

Exercise Induced Cardiac Fatigue Following Prolonged Exercise in Road Cyclists

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Abstract

The purpose of this study was to examine cardiac function following a 100-mile ride in high ambient temperatures by healthy, competitive cyclists. Methods: Subjects were six (n=6) competitive cyclists racing in a 100-mile road race. Measures (pre/post) included: body mass (kg); E:A ratio (ventricular compliance); stroke volume (ml); ejection fraction (%) through echocardiography; age (y); training status (hrs*week⁻¹); years of racing experience (YE); race finish time (hrs); height (cm); mean race heart rate (b*min⁻¹), and post race blood troponin I (cTnI) to assess myocyte damage. Results: subject means (±SE) were the following: age, 24.2 (1.2) y; height, 181.1 (5.5) cm; training status, 18 (2.4) hrs*week⁻¹; racing experience, 5.8 (4.6) y; race heart rate, 159.3 (3.9) b*min⁻¹; pre/post E:A ratio, 2.04(.41)/ 1.27(.39); pre/post stroke volume, 98.6 (21.6)/ 72.6(11.8) ml*min⁻¹; cTnI, 0.13 (.15); ejection fraction pre/post, 67.3 (3.8)/ 65.1(2.2)%; finish time 4.05 (0.54) hrs. Significant (p< 0.05) differences were determined pre/post for E:A ratio, stroke volume, and pre/post body mass, 76.4 (5.9)/ 72.4 (1.8) kg. cTnI was elevated above established levels of 0.03 ng*ml⁻¹ for cellular disruption. Conclusion: The differences in E:A ratio (i.e., ventricular compliance), stroke volume and elevated cTnI indicate reduced cardiac function indicative of cardiac fatigue.

Key Words: echocardiography, cardiac damage.

Introduction

Exercise induced cardiac dysfunction is generally associated with cardiovascular disease. However, a transient reduction in systolic and diastolic performance after prolonged exercise has been successfully demonstrated by many researchers (Bonetti et al., 1996; Douglas, O'Toole, Hiller, Hackney & Reichel, 1987; Konig et al., 2003; Middleton et al., 2007; Niemela, Palatsi, Ikaheimo, Takkunen & Vuori, 1984; Rafai, Douglas, O'Toole, Rimm & Ginsberg, 1999; Rowe, 1993; Seals et al., 1988; Shave et al., 2004; Tulloh, et al., 2006; Vanoverschelde et al., 1991). This can be identified by various signs, such as decreased cardiac contractility, altered diastolic function and septal wall motion abnormalities. Additionally, transitory elevation of cardiac markers, indicative of cardiac damage are shown following prolonged duration of exercise (Koller, 2003; Middleton et al.; Neumayr, et al., 2001).

It is well recognized that chronic cardiac endurance training induces a number of morphological and cardiovascular adaptations such as decreased resting heart rate, left ventricular hypertrophy, and increased stroke volume (Middleton, Shave, George, Whyte, Hart, & Atkinson, 2006). As cardiac output is a product of heart rate and stroke volume, increased requirement of oxygen during prolonged exercise demands increased cardiac activity (Braunwald et al., 2001; Sagiv, Ben-Sira, Goldhammer & Soudry, 2000). This increase in cardiac workload for a prolonged

duration may result in a transient impairment in cardiac function (Middleton et al.). In the absence of any underlying cardiovascular diseases, this impairment may be attributed to a condition referred to as exercise induced cardiac fatigue (EICF) (Middleton et al.; Starnes, Wilson & Erecinska, 1985; Whyte et al., 2000). Yet, some research indicates a lack of evidence toward a decrease in cardiac performance after prolonged exercise (Goodman, McLaughlin & Liu, 2001). This may be attributed to variations in the methods employed, specifically the exercise duration and the training status of participants (Middleton et al.).

