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1 **Global and Regional Left Ventricular Circumferential Strain**
2 **during Incremental Cycling and Isometric Knee Extension**
3 **Exercise**

4

5 Running title: Circumferential strain during exercise

6

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1 ABSTRACT

2 **Background:** The objective of this study was to investigate left ventricular (LV)
3 circumferential strain responses to incremental cycling and isometric knee extension
4 exercises.

5 **Methods:** Twenty-six healthy male participants (age= 30±6 years) were used to study LV
6 global (GCS) and regional circumferential strain at the apex (ACS) and base (BCS) during
7 incremental cycling at 30% and 60% work rate maximum (W_{max}) and short duration (15s
8 contractions) isometric knee extensions at 40% and 75% maximum voluntary contraction
9 (MVC) using two-dimensional speckle-tracking echocardiography.

10 **Results:** During cycling (n=22), GCS increased progressively from rest to 60% W_{max} (-
11 22.85±3.26% to -29.87±2.59%, $p<0.01$). ACS increased from rest to 30% W_{max} (-
12 26.29±4.84% to -36.84±6.94%, $p<0.01$) and then remained unchanged to 60% W_{max} (-
13 40.72±4.06%, $p=0.068$). BCS decreased from rest to 30% W_{max} (-19.41±2.79 to -
14 17.51±4.66%, $p=0.05$) then remained unchanged to 60% W_{max} . During isometric knee
15 extension (n=23), GCS decreased from rest to 40% MVC (-22.63±3.46 to -20.10±2.78%,
16 $p<0.05$), then remained unchanged to 75% MVC. Similarly, BCS decreased from rest to 40%
17 MVC (-19.21±2.58% to -13.55±3.45%, $p<0.01$) and then remained unchanged, whereas ACS
18 did not change with exercise intensity (rest, -26.05±5.34%; 40% MVC, -26.64±4.53% and
19 75% MVC -27.22±5.34%, all $p>0.05$).

20 **Conclusion:** GCS increased stepwise during incremental cycling, mediated by the apex with
21 trivial changes at the base. In contrast, GCS decreased during the isometric knee extension to
22 40% MVC then plateaued, due to decreased BCS since ACS was maintained. A novel finding
23 is that the GCS response appears to be exercise modality dependant and are the consequence
24 of region-specific changes.

25 **Keywords:** exercise; deformation; left ventricle; speckle tracking echocardiography; strain

1. INTRODUCTION

Myocardial strain mechanics are used as markers of left ventricular (LV) function¹, and are assessed in three planes of motion; radial, longitudinal and circumferential². Circumferential strain reflects the change in length around the LV perimeter and during systole as the myocardium shortens the circumference of the LV cavity reduces^{3,4}. The healthy heart demonstrates a basal-to-apical gradient in circumferential strain, with higher strain in the apex, which highlights the non-uniform distribution of shortening about the long-axis of the ventricle⁵.

Assessment of cardiac strain during exercise stress provides important information pertaining to the physiological capabilities of the LV to alter its function in response to an increased cardiac demand. Interrogation of circumferential strain during exercise will add additional knowledge regarding LV shortening during contraction, supplementary to the previously reported longitudinal strain during dynamic and isometric exercise^{6,7}.

During incremental dynamic exercise, studies reported a plateau⁸ or progressive increase⁶ in global circumferential strain (GCS). Still, Doucende et al.⁶ did not observe a statistically significant increase between final work intensities, making it difficult to determine whether at 40% maximal workload, GCS begins to plateau thereafter or larger workload increments are necessary to elicit notable differences between exercise intensities. Further, circumferential shortening during exercise also show regional disparity between apical and basal planes, with increases at the apex (ACS) without changes at the base (BCS)^{9,10}, which however, contrasts another investigation having reported a reserve in BCS compared with baseline¹¹.

Data pertaining to circumferential strain during resistance exercise are limited. Reductions in GCS were noted during isometric hand-grip exercises¹³, however, regional strains were not independently reported. In contrast, more recently short-duration double-leg

1 press transiently reduced BCS and ACS ¹³. Although, this was not traditional resistance
2 exercise, since image acquisition was performed during an isometric hold following a brief
3 near-complete leg extension. Therefore, the global and regional circumferential strain
4 responses during incremental short-duration resistance exercise concerning sustained
5 isometric work of the lower extremities remains to be determined.

