 ± 3.9% to 22.9 ± 2.5% ($P < 0.001$). The ratio of left ventricular transmitral Doppler early velocity (E) to tissue-doppler imaging early annular velocity (e′) increased from 5.1 ± 1.8 to 6.2 ± 1.3 ($P < 0.01$).

Conclusion: In recreational marathon runners, there is a marked increase in first-phase ejection fraction after the race despite no other significant change in cardiac performance or conventional measure of systolic function. More detailed physiological studies are required to elucidate the mechanism of this increase.

Keywords

Ejection fraction, systolic function, diastolic function, endurance, long distance, aerobic capacity

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Introduction

During physical exercise, the cardiovascular system undergoes complex integrated adjustments largely to support the metabolic demand and heat dissipation generated by exercising muscles. The beneficial effects of moderate aerobic exercise on cardiovascular health are well known[1] and extend to marathon running.[2] Despite this, some studies have reported deleterious effects in cardiac function following high-intensity and/or prolonged exercise. Exercise-induced cardiac

[1]Department of Clinical Pharmacology, King's College London, British Heart Foundation Centre, London, UK
[2]Academic Department of Military Medicine, Research and Clinical Innovation, Royal Centre for Defence Medicine, Birmingham, UK
[3]Department of Diabetes & Endocrinology, Imperial College, London, UK
[4]Research Institute for Sport, Physical Activity and Leisure, Leeds Beckett University, Leeds, UK

Corresponding author:
Luca Faconti, Clinical Pharmacology, St Thomas' Hospital, London, UK, SE1 7EH.
Email: luca.faconti@kcl.ac.uk

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fatigue (EICF)[3] is a term often used to describe measurable decreases in cardiac function, in seemingly normal healthy hearts, after bouts of prolonged strenuous exercise. The alterations described vary according to the type of physical activity performed and population studied but can include transient reductions in biventricular systolic and/or diastolic relaxation.[4] However, EICF, as a concept, remains controversial[4] and there is conflicting evidence on whether cardiac fatigue occurs following marathon running,[5–9] which in a recreational population is generally described as prolonged (but not strenuous) exercise.[4,10]

First-phase ejection fraction (EF1) is a novel integrated index of contractility and systo-diastolic coupling.[11] EF1 represents the early phase of contraction up to the time of peak aortic flow[12] when the maximum velocity of shortening of the cardiac muscular fibres occurs. This early systolic peak (which is then followed by a subsequent fall in myocardial wall stress) facilitates relaxation in diastole. Previous studies in subjects with hypertension[11] have shown that EF1 is related to diastolic function and it may be a more sensitive index of left ventricular (LV) dysfunction and systo-diastolic coupling than conventional echocardiographic measures of systolic function. We hypothesized that EF1 would be sensitive to changes in systolic function induced by marathon running and the aim of the present study was to perform an echocardiographic evaluation of cardiac function including EF1 before and after a marathon in recreational runners.

Methods

Experimental protocol

Ethical approval was provided by the National Health Service Health Research Authority (London – South East) Research Ethics Committee (approval reference 19/LO/0340) and complied with the standards set in the Declaration of Helsinki (Fortaleza). All subjects gave written informed consent before participation. Recreational runners (>18 years) registered for the 2019 Brighton marathon were recruited by open invitation one or two days before the race (pre-race measurements) and had anthropometric measurements, hemodynamic data and a 2D trans-thoracic cardiac ultrasound (TTE) performed. All the individuals were then invited to repeat the same investigations after completing the marathon when post-race measurements were collected after crossing the finish line (within 30 min from the end of exercise). Subjects with a positive history of cardiovascular disease, on treatment with cardiovascular medications, showing rhythm abnormalities and/or valvular disease were excluded from the analysis.

Anthropometric measurements and hemodynamic data

Height was measured using a stadiometer. Weight was measured using a bioimpedance multifrequency scale (MC-780MA P, TANITA, Tokyo, Japan) with subjects standing barefoot both during pre- and post-race measurements. Brachial blood pressure (BP) was measured by a trained observer using Omron HEM 705-CP semi-automatic oscillometric recorder (Omron Health Care, Tokyo, Japan) with appropriate size arm cuff supine after at least 5 min of rest. The average of two consecutive readings of systolic BP (SBP) and diastolic BP (DBP) and heart rate (HR) was used for the analysis. Central hemodynamics (aortic systolic blood pressure, aoSBP; aortic diastolic blood pressure, aoDBP; aortic pulse pressure, aoPP) were estimated using a high-fidelity micromanometer (SPC-301; Millar Instruments, Houston, Texas, USA) applied to the radial artery and processed using a SphygmoCor device (AtCor Medical, Sydney, Australia) calibrated from peripheral BP. A single operator (BF) performed all the measurements both before and after the marathon and an operator index > 85% was required for the measurements to be included in the analysis.