The study of exercise induced cardiac fatigue has mainly focused on trained athletes participating in prolonged endurance events such as triathlons, marathon running and cycling. These studies have been limited by various confounding factors such as duration, intensity, and environmental conditions. Individuals not competitively engaged in an endurance exercise program appear to have a much lower threshold and less tolerance for prolonged endurance exercise. Thus, these non-competitive individuals may experience cardiac fatigue after a shorter amount of time and lower intensities of exercise than competitive endurance athletes (Seals et al., 1988; Vanoverschelde et al., 1991). Although there is no unanimity to the cause of exercise induced cardiac fatigue, many hypotheses have been used to explain the cardiac dysfunction experienced in the absence of cardiovascular disease. These include fatty acid accumulation, prolonged tachycardia, and catecholamine elevations (Rifai et al., 1999). Decreased systolic function of the heart has been attributed to a depressed inotropic state (Douglas et al., 1987; Douglas, O'Toole & Woolard, 1990; Mole & Coulson, 1995; Niemela, Palatsi, Ikaheimo, Airaksinen & Takkunen, 1987; Niemela et al., 1984; Seals et al., 1988; Vanoverschelde et al., 1991) while diastolic dysfunction has been attributed to altered volume loading (Douglas et al.; Niemela et al.). Septal wall abnormalities suggestive of ischemia have also been identified (Douglas et al.). Following the completion of prolonged strenuous exercise, athletes often exhibit left ventricular dysfunction (Middleton et al., 2006). Additionally, elevated levels of cardiac enzymes indicative of myocyte damage, such as creatinine kinase MB (CK-MB), cardiac troponin-T (cTnT), and cardiac troponin- I (cTnI) may be noted following endurance events. Cardiac troponin-T and cTnI are not normally detected in the serum of healthy subjects at rest and are therefore highly sensitive and specific indicators of injury to the heart (Bonetti et al., 1996; Rifai et al., 1999; Shave et al., 2002). Currently, cTnI is the most sensitive and specific marker for the myocardial necrosis detection even in the presence of damage to skeletal muscles (Denvir et al., 1999; Koller, 2003; Neumayr et al., 2001).

Lastly, cardiac fatigue in the absence of myocardial necrosis has been previously described as myocardial stunning (Whyte et al., 2000). This may be the result of transient ischemia during exercise and associated with the accumulation of oxygen free radicals (Whyte et al.). Therefore, it is the purpose of this study to examine cardiac fatigue following a 100 mile ride in a high ambient

temperature environment by healthy, competitive cyclists. It is hypothesized that following an extended period of work associated with endurance performance (i.e., competitive cycling), markers for cardiac fatigue will be noted through echocardiography and elevated blood cTnI levels. Utilizing an environment of work (i.e., 100 m bike ride) coupled with high ambient temperature conditions (98.6° F) the researchers purposely chose this venue for eliciting possible EICF. The examination of the aforementioned blood markers and echocardiography in the current study provides a multifaceted approach to confirmation of cardiac fatigue. From these findings, future research may focus on recovery markers resulting from the associated cardiac fatigue. Recognition or confirmation of cardiac fatigue recovery in competitive endurance athletes provide evidence of specific stress markers associated with specific adaptation responses.

Methods

The Hotter-N-Hell™ Hundred is one of the oldest and largest one day cycling events in the United States. It is held each year in August when temperatures often exceed 100°F during later portions of the race. Six (6) subjects participating in this bicycle ride were selected for this study. Prior to testing, all subjects were administered a medical health questionnaire, a PAR-Q Fitness Readiness questionnaire and signed a Midwestern State University Institutional Review Board approved informed consent. Pre-race measurements were taken 36 hours (h) before the race. Post-race measurements were taken immediately following each individual’s finish of the race.

Pre Race Measurements

Subjects descriptive characteristics included mean (+SE) for the following; age (y), gender (M/F), height (m), body mass (kg), body mass Index (BMI), training status (hrs*week⁻¹), and years of experience (YE). Body mass was measured on a Health o meter™ beam scale (Jarden Corporation, Providence, RI) with subjects in bare feet and shorts. A two dimensional echocardiographic assessment was completed by a single, experienced sonographer, in accordance with the guidelines established by the American Society of Echocardiography. Assessment was completed by using a Hewlett-Packard Philips Sonos 5500™ (Palo Alto, CA). Subjects were instructed to lie in the left lateral decubitus position. Stroke volume (L*min⁻¹), ejection fraction (%) along with peak early filling (E waves/cm) and peak late filling (A wave/cm) velocities were measured. Additionally, the ratio of early to late diastolic filling (E:A) was calculated in order to establish diastolic function of the heart (Schiller, Shah, Crawford, Demaria, Devereux, Feigenbaum, Gutgussel, Reichek, Sahn, Schittger, Silverman & Tajik, 1989). Three to five measures were obtained with three consecutive and consistent measures averaged. This was done to maintain tester reliability within each measure.