6 Taken together, despite the aforementioned reports of circumferential strains during
7 exercise, a full description, within the same investigation, of global and region-specific
8 circumferential strains during incremental exercise are lacking at present and the responses
9 during dynamic and static modalities remain incompletely understood. Also, there is some
10 confusion in the literature regarding the effect of exercise on the different levels of the LV at
11 which circumferential strain can be measured. Additionally, dynamic exercise predominantly
12 increases preload, while isometric (static) exercise elevates afterload on the LV ¹⁴. However,
13 the response to these different loading patterns have not been previously assessed in the same
14 individuals, which is of importance considering comparisons in the cardiovascular responses
15 during exercise are frequently made between dynamic and static modalities.

16 Accordingly, the present study aimed to investigate the influence of incremental
17 dynamic cycling and isometric knee extension on LV regional and global circumferential
18 strain. It was hypothesized that; (1) GCS would increase incrementally during cycling,
19 mediated through increased ACS. (2) Both BCS and ACS would initially decrease during
20 isometric exercise and as a result, would decrease GCS.

21

1 **2. METHODS**

2 **2.1 Study design and population**

3 Twenty-seven healthy males (18-40 years) of differing exercise habits (runners n=8;
4 triathletes n=9; resistance exercisers, n=5 and no regular habits, n= 5) were recruited for this
5 cross-sectional study. A medical questionnaire was used to exclude a past history or known
6 current diagnosis of coronary heart disease, hypertension, diabetes mellitus, myocardial
7 infarction, peripheral artery disease or sudden cardiac death in immediate family members.
8 Participants were required to avoid vigorous physical activity, and consumption of alcohol
9 (24 hours) and caffeine (12 hours) prior to data collection. Before initiation of this study, the
10 local university ethics committee reviewed and approved the protocol which was conducted
11 in accordance with the declaration of Helsinki. The participants in the present study are the
12 same population as reported in our previous publication ¹⁵. Further, all methods have been
13 fully detailed previously ¹⁵, however, a synopsis of measurement procedures and
14 experimental protocols are provided below.

15

16 **2.2 Protocol and experimental procedures**

17 Participants attended the Sport Science Laboratories twice at the same time of day with each
18 visit separated by at least 24 hours, but <7 days. Demographic information, physiological
19 assessment and a baseline (resting) echocardiographic assessment were collected/completed
20 on the first visit. During visit 2 each participant completed submaximal cycling and isometric
21 knee extension protocols to obtain circumferential strain data during exercise.

22 After 5 min supine rest, heart rate (HR) (FS1, Polar Electro Oy, Kempele, Finland),
23 systolic (SBP) and diastolic blood pressures (DBP), using manual sphygmomanometry, were
24 recorded and used to calculate rate-pressure product, as HR*SBP and mean arterial pressure
25 (MAP) ¹⁶. After a resting echocardiographic examination, participants completed an

1 incremental exercise test to exhaustion on a dedicated semi-supine ergometer (eBike-L,
2 ergoline GmbH, GE Healthcare) using breath-by-breath expired gas analysis using a
3 ergospirometer (Metalyser 3B, Cortex, Germany). Work rate maximum (W_{\max}) was
4 calculated using the equation: $W_{\max} = W_{\text{com}} + \left(\frac{t}{60}\right) \times W$ ¹⁷. We elected to use 30% and 60%
5 W_{\max} to enable a doubling of exercise workload while ensuring an exercise intensity with
6 suitable image acquisition.

7 **2.3 Cycle ergometry and isometric knee extension protocols**

8 Following a 10 min rest on the semi-supine (45°) ergometer (eBike-L, ergoline GmbH, GE
9 Healthcare), participants performed incremental exercise of 2 x 5 min stages at 30% and 60%
10 W_{\max} and echocardiographic images were collected during the last 3 min of each stage. HR
11 and manual blood pressures were recorded at the end of, yet before, the termination of each
12 exercise stage.