Echocardiographic assessment

A conventional TTE was performed using a Philips CX50 ultrasound system (Phillips, Amsterdam, Netherlands) in accordance with the American Society of Echocardiography and the European Association of Cardiovascular Imaging[13] recommendations. Measurements were performed by two operators (LF and IP) and analyzed by a single operator (LF) who was blind to the hemodynamic data. Acquisitions were individually optimized for depth, gain and frame rate to maximize image quality and minimize inconsistency in acoustic windows.

Morphological evaluation

Inferior vena cava (IVC) bidimensional diameters were recorded in expiration using the subcostal long-axis view during spontaneous breathing.[14] Left ventricular mass was calculated using the cube formula and indexed to body surface area to obtain left ventricular mass index (LVMI).[13] Relative wall thickness (RWT) was calculated as the ratio of two times posterior wall thickness divided by LV diastolic diameter. Left atrium volume was measured from standard apical four-chamber views at end-systole just before mitral valve opening using biplane method. Automated measurements of LV end-diastolic volume (EDV) and end-systolic volume (ESV) were obtained from four-chamber views using the image analysis software

a2DQ (Philips QLAB) which has proven to be an accurate and reproducible tool for volume measurements.[15]

LV systo-diastolic function

LV systolic function was evaluated by conventional TTE indexes including ejection fraction (EF), peak systolic tissue-doppler imaging (TDI) of the S′ wave (averaged between the septal and lateral mitral annulus) and global longitudinal strain (GLS) assessed by two-dimensional speckle-tracking echocardiography. In addition, the novel measure of early systolic function EF1 was calculated as the percentage change in LV volume from end-diastole to the time of peak aortic blood flow as previously described.[11] Diastolic function of the left ventricle was estimated by conventional Doppler mitral inflow (ratio of transmitral Doppler early (E) to late (A) filling velocity (E/A)) and TDI of the mitral annulus (ratio of E to TDI early diastolic mitral annular velocity (e′), as per recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[16] TDI of late diastolic velocity (A′) was also recorded and averaged between septal and lateral wall for the analysis.

Cardiovascular performance and arterial-ventricular coupling

Stroke volume (SV) was estimated by the difference between the LVEDV and LVESV and then multiplied for HR to obtain cardiac output (CO). Cardiac power output-to-mass (CPOM) was calculated as the product of CO and mean systemic BP[17] in relation to LV mass. CPOM represents the number of watts that are developed by 100 g of myocardial tissue mass[18] and is considered an integrative measure of overall cardiac function as it accounts for both flow- and pressure-generating capacities of the heart. Non-invasive assessment of arterial ventricular coupling was estimated as the ratio of arterial elastance (Ea) to end-systolic LV elastance (Ees), where Ea is an integrated index of net arterial load that is imposed on left ventricle work and Ees is an index of contractility and systolic stiffness of the myocardium.[19] Ea was calculated as the ratio of central end-systolic pressure (derived from the arterial waveform) to SV and Ees as the ratio of central end-systolic pressure to EDV.

Right ventricular systo-diastolic function

Right ventricular (RV) systolic function was evaluated by conventional TTE indexes including tricuspid annulus plane systolic excursion (TAPSE) and peak systolic TDI of the S′ wave. Diastolic function was estimated by conventional Doppler mitral inflow (E/A) and TDI of the tricuspid annulus (E/e′).

Statistical analysis

Data are presented as mean ± standard deviation and as numbers and percentages for categorical variables. Differences between pre- and post-marathon values were assessed via a paired *t*-test. A χ^2 test was used for categorical values. $P < 0.05$ was considered statistically significant and all tests were two-tailed. SPSS Statistics Version 25 (IBM Corporation) was used for all statistical analysis. Univariate regression analysis was used to explore correlations between EF1 and hemodynamic changes. Subjects were stratified into tertiles of time taken to complete the marathon to explore potential differences between 'faster' and 'slower' runners. GraphPad Prism 8 (GraphPad Software Inc, California) was used for graphical representation of data. A formal sample size calculation was not performed but our group size was similar to other echocardiographic studies examining changes in cardiac function following marathon running.

