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Cardiac electromechanical delay is increased during recovery from 40 km cycling but is not mediated by exercise intensity

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Cardiac electrical-mechanical delay (cEMD), left ventricular (LV) function, and cardiac troponin I (cTnI) were assessed after 40 km cycle time trials completed at high (HIGH) and moderate (MOD) intensities in 12 cyclists. Echocardiograms and blood samples were collected before, 10, and 60 min after cycling. cEMD as assessed by time from QRS onset to peak systolic (S') tissue velocity was lengthened after both bouts of cycling but was not mediated by cycling intensity (HIGH: 174 ± 52 vs 198 ± 26 ms; MOD: 151 ± 40 vs 178 ± 52 ms, $P < 0.05$). Global LV systolic function was unaltered by exercise. cEMD from QRS to peak early (E') diastolic tissue velocity was also increased post-exercise (HIGH: 524 ± 95 vs 664 ± 68 ms; MOD: 495 ± 62 vs 604 ± 91 ms, $P < 0.05$). Indices of LV diastolic function was reduced after cycling but were not mediated by exercise intensity. cTnI was elevated in two participants after HIGH trial (0.06 ug/L; 0.04 ug/L) and one participant after MOD trial (0.02 ug/L). While cEMD is lengthened and LV diastolic function was reduced post-cycling, altering time-trial intensity had little impact upon cEMD, LV function, and cTnI release.

Multiple reports provide evidence of a transient depression in left ventricular (LV) global and regional myocardial function after prolonged exercise (e.g. Neilan et al., 2006a). A recent observation of extended cardiac electro-mechanical delay (cEMD, Chan-Dewar et al., 2010a) after prolonged running suggests that the mechanism(s) underpinning changes in cardiac function might be intrinsic to myocardial cells. These initial cEMD observations, obtained during a field study at a competitive 89 km foot race, require verification and further evaluation. Specifically, we do not know whether changes in cEMD occur after shorter exercise bouts or are mediated by the controlled manipulation of exercise intensity.

Substantial descriptive evidence of changes in LV function after prolonged exercise (Middleton et al., 2006; Shave et al., 2008; Oxborough et al., 2010) have been derived from field-based studies. Such studies lack control and thus provide limited insight into specific facets of exercise stimulus that may mediate functional changes (Scott & Warburton, 2008). A recent laboratory-based study indicated that LV function was reduced more after 150 min of high-intensity (80% maximal aerobic power) compared to moderate-intensity (60% maximal aerobic power) running (Banks et al., 2010). Whether differences in LV function are apparent after cycling, at different intensities, is currently unknown. Further, with continuing technical developments we can now deploy speckle-tracking (Helle-Valle et al., 2005) echocardiography to assess myocardial tissue strain (deformation) in multiple planes of motion. This provides additional LV functional data beyond ejection fraction (EF) and peak Doppler LV filling velocity ratios (E/A) that have been used to represent global contraction and relaxation, respectively. Indeed, multiple measures of LV strain may better characterize the true motion of the heart (Oxborough et al., 2010) but have not been used after controlled bouts of prolonged cycling.

Changes in LV function after prolonged exercise may be linked to "cardiac damage" (Neilan et al., 2006a). The release of cardiac biomarkers, such as cardiac troponin I (cTnI), a cardiac-specific marker indicative of myocyte insult, has been observed in many prolonged exercise settings (e.g. Fortescue et al., 2007), but whether a link exists between cTnI release and LV function during recovery remains controversial (Shave et al., 2010). Further, specific factors related to the stimulus bout of exercise that might promote cTnI appearance have been the focus of some recent debate. Two subsidiary analyses

from a meta-analysis are illuminating (Shave et al., 2007). First, increased exercise duration was associated with a decreased appearance of cTn. The authors speculated that this may have been associated with reduced exercise intensity but the direct assessment of intensity of exercise was not possible due to limited data presentation in the original studies. Second, studies employing cycling as the exercise mode reported roughly half the frequency of appearance of cTn compared to running or multisport prolonged events. Recently, Serrano-Ostariz et al. (2011) adopted a controlled, repeated-measures approach to assess the impact of exercise intensity and duration on cTn appearance after prolonged running. These authors reported that exercise intensity might be more important than duration in determining cTn appearance after exercise. This approach has not been adopted in similar controlled studies of cycling in combination with assessment of LV function and cEMD.

The focus of the present study is to investigate the magnitude of cEMD, changes in LV function and cTnI appearance during recovery from prolonged cycling at different exercise intensities. Building on previous research, we employed a controlled laboratory-based research design and employed echocardiographic modes to facilitate the assessment of cEMD and LV motion in three planes. We hypothesized that greater changes in cEMD, LV function, and a higher prevalence of detectable cTnI would be apparent after HIGH compared to MOD intensity cycling.

