Left ventricular contractile function is preserved during prolonged exercise in middle-aged men

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Submitted 8 April 2008; accepted in final form 20 November 2008

Goodman JM, Busato GM, Frey E, Sasson Z. Left ventricular contractile function is preserved during prolonged exercise in middle-aged men. J Appl Physiol 106: 494–499, 2009. First published November 26, 2008; doi:10.1152/japplphysiol.90506.2008.—We examined left ventricular (LV) performance before, during, and following prolonged exercise (EX) in 12 healthy middle-aged men [means ± SE: age = 43.5 ± 1.9 yr; maximal O2 uptake (V\textsubscript{O\textsubscript{2max}}) = 51.7 ± 1.5 ml·kg\textsuperscript{-1}·min\textsuperscript{-1}]. Subjects cycled for 120 min at 65% V\textsubscript{O\textsubscript{2max}} (75% of maximal heart rate). Two-dimensional echocardiography (ECHO) to determine tissue-Doppler longitudinal myocardial strain and strain rate, LV ejection fraction (EF), end-diastolic (EDV), end-systolic (ESV), and stroke volume (SV) at baseline and after 5, 30, and 120 min of EX and following 30 min of recovery. In addition, hematocrit and plasma norepinephrine (NE) were measured. From baseline to 5 min of EX, there were significant increases in LV longitudinal strain (+23.20 ± 0.87 to −27.63 ± 1.07%; \(P < 0.01\)), strain rate (−1.50 ± 0.15 to −2.08 ± 0.14 s\textsuperscript{-1}; \(P < 0.01\)), and EF (56.3 ± 2.2 to 77.1 ± 1.0%; \(P < 0.05\)) with continued increases by both at 30 min of exercise vs. EDV, ESV, and SV, which remained constant. After 120 min of EX, HR and NE increased further with reductions in SV, cardiac output, and systolic blood pressure without changes in strain or strain rate. EDV decreased after 120 min of EX (−9.2- vs. 30-min value; \(P = 0.05\)) along with a hemoconcentration (baseline = 41.3 ± 1.0 vs. EX = 45.1 ± 1.2%; \(P < 0.001\)) and significant reduction in body mass despite a mean fluid consumption of 1.8 ± 0.2 liters throughout EX. After 30 min of recovery, LV longitudinal strain was depressed relative to baseline (−23.20 ± 0.87 to −19.57 ± 1.21%; \(P < 0.01\)). The reduction in LV SV during prolonged EX occurred without changes in the LV contractile state and is likely secondary to reduced LV preload. A reduction in LV contractility despite a reduced afterload following exercise may be due to factors unique to the recovery period and do not appear to contribute to a reduction in SV during prolonged exercise.

echocardiography; stroke volume; end-diastolic volume; end-systolic volume

THE LEFT VENTRICULAR (LV) response to prolonged strenuous exercise is characterized by a gradual rise in heart rate (HR) and concomitant reduction in stroke volume (SV). This response has been termed “cardiovascular drift” (2, 8, 30). The progressive decline in SV and pulmonary and systemic mean arterial pressures, along with the rise in HR (14) at a constant cardiac output (Q) (8, 19, 33), was once considered to be secondary to a reduction in LV filling time due to an elevated HR (43), limiting end-diastolic volume (EDV) (18, 19) and reducing SV (37). It is now known that these responses are also brought about by a sympathetically mediated rise in HR (9) related to an increased core temperature. Combined, these responses and the accompanying plasma volume loss and reduced LV filling pressures are thought to contribute significantly to cardiovascular drift (2, 8, 30).

More recent data from controlled experimental conditions indicated that maintenance of preload (thereby maintaining central venous pressure and LV filling pressure) throughout exercise can arrest the reduction in SV (5, 16), suggesting that the reduction in SV during prolonged exercise is highly preload dependent. Therefore, this study and others examining the effects of prolonged exercise on LV function have assessed systolic function in the immediate postexertional period, when HR and hemodynamic loading conditions change rapidly. Such studies have reported transient reductions in LV systolic (1, 6, 7, 35, 36, 42, 46) and diastolic (1, 5, 10, 16, 24, 25, 36, 46) function during the recovery period, a phenomenon termed “cardiac fatigue.” Notwithstanding, it remains unclear whether a decline in LV contractile (i.e., inotropic) function is coincident in the reduction in SV during prolonged exercise. There are limited data describing LV function during exercise; a constant systolic pressure volume ratio (SPVR) was observed during (12) and immediately after 120 min of exercise (4), and similar data were reported in cyclists after ~2.5 h of exercise (40) using systolic blood pressure and LV dimensional data. Although an accepted index of contractility, the SPVR is limited by a single and surrogate measure of end-systolic pressure (systolic arterial blood pressure) and a lack of sensitivity (34), whereas novel measures of LV strain and strain rate (50) are now considered superior measures of LV contractility given the avoidance of LV volume determinations that are influenced by papillary tethering (27) and, in particular, global measures of LV function such as ejection fraction (EF), which is highly influenced by loading conditions (27, 38). Finally, there are few data characterizing these responses in older individuals who represent both the largest and the fastest growing cohort in mass-participation endurance events (32). Observations of an age-dependent reduction in β-adrenergic receptor sensitivity (47) may increase the likelihood of impaired systolic contractile performance during exercise in these individuals, yet little data exist in either this population or following exercise durations that more closely match chronic training regimes compared with competitions of longer duration. Accordingly, the purpose of this study was to examine the effects of prolonged strenuous exercise on LV systolic function to test the hypothesis that cardiovascular drift during exercise is due in part, to a reduction in LV contractility.

