Left ventricular performance during prolonged exercise: absence of systolic dysfunction

Jack M. GOODMAN*, Peter R. McLAUGHLIN† and Peter P. LIU†
*Faculty of Physical Education and Health, University of Toronto, 55 Harbord Street, Toronto, Ontario, Canada M5S 2W6, and †Heart & Stroke/Richard Lewar Centre of Excellence, Faculty of Medicine, University of Toronto, 150 College Street, rm 8, Fitzgerald Building, Toronto, Ontario, Canada M5S 3E2

ABSTRACT

We assessed left ventricular systolic and diastolic performance during and after prolonged exercise under controlled conditions in a group of healthy, trained men. Previous studies have examined the effects of prolonged effort on left ventricular function, yet it remains unclear whether or not left ventricular dysfunction (e.g. cardiac fatigue) can be produced under such conditions. We studied 15 healthy men, aged 27 ± 1 years (mean ± S.E.M.). Subjects exercised on bicycles at a constant work rate (60% of maximum oxygen uptake per min) for 150 min. Measurements of gas exchange, blood pressure and haematocrit were obtained, concurrent with the assessment of left ventricular function using equilibrium radionuclide angiography, at rest, during exercise (every 30 min) and after 30 min of recovery. Fluid replacement was provided and monitored during the exercise period. The baseline resting and exercise ejection fractions were 66 ± 2% and 78 ± 2% respectively. During exercise, subjects consumed 1816 ± 136 ml of fluid, and the haematocrit had increased at 120 min of exercise (from 47.2 ± 0.6 to 49.9 ± 0.8%; P < 0.05). There was no change in either systolic or diastolic blood pressure throughout the exercise period, but heart rate drifted upwards from 141 ± 2 beats/min after 30 min to 154 ± 3 beats/min after 150 min (P < 0.05). There was a small decline (8%; P < 0.05) in end-diastolic volume at 150 min. No changes were observed in left ventricular ejection fraction, the pressure/volume ratio or end-systolic volume. After 30 min of sitting in recovery, heart rate was still higher than the pre-exercise value (84 ± 3 compared with 69 ± 2 beats/min; P < 0.05), as were measures of peak filling rate and time to peak filling (P < 0.05). The ejection fraction in the post-exercise recovery period was similar to the pre-exercise value. The results indicate that prolonged exercise of moderate duration may not induce abnormal left ventricular systolic function or cardiac fatigue during exercise.

INTRODUCTION

The normal left ventricular (LV) response to brief submaximal exercise in the upright position has been well characterized [1,2], and includes increases in both heart rate (HR) and cardiac output, the latter increasing during low to moderate intensities of exercise due to augmented HR and stroke volume. Increases in stroke volume are brought about largely by increased LV filling [1,3], particularly during exercise performed at a low to moderate intensity. Beyond this point, further increases in cardiac output are brought about by continued increases in HR, and a decrease in end-systolic volume (ESV) secondary to increased contractility [1,3]. During prolonged exercise, an upward ‘drift’ in HR and a decline in stroke volume characterize the car-
driovascular response [4–6]. These responses are thought to be largely the result of gradual reductions in ventricular filling pressures and systemic blood pressure. The responses reflect a gradual decline in central blood volume, probably occurring secondary to a redistribution of blood volume to the venous capacitance vessels of the cutaneous circulation through peripheral vasodilatation [4,6,7]. This circulatory adjustment has been termed ‘cardiovascular drift’ [7]. It remains unclear if LV dysfunction during such activity contributes to the decrease in stroke volume. Some investigations have described an impairment of LV function following exercise of a prolonged nature [8–15]. It is possible that a decline in ventricular output involves a depression in the diastolic filling characteristics [9,13,16], several studies have failed to report a decline in LV filling pressures and stroke volume [22–25]. In addition, most were conducted under field conditions that failed to control for either the intensity of effort or the exercise time. Moreover, in the majority of cases, LV function was assessed at varying times during supine recovery. In those studies reporting an impairment of systolic function, the finding is typically transient, with normal values reported after 12–24 h of recovery; hence the term cardiac ‘fatigue’. Despite a low prevalence of cardiac events during long-distance events such as the marathon (one event per 50000 participants) [26], certain individuals remain predisposed to cardiac dysfunction and cardiac sudden death during exercise [27]. Thus a more thorough understanding of the LV response to prolonged exercise is warranted.