Post Race Measures

Following the race, each subject immediately came to the established medical tent where post race measures were conducted. Initially, subject hydration status was checked for any evidence of dehydration through urine sample color followed by body mass (kg) and mean heart rate (b*min⁻¹). Hydration was measured to ensure

blood volume was not a factor associated with altered cTNI levels. Once they were stabilized (i.e, recovered) in the supine position, the blood measurements and echocardiography were taken. These measures were approximately 15 min post race with the blood stored in a cooler with dry ice for later analysis. Cardiac troponin I levels (cTnI) were determined by immunochemiluminescence (ECL) technology employed within the Beckman Coulter DXI Analyzer™ (Brea, CA). The established cut off value for myocardial injury for cTnI is 0.5 ng*ml⁻¹ and detection limit (i.e., elevation detection) was 0.03 ng*ml⁻¹ (Collinson, Boa & Gaze, 2001).

Statistics

Mean (SE) was determined for descriptive data. To determine pre/post race statistical differences, a dependent samples t-Test was performed. Cardiac troponin I levels were analyzed for clinical significance established at 0.03 ng*ml⁻¹ utilizing a □square test for single sample. Correlation analyses were performed using a Pearson Product R Correlation Coefficient to determine possible bivariate associations between variables. Alpha (p) value for statistical significance was set a priori at p ≤ 0.05. All statistics were performed using Statistica-7™ (Tulsa, OK).

Results

The subjects were six (6) college aged male cyclists participating in the Hotter-N-Hell™ 100 mile bicycle ride with the following descriptive measures (mean ± SE) in Table 1.

Table 1. Subject Mean (SE) Descriptive Measures

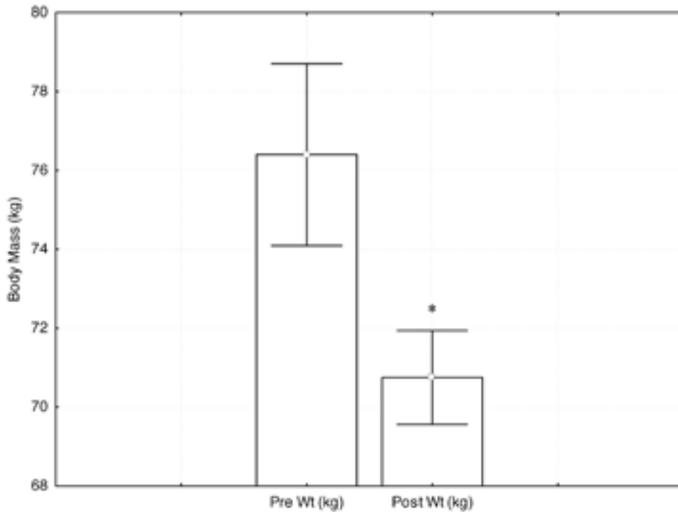
Measure	Mean	SE
Age (y)	24.2	0.47
TS (hrs*wk-1)	18	1.00
YE (y)	5.83	1.87
Height (cm)	181	2.00
Pre Body Mass (kg)	76.4	2.43
Post Body Mass (kg)	70.75*	1.25
Race HR (b*min-1)	159.3	1.59

Note: TS - Training Status; YE-years of cycling experience; HR-heart rate; *Statistically significant at p=0.02

Out of six, four completed the 100 miles in 4.40±0.04 hrs, while two finished 80 miles after being dropped by the leaders of the race. The two that rode 80 m were not excluded because the endurance time on the bike exceeded four (4) hours and the ambient temperature during the ride reached 98.6° F. Body mass pre race 76.4±5.94 kg was significantly (p= 0.02, t=3.55) reduced post race 70.7±3.18 kg (See Figure 1). Mean (SE) heart rate was 159.3 ± 1.59 b*min⁻¹. Correlation analysis revealed no significant associations between measured variables.

Figure 1

Mean (SE) Pre-Post Race Measures of Body Mass.