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METHODS

Subjects. A total of 12 healthy men (40–52 yr) participated in the study. Subjects were recruited from advertisements posted in local running and cycling clubs. Subjects were free of medications and were excluded if there was evidence of any prior history of cardiovascular disease or a >5% likelihood of coronary disease from their clinical history. The protocol and informed, written consent obtained from all subjects before their participation was approved by the University of Toronto and Mt. Sinai Hospital research ethics board pertaining to human subjects, which is in full conformity with the Helsinki Declaration on the use of human subjects.

General experimental design. Subjects initially underwent graded cycle exercise testing to determine maximal O2 uptake (VO2max). These data were then used to establish the individual exercise intensity for the prolonged exercise challenge, conducted on a separate occasion within a 2-wk period in a controlled laboratory setting. A trial session was initially conducted (after exercise testing) to habituate the subjects and to establish the workrates used during prolonged exercise session performed on their personal road bikes set on “turbo trainers.” A workload (gear setting and rpm) was determined to elicit a steady-state target HR equal to ~75% of maximal HR (HRmax) or 60–65% VO2max. To perform cardiac imaging, subjects transferred from their road bikes to an imaging table ergometer positioned adjacently; this procedure and the workrate on the ergometer was also established during the trial session to ensure that subjects rapidly matched the heart rate during cardiac imaging to that observed immediately before the transfer; these workrates would remain fixed for all cardiac imaging throughout the exercise session.

Initial exercise testing (VO2max). Graded exercise testing was performed to exhaustion on a cycle ergometer (Lode B.V. Groningen-Holland Medical Technology) to assess VO2max and HRmax. Expired gases were collected from breath-by-breath samples and reported as 20-s averages using a calibrated metabolic cart (Sensormedics 2900), whereas HR was measured continuously (Polar 810i) and recorded electronically (HRTrak II Heart Rate Tracker, Equilibrate Bio Systems). Cycling was performed at a pedaling frequency of 70 rpm. Following a 3-min warm-up at 50 W, the workrate was progressively increased by 25 W every 30 s until maximal effort was achieved, demonstrated by a plateau in O2 uptake. Secondary measures of maximal effort included attainment of the age-predicted maximal HR and a respiratory exchange ratio of 1.15 or higher.

Prolonged exercise protocol. Within 2 wk of graded exercise testing, subjects performed the prolonged exercise challenge. Subjects were asked to refrain from caffeine or alcohol 24 h before the study. Sixty minutes before exercise, subjects drank 500 ml of water to ensure an adequate preexercise hydration status. Subjects were weighed on a calibrated scale (Health-O-Meter, Bridgeview, IL) to determine dry body weight before exercise. Each subject was fitted with 12 electrocardiographic (ECG) leads in the standard fashion (Case 16 Exercise Testing System, Marquette Medical Systems, Milwaukee, WI) for HR assessment and echocardiography gating. The prolonged exercise challenge began with a 3-min warm-up, and after an additional 5 min the predetermined workrate was established and held constant to elicit the desired intensity for 120 min of cycling. After 5, 30, and 150 min, subjects transferred to the imaging table ergometer and immediately resumed cycling at the preset intensity as described earlier (requiring ~20–30 s to complete the transfer). Cardiac imaging and blood sampling occurred only after the steady-state HR before the transfer was reestablished. HR was continuously monitored throughout the exercise (Polar 810i). Participants were required to drink 250 ml of water every 20–30 min to maintain hydration during the exercise bout. Following the prolonged exercise challenge, subjects cooled down for a minimum of 10 min at a low intensity, after which dry body weight was determined again.