To date, there is very little information describing serial changes in LV function during prolonged exercise under controlled conditions, and it remains unclear if a

Table 1  Studies examining LV systolic and/or diastolic function during prolonged exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>Distance/duration</th>
<th>Measurement technique</th>
<th>Timing of measurement</th>
<th>Position/recovery or exercise data</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas et al. [12]</td>
<td>Ironman Triathlon</td>
<td>Doppler echo</td>
<td>20 min post-exercise</td>
<td>Supine/recovery</td>
<td>↓ EDD</td>
</tr>
<tr>
<td>Douglas et al. [10]</td>
<td>Ironman Triathlon</td>
<td>Doppler echo</td>
<td>3–23 min post-exercise</td>
<td>Supine/recovery</td>
<td>↓ EDD, FS</td>
</tr>
<tr>
<td>Ketelhut et al. [13,17]</td>
<td>60 min cycling</td>
<td>M-mode echo</td>
<td>Immediately after 5 min and 60 min of exercise</td>
<td>Supine/exercise</td>
<td>↓ SV, Q, EF, FS; ↓ ESD</td>
</tr>
<tr>
<td>Lucia et al. [21]</td>
<td>Marathon (42 km)</td>
<td>M-mode and Doppler echo</td>
<td>Immediately before and after exercise, and after 24–36 h of recovery</td>
<td>Supine/recovery</td>
<td>↓ EF, mV&lt;sub&gt;0&lt;/sub&gt; during recovery (vs. pre-exercise); ↓ E/A ratio</td>
</tr>
<tr>
<td>Niemelä et al. [8]</td>
<td>24 h run</td>
<td>M-mode echo</td>
<td>Immediately to 25 min post-exercise</td>
<td>Supine/recovery</td>
<td>↓ EDD, ESO, FS, mV&lt;sub&gt;0&lt;/sub&gt;</td>
</tr>
<tr>
<td>Niemelä et al. [9]</td>
<td>24 h run</td>
<td>M-mode echo</td>
<td>Immediately post-exercise</td>
<td>Supine/recovery</td>
<td>↓ FS, DFR, EDD, E/A</td>
</tr>
<tr>
<td>Palatini et al. [20]</td>
<td>50 min cycling</td>
<td>M-mode echo</td>
<td>During exercise at 10 min intervals</td>
<td>Semi-supine/recovery</td>
<td>↓ EF, SV, PVR; ↓ EDV</td>
</tr>
<tr>
<td>Perrault et al. [19]</td>
<td>42 km run</td>
<td>M-mode echo</td>
<td>Immediately to 40 min post-exercise</td>
<td>Supine/recovery</td>
<td>↓ SBP, ↔ EF, mV&lt;sub&gt;0&lt;/sub&gt;, ESD, EDD</td>
</tr>
<tr>
<td>Seals et al. [14]</td>
<td>Treadmill walking</td>
<td>M-mode echo</td>
<td>10 min post-exercise</td>
<td>Supine/recovery</td>
<td>↓ FS, mV&lt;sub&gt;0&lt;/sub&gt;, EDD</td>
</tr>
<tr>
<td>Upton et al. [18]</td>
<td>120 min cycling</td>
<td>First-pass RNA</td>
<td>During exercise at 60 min (submaximal) and 120 min (maximal)</td>
<td>Upright/recovery</td>
<td>↔ EDV or EF at 60 min</td>
</tr>
<tr>
<td>Vanoverschelde et al. [15]</td>
<td>20 km run</td>
<td>M-mode and Doppler echo, carotid pulse tracings</td>
<td>5 min after brief and prolonged exercise</td>
<td>Supine/exercise and rest</td>
<td>↑ ESD, ↓ EDD, SBP, FS, EF (vs. rest), SV</td>
</tr>
<tr>
<td>Whyte et al. [16]</td>
<td>Half and full Ironman Triathlon</td>
<td>M-mode and Doppler echo</td>
<td>2 weeks pre-race; immediately after race and 24 h recovery</td>
<td>Supine/recovery</td>
<td>↓ EDD, SV, EF for full Ironman only; ↓ E/A ratio in both; normal 48 h ratio</td>
</tr>
</tbody>
</table>

DFR, diastolic filling rate; E/A ratio, early/late diastolic flow velocity; EDD, end-diastolic dimension; ESD, end-systolic dimension; FS, fractional shortening; PVR, pressure/volume ratio; Q, cardiac output; SV, stroke volume; SBP, systolic blood pressure; mV<sub>0</sub>, mean velocity of circumferential shortening; 2D, two-dimensional.
true decline in LV systolic performance actually contributes to a reduction in stroke volume and/or a reduction in cardiovascular performance. Therefore the purpose of the present study was to examine, using radionuclide techniques, LV function during constant-load exercise and after recovery under controlled laboratory conditions.