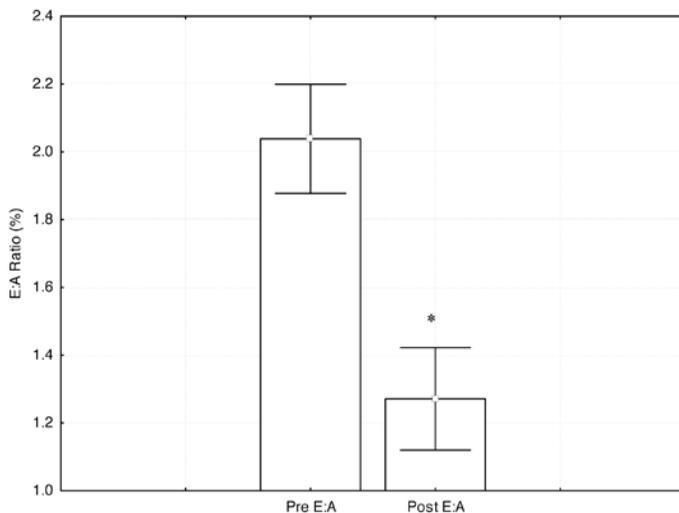
*Statistically significant at $p=0.02$

Echocardiographic Data

Early (E) and late (A) diastolic filling were not significantly reduced ($p=0.06$). However, the resultant early to late diastolic filling ratio (E:A) between pre and post race were significantly different ($p=0.002$, $t=5.75$). Graphic comparisons of E:A ratio pre and post race can be seen in Figure 2.

Figure 2

Mean (SE) Pre-Post Race Measures in Diastolic function (E:A ratio)

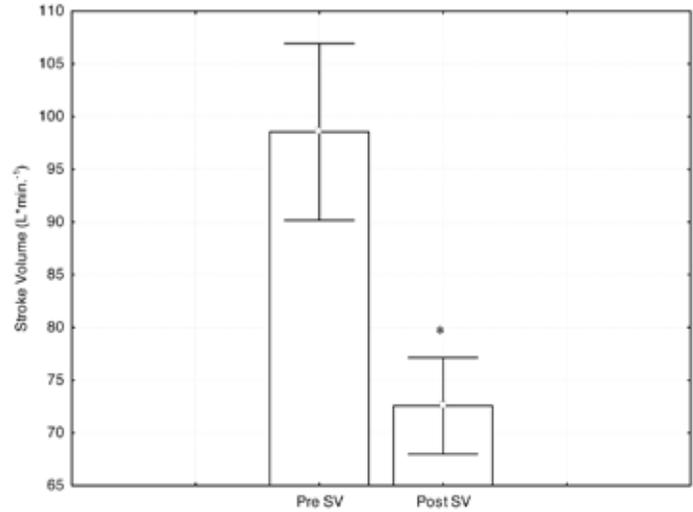


*Statistically significant $p=0.002$

Stroke volume ($L \cdot \text{min}^{-1}$) was significantly reduced ($p=0.02$, $t=3.21$) post race in all subjects (Figure 3).

Figure 3

Mean (SE) Pre-Post Race Measures in Stroke Volume.



*Statistically significant $p=0.02$

While ejection fraction was reduced, it did not reach statistical significance ($p=0.29$, $t=1.16$).

Blood Data

Following the race, cTnI levels increased in all subjects. The increase was moderate or indeterminate grade (i.e. between 0.03 - $0.5 \text{ ng} \cdot \text{ml}^{-1}$) with a mean of $0.13 \pm 0.06 \text{ ng} \cdot \text{ml}^{-1}$. One subject showed increase in cTnI level of $0.45 \text{ ng} \cdot \text{ml}^{-1}$, which nears the acute myocardial infarction cutoff value of $0.5 \text{ ng} \cdot \text{ml}^{-1}$ (Collinson et al., 2001). This indicates that there was myocardial cellular disruption, though statistically not significant ($p=0.17$). While subject values varied within the group, they were maintained with analysis primarily focused toward clinical implications toward the aforementioned cTnI levels (i.e., 0.03 - $0.5 \text{ mg} \cdot \text{ml}^{-1}$). All subjects exceeded clinical levels of cTnI indicating myocardial disruption in their post race blood analysis.