Materials and methods

Subjects

Twelve healthy male recreational cyclists (mean ± SD, age: 34 ± 9 years, weight: 80.3 ± 11.3 kg, height: 178 ± 6 cm) performed two 40 km cycling time-trials at different exercise intensities. Participants self-reported no personal or early family history of cardiovascular disease, and no illness, injury or medication use during the study period. Participants were recruited from the University and North-West England cycling clubs via advertisement. They were given an information sheet and had the protocol explained. All participants gave written informed consent after local ethics approval. *A priori* sample size estimation was based on detecting a post-cycling drop in EF of 5% with a power of 80%. This resulted in a target sample size of 10; therefore, allowing for drop-outs, 12 participants were recruited.

Experiment design

In an ecologically-driven design the HIGH intensity-trial was performed as a "true" time-trial with subjects asked to complete the distance as quickly as possible. For the MOD-intensity trial, all cyclists performed at intensity akin to a "steady training ride." Prior experience of the cyclists and experimenters suggested that heart rate (HR) for each trial would equate to 80–95% and 60–75% of age-predicted maximal HR max. During the time trials, HR was assessed using short-range telemetry devices (HR, Polar Electro Sport Testers, Kempele, Finland) to provide constant biofeedback to the cyclists and experimenters to guide exercise intensity. Both cycling-trials were completed on a computerized cycle training system (Computrainer pro 8002, Race Mate, Seattle WA, USA) in a controlled environment (20°C, 50% relative humidity) at the same time of the day. The trial order was randomized and separated by at least five days recovery. The setup for the cycle was individualized to the rider and replicated for the second trial. Participants were required to perform no strenuous exercise in the 24 h prior to the test and take no major meal/caffeine/alcohol for the 3 h before each trial. Water was allowed ad libitum before and during trials to promote euhydration. Assessments of LV function were made before (pre) as well as 10 min and 60 min after (post) each time trial. The controlled laboratory approach adopted allowed us to closely standardize these timings.

Echocardiographic Data collection

Echocardiographic measurements were taken by an experienced sonographer using a combination of color tissue velocity imaging (TVI), 2D, M-mode, Doppler, and myocardial speckle tracking modalities. A commercially available ultrasound system (Vivid 7, GE Medical, Horton, Norway) and a 1.5–4 MHz phased array transducer were employed. Images were captured with the participant lying in the left lateral decubitus position, stored digitally, and were analyzed by a single experienced technician and included a minimum of three cardiac cycles (Echopac software, GE Medical, Horton, Norway). Care was taken to optimize all images by modification of gain, compression, dynamic range, and appropriate adjustment of focal length to produce the best possible endocardial definition. For repeat assessments of the same individual every effort was made to replicate acoustic windows, insonation angle, and depth of image.

Apical 4-chamber views of the LV were imaged and then focused on the LV to allow color TVI cine loops to be stored for off-line assessment of peak systole (S'), early diastole (E'), and late diastole (A') tissue velocities. The sample volume was placed in the basal septum and lateral wall parallel to the plane of tissue motion. A single lead ECG was monitored throughout the scan to assess HR, QRS duration, and the time delay (cEMD) between QRS onset and peak S', peak E'. Overall, cEMD was averaged over the two sites.

From a 2D-parasternal long axis acoustic window M-mode traces of the LV were taken at the tips of the mitral valve and perpendicular to the long axis of the ventricle for assessing LV diastolic and systolic internal dimensions (LVIDd and LVIDs). This facilitated the estimation of end-diastolic and end-systolic volumes (LVEDV and LVESV), EF, fractional shortening (FS), and stroke volume (SV) using the Teicholz formula. Pulsed-wave Doppler was employed in apical 4-chamber view to assess peak transmitral flow velocities during early diastole (E) and atrial systole/late diastole/ (A). The E/A ratio were calculated.

Myocardial speckle tracking was employed to assess strain (deformation) and strain rates (Sr; rate of deformation) in circumferential, radial, and longitudinal planes. Further, rotation and torsion were derived from circumferential motion. Peak Sr were determined in systole (SSr), early diastole (ESr), and late diastole (ASr). Circumferential and radial strain and Sr were derived from parasternal short axis images at basal (mitral valve) and apical (using anatomical guidance from inferior border of papillary muscle and the point of systolic cavity obliteration) levels of the LV. Semi-automated off-line analysis followed manual tracing of LV endocardial borders. The software automatically applied regions of interest which were intrinsically assessed as adequate or not, although these could be manually adjusted to endure adequate and full wall depth tracking. The LV was automatically separated into six transmural wall segments (septum, lateral, inferior, anterior, posterior, and anteroseptal) for the determination of regional data for peak strain and Sr. Global strain and Sr data were derived by averaging wall segments at both basal and apical levels. Peak rotation was assessed at both basal and apical levels, and peak LV torsion was estimated. From an apical 4-chamber view, longitudi-