METHODS

Subjects
A total of 15 male subjects between the ages of 20 and 30 years were recruited for the study, and each gave informed consent. The protocol was approved by the University of Toronto Committee on Human Research. All subjects had been involved with competitive cycling for a period of at least 1 year, and were studied after the competitive cycling season. All subjects were free of any medication during the course of the study.

Experimental design
All subjects performed two exercise sessions, separated by a period not exceeding 7 days. Exercise was performed in a 2-h fasted state, in a laboratory maintained at a temperature between 21 and 22 °C and a relative humidity between 40% and 50%. Baseline data were obtained during a preliminary graded exercise test before the prolonged exercise study.

Control data and preliminary exercise test
Prior to exercise, gated equilibrium radionuclide angiography was performed at rest to determine resting LV function, as described below. Subjects then performed a graded exercise test to maximum on a cycle ergometer (Monarch 850), with maximum oxygen uptake (VO2max) determined by the open-circuit method, with expired gases collected and analysed on a 15 s average basis using a calibrated metabolic cart (Senormedics 4400). Following a 45 min rest period, subjects performed an additional 4 min of exercise at an intensity equivalent to approx. 60–70% of VO2max (as determined earlier) for determination of LV function during submaximal exercise. This assessment was used as a ‘baseline’ (e.g. short-term exercise) measurement of LV ejection fraction (EF) during exercise. Each min during exercise, a 12-lead ECG was obtained (Hewlett Packard 4700A), as were measurements of arterial systolic blood pressure using an automated blood pressure cuff (Infrasound D4000), verified by manual auscultation.

Prolonged exercise study
On the second visit, subjects performed prolonged exercise of 150 min in duration, with the work rate held constant at 70–74% of the maximal HR determined during the initial graded exercise test. A venous catheter was first positioned in the right antecubital vein, with line patency maintained with a saline drip during the course of exercise. Subjects performed prolonged exercise on ‘turbo-trainers’, which are stationary training devices upon which a bicycle is fixed, allowing a rear wheel to rotate a friction-driven wind turbine which generates pedalling resistance. The pedalling rate was fixed to a given subject’s preference (70–80 rev./min), with the pedalling resistance adjusted by altering the bicycle gear. This was fixed for the entire exercise session once a plateau in target HR equal to 70–74% of maximum HR was obtained within the first 10 min of exercise. Once the pedalling rate and resistance were set, they were monitored every 10 min throughout the exercise session and kept constant. HRs were monitored continuously throughout exercise using a portable HR monitor (Sport Tester PE 3000).

Cardiorespiratory function
After every 30 min of exercise, subjects were transferred immediately to a cycle ergometer (within 30 s) and resumed their exercise for 5 min before assessment of cardiorespiratory function. Each subject’s work rate (in W) was adjusted to elicit the exercise HR measured immediately before switching from the turbo trainers, and this work rate was used for each subsequent assessment. Both systolic and diastolic blood pressures were monitored during this sequence of exercise, using an automated cuff monitor (Infrasound D4000). Expired gases were collected for a period of 2 min and reported as an average during this time period. From these data, minute ventilation, oxygen consumption (VO2) and the respiratory exchange ratio [RER; CO2 production (VCO2)/VO2] were determined. All measurements were made in the 3rd and 4th min of steady-state exercise. Blood samples for determination of the haematocrit were obtained at rest and immediately before cardiorespiratory measurements, and were analysed in triplicate immediately after sampling using a microhaematocrit scale. In addition, a general rating of perceived exertion was obtained every 30 min using the 20-point Borg scale.