13 After 10 min seated rest, participants lay fully supine on an isokinetic dynamometer
14 (Kin-Com 125E Plus, Chattecx Corporation, Chattanooga, USA). A full supine position was
15 used to enable optimal echocardiographic image acquisition. The dominant leg was used for
16 all isometric contractions of the quadriceps, which were performed at a fixed knee extension
17 angle of 130° with the knee joint centre was aligned with the axis of the dynamometer crank
18 arm ¹⁸. A warm-up of 5-10 submaximal isometric contractions was performed prior to the
19 maximal voluntary contraction (MVC) assessment, which was determined from the greatest
20 of 3 maximal isometric contraction attempts interspersed with a 1 min recovery ¹⁹. Following
21 5 min rest, participants completed an incremental protocol consisting 2 x 15s isometric
22 contractions, separated by 2 min passive recovery, at both intensities corresponding to 40%
23 and 75% MVC. An initial intensity of 40% MVC was chosen to match that of a previous
24 isometric hand-grip study ²⁰ and an upper intensity of 75% MVC chosen as the highest

1 relative intensity while attempting to limit the Valsalva manoeuvre. At the termination of
2 contraction, five cardiac cycles, HR and manual blood pressures were recorded.

3

4 **2.4 Echocardiography**

5 All participants underwent two-dimensional transthoracic echocardiographic examinations at
6 rest in the left lateral decubitus position and during both exercise modalities using
7 commercially available ultrasound equipment (Vivid 7, GE Medical, London) with a phased
8 array transducer (3S 1.4-3.8 MHz). Image acquisition and measurement procedures were
9 conducted by the same investigator (AB) in accordance with established guidelines²¹⁻²³. Five
10 cardiac cycles were obtained at end-expiration, with data analysis performed from a
11 minimum of 2 consecutive cycles when 3 were not available. Conventional parameters at rest
12 included LV structure, systolic and diastolic function.

13

14 **2.5 Speckle tracking derived circumferential strain**

15 Circumferential strain was measured at rest and during both submaximal cycling and
16 isometric knee extension protocols. Resting data obtained during visit 1 were used to
17 compare with both the cycling and isometric exercise protocols. Frame rate ranged between
18 70 – 80 frames per second which was consistent within each individual across all conditions
19 and also the same for apical and basal image acquisition. Using the parasternal short-axis
20 view, the basal level was determined as the highest imaging plane at which full myocardial
21 thickness was present with the observation of surrounding mitral valve at end-systole and
22 positioned as circular as possible with no visible papillary muscles²⁰. Apical images were
23 captured proximal to the end-systolic luminal obliteration of the LV cavity with as much
24 accuracy as possible²⁴.

1 Images were analysed offline using semi-automated software (EchoPac software, GE
2 Healthcare, UK) by one investigator. After manual endocardial border detection, the region
3 of interest was first automatically and then manually adjusted until the epicardal border was
4 correctly aligned to encompass the entire LV wall thickness whilst avoiding the echogenic
5 pericardium²²²²²²²². ACS and BCS were recorded as the peak value, reflective of mid-layer
6 strain, from the average of all fully tracked myocardial segments, with GCS then calculated
7 as the average of BCS and ACS.

8 The quality of echocardiographic images obtained during exercise, in addition to the
9 grading system employed have been reported previously¹⁵.

10

11 **2.6 Intra-observer reproducibility**

12 Intra-observer reproducibility (coefficients of variation (CV)) was determined within-day at
13 rest and between-day during both dynamic cycling and isometric knee extension exercise
14 (Table 1). CV was calculated for each individual between trial 1 and trial 2 using the
15 calculation: $CV = \left(\frac{\text{standard deviation}}{\text{mean}} \right) \times 100$. An average of each individual CV was then
16 obtained to determine a global CV.