Table 1. Peak tissue velocities and time to peak velocity (R-R adjusted) before and after HIGH and MOD intensity 40 km cycling time trials

	HIGH (mean ± SD)			MOD (mean ± SD)			P value		
	Pre	Post-10 min	Post-60 min	Pre	Post-10 min	Post-60 min	Int	Time	Int × Time
QRS duration (ms)	103 ± 15	98 ± 11	105 ± 12	105 ± 11	101 ± 12	106 ± 13	0.16	0.16	0.66
Peak S' velocity (cm/s)	6.3 ± 1.3	6.4 ± 1.6	7.2 ± 1.5	6.9 ± 1.5	6.9 ± 1.5	7.0 ± 1.4	0.17	0.28	0.22
Peak E' velocity (cm/s)	9.8 ± 2.1	9.0 ± 2.4	9.6 ± 2.7	10.3 ± 2.5	9.2 ± 2.7	9.4 ± 2.8	0.66	0.01	0.16
Peak A' velocity (cm/s)	–5.5 ± 2.9	–4.5 ± 1.9	–5.3 ± 2.8	–4.6 ± 1.5	–4.6 ± 1.3	–5.5 ± 1.4	0.13	0.27	0.57
Time to peak S' (ms)	174 ± 52	198 ± 26	183 ± 30	151 ± 40	178 ± 52	190 ± 37	0.27	0.04	0.06
Time to peak E' (ms)	524 ± 95	664 ± 68	604 ± 80	495 ± 62	604 ± 91	568 ± 82	0.11	0.00	0.56

HIGH, high intensity exercise; MOD, moderate intensity exercise; int, intensity; S', systolic; E', early diastolic; A, late diastolic.

nal peak strain and Sr were assessed off-line using the same approach to endocardial tracing and region of interest generation. Although strain and Sr data were generated for six wall segments, (base, mid, and apex for both the septum and lateral wall) global data was calculated by averaging two basal and two apical segments to mirror the LV "cuts" derived for circumferential and radial strain.

For all images used for speckle-tracking frame rates were as high as possible, but below 90 fps, to optimize resolution when scans were obtained at different HR. Quality control for cEMD and speckle-tracking echocardiographic assessment in our laboratory has been reported previously (Chan-Dewar et al., 2010a, b) with no systematic bias and intra-class correlations ranging from 0.693 to 0.993 (all $P < 0.05$).

Venous blood (5 mL) was collected via repetitive brachial venipuncture and drawn into serum gel tubes. Blood was allowed to clot (about 45 min), spun, and the serum stored at −80°C for later analysis. cTnI was determined using the TnI-Ultra assay for the Advia Centaur XP immunoassay system (Siemens Medical Solutions Diagnostics, Frimley, Surrey). Assay detection limit was 0.006 ug/L with a linear calibration range up to 50 ug/L (Apple et al., 2008). Assay precision in our laboratory was estimated as 10% CV at 0.045 ug/L (Collinson et al., 2009).

Statistical analysis

Performance data in the two trials were compared by paired *t*-tests. Comparisons of pre-exercise and post-exercise (post-10 min and post-60 min) data from both trials were made using repeated measures two-way ANOVA and Bonferroni's method to assess post-hoc pair-wise differences where significant main effects or interactions were reported. Pearson's product-moment correlations assessed the degree of association between pre-post exercise change in cEMD and pre-post exercise changes in S', E', EF, and peak longitudinal strain. cTnI data were reported descriptively due to the likely lack of any detectable data in pre-cycling samples. All data were presented as mean ± SD. Critical alpha was set at $P < 0.05$. Statistical analysis was performed using SPSS (Version 15.0).

Results

All 12 participants completed both 40 km trials. Mean values for HR, finishing time, speed, and power output in HIGH vs MOD trials were 155 ± 4 vs 131 ± 2 beats/min; 69 ± 7 vs 76 ± 9 min; 34.6 ± 3.4 vs 31.8 ± 3.6 km/h; 223 ± 53 vs 182 ± 47 W (all $P < 0.05$). Body mass was decreased after both HIGH (80.3 ± 11.3 to 79.8 ± 11.2 kg) and MOD trials (80.7 ± 11.1 to 80.2 ± 11.0 kg) ($P < 0.05$).