Radionuclide angiography and LV function
Concurrent with measurements of expired gases (described above), gated equilibrium radionuclide images were obtained during exercise, as described previously [1]. Briefly, each subject received an intravenous injection of 2 mg of stannous pyrophosphate 15 min before modified in vitro labelling of the red blood cells with 925 MBq of 99mTc pertechnetate. Images for determination of LV EF during exercise counts were acquired by a high-sensitivity γ-radiation camera (Elscint Apex 409 AG/ECT), with subjects positioned in the left anterior oblique 35–45° position, with 15° caudal angulation to optimize right ventricle and LV separation. The LV EF was determined by semi-automated edge detection of the
averaged time–activity curve (using 300 cardiac cycles) corrected for background activity, with a correlation coefficient of 0.98 and < 2% standard error of the estimate. LV end-diastolic volume (EDV) and ESV were determined by a count-based technique [28], which has a correlation coefficient of 0.96 and a standard error of the scintigraphic estimate equal to 15.8 ml [29] in our laboratory. An index of contractility was determined by using the systolic blood pressure/ESV ratio [30]. Stroke volume and cardiac output data were derived from the ventricular volume data. All data for EDV and ESV (for serial comparison purposes) were corrected for the physical decay of 99mTc and for changes in peripheral haematocrit obtained at each sampling time period. Resting diastolic filling rates were determined using standard techniques [31] at rest and after a 30 min recovery period following prolonged exercise. A 4 min acquisition of a minimum of 200 cardiac cycles was performed, which allowed determination of the rapid filling phase, time to peak filling, peak filling rate, and atrial kick phase (%).

Fluid intake
Subjects were provided with fluids ad libitum, and were encouraged to consume water during exercise (200–300 ml every 30 min) in an attempt to maintain iso-volaemic status. Subjects received intravenous saline [with 5% (w/v) dextrose] throughout exercise, at a rate sufficient to maintain catheter patency during the 150 min period. Total fluid consumption (saline and oral consumption) was recorded over the 150 min exercise period for each subject. Body mass (kg) was measured without clothing and free of perspiration before and after the exercise session.

Statistical analysis
Differences for each variable between baseline and exercise measures were analysed using ANOVA for repeated measures [Statistical Analysis System (SAS), Cary, NC, U.S.A.]. A post hoc analysis was performed to determine specific differences between each sample time period using a Student–Newman–Keuls test. Baseline and recovery measurements of diastolic filling rates were compared using the Student’s t-test for paired samples. A probability level of $P < 0.05$ was required for significance.

RESULTS

Subject characteristics
All 15 subjects completed the study. The mean age of the group was 27 ± 1 years ($\pm$ S.E.M.). The mean height and body mass for the group were 1.78 ± 0.2 m and 71.9 ± 2.0 kg respectively.

Baseline maximal exercise data
The mean $V_{O_{2\text{max}}}$ of the group was 55.9 ± 2.0 ml·min$^{-1}$·kg$^{-1}$, or 4.06 ± 0.17 litres/min. Subjects achieved a maximal work rate of 338 ± 11 W, reaching a maximal HR of 191 ± 3 beats/min. The maximal RER was 1.20 ± 0.19, and the maximal venous blood lactate (obtained 3 min post-exercise) was 14.5 ± 0.65 mmol/l. The baseline LV EF at rest and at 70% $V_{O_{2\text{max}}}$ was 66 ± 2% and 78 ± 2% respectively.

Prolonged exercise study: cardiorespiratory and metabolic data
Mean data describing all ventilatory and metabolic measures are summarized in Table 2. $V_{O_{2}}$ remained constant throughout the exercise session, with only minor variations evident. A significant decrease in the RER was observed by 150 min ($P < 0.05$). Venous blood lactate was unchanged throughout the exercise session. Ratings of perceived exertion increased by 38% by the end of exercise ($P < 0.01$), despite a constant work rate throughout exercise. Systolic and diastolic blood pressures remained constant during exercise. However, there was small and insignificant downward trend in diastolic pressure.

LV function
Data describing LV function during exercise are presented in Figures 1–3. By the completion of the exercise period at 150 min, a significant reduction in EDV ($P < 0.05$), without any change in ESV, was observed (Figure 1). Consequently the drop in stroke volume after 90 min of exercise ($P < 0.05$) was largely due to a decrease in LV EDV (Figure 1). HR demonstrated a progressive and significant increase throughout exercise, increasing by 12% during the course of the exercise period (Figure 2) ($P < 0.01$). Indices of systolic performance were unchanged during exercise (Figure 3), as EF remained stable, within 2% (range 76–78%) of the 30 min value at all time points and almost identical to the EF measured at 75% $V_{O_{2\text{max}}}$ during the initial exercise test (78.6 ± 2.1%). The systolic pressure/volume ratio was also unchanged throughout exercise (Figure 3). There was no significant difference between measures of LV function after 30 min compared with the control values obtained during the baseline test.