17 A separate cohort of 14 participants rested for 5 min in the supine position, two
18 echocardiographic examination were performed 5 min apart. During both cycling (n=12) and
19 knee extension (n=12) exercise, participants attended twice at the same time of day within 7
20 days of each other. Similar to the main data collection, participants were asked to abstain
21 from vigorous physical activity and alcohol for 24 hours and caffeine for 12 hours prior to
22 testing. The submaximal cycling consisted of 2 x 4 min bouts corresponding to 70 watts and
23 170 watts. Basal and apical images were collected at the end of each bout with image
24 acquisition as described in section, '*Speckle tracking derived circumferential strain*'. The

1 isometric knee extension exercise was performed as described in section, '*Cycle ergometry*
2 *and isometric knee extension protocols*', with images collected at 40% and 75% MVC.

3

4

INSERT TABLE 1 NEAR HERE

5

6 **2.7 Statistical analysis**

7 Data presented as means \pm standard deviation or median (interquartile range). Normality of
8 data distribution was assessed by Shapiro-Wilks test. For normally distributed data,
9 haemodynamic measures and circumferential strains assessed during exercise were compared
10 using one-way repeated measures analysis of variance (ANOVA) with post hoc Bonferroni
11 correction. For non-normally distributed data a Friedman test was employed followed by
12 Wilcoxon signed-rank test to test for pairwise comparisons. A manual Bonferroni correction
13 was applied to non-parametric tests to ensure accurate interpretation of potential statistically
14 significant differences. All analyses were conducted using SPSS (Version 21; IBM Company,
15 SPSS Inc., Chicago, USA) and statistical significance granted at $p \leq 0.05$.

16

17

18 **3. RESULTS**

19 **3.1 Participant numbers for echocardiography**

20 All participants completed the full protocol and echocardiographic data was determined in all
21 participants at rest. However, cardiac images during all exercise conditions could not be
22 obtained for one participant leading to exclusion from the study, resulting in a total sample of
23 twenty-six participants available for statistical analyses (age, 30 ± 6 years; height, 1.77 ± 0.08
24 m; mass, 75.87 ± 9.90 kg). Peak oxygen uptake, resting left ventricular structure, systolic and
25 diastolic function for the present study group have been published elsewhere ¹⁵. Furthermore,

1 due to poor image quality, circumferential strain data were not acquired during cycling at
2 30% W_{\max} ($n = 2$) and 60% W_{\max} ($n = 3$) and during knee extension at 75% MVC ($n = 3$).
3 Consequently, 22 and 23 participants were included during cycling and knee extension,
4 respectively. The reasons for missing data for blood pressure have been detailed previously
5 ¹⁵.

6

7 **3.2 Maximal physiological and haemodynamic parameters**

8 Following the maximal incremental exercise test and MVC, group physiological parameters
9 were, W_{\max} 277 ± 49 W; 30% W_{\max} 83 ± 15 W; 60% W_{\max} , 166 ± 29 W; MVC, 1103 ± 267 N;
10 40% MVC, 441 ± 107 N and 75% MVC, 828 ± 200 N. All haemodynamic data during
11 cycling and knee extension are presented in Table 2. HR, SBP, DBP, MAP and RPP
12 significantly (all $p < 0.01$) increased with progressive exercise intensity from rest during both
13 cycling and knee extension exercises. Exercise workloads at maximum and relative
14 percentages, in addition to all haemodynamic data, with the exception of RPP, have been
15 reported previously ¹⁵.

16

17

INSERT TABLE 2 NEAR HERE

18

19 **3.3 Circumferential strain during exercise**

20 LV GCS, ACS and BCS during cycling and isometric exercise are presented in Figure 1a-b.
21 During semi-supine dynamic cycling, GCS increased from rest ($-22.85 \pm 3.26\%$) to 30%
22 W_{\max} ($-27.17 \pm 4.63\%$, $p = 0.002$) and then further increased to 60% W_{\max} ($-29.87 \pm 2.59\%$, p
23 $= 0.031$). ACS increased from rest ($-26.29 \pm 4.84\%$, $p < 0.001$) to 30% W_{\max} ($-36.84 \pm$
24 6.94%) and then remained unchanged to 60% W_{\max} ($-40.72 \pm 4.06\%$, $p = 0.068$). In contrast,

1 there was a statistically significant decrease in BCS from rest ($-19.41 \pm 2.79\%$) to 30% W_{\max}
2 ($-17.51 \pm 4.66\%$, $p = 0.049$) which then remained statistically unchanged thereafter to 60%
3 W_{\max} ($-19.03 \pm 4.14\%$, $p = 0.506$).