Results

The study population (Table 1) consisted of 25 recreational marathon runners (17 male), aged between 23 and 63 years, who completed the race in a mean time of 4 h 10 min ± 47 minutes during a minimum daytime ambient temperature of 8 °C and maximum of 12 °C. All subjects were free from cardiovascular disease and with no sign of impairment of LV systo-diastolic function at baseline. Average LVMI was 74.3 ± 15.93 g/m^2 with no subjects fulfilling the criteria for LV hypertrophy. After stratifying the population in tertiles according to the race time we found that faster runners (3 h 13 min ± 9 min) were mostly male compared to slower runners (5 h 7 min ± 19 min) but other characteristics were similar between the two groups.

Anthropometric measurements and hemodynamic data

Compared to pre-race measurements, the body weight of runners decreased by 1.81 ± 1.37 kg (corresponding to a change of 2.51 ± 1.72%, $P < 0.01$). A significant reduction in SBP and DBP (–10.83 ± 6.24 mmHg and –7.48 ± 8.73 mmHg, respectively) and increase in HR (+24.83 ± 9.51 bpm), were observed (Table 2, all $P < 0.001$). Central BP components including aoSBP, aoDBP and aoPP were also reduced significantly from pre- to post-race (Table 2).

Table 1. Baseline characteristics of study population.

Variable	Mean (± SD)/%
Age (years)	39.40 ± 9.31
BMI (kg/m^2)	23.46 ± 2.34
Ethnicity	24/25 WB, 1/25 Mixed
Gender (number of male)	17
LVMI (g/m^2)	74.28 ± 15.93
RWT	0.34 ± 0.05

BMI: body-mass index; LVMI: left-ventricular mass index; LVM: left-ventricular mass; RWT: relative wall thickness; WB: White-British.

Echocardiographic parameters

Morphological evaluation. After completing the marathon race, IVC diameter was significantly decreased in expiration by 0.513 ± 0.55 cm ($P = 0.001$). LV volumes were reduced by 6.03 ± 24.42 mL for EDV and 7.56 ± 13.80 mL for ESV (both $P < 0.05$). A similar trend was observed for LAV but this did not reach statistical significance (Table 2).

Systo-diastolic function of the left and right ventricles. Conventional indices of LV systolic function (EF, GLS and S′) were similar pre- and post-race (Table 2). In contrast, EF1 increased approximately by 48% from 16.28 ± 3.88% units to 22.93 ± 2.53% units ($P < 0.001$, Figure 1). The time to peak aortic flow was reduced from 124.50 ± 18.20 ms to 107.50 ± 18.60 ms ($P < 0.01$). There was no significant correlation between the increase in EF1 and the decrease in BP ($R^2 = 0.018$, $P = 0.624$), change in body weight ($R^2 = 0.024$, $P = 0.563$), change in HR ($R^2 = 0.03$, $P = 0.536$) or change in ventricular volumes. Baseline values of EF1 and the increase in EF1 post-race was similar in faster vs slower runners (6.43 ± 1.67% vs 6.05 ± 4.46% in faster vs slower runners, respectively, $P = 0.153$).

The E/A ratio was significantly reduced post-race by 0.517 ± 0.582, $P < 0.001$ largely due to an increase in peak velocity of the A wave with no significant change in E wave. TDI indices E′ but not A′ were reduced post-race and the ratio E/E′ increased significantly by 1.18 ± 1.88 ($P = 0.005$, Table 2).

Indices of RV systolic and diastolic function remained similar pre- and post-race (Table 2).

Cardiovascular performance. Compared to pre-race measurements, CO increased significantly post-race by 1.12 ± 0.97 L/min ($P < 0.01$) due to an increase in HR while SV decreased by 8.97 ± 13.7 mL ($P = 0.004$). CPOM was similar between pre-race and post-race measurements and no significant differences were observed in Ea, Ees and Ea/Ees (Table 2).

Table 2. Hemodynamic profile and cardiovascular indices of study population pre- and post-race.