Discussion

The findings of this study indicate that after prolonged exercise in high ambient temperatures, cardiac dysfunction as well as myocardial cellular disruption in competitive, healthy male cyclists is evident. The current study found a significant decrease in diastolic function denoted by the decreased E:A ratio. The significant decrease in stroke volume and decrease in ejection fraction indicates additional systolic dysfunction. While the mechanisms of this systolic and diastolic dysfunction are not clear, a number of possibilities have been proposed. Additionally, this study found evidence of myocardial cellular disruption indicated by moderate elevations of cTnI after the race. A Pearson Product R Correlation Coefficient did not reveal associations between the significant decline in cardiac function and other measures included in the study. Considering the aforementioned definition of fatigue, the decrease in cardiac function of the heart following such a prolonged exercise in this study may be referred to as cardiac fatigue. However, because this analysis utilized a small sample

size, these findings should be interpreted with caution.

Echocardiographic Data

The subjects in this study showed a statistically significant decrease in E:A ratio immediately post-race compared to pre-race measures. This may contribute to the phenomenon of exercise induced cardiac fatigue. The decrease in diastolic function has been confirmed by many researchers (Douglas et al., 1987; Miki, Yokota, Seo & Yokoyama, 1994; Niemela et al., 1987; Rowe, 1993; Seals et al., 1988; Tulloh et al., 2006; Whyte et al., 2000).

An immediate post race decrease in E:A ratio indicates that diastolic filling is compromised and left ventricular compliance is reduced (Whyte et al., 2000). The increased velocity of atrial or late diastolic inflow results in a decrease in early to late diastolic flow velocities as the current study indicates. As diastolic performance depends on many factors such as ventricular loading and contractile conditions, it is difficult to speculate as to a specific cause for this dysfunction (Douglas et al., 1987). Such abnormal filling patterns may be due to reduced ventricular compliance or increased myocardial stiffness. Another possibility for the increased late diastolic filling velocity is simply an increase in the force of left atrial contraction. This results in a higher velocity of blood flow during atrial systole. It should be noted that while transient, it is not known whether this reduction has any impact on subsequent prolonged endurance exercise performance (Whyte et al.).

The current study found a significant decrease in post race stroke volume. Stroke volume is an indicator of systolic performance of the heart and is dependent on two factors: preload on the cardiac muscle and the level of contractility (Guyton & Hall, 2005). Frank-Starling's Law of the Heart simply states that an increase in diastolic filling and pre-load enhances contractility of the heart. As per Starling's mechanism, the force of ventricular contraction is a function of the end diastolic length of the cardiac muscle fibers indicating a close relationship to end diastolic volume (Braunwald et al., 2001; Guyton & Hall). The fractional shortening of myocardial fibers (length of myocardial fibers) is one of the indices of myocardial performance. This is dependent on the preload. Decreased preload because of blood volume redistribution or reduced venous return leads to a reduction in end diastolic volume and subsequent reduced stroke volume (Douglas et al., 1987). In the current study, subjects were exposed to a long duration event as well as high ambient temperatures. Mole and Coulson (1995) note that demands on circulation become exacerbated with an increase in high ambient temperatures. As the increased temperature increases core body temperature, there is a resultant need to redistribute blood flow to the skin as part of the cooling mechanism. Additionally, blood volume and more specifically plasma volume are reduced because of sweating. This subsequently leads to a decreased central blood volume which ultimately reduces cardiac filling allowing for the aforementioned decrease in stroke volume. A fluid shift may affect the contractile and relaxation properties of the myocardium. Therefore, this dysfunction may be attributed to altered cardiovascular loading conditions during prolonged exercise in extreme environments (Middleton et al., 2006). Other factors such as exercise duration, intensity and training status of the subjects contribute to this phenomenon of exercise induced cardiac fatigue (Middleton et al.). Utilizing the equation $220 - \text{age}$

for estimating maximal heart rate and noting the average heart rate of the group during the race, it was determined that the subjects raced at an average of 81% of their maximal output.