4 During isometric knee extension, GCS decreased from rest ($-22.63 \pm 3.46\%$) to 40%
5 MVC ($-20.10 \pm 2.78\%$, $p = 0.031$) and then remained unchanged to 75% MVC ($-19.72 \pm$
6 2.91% , $p = 1.00$). Similarly, BCS decreased from rest ($-19.21 \pm 2.58\%$) to 40% MVC (-13.55
7 $\pm 3.45\%$, $p < 0.001$) and then remained unchanged to 75% MVC ($-12.21 \pm 2.89\%$, $p = 0.162$),
8 whereas ACS did not change with exercise intensity (rest, $-26.05 \pm 5.34\%$; 40% MVC, -26.64
9 $\pm 4.53\%$ and 75% MVC $-27.22 \pm 5.34\%$, all $p = 1.00$).

10

11

INSERT FIGURE 1 NEAR HERE

12

13 **4. DISCUSSION**

14 This study is the first to investigate the influence of both incremental dynamic and static
15 (isometric) exercises on LV global and regional circumferential strain in the same
16 participants. Accordingly, the principle findings were that, (1) during dynamic and static
17 exercise, opposing GCS responses were observed. During aerobic exercise, there was a
18 stepwise increase in GCS, whereas during the static exercise GCS decreased to 40% MVC
19 but plateaued thereafter. In addition, the GCS responses in both exercises modalities were
20 due to different circumferential strain mechanics. (2) During aerobic exercise, the increase in
21 GCS was mediated by increasing ACS with trivial effects on BCS. (3) In contrast, static
22 exercise had no effect on ACS with the GCS changes being mediated by a decrease in BCS
23 from rest. Therefore, it appears that exercise modality plays some role in the responses of
24 circumferential strain.

1 These observations present a novel finding which adds to work having been
2 performed thus far, and at higher intensities than have previously been used, highlighting that
3 GCS alterations are the consequence of opposing physiological responses between the basal
4 and apical regions. Global strain provides a good indication of deformation encompassing the
5 entire LV; apical and basal strain may compliment the global derivative (when calculated as
6 an average of apical and basal planes) by determining the regional contributions.

7 8 **4.1 Circumferential strain during semi-supine cycling**

9 GCS increased with exercise initiation and further increased between exercise intensities
10 which agrees with our first hypothesis. These observations concur²⁵ and contrast with prior
11 studies, of which found no statistically significance increase between penultimate and final
12 exercise intensities^{6,8}. Although a lack of statistical significance does not imply the changes
13 are not biologically meaningful, the present study extends previous work and clarifies the
14 position that beyond low-moderate intensities and up to moderate intensity cycling, GCS
15 does not plateau. In this study, exercise intensity was greater than the absolute⁸ and relative
16 workloads⁶ employed previously and in particular, larger intervals between workloads were
17 used compared with the protocol of Doucende et al.⁶. Thus, discrete differences in
18 circumferential strain may only become evident with higher intensities and/or wider
19 categories. Moreover, Unnithan et al.⁸ used upright cycling compared to semi-supine cycling
20 in the present study, and therefore, a postural effect during the exercise cannot be ruled out.
21 The studied population should also be considered; Unnithan et al.⁸ used adolescents whereas
22 we recruited adults, whether the circumferential strain response differs between adolescents
23 and adults or are influenced by posture are intriguing prospects that may wish to be explored
24 further.