Cardiac data during recovery from both trials are detailed in Table 1. Baseline data were not significantly different between HIGH and MOD trials. A significant main effect for time was observed for HR which increased from pre- to 10 min post-cycling (HIGH: 63 ± 11 vs 85 ± 10; MOD: 59 ± 10 vs 73 ± 13 beats/min). Systolic blood pressure fell by 8 mmHg after HIGH-trial but did not change after MOD-trial.

Data for QRS duration was not altered by time or trial (see Table 1). There was a significant main effect of time for the delay between QRS to peak S' but no time-by-trial interaction. The extension of cEMD at 10 min post-exercise was partially lost by 60 min post-exercise (Table 1). Likewise, there was a significant main effect for time but no time-by-trial interaction for the delay between QRS and peak E'. The increase from rest to 10 min post-exercise was partially recovered at 60 min post-exercise.

Both EF (Table 2) and peak S' were not altered after both cycling trials, and any individual changes in these variables were not correlated with changes in cEMD ($P > 0.05$). A significant main effect of time but no time-by-trial interaction was observed for peak basal but not apical, longitudinal strain (Table 3) with a decrease at 10 min post-exercise and partial recovery at 60 min post-exercise. This change was not significantly correlated with pre-post exercise changes in cEMD ($P > 0.05$). There were no significant main effects or interactions for peak strain in circumferential and radial planes at both the base and apex. No main effect or interaction was recorded for peak SSr, peak rotation, or torsion data.

A significant main effect for time, but no time-by-trial interaction, was also noted with respect both peak E and A transmittal flow velocities. Both E and A were reduced to a similar extent after both cycle trials but had largely returned to baseline after 60 min recovery. A significant main effect for time, but no time-by-trial interaction, was also observed for peak E' with a drop at 10 min post-exercise and partial recovery at 60 min. While there was a temporal association between a drop in E' and an increase in cEMD (QRS to peak E') post-exercise, this was not significant on individual pair-wise correlation ($P > 0.05$). A significant main effect, but no time-by-trial interaction, was apparent for longitudinal plane peak ESr

Table 2. Cardiovascular data collected before and after HIGH and MOD intensity 40 km cycling time trials

	HIGH (mean ± SD)			MOD (mean ± SD)			*P*-value		
	Pre	Post-10 min	Post-60 min	Pre	Post-10 min	Post-60 min	Int	Time	Int × Time
LVIDd (cm)	4.8 ± 0.5	4.7 ± 0.4	4.8 ± 0.4	4.8 ± 0.3	4.8 ± 0.3	4.8 ± 0.3	0.10	0.64	0.93
LVIDs (cm)	3.2 ± 0.5	3.3 ± 0.4	3.3 ± 0.4	3.3 ± 0.3	3.4 ± 0.3	3.3 ± 0.4	0.10	0.53	0.73
EDV (cm)	106 ± 24	104 ± 18	107 ± 21	111 ± 16	108 ± 17	111 ± 17	0.12	0.65	0.99
ESV (cm)	41 ± 15	45 ± 13	45 ± 14	45 ± 10	49 ± 10	46 ± 12	0.17	0.47	0.80
EF (%)	62 ± 9	58 ± 7	57 ± 9	59 ± 5	55 ± 8	59 ± 7	0.39	0.15	0.41
FS (%)	34 ± 7	30 ± 5	31 ± 6	32 ± 3	29 ± 5	31 ± 5	0.34	0.16	0.69
SV (ml)	65 ± 13	59 ± 10	62 ± 15	65 ± 10	60 ± 14	65 ± 12	0.45	0.12	0.82
Peak E (m/s)	0.71 ± 0.12	0.63 ± 0.09	0.69 ± 0.13	0.73 ± 0.12	0.66 ± 0.13	0.68 ± 0.11	0.48	0.01	0.59
Peak A (m/s)	0.43 ± 0.06	0.40 ± 0.08	0.47 ± 0.05	0.45 ± 0.09	0.43 ± 0.07	0.47 ± 0.05	0.31	0.02	0.86
E/A	1.65 ± 0.17	1.63 ± 0.31	1.52 ± 0.34	1.65 ± 0.28	1.60 ± 0.48	1.47 ± 0.23	0.76	0.09	0.86

LVIDd, LV internal dimension (diastole); LVIDs, LV internal dimension (systole); EDV, end diastole volume; ESV, end systole volume; EF, ejection fraction; FS, LV fraction shortening; SV, stroke volume; Peak E, LV peak early diastole flow velocity; Peak A, LV peak late diastole flow velocity; E/A, ratio beween peak E and peak A.