Resting and recovery diastolic filling measurements
Resting diastolic filling rates obtained before and after a 30 min recovery period demonstrated a significant increase in the time to peak filling (0.174 ± 0.01 and 0.201 ± 0.013 ms respectively; $P = 0.02$), with no significant change in the peak filling rate (2.72 ± 0.14 and 3.28 ± 0.19 EDV/s respectively; $P = 0.34$). The atrial contribution to stroke volume was unchanged (22.4%...
Table 2  Cardiorespiratory and metabolic response during 150 min of exercise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Duration of exercise (min)…</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\dot{V}O_2$ (ml)</td>
<td></td>
<td>2458 ± 120</td>
<td>2408 ± 103</td>
<td>2461 ± 115</td>
<td>2451 ± 108</td>
<td>2476 ± 109</td>
</tr>
<tr>
<td>RPE</td>
<td></td>
<td>60 ± 3</td>
<td>59 ± 3</td>
<td>62 ± 3</td>
<td>60 ± 3</td>
<td>61 ± 4</td>
</tr>
<tr>
<td>RER</td>
<td></td>
<td>1.04 ± 0.01</td>
<td>1.00 ± 0.01</td>
<td>0.98 ± 0.01</td>
<td>0.95 ± 0.01*</td>
<td>0.93 ± 0.01*</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td></td>
<td>2.8 ± 0.3</td>
<td>2.7 ± 0.4</td>
<td>2.6 ± 0.4</td>
<td>2.5 ± 0.3</td>
<td>2.7 ± 0.3</td>
</tr>
<tr>
<td>Systolic pressure (mmHg)</td>
<td></td>
<td>158 ± 4</td>
<td>164 ± 4</td>
<td>163 ± 3</td>
<td>168 ± 3</td>
<td>165 ± 3</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td></td>
<td>79 ± 2</td>
<td>77 ± 2</td>
<td>75 ± 3</td>
<td>73 ± 3</td>
<td>76 ± 3</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td></td>
<td>105 ± 2</td>
<td>106 ± 3</td>
<td>104 ± 3</td>
<td>104 ± 3</td>
<td>105 ± 3</td>
</tr>
<tr>
<td>RPE</td>
<td></td>
<td>10.6 ± 0.6</td>
<td>11.4 ± 0.5</td>
<td>12.2 ± 0.4</td>
<td>13.4 ± 0.3*</td>
<td>14.7 ± 0.5*</td>
</tr>
</tbody>
</table>

Hydration status: body mass, fluid intake and haematocrit

The mean oral fluid intake was 1373 ± 116 ml during the course of exercise. In addition, the mean intake of intravenous saline was 443 ± 11 ml, amounting to a mean total fluid intake of 1816 ml. Haematocrit increased from 47.2 ± 0.6 % at rest to 48.0 ± 1.0 % after 30 min of exercise. Thereafter a slow rise in haematocrit was observed to 150 min of exercise, increasing to 49.9 ± 0.8 % after 60 min, 49.2 ± 0.8 % after 90 min and 49.0 ± 0.8 % at 120 min. The value at 150 min (49.7 ± 0.9 %) was significantly higher than that observed at 30 min ($P < 0.05$). Body mass decreased slightly from 70.9 ± 2 kg to 70.2 ± 2 kg immediately after exercise, but the decrease was not significant.

**DISCUSSION**

The decrease in stroke volume and EDV associated with prolonged exercise is a well established observation [4–7]. We observed a classic upward drift in HR and a decrease in EDV during 150 min of constant-load exercise. The decline in EDV led to a non-significant decline in stroke volume, with no decrease in systolic performance during recovery.
exercise. In addition, although we observed a delay in the
time to peak filling, no other abnormality in LV filling
characteristics (peak filling rate or atrial kick) was 
observed, nor was there evidence of depressed systolic 
performance during the recovery period.