1 Region-specific function was noted during cycling exercise, ACS initially increased
2 from rest and then demonstrated a trend toward an increase between exercise intensities,
3 which underlines the functional reserve capacity of the apex in response to cardiovascular
4 exercise stress, whereas BCS decreased initially and was unchanged thereafter. Despite a
5 statistically significant change in BCS following the transition of rest to exercise, the
6 biological significance of this small reduction (~2% strain) is likely to be trivial. Although,
7 lower basal shortening as seen in this study compared to the apex may not necessarily reflect
8 a lower contribution to physiological contraction²⁶. Nonetheless, from the present data, GCS
9 (when averaged from the base and apex) is predominantly the consequence of changes within
10 the apex during dynamic exercise and are similar to previous studies having shown increased
11 ACS, but unchanged BCS^{9,10}. In contrast, others reported a strain reserve in BCS during
12 cycling compared with baseline¹¹ and disagrees with the present study, which is indicative of
13 limited-to-no functional reserve, at least up to 60% W_{max} . Pielek et al.¹¹ studied an adolescent
14 cohort; whether younger individuals demonstrate alternate circumferential mechanics to
15 adults during incremental exercise is difficult to determine since ACS was not reported,
16 whereby preventing a direct comparison; yet, as alluded to previously, such possibilities of an
17 age-dependant response require future study.

18

19 **4.2 Circumferential strain during isometric knee extension**

20 During incremental isometric knee extension exercise, GCS reduced from rest to 40% MVC
21 and then remained unaltered to 75% MVC, which is in agreement with our second
22 hypothesis. The reduction in GCS concurs with previous reports utilising upper-body
23 isometric hand-grip exercises^{7,12} and suggests the GCS responses during upper and lower
24 body based isometric exercise are independent of the exercise modality. Similar to the
25 cycling exercise, we found regional differences in circumferential strain between the apex

1 and base. However, unlike during dynamic exercise, ACS remained unchanged through the
2 incremental protocol while BCS was reduced. These observations are in partial agreement
3 with our second hypothesis, with respect to BCS, yet are at odds in regards to the responses
4 observed at the apex. The regional BCS responses during isometric exercise are similar to
5 another study having used incremental resistance exercise¹³. In contrast, ACS was reduced in
6 their study but unchanged in ours and the reasons for this disagreement are unknown at
7 present. Herein a supine unilateral knee extension was performed, whereas Stohr et al.¹³ used
8 a seated double-leg press held isometrically (90° knee flexion) for a short duration following
9 a near-complete leg extension. Blood pressure during their experimental protocol^{13,27} far
10 exceeded those of the present; the larger work required to perform the resistance exercise
11 even at similar relative workloads would have accentuated the afterload exposure.
12 Nonetheless, this does suggest that changes in BCS are consistent across a broad range of
13 afterloads and, may be more sensitive to small increases in afterload than ACS.

14 Although we can only speculate on the responsible mechanisms for the global and
15 regional observations herein, changes in fibre length during the isometric exercise may
16 adversely affect the ensuing shortening and tension developed and as a consequence LV
17 function²⁰. The unique myocardial fibre orientation should also be considered and in addition
18 to a circumferential strain basal-to-apical gradient, an epicardial-to-endocardial strain
19 gradient exists in both basal and apical regions⁵; examination of such layers may provide
20 further insight.

21 The implications of an immediate reduction in GCS and BCS remain to be explored
22 and more so, the magnitude of reduction required before it can be considered biologically
23 important (e.g. it significantly alters LV output and thus cardiac performance) is yet to be
24 fully elucidated. Stohr et al.¹³ identified only transient reductions following a restoration to
25 baseline levels during recovery intervals, yet the long-term ramifications of repeated bouts

1 and exposure to transient reductions in circumferential strain over multiple years are
2 unknown. GCS was significantly reduced in resistance trained athletes compared with normal
3 controls ^{28,29}, although more studies are required in those who perform repetitive resistance
4 exercise for both competition (i.e. highly trained athletes) and recreation.

5

6 **4.3 Limitations**

7 We have previously acknowledged the experimental protocol limitations ¹⁵, with regards to
8 the potential error of the blood pressure measurements and the confirmation of afterload
9 exposures. Also, we included only young, healthy males so the findings of this study may not
10 reflect the entire population including females, older aged individuals or special, clinical
11 populations. At rest images were obtained in the supine position, whereas during cycling they
12 were collected in the semi-supine position. However, despite a reduction in LV preload
13 following a transition from supine to head-up tilt position, LV circumferential strain was
14 comparable between body positions ³⁰. Thus, the physiological increases in regional and
15 global circumferential strain observed in this study, during dynamic exercise, are unlikely to
16 be attributed to the differences in resting and exercising body positions when acquiring
17 echocardiographic images.