Variable	Pre-marathon	Post-marathon	*P* value
Hemodynamic			
SBP (mmHg)	131.40 ± 9.63	120.56 ± 10.39	<0.001
DBP (mmHg)	78.40 ± 9.78	70.93 ± 5.47	0.001
HR (bpm)	55.40 ± 8.48	80.23 ± 10.77	<0.001
aoSBP (mmHg)	119.10 ± 12.84	102 ± 9.74	<0.001
aoDBP (mmHg)	79.55 ± 10.18	72.80 ± 5.92	0.003
aoPP (mmHg)	39.55 ± 10.52	29.20 ± 6.61	<0.001
Cardiac morphology			
IVC diameter (cm)	1.91 ± 0.47	1.40 ± 0.39	0.001
LAV (mL)	45.46 ± 14.09	40.50 ± 13.65	0.053
LVEDV (mL)	129.55 ± 27.16	113.51 ± 25.71	0.004
LVESV (mL)	55.87 ± 14.90	48.31 ± 12.78	0.013
LV systolic function			
EF (%)	57.64 ± 5.09	57.55 ± 5.25	0.938
S′ (cm/s)	11.60 ± 2.23	11.78 ± 1.88	0.743
GLS (%)	−15.9 ± 2.83	−16.3 ± 4	0.677
EF1 (%)	16.28 ± 3.88	22.93 ± 2.53	<0.001
LV diastolic function			
E (cm/s)	0.856 ± 0.194	0.797 ± 0.162	0.180
A (cm/s)	0.563 ± 0.135	0.752 ± 0.175	<0.001
E/A	1.61 ± 0.580	1.09 ± 0.272	<0.001
E′ (cm/s)	15.07 ± 2.66	12.91 ± 1.93	<0.001
A′ (cm/s)	11.76 ± 2.99	11.32 ± 2.73	0.521
E/E′	5.06 ± 1.80	6.24 ± 1.34	0.005
RV systolic function			
TAPSE (mm)	26.30 ± 6.24	27.00 ± 3.40	0.609
S′ (cm/s)	15.37 ± 3.01	16.81 ± 5.47	0.292
RV diastolic function			
E (cm/s)	0.582 ± 0.141	0.586 ± 0.140	0.921
A (cm/s)	0.4223 ± 0.113	0.477 ± 0.115	0.187
E/A	1.49 ± 0.570	1.31 ± 0.490	0.227
E′ (cm/s)	13.01 ± 3.19	16.92 ± 12.3	0.161
A′ (cm/s)	14.76 ± 6.80	16.81 ± 6.32	0.332
E/E′	4.68 ± 1.61	4.00 ± 1.23	0.129
Cardiovascular performance			
SV (mL)	74.17 ± 13.93	65.20 ± 15.92	0.004
CO (L/min)	3.89 ± 0.83	5.02 ± 1.13	<0.001
CPOM (W/100 g)	0.632 ± 0.115	0.706 ± 0.187	0.149
Ea (mmHg/mL)	1.90 ± 0.39	1.79 ± 0.51	0.404
Ees (mmHg/mL)	2.63 ± 0.89	2.42 ± 1.02	0.391
Ea/Ees	0.755 ± 0.19	0.780 ± 0.21	0.661

SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; cSBP: central systolic blood pressure; cDBP: central diastolic blood pressure; cPP: central pulse pressure IVC: inferior vena cava; LAV: left-atrial volume; LVEDV: left-ventricular end-diastolic volume; LVESV: left-ventricular end-systolic volume; EF: ejection fraction; S': peak systolic tissue-doppler imaging (TDI) of the S′ wave EF1: first-phase ejection fraction; GLS: global longitudinal strain; E: transmitral Doppler early filling velocity; A: transmitral Doppler late filling velocity; E′: TDI early diastolic annular velocity; A′: TDI of late diastolic velocity; TAPSE: tricuspid annulus plane systolic excursion; SV: stroke volume; CO: cardiac output; CPOM: cardiac power output-to-mass; Ea: arterial elastance; Ees: end-systolic elastance.

Discussion

This is the first study to demonstrate that after a marathon race EF1 is increased in recreational runners despite no change in other measures of systolic

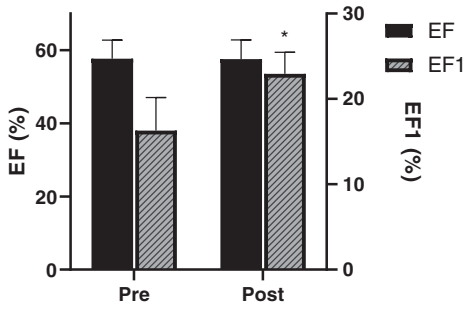

Figure 1. Ejection fraction (EF) and first-phase ejection fraction (EF1) measured before and after the marathon. The left *y*-axis represents EF and the right *y*-axis represents EF1. $* = P < 0.001$.

function. The increase in EF1 may suggest an increase in myocardial efficiency in the early phase of LV contraction.