Echocardiography. Echocardiographic imaging was obtained with subjects exercising on an electronically braked cycle ergometer (Su-
Systolic blood pressure progressively decreased with exercise from baseline to 108.0 (P < 0.05) (Table 2; Fig. 1). This was accompanied by a significant reduction in cardiac output (Q) observed between 30 and 120 min of prolonged exercise (−7.4%; P < 0.05) (Table 2; Fig. 1). Systolic blood pressure progressively decreased with exercise (185.0 ± 6.7 mmHg at 5 min to 171.0 ± 6.4 mmHg at 120 min; P < 0.05) and a postexercise hypotension was evident following the 30-min recovery period (120.0 ± 2.4 mmHg at baseline to 108.0 ± 1.7 mmHg at recovery; P < 0.001). Throughout the exercise bout, there were reductions in EDV (−9.2%; P = 0.05), EF (−3.8%, P = 0.11), and the systolic pressure-to-volume ratio (−11%; P = 0.22). In addition, systolic wall stress steadily declined throughout the exercise period (3.9 ± 0.2 g/cm² at 5 min to 2.83 ± 0.23 g/cm² at 120 min; P < 0.001). Relative changes in variables during exercise compared with the 5-min exercise value (% change) are depicted in Fig. 2.

All strain and strain rate measures of the LV were taken from the distal septal region, since proximal septal images were unsuitable for analysis due to motion artifact during exercise. As per convention, systolic strain and strain rate are expressed as negative values where greater deformation (i.e., contractility) is reported as more negative. The average LV strain significantly increased from baseline to 5 min of exercise (−23.20 ± 0.87 to −27.63 ± 1.07%; P < 0.01) (Table 2; Fig. 3). Thereafter, no change in the mean strain was observed during exercise; however, there was a significant reduction during recovery compared with baseline values (−23.20 ± 0.87 to −19.57 ± 1.21%; P < 0.01). In addition, peak systolic strain rate was also reduced in the recovery period compared with preexercise measures, although this failed to reach statistical significance (−1.50 ± 0.15 to −1.21 ± 0.11 s⁻¹; P = 0.07). The peak systolic strain rate significantly increased from baseline to 5 min (−1.50 ± 0.44 to −2.08 ± 0.41 s⁻¹) and from 5 to 30 min of exercise (−2.08 ± 0.14 s⁻¹ to −2.66 ± 0.16 s⁻¹; P < 0.05). A significant reduction in the recovery period compared with baseline values was also observed (−23.20 ± 0.87 to −19.57 ± 1.21%; P < 0.01) (Table 2; Fig. 3). Changes in average strain and peak systolic strain rate are depicted in Figs. 3 and 4, respectively.

A moderate hemococoncentration was observed throughout the exercise protocol, with hematocrit rising from 41.3 ± 1.0% at baseline to 43.6 ± 1.1% and 45.1 ± 1.2% after 30 and 120 min of exercise, respectively (P < 0.001). Plasma levels of norepinephrine (NE) increased steadily throughout the exercise bout (3.1 ± 0.4 at baseline to 11.0 ± 1.5 nM at 120 min; P < 0.001) (Table 2; Fig. 2).

**DISCUSSION**

This study demonstrated that LV systolic performance during prolonged exercise in middle-aged endurance-trained men is well regulated during the first 30 min of exercise through the combined effects of increased LV filling (preload) and LV contractility. The cardiovascular drift evident in the later stages of exercise is secondary to a reduction in LV preload (EDV)
while systolic performance and indexes of LV contractility were preserved. A novel feature of this study was the measurement of LV function during exercise, thereby avoiding rapidly changing hemodynamic loading conditions. This is relevant given our finding that postexercise reductions in LV systolic performance were dissociated from that observed during exercise, suggesting that a decline in LV contractility following prolonged exercise may be unique to the recovery period.

These data extend earlier work by this author (12), which reported classic signs of cardiovascular drift after 30 min of continuous exercise, the magnitude of which is similar to previous studies examining mildly to moderately dehydrated individuals (2, 11, 22). In agreement with prior observations (13), LV output was increased early (5 min) during exercise by enhanced preload and contractility. The Frank-Starling mechanism has been considered the primary factor responsible for increased SV during early stages of exercise (29), and although contractility increased at this point (5 min), further increases were observed after 30 min, concurrent with a significant increase (+139%) in plasma NE. At this point of steady-state exercise, LV filling reaches an asymptote well above resting levels. It is well known that prolonged exercise is associated with significant elevations in NE, contributing to increased glycogenolysis and myocardial contractility (49). We observed a steady rise in plasma NE (Fig. 2) with robust LV systolic function throughout exercise, as seen in all measures of LV function from 5 to 120 min of exercise (Table 2; Figs. 3 and 4). Paralleling these increases were measures of systolic strain and strain rate, with no evidence of diminished LV contractility between 30 and 120 min of exercise (Figs. 3 and 4), which is similar to previous reports that measured LV systolic function during exercise using radionuclide techniques (12, 44) or echocardiography immediately after exercise (26). LV systolic strain and strain rate have the advantage of being independent of myocardial tethering of the papillary muscles (23, 27, 38, 48), are less sensitive to influences of LV loading, and are more representative of global and regional contractility. Sustained LV systolic function during prolonged exercise was associated with a diminution in LV wall stress and LV afterload (Table 2), which in turn favors LV emptying.