Table 3. Left ventricular strain and strain rate parameters before and after HIGH and MOD intensity 40 km cycling time trials

	HIGH (mean ± SD)			MOD (mean ± SD)			*P*-value		
	Pre	Post-10 min	Post-60 min	Pre	Post-10 min	Post-60 min	Int	Time	Int × Time
Basal Circ									
Strain (%)	–13.7 ± 4.1	–11.6 ± 3.7	–13.4 ± 3.0	–15.4 ± 4.3	–13.8 ± 2.4	–13.5 ± 3.2	0.10	0.14	0.41
S Strain rate (s^{-1})	–1.4 ± 0.2	–1.5 ± 0.3	–1.6 ± 0.4	–1.6 ± 0.2	–1.6 ± 0.3	–1.8 ± 0.4	0.14	0.12	0.56
E Strain rate (s^{-1})	1.6 ± 0.4	1.4 ± 0.4	1.5 ± 0.4	1.6 ± 0.3	1.6 ± 0.3	1.4 ± 0.5	0.60	0.34	0.33
A Strain rate (s^{-1})	0.8 ± 0.2	1.4 ± 0.7	1.3 ± 0.4	0.8 ± 0.2	0.8 ± 0.2	1.0 ± 0.3	0.11	0.08	0.20
Basal Radial									
Strain (%)	25.5 ± 12.2	17.3 ± 9.9	17.9 ± 7.2	33.7 ± 17.3	28.2 ± 19.7	25.3 ± 20.7	0.06	0.11	0.76
S Strain rate (s^{-1})	1.9 ± 0.7	2.3 ± 1.4	2.3 ± 0.9	1.7 ± 0.4	2.8 ± 1.9	2.7 ± 1.7	0.44	0.07	0.57
E Strain rate (s^{-1})	–1.6 ± 1.1	–1.6 ± 0.7	–1.8 ± 0.7	–1.6 ± 0.6	–1.4 ± 0.5	–1.6 ± 0.8	0.64	0.63	0.77
A Strain rate (s^{-1})	–1.0 ± 0.6	–1.6 ± 1.0	–1.5 ± 1.5	–0.9 ± 0.3	–1.1 ± 0.4	–1.3 ± 0.7	0.20	0.39	0.75
Basal Long									
Strain (%)	–19.6 ± 3.1	–16.6 ± 3.9	–17.0 ± 3.1	–18.7 ± 2.5	–15.3 ± 2.3	–17.9 ± 3.2	0.06	0.01	0.40
S Strain rate (s^{-1})	–1.4 ± 0.3	–1.3 ± 0.4	–1.4 ± 0.3	–1.3 ± 0.3	–1.4 ± 0.4	–1.3 ± 0.4	0.67	0.89	0.52
E Strain rate (s^{-1})	2.0 ± 0.4	1.6 ± 0.4	1.5 ± 0.3	1.7 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	0.07	0.00	0.41
A Strain rate (s^{-1})	0.8 ± 0.3	0.9 ± 0.3	0.9 ± 0.2	0.9 ± 0.3	1.0 ± 0.2	1.2 ± 0.4	0.08	0.03	0.30
Apical Circ									
Strain (%)	–16.0 ± 7.0	–17.8 ± 3.1	–20.2 ± 6.1	–18.8 ± 3.6	–18.7 ± 3.8	–17.8 ± 2.3	0.67	0.52	0.21
S Strain rate (s^{-1})	–1.3 ± 0.3	–1.4 ± 0.2	–1.8 ± 0.4	–1.4 ± 0.2	–1.6 ± 0.2	–1.5 ± 0.3	0.62	0.01	0.05
E Strain rate (s^{-1})	1.8 ± 0.5	1.7 ± 0.3	2.0 ± 0.6	2.0 ± 0.4	1.8 ± 0.4	1.7 ± 0.3	0.87	0.71	0.17
A Strain rate (s^{-1})	0.8 ± 0.3	1.3 ± 0.6	1.1 ± 0.4	0.8 ± 0.3	0.9 ± 0.2	1.0 ± 0.3	0.25	0.20	0.07
Apical Radial									
Strain (%)	40.7 ± 24.9	38.2 ± 14.1	41.5 ± 17.0	47.6 ± 14.9	39.4 ± 11.6	44.9 ± 17.7	0.32	0.42	0.82
S Strain rate (s^{-1})	1.9 ± 0.6	1.8 ± 0.4	2.4 ± 0.7	1.9 ± 0.7	1.8 ± 0.4	2.1 ± 0.6	0.47	0.07	0.49
E Strain rate (s^{-1})	–1.8 ± 0.5	–1.9 ± 0.7	–2.1 ± 0.7	–2.5 ± 0.6	–2.3 ± 0.8	–2.2 ± 0.5	0.08	0.98	0.17
A Strain rate (s^{-1})	–1.3 ± 0.3	–1.7 ± 1.0	–1.2 ± 0.5	–1.5 ± 0.7	–1.3 ± 0.4	–1.2 ± 0.4	0.81	0.45	0.27
Apical Long									
Strain (%)	–19.1 ± 4.6	–18.4 ± 5.1	–21.7 ± 6.6	–18.3 ± 5.8	–20.2 ± 4.4	–20.9 ± 5.5	0.95	0.20	0.39
S Strain rate (s^{-1})	–1.3 ± 0.3	–1.2 ± 0.2	–1.5 ± 0.5	–1.3 ± 0.3	–1.3 ± 0.4	–1.3 ± 0.4	0.65	0.10	0.17
E Strain rate (s^{-1})	2.2 ± 0.6	2.0 ± 0.6	2.1 ± 1.0	2.2 ± 0.8	2.0 ± 0.7	2.2 ± 0.8	0.93	0.40	0.98
A Strain rate (s^{-1})	0.9 ± 0.5	1.0 ± 0.6	0.9 ± 0.3	1.0 ± 0.7	0.8 ± 0.3	1.3 ± 1.0	0.39	0.41	0.22
Rotation Basal (°)	–3.4 ± 6.1	–3.8 ± 4.5	–3.5 ± 5.1	–4.2 ± 5.1	–2.9 ± 5.8	–3.0 ± 6.2	0.83	0.85	0.80
Rotation Apical (°)	0.4 ± 6.2	–0.5 ± 3.8	1.1 ± 6.6	2.7 ± 4.4	0.1 ± 5.1	–0.6 ± 4.5	0.58	0.33	0.41
Torsion (°)	3.8 ± 6.5	3.4 ± 4.8	4.6 ± 9.5	6.9 ± 4.8	3.0 ± 8.4	2.4 ± 7.4	0.90	0.41	0.50