Studies performed during the Ironman™ Triathlon and other ultra-endurance events support the theory that EICF is duration dependent (Niemela et al., 1987; Niemela et al., 1984; Shave et al., 2002). Additional studies indicate that systolic dysfunction is apparent only after aerobic exercise of greater than six hours duration while shorter duration exercises can produce diastolic dysfunction (Whyte et al., 2000). Moreover, research indicates that time of occurrence is sooner for noncompetitive or untrained healthy subjects (Niemela et al., 1987; Seals et al., 1988). The results of the current study indirectly support the conclusion that EICF seems dependent on the duration of exercise as well as the environmental conditions (Middleton et al., 2007).

It is clear that the etiology of EICF is multi-factorial. With the aforementioned mechanical factors (i.e., loading, contraction) researchers have suggested that elevated plasma free fatty acids and reduced cardiac glycogen subsequent to prolonged exercise can lead to a reduced contractile state of the myocardium (Lucia, Serratos, Saborido, Pardo, Boraita, Moran, Bandres, Megias & Chicharro, 1999; Niemela et al., 1984). Others report that increased levels of beta natriuretic peptide (BNP) might be a marker of impaired left ventricular performance (Konig et al., 2003). Lastly, it has been hypothesized that left ventricular segmental wall motion abnormalities reduce systolic and diastolic performance of the heart after prolonged exercise (Douglas et al., 1990).

Blood Data

Cardiac isoforms of troponin I (cTnI) and T (cTnT) are highly specific markers of myocardial injury. This study showed moderate increases in levels of cTnI following the race although not statistically significant when compared to clinical norms. One hypothesis that explains this exercise induced myocyte cell disruption is that under the stress of increased oxygen demand by the myocardium there is an increased release of catecholamines. This causes coronary vasospasm and endothelial injury that may result in asymptomatic focal myocardial necrosis resulting in increased troponin levels (Neumayr et al., 2001).

Another explanation to this increase rather than a marker of disruption of contractile proteins, is simply membrane leakage of the cytolytic component of cardiac troponin. This could be because of a transitory increase in membrane permeability. Return of troponin levels after recovery indicates this reversible shift in membrane permeability may be the result of a stress induced overload of free radicals with a resultant production of antioxidants to prevent further myocardial damage (Whyte et al., 2005).

The current study findings of increased levels of cTnI concentrations immediately after the race indicating myocardial injury, are in agreement with several studies (Koller, 2003; Neumayr et al., 2001; Rifai et al., 1999). Based on the YE (Table 1) for each cyclist and their continued participation in bicycle racing, it is surmised that the increase is due to reversibly injured myocytes occurring due to a disruption of cell membranes. The rapid repair mechanisms allow for a prevention of further damage. Because these subjects have experienced this level of athletic stress prior to this study, the myocyte disruption may be part of

the stress-adaption response. Signal influx and efflux through disruptions can initiate changes in gene expression in the disrupted cells and its neighbors promoting long term repair and adaptive responses at both the cellular and tissue level (Koller). Middleton et al. (2007) determined that along with increased cTnI or cTnT following myocardial injury, there is an increase in other cardio-protective proteins such as heat shock proteins. Heat shock proteins aid in myocardial adaptation to EICF and possibly provide future resistance to the damage of ischemia or infarction (Middleton et al.). Lastly, studies have successfully correlated myocyte disruption with depressed ejection fractions and abnormal wall motions on echocardiography following extreme endurance efforts (Koller; Tulloh et al., 2006; Whyte et al., 2000). They concluded that abnormal systolic function is a result of combined cardiac fatigue and myocardial cellular disruption.

Conclusions

Within the limitations of this study, the results suggest that intense prolonged endurance exercise in high ambient temperatures does induce cardiac fatigue in competitive healthy cyclists. This is reflected in changes in blood cardiac markers and echocardiographic data. Athletes involved in high level cardiac performance could be exposed to asymptomatic myocyte disruption as they are putting more stress on their hearts by pushing harder and longer than regular associated stresses (Neumayr et al., 2001). Without histological examination to confirm this disruption, it is possible that the increase in cTnI is a normal part of an adaptation process and not of patho-physiological significance. The changes evidenced after such ultraendurance events can provide a trigger for further adaptation allowing cellular and tissue level resistance to future stressful events. It is possible that findings of the current study are normal and part of an adaptation process with no patho-physiological significance. Therefore future research involving endurance athletes should investigate a timeline of cardiovascular examinations (i.e., post-echocardiography, post-cTnI) looking for any evidence of myocardial disruption and subsequent adaptation.

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