Although the focus of this investigation was LV function during exercise, it is noteworthy that studies reporting evidence of LV systolic and diastolic dysfunction following prolonged exercise have used resting pre- and postexercise (recovery) measures, the latter subject to rapidly changing loading and metabolic conditions. As with other reports (1, 6, 7, 35, 36, 42, 46), we observed a postexercise (30-min recovery) depression of LV systolic performance, yet no change during exercise (Figs. 3 and 4). This dissociation is difficult to explain other than by abrupt reductions in venous return and sympathetic withdrawal following exercise. Further study is required to reconcile these observations, but our data suggest the decline in SV is independent of altered systolic performance (12, 44).

The reduction in LV SV during prolonged exercise is likely secondary to numerous factors related to loading conditions. We did observe a reduction in systolic arterial blood pressure, which can reduce LV filling. The upward drift in HR may in
turn compromise LV filling time (43), reducing EDV and SV (37). In addition, a reduction in SV during prolonged exercise can be prevented by clamping HR using beta-blockade (9). Acute blood volume expansion studies (22) suggest that hypovolemia accounts for ~50% of the decline in SV observed during PSE (2). Indeed, the maintenance of preload during exercise can virtually obliterates exercise-induced changes in indexes of systolic and diastolic function (5, 16), and the modest hemoconcentration and reduction in body mass seen in the present study likely contributed to a reduction in preload and resultant decline in SV after 120 min of exercise. However, reports of diastolic dysfunction following exercise despite preload augmentation (15) and discordance between changes in diastolic function and loading conditions or HR (10) suggests that altered intrinsic LV relaxation during exercise cannot be ruled out. Fusion of the early and atrial transmitral filling velocities that occurs with heart rates above ~100 beats/min (31) prevented us from such measures, yet slowing of diastolic myocardial energetics or beta-adrenergic receptor desensitization remain possible mechanisms to explain the decline in EDV during exercise (21, 28, 39).

Limitations

Our study is not without limitations. Acquiring high-fidelity echo images during exercise is technically challenging but allows for interrogation of the LV under the true loading conditions of exercise. However, due to motion artifact, we could only analyze tissue-Doppler images from the distal septum. Although it has been argued that LV strain is indicative of global contractility and that regional measures are comparable (27, 38), we were limited at the time by imaging and analysis software. Analysis of diastolic function remains elusive during exercise and limits our understanding of the factors that may contribute to systolic dysfunction following exercise, particularly given the observation that diastolic dysfunction may precede systolic abnormalities (5). In addition, TDI-derived strain and strain rate are dependent on the ultrasound probe angle relative to the direction of myocardial movement and is limited to a single-dimensional measure (3). Finally, the assessment of LV function during prolonged exercise remains problematic given the upward drift of HR and the potentially confounding influence of the Bowditch effect (17). We did not normalize HR to early exercise values to characterize the cardiovascular response to exercise during a steady-state condition. There is also a possibility that LV loading conditions were altered as subjects transitioned from their training bicycles to the imaging ergometer, although subjects were secured against a foam wedge at a 60° angle, with the torso clearly in an upright orientation. In addition, all imaging was performed in this manner and was not performed until a steady-state HR was re-established, ensuring the cycling condition was matched as closely as possible. Finally, we were unable to obtain measures of hemoglobin, limiting our estimation of the changes in plasma volume, yet the loss in body mass following exercise provides supportive evidence.

In conclusion, the acute, early response to submaximal exercise in masters recreational athletes is characterized by an increased end-diastolic volume secondary to the Frank-Starling effect with augmented LV contractility and HR, which continue from 5 to 30 min of exercise. After 120 min of exercise, a reduction in LV SV occurred concomitant to a decline in LV EDV. These changes were likely secondary to a reduction in preload through reductions in arterial blood pressure and plasma volume. These data indicate that a reduction in SV during prolonged exercise is independent of LV contractility, which remains well preserved throughout exercise.

ACKNOWLEDGMENTS

The authors thank Joan Persaud for technical assistance.

GRANTS

The authors thank the Heart and Stroke Foundation for funding.

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J Appl Physiol • VOL 106 • FEBRUARY 2009 • www.jap.org
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