HIGH, high intensity exercise; MOD, moderate intensity exercise; Int, intensity; Circ, circumferential; Long, longitudinal; S, systolic; E, early diastolic; A, late diastolic.

at the basal level ($P < 0.05$). The decline in peak ESr at 10 min post-exercise had not recovered at 60 min. The change in peak basal longitudinal ESr post-exercise was not significantly correlated with cEMD ($P > 0.05$). There were no significant main effects or interactions present for all other ESr and no significant main effects or interaction terms for ASr data apart from a main effect for time for basal ASr in the longitudinal plane.

Concentrations of cTnI were below detection limits in all samples pre-exercise. At 60 min post-cycling cTnI was elevated in two participants after the HIGH trial (0.04 and 0.06 ug/L) and one participant after the MOD trial (0.02 ug/L).

Discussion

The key findings of the study are that prolonged cycling at both HIGH and MOD intensities resulted in a transient increase in cEMD. This effect was independent of exercise intensity. Few changes in systolic LV function were noted post-exercise despite the alteration in cEMD. A transient reduction in global diastolic flow parameters as well as longitudinal indices of tissue motion in diastole at the LV base was also observed but independent of exercise intensity. Finally, cTnI appearance post-exercise was sporadic and not different between trials.

Impact of prolonged exercise on cEMD and systolic LV function

A delay between the electric signal (QRS) and the peak S' tissue velocity was observed at 10 min post both trials. This cEMD has been reported previously after ultra-endurance exercise (Chan-Dewar et al., 2010a), but it is the first time this has been observed after shorter duration cycling. A partial recovery of cEMD by 60 min post-exercise has not been recorded previously and this suggests that, like most other changes in LV function after prolonged exercise, alterations in cEMD are transient and rapidly reversible with rest and recovery. This would support the notion that post-exercise alterations in cEMD are physiological and have little consequence for long term LV function/health. In the current study, changes in cEMD were not associated with pre-post exercise alterations in EF, E/A, S', E', and/or peak basal longitudinal strain and ESr. Thus, unlike in a previous study (Chan-Dewar et al., 2010a), an altered cEMD may not be obligatory in terms of progression to functional change. The exact cause of the change in cEMD cannot be determined from the current study but some comment and speculation is relevant. Zhou (1996), when assessing EMD in skeletal muscle after exercise, suggested that candidates for a delayed EMD, or in this case development of peak tissue velocity, are speculative but could include altered membrane excitability, reduced cytosolic Ca2+ concentration, reduced myofibrillar Ca2+ sensitivity, and/or some form of metabolic derangement. Consistent with previous data (Chan-Dewar et al., 2010a), the lack of change in QRS duration would seem to rule out alterations in membrane excitability, and thus transduction of the electrical signal into the cardiomyocytes and so locates the mechanism for changes in cEMD to those intrinsic to the internal environment of the myocycte. The lack of association between changes in cEMD and cardiac function may not be surprising given the lack of change in most parameters of global systolic function. Whether post-exercise alterations in cEMD reflect an early or sensitive marker of cardiac fatigue may be the focus of ongoing research.