18 Technical limitations of echocardiography are especially pertinent when acquiring the
19 basal and apical imaging planes. First, with two-dimensional echocardiography basal and
20 apical images are obtained within different heart beats and thus in this study, obtained during
21 two separate contractions during the isometric knee extension. Second, obtaining the
22 consistent imaging planes is challenging which may affect intra-subject variability ⁶. Indeed
23 this intrinsic limitation of two-dimensional imaging may be overcome with the use of three-
24 dimensional which facilitates the detection of deformation in and out of plane^{4,22}.
25 Nevertheless, the resting within-day intra-observer reproducibility reported in this study are

1 consistent with previous reports ^{8,31}. As would be anticipated, the CV were greater during
2 both dynamic and static exercises compared with rest, yet were similar to another incremental
3 exercise study, albeit in an adolescent population and performing upright cycle ergometer
4 exercise ⁸. During isometric exercise, BCS demonstrated the largest CV which should
5 therefore be considered when interpreting the findings of this study, especially since BCS
6 was the largest respondent during isometric knee extension. However, the changes in BCS
7 from rest to 40% (29.46%) and 75% MVC (36.44%) were greater than the intra-observer CV
8 at 40% and 75% MVC. Still it is possible that the magnitude of decrement in BCS could have
9 been influenced by the reproducibility.

10

11 **5. CONCLUSIONS**

12 This study is the first to investigate global and region-specific circumferential strain during
13 both incremental dynamic cycling and isometric knee extension exercises in the same
14 participants. GCS progressively increased during dynamic exercise but decreased during
15 short-duration isometric work. These acute, global alterations were due to apical increase
16 during cycling, yet basal reductions during isometric knee extension. Cardiac strains,
17 circumferentially determined, appear to be modality dependant following region-specific
18 changes within the myocardium, concomitant with exercise stress of differing physiological
19 demands.

1 **References**

- 2 1. Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging:
3 how useful is it in clinical decision making? *Eur Heart J*. 2016;37:1196–1207.
- 4 2. Blessberger H, Binder T. Two dimensional speckle tracking echocardiography: basic
5 principles. *Heart*. 2010;96:716–722.
- 6 3. Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. *Indian*
7 *Heart J*. 2013;65:117–123.
- 8 4. Biswas M, Sudhakar S, Nanda NC, Buckberg G, Pradhan M, Roomi AU, Gorissen W,
9 Houle H. Two- and Three-Dimensional Speckle Tracking Echocardiography: Clinical
10 Applications and Future Directions. *Echocardiography*. 2013;30:88–105.
- 11 5. Shi J, Pan C, Kong D, Cheng L, Shu X. Left Ventricular Longitudinal and
12 Circumferential Layer-Specific Myocardial Strains and Their Determinants in Healthy
13 Subjects. *Echocardiography*. 2016;33:510–518.
- 14 6. Doucende G, Schuster I, Rupp T, Startun A, Dazat M, Obert P, Nottin S. Kinetics of
15 Left Ventricular Strains and Torsion During Incremental Exercise in Healthy Subjects:
16 The Key Role of Torsional Mechanics for Systolic-Diastolic Coupling. *Circ Cardiovasc*
17 *Imaging*. 2010;3:586–594.
- 18 7. Balmain B, Stewart GM, Yamada A, Chan J, Haseler LJ, Sabapathy S. The impact of an
19 experimentally induced increase in arterial blood pressure on left ventricular twist
20 mechanics: Exercise-induced afterload increase and ventricular twist mechanics. *Exp*
21 *Physiol*. 2016;101:124–134.
- 22 8. Unnithan VB, Rowland T, Lindley MR, Roche DM, Garrard M, Barker P. Cardiac
23 strain during upright cycle ergometry in adolescent males. *Echocardiogr Mt Kisco N*.
24 2015;32:638–643.
- 25 9. Stembridge M, Ainslie PN, Hughes MG, Stöhr EJ, Cotter JD, Tymko MM, Day TA,
26 Bakker A, Shave R. Impaired myocardial function does not explain reduced left
27 ventricular filling and stroke volume at rest or during exercise at high altitude. *J Appl*
28 *Physiol*. 2015;119:1219–1227.
- 29 10. Stöhr EJ, McDonnell B, Thompson J, Stone K, Bull T, Houston R, Cockcroft J, Shave
30 R. Left ventricular mechanics in humans with high aerobic fitness: adaptation
31 independent of structural remodelling, arterial haemodynamics and heart rate. *J Physiol*.
32 2012;590:2107–2119.
- 33 11. Pielles GE, Gowing L, Forsey J, Ramanujam P, Miller F, Stuart AG, Williams CA. The
34 relationship between biventricular myocardial performance and metabolic parameters
35 during incremental exercise and recovery in healthy adolescents. *Am J Physiol Heart*
36 *Circ Physiol*. 2015;309:H2067-2076.
- 37 12. Murai D, Yamada S, Hayashi T, Okada K, Nishino H, Nakabachi M, Yokoyama S, Abe
38 A, Ichikawa A, Ono K, Kaga S, Iwano H, Mikami T, Tsutsui H. Relationships of left