Metabolic and respiratory data
All subjects performed exercise under controlled con-
ditions, yielding an intensity equivalent to 60–70% of 
\( V_\text{O}_{2\text{max}} \). There was very little variation in intensity 
according to measures of \( V_\text{O}_2 \) (Table 2), although the 
ratings of perceived exertion rose steadily with time. 
Respiratory data (RER) suggest a shift towards fat 
metabolism during the latter stages of exercise, with the 
blood lactate concentration remaining steady throughout 
the exercise challenge.

LV volumes
Our results are in agreement with previous data de-
scribing a decrease in LV EDV during prolonged exercise 
[8–16]. We have described a small, non-significant re-
duction in stroke volume (6%) during prolonged effort, 
secondary to a decrease in EDV late in the exercise 
session; this decrease is markedly less than in some 
studies, but comparable with that in one echo-
cardiography study [19]. However, previous studies have 
examined subjects after endurance events ranging from 
60 min in duration [13] to 42 km in length (e.g. marathon) 
[19] to the Ironman Triathlon [10–12,16] to a 24 h run 
[8,9]. Comparison between previous studies and the 
present data remains problematical, because most of 
the former assessed LV function in the supine position, 
and none monitored fluid consumption. A redistribution 
of central blood volume to the skin vasculature due to 
thermoregulatory adjustment would theoretically con-
tribute to reduced ventricular filling according to the 
Frank–Starling relationship [6,7]. In fact, it has been the 
generally accepted view that cardiovascular drift is indeed 
secondary to a rise in cutaneous blood flow, with a 
decrease in stroke volume as core temperature rises [7]. 
As a compensatory measure to mitigate this response, 
HR increases progressively in order to maintain cardiac 
output. It is possible that we attenuated the declines in 
EDV and stroke volume by minimizing plasma volume 
loss with fluid replacement. Hamilton et al. [32] showed 
that fluid replacement during prolonged exercise arrests 
the decline in stroke volume and attenuates the rise in HR 
during 120 min of cycling at 70% of \( V_\text{O}_{2\text{max}} \). Despite our 
efforts to maintain regular fluid intake (approx. 250 ml/ 
20 min), we observed a modest decrease in body mass and 
a haemoconcentration, suggestive of fluid loss. While 
some of this response may be due to compartmental 
shifts observed during exercise, such changes are nor-
mally restricted to the initial 10–15 min of exercise [33], 
and changes in plasma volume of this magnitude would 
not contribute to altered haemodynamics [34].

The direct role of cutaneous blood flow in causing 
cardiovascular drift has recently been challenged [35]. 
Fritzehe and colleagues used a selective \( \beta \)-blocker during 
60 min of exercise (57% peak effort), and found that the 
reduction in stroke volume was related to HR, but not to 
cutaneous blood flow [35]. Thus ventricular filling time 
or other factors affecting ventricular diastolic function 
may play a dominant role in the diminished stroke 
volume response.

Abnormal diastolic filling has been observed during 
recovery from prolonged exercise [9,10,14,16,21], sug-
gesting impairment of LV relaxation and/or changes in 
compliance. We observed an increase in the time to peak 
filling after 30 min of recovery. However, these changes 
were concomitant with an increase in HR, which is 
related directly to the peak filling rate and inversely to the 
time to peak filling [36]. It is therefore difficult to make 
meaningful conclusions about diastolic filling owing to 
the complexity of its nature and the interactive effects of 
HR. These limitations can also be applied to previous 
studies reporting impaired diastolic function in recovery. 
Although EF can also influence diastolic filling rates 
[31,36], there was no change in EF during recovery 
compared with pre-exercise values. Afterload reduction 
can also enhance diastolic filling, making it difficult to 
draw conclusions about ventricular compliance. Our 
subjects demonstrated a decrease in systolic blood 
presure during recovery (compared with pre-exercise 
resting values), which may in part account for the increase 
in the peak filling rate. While others have reported 
diminished filling characteristics after exercise [9,11,13], 
these data were derived from subjects in the supine 
position, and obtained while HRs remained elevated.