Whether prolonged exercise results in a decline in LV systolic function is controversial and seems to be partially mediated by exercise duration/volume as well as training status (Middleton et al., 2006). A decline in global indices of LV systolic function has been reported previously after ultra-endurance exercise (Neilan et al., 2006b; Scott et al., 2009), but shorter durations of exercise have produced no changes in EF or FS during recovery (Goodman et al., 2001; George et al., 2005; Whyte et al., 2005), and thus the current data support past research. Single bouts of endurance cycling have seen similarly marginal changes in standard EF measurements of about −4% ($P > 0.05$, Shave et al., 2004) and −3.8% ($P = 0.11$, Goodman et al., 2009).

The lack of change in peak basal septal S' post-cycling supports previous data reported after marathon races (George et al., 2006; Oxborough et al., 2006). As with global measures like EF, peak S' has been observed to be depressed during recovery from much longer bouts of exercise (Scott et al., 2009). While there was no change in peak S' in the basal septum, there was a decline in peak strain in the longitudinal plane at the basal level. No changes in strain were reported in radial or circumferential (basal or apical) planes. Likewise, there was no evidence of a decline in peak SSr in any plane and no alteration in peak LV rotation or torsion. Previous studies have reported decreased peak strain and peak SSr in multiple planes of cardiac motion when assessing recovery from exercise of much longer duration (George et al., 2009; Nottin et al., 2009; Scott et al., 2009). While the current study presents the first strain and SSr data after prolonged cycling it seems, as with other forms of exercise, that a volume of exercise greater than assessed in the present study (about 70 min) is required to detect meaningful changes in global or regional LV function.

Impact of prolonged cycling exercise on cEMD and diastolic LV function

After both HIGH and MOD intensity trials, the cEMD from Q to peak E' was significantly increased, which also mirrors data reported by Chan-Dewar et al. (2010a), but uniquely, the data suggest some recovery by 60 min. While temporally the increase in time delay to peak E' occurred at the same time as a reduction in E, E', and basal longitudinal ESr, there was no significant pair-wise correlation between the timing delay and indices of diastolic flow and tissue relaxation. As with the link between cEMD and peak systolic function, it may not be that the delay in QRS to E, E' or ESr is obligatory in the evolution of diastolic changes in the LV after prolonged exercise.

Data from the meta-analysis (Middleton et al., 2006), as well as individual studies from marathons (Neilan et al., 2006c) to Ironman triathlon (Nottin et al., 2009), suggest that changes global and segmental diastolic parameters after prolonged exercise are more consistent, seemingly independent of exercise duration/volume and thus may occur before LV systolic functional changes. In a previous study of a 100-mile cycling time-trial, a similar small decline in post-exercise E (83 ± 11 vs 72 ± 9 cm/s; $P < 0.05$) contributed to a change in E/A ratio (2.3 ± 0.6 vs 1.4 ± 0.4; $P < 0.05$) (Shave et al., 2004).

Data related to E, E', and ESr are associated with both early recoil and active relaxation of the LV. These data were altered in the longitudinal plane which is important in the development of the left-atrial-LV pressure gradient and LV suction. The question remains why early diastolic flow and longitudinal tissue motion were depressed after cycling. While alterations in load and rate have been implicated previously (Hassan et al., 2006), this is unlikely to be the only explanation here with only small changes in LVEDV and HR apparent post-exercise, and reductions or no change in blood pressure. It is unlikely that cellular damage (see later cTnI data) is responsible. Whether the increased cEMD from QRS to peak E' is a consequence or cause of altered LV diastolic motion in the longitudinal plane cannot be deduced in the current study. Data for ASr were not significantly altered with exercise or the time-trial intensity except for basal ASr in the longitudinal plane. This and other minor changes tended to be increases in ASr post-cycling (independent of trial) which could reflect an alteration in atrial contractility in compensation for changes in early diastolic deformation. Alternatively, these subtle alterations may be related to an elevated HR post-exercise. Fundamentally, changes in ASr were small compared to the relatively large inter- and intra-individual variability.