The physiological mechanisms of an increase in myocardial efficiency are likely to be complex and multifactorial particularly in the context of a marathon race. The prolonged physical activity has an impact on cardiac pre-load due to dehydration and redistribution of blood flow to peripheral non-working tissue associated with thermoregulation. An increase in EF1 would not have been expected according to the Frank-Starling mechanism.[20] This states that an increase in venous return dilates the ventricle(s), stretching the myocardium thereby increasing the contractility of the muscle and increasing the SV, while a decrease in pre-load is expected to elicit opposite effects. Moreover, the increase in EF1 was not simply the result of an extended time to peak aortic flow, which on the contrary was reduced.

A decrease in afterload secondary to pre-load reduction and release of vasodilatory mediators responsible for post-exertional hypotension[21] could have contributed to an increase in EF1, but we did not see a correlation between the increase in EF1 and fall in BP. However, this negative finding could have been due to the limited sample size. A major factor likely to have contributed to the increase in EF1 was an increase in sympathetic activity and HR.[22] Previous studies have demonstrated that training leads to an array of sympathovagal adjustments, leading to bradycardia and vagal predominance at rest.[23] Parasympathetic tone appears to predominate at rest and that the initial increase in HR at the onset of exercise is believed to be primarily due to parasympathetic withdrawal.[24] As the intensity of exercise increases to more vigorous levels, the sympathetic system is activated and the cardiovascular response is largely characterized by a decrease in SV, with the CO maintained by an increase in HR[25] (cardiovascular drift). We did not find a significant correlation between EF1 and change HR, but this may again be because of the limited sample size or a confounding effect of training adaptation.

Despite the increase in EF1, we found no significant change in other measures of LV systolic function. This finding is largely consistent with previous studies performed in runners although discrepancies have been reported in literature with some studies reporting an increased,[9] unaltered or impaired[2,9] LV (and in some cases RV) systolic function as assessed through 2 D-echocardiography[5,6,8,26] and speckle-tracking echocardiography.[8,27] Reasons for these discrepancies are likely to be multifactorial and probably related to type of exercise,[28] training status, environmental conditions, type of investigation performed and time interval between exercise and data recording.

In line with previous observations reporting changes in LV diastolic function in the absence of a change in conventional measures of systolic function,[6,7,9,26] we observed a decrease in E wave, E/A ratio and E′, while E/E′ increased. This may suggest an attenuation of early LV filling although this alone may not represent a diastolic impairment in otherwise normal heart. In fact, none of the TTE indices used to study diastolic function are entirely load-independent and the literature on the topic is controversial.[29,30]

Compared to pre-race measurements, CO increased while CPOM and the non-invasive indices of arterial-ventricular coupling were not affected. These data suggest that post marathon an optimal stroke work and energetic efficiency of the heart is preserved. In fact, cardiovascular performance is dependent on the interaction of both the ventricular and vascular systems which are both represented in CPOM (which accounts for both flow- and pressure-generating capacities of the heart in relation to the myocardial mass) and in Ea/Eees.

Our study is subject to several limitations. Our sample size (although in line with many other cohorts in the literature) is relatively small. Data were collected only before and immediately after physical exercise with no long-term follow-up data available. Subjects involved in the analysis had free access to fluid and food during the race and this might have affected the results reported. Information regarding training level and physical activity level were not collected prior to the race. We did not relate changes in EF1 to electrocardiographic features. The strength of our analysis is the comprehensive approach that we used for the evaluation of LV systolic function and cardiac performance with a direct estimation of central hemodynamic performed with applanation tonometry. More detailed studies will be required to delineate the individual hemodynamic factors contributing to the increase in EF and individual characteristics of the runners that determine the degree of increase.

Conclusion

In recreational marathon runners, there is a marked increase in EF1 after the race despite no other significant change in cardiac performance or conventionally measured systolic function. More detailed physiological studies are required to elucidate the mechanism of this increase.

Perspective

Running a marathon has been equivocally associated with acute changes in cardiac performance. We have provided the first evidence that in recreational amateur runners a novel index of left ventricular systo-diastolic function (EF1) is increased after the race, which may suggest an enhancement rather than an impairment in myocardial contractility.

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None

Contributorship

L Faconti, IP, MS, NH, DW and PC conceived and designed the experiment.
L Faconti, IP, BF and RM collected the data.
L Fang and LN contributed data or analysis tools.
L Faconti, BF and RM interpreted the data performed the analysis.
RM and BF devised the figures and tables.
L Faconti and RM drafted the majority of the manuscript, with revisions and edits from all authors

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Guarantor

Phil Chowienczyk, Clinical Pharmacology, St Thomas' Hospital, London.

ORCID iD

Ryan McNally https://orcid.org/0000-0003-2395-183X

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