LV systolic performance
A rise in EF of at least 5% is considered a normal LV 
response to exercise, with EF increasing throughout 
incremental exercise [1–3]. While EF has been used 
widely as a global measure of systolic performance, few 
studies have measured it during prolonged exercise in the 
upright position. We observed no change in EF through-
out 150 min of exercise, in agreement with a previous 
study [18] that reported no change in EF after 60 min of 
exercise, or after 120 min at maximal effort. It is highly 
unlikely that prolonged exercise in itself induces myo-
cardial damage. Abnormal myocardial enzyme levels 
after marathon running have been reported previously 
[37]. However, increases in the creatine kinase MB 
fraction may accompany skeletal muscle damage, as small 
quantities of this isoenzyme have been detected in skeletal 
muscle [38]. In fact, elevated creatine kinase enzyme 
levels were reported in subjects after an ultramarathon
event [39]. However, a later report by the same authors using a more sensitive cardiac-specific troponin T immunoassay failed to duplicate these findings, and could not detect myocardial damage [40]. Similar results were observed in subjects after completion of a marathon: the authors failed to demonstrate evidence of myocardial damage using specific markers for troponin T and troponin I [21]. In contrast with these studies, a recent study did observe a small increase in troponin T levels in subjects after a half-Ironman and a full Ironman competition [16]. However, pre-race values were obtained 2 weeks before the race, and the authors reported that troponin T levels had returned to normal after 48 h, which is much earlier than the expected 5–14-day time course normally expected if myocyte damage were present. Furthermore, the value for early measurements of troponin T (< 6 h after suspected myocardial damage) may be unreliable [41]; this aspect requires further study, particularly as it relates to endurance exercise.

In pathological states, the inability to reduce ESV in the presence of afterload reduction can indicate depression of LV systolic function [42]. Despite limited data from animals that describe impaired myocardial calcium uptake during prolonged exercise [43,44], studies in humans remain limited to load-dependent measures of contractility. For example, observations of a decrease in fractional shortening [9,10,12–15] are confounded by the observation of afterload reduction in long-distance athletes after prolonged effort [17,34]. Since many of these indices of myocardial contractility (e.g. fractional shortening) are load-dependent [11], they have limited value. The study of Seals et al. [14], which is most similar to the present study in terms of exercise intensity (approx. 70% of \( \dot{V}O_{2\text{peak}} \)), demonstrated a decrease in LV fractional shortening, despite a reduction in wall stress, after 170 min of treadmill running in 12 athletes. However, the limitations of load-dependent measures of contractility used in echocardiography are well recognized, and are difficult to compare with the present investigation. Unlike previous studies that based their conclusions on post-exercise recovery data, Palatini et al. [20] observed no change in systolic performance using exercise data. Similar to our design, they provided some fluid replacement, and concluded that limited fluid consumption and use of recovery data may account for the discrepant results among these studies. We observed no change in the pressure/volume ratio during exercise, and, although this index of contractility has its limitations [30], particularly because peak systolic pressure is not measured, it is not afterload-dependent. In addition, we avoided using the recovery data to compare against the exercise data, and obtained them much later (30 min) than in most studies, when LV dimensions are less liable to undergo rapid change [20]. Ketelhut et al. [17] reported that abnormal ventricular function after 60 min of exercise may be independent of decreases in arterial pressure. However, in that particular study, data were obtained from subjects in the supine position during exercise and therefore are limited. In addition, the extent of post-exercise hypotension can vary greatly and is strongly linked to various factors, including hydration state, blood volume shifts to the periphery, thermal stress and sympathetic activation [34].

**Limitations of the study**

We chose to evaluate LV function under conditions that would mimic typical steady-state exercise conditions; that is, exercise intensity was held constant and HR was allowed to drift upwards. We are the first to report LV volumes and systolic performance under controlled conditions over 120 min using non-geometric-based measurements to determine volumes. Nevertheless, count-based measures of LV volume used with equilibrium radionuclide angiography are not without limitations. Movement artifact may have contributed to the large variability in the findings (e.g. EDV), leading to an underestimation of the reported decline in stroke volume. However, this technique still avoids potential changes in cavity shape and allows for serial measurements without added exposure to radiation [29,31]. Furthermore, data from the present study were acquired during upright exercise, allowing for more physiologically relevant conclusions than those acquired during recovery in the supine position. A further limitation may be the trained nature of the subjects. In light of the evidence that training attenuates cardiovascular drift, the application of our findings to less-trained individuals may be limited [45] and could underestimate the risk of participation in such events.

**Conclusions**

We could not detect diminished LV systolic function during prolonged effort in conditioned young adults. Despite fluid replacement, cardiovascular drift occurred as exercise time increased, characterized by a progressive increase in HR and a decrease in EDV. This response was not accompanied by any evidence of LV systolic dysfunction during exercise or in the recovery period.

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