Prolonged cycling and cTnI appearance

The release of the cTnI was apparent in only three participants, and exercise intensity had little mediating role. Previous data is somewhat conflicting in relation to the influence of exercise parameters on cTn appearance during recovery. In a recent meta-analysis, Shave et al. (2007) reported a reduced appearance rate for cTnT as event duration increased; suggesting that changes in exercise intensity might have been involved. This idea was given some support when Serrano-Ostariz et al. (2011) reported that higher exercise intensity produced a greater cTn response after prolonged running when compared to the effect of altered duration. Conversely, we have shown that even low levels of exercise (walking), if sustained long enough can result in cTn elevation (Eijsvogels et al., 2010). The fact that the current data do not support the work of Serrano-Ostariz et al. (2011) may again reflect differences in cTn response to cycling and running, also alluded to in the meta-analysis of Shave et al. (2007). Further, variations in number and timing of blood samples collected between the current study and the work of Serrano-Ostariz et al. (2011) may partially explain these differences. In those cyclists where cTnI was released post-cycling, the mechanism responsible and the clinical and/or performance implications are still being debated. Given the absence of other signs and symptoms of cardiovascular insult either during exercise or recovery, we suggest that the response is likely physiological rather than pathological (Shave et al., 2010). Recent work from Middleton et al. (2008) suggests that, if enough blood samples are taken during exercise and recovery, a "positive cTn" will be observed in nearly all participants. Further work regarding the mechanisms underpinning the release of cTn during and after prolonged exercise is required.

The effective of exercise intensity

The primary focus of the current paper was to assess the impact of prolonged cycling at two different intensities on cEMD, LV function, and cTnI appearance post-exercise. The overall impact of intensity in the current design is negligible. For practical application and implication, we set these intensities at self-selected paces associated with peak time-trial performance (HIGH) and an easy training ride (MOD) over the same distance. Despite significant differences in speed, power output, and HR between the trials, there was no noticeable impact on cEMD, LV function or cTnI appearance after both trials. This lack of impact of exercise intensity contradicts suggestions made in a meta-analysis (Middleton et al., 2006) and the only piece of controlled laboratory/field research performed with running activity (Banks et al., 2010; Serrano-Ostariz et al., 2011). Several plausible explanations exist. First, it may be that exercise volume rather than intensity is responsible for development of cardiac fatigue, and so both cycling bouts were too short in duration and low in total volume compared to other field-based studies (Nottin et al., 2009). Second, the difference in intensities employed was relatively small thus may not have provided the optimal difference from a scientific perspective to investigate the effect of exercise intensity. While this may be the case, and the running example did employ a greater difference of 60% vs 80% maximal aerobic power, we choose these trials to provide a "real-world" setting to the study, and cycling at any intensity lower than the MOD trial would have no external validity. Finally, it may be that cycling per se and differences in cycling intensity have smaller effects on LV function during recovery than do running or multi-sport endurance tasks; to date the vast majority of "cardiac fatigue" literature has been based on running or multisport tasks (Middleton et al., 2006; Oxborough et al., 2010). With individual's weight supported, a different body position and

potential differences in hemodynamic loading during cycling might provide less cardiovascular stress at optimal self-selected paces than running, although this requires experimental verification.

Limitations

It is pertinent to recognize some limitations. Specifically, EF derived from M-mode dimensions is limited compared to the use of Simpson's biplane convention. A lack of image optimization/storage in 2-chamber and 4-chamber views restricted our analysis. Further, we note different HR in pre- and post-cycling scans that will result in minor alterations in temporal resolution. We tried to maximize fps on all scans while staying within acknowledged limits for. While we report interesting and new data for cEMD, we must acknowledge that our understanding of cEMD is still limited. Direct comparison to EMD changes in skeletal muscle post-exercise is complex and challenging due to different tissue properties and motion in cardiac and skeletal muscle. Finally, we collected only two blood samples during recovery and would note that more samples would provide a better cTnI "kinetic" profile post-cycling.

In conclusion, **c**ompletion of 40 km cycling time-trial resulted in a transient increase in cEMD that was temporally associated with a depression in longitudinal LV function and early diastolic peak flow velocities. No changes were observed in LV systolic function after prolonged cycling bouts and cTnI appearance was sporadic. In all cases, altering cycling intensity over a 40 km time-trial had no further effect on these parameters in a controlled repeated-measures design.

Perspectives

This study presents unique evidence of cEMD after prolonged bouts of cycling that are temporally associated with alterations in LV diastolic functional parameters. These changes were transitory with movement back toward baseline after 60 min of recovery. It is also noteworthy that changes in cEMD post-exercise were not associated with any change in global or regional LV systolic function. Taken together with only minor alterations in cTnI appearance, it seems that these changes are likely to be physiological and thus quickly reversible. The impact of altering the intensity of the cycling time-trial was negligible, and it seems that the cardiac work of prolonged but high intensity cycling is handled well in this group of trained cyclists. Future work should extend our knowledge in this field. More controlled laboratory-based studies with specific exercise manipulations in different subject groups are warranted to increase our understanding of these phenomena.

Key words: cardiac fatigue, diastolic function, tissue velocities, strain imaging.

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