- 1 ventricular strain and strain rate to wall stress and their afterload dependency. *Heart*
2 *Vessels*. 2017;32:574–583.
- 3 13. Stöhr EJ, Stembridge M, Shave R, Samuel TJ, Stone K, Esformes JI. Systolic and
4 Diastolic LV Mechanics during and following Resistance Exercise. *Med Sci Sports*
5 *Exerc*. 2017;
- 6 14. Mitchell JH, Haskell W, Snell P, Van Camp SP. Task Force 8: classification of sports. *J*
7 *Am Coll Cardiol*. 2005;45:1364–1367.
- 8 15. Beaumont A, Hough J, Sculthorpe N, Richards J. Left ventricular twist mechanics
9 during incremental cycling and knee extension exercise in healthy men. *Eur J Appl*
10 *Physiol*. 2017;117:139–150.
- 11 16. Weippert M, Behrens K, Rieger A, Stoll R, Kreuzfeld S. Heart rate variability and blood
12 pressure during dynamic and static exercise at similar heart rate levels. *PLoS One*.
13 2013;8:e83690.
- 14 17. Kuipers H, Verstappen FT, Keizer HA, Geurten P, van Kranenburg G. Variability of
15 aerobic performance in the laboratory and its physiologic correlates. *Int J Sports Med*.
16 1985;6:197–201.
- 17 18. Kong PW, Haselen JV. Revisiting the influence of hip and knee angles on quadriceps
18 excitation measured by surface electromyography : original research article. *Int*
19 *SportMed J*. 2010;11:313–323.
- 20 19. Adler Y, Fisman EZ, Koren-Morag N, Tanne D, Shemesh J, Lasry E, Tenenbaum A.
21 Left ventricular diastolic function in trained male weight lifters at rest and during
22 isometric exercise. *Am J Cardiol*. 2008;102:97–101.
- 23 20. Weiner RB, Weyman AE, Kim JH, Wang TJ, Picard MH, Baggish AL. The impact of
24 isometric handgrip testing on left ventricular twist mechanics: Handgrip testing and left
25 ventricular twist. *J Physiol*. 2012;590:5141–5150.
- 26 21. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner
27 AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the
28 Evaluation of Left Ventricular Diastolic Function by Echocardiography. *J Am Soc*
29 *Echocardiogr*. 2009;22:107–133.
- 30 22. Mor-Avi V, Lang RM, Badano LP, et al. Current and Evolving Echocardiographic
31 Techniques for the Quantitative Evaluation of Cardiac Mechanics: ASE/EAE Consensus
32 Statement on Methodology and Indications Endorsed by the Japanese Society of
33 Echocardiography. *Eur J Echocardiogr*. 2011;12:167–205.
- 34 23. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for Cardiac Chamber
35 Quantification by Echocardiography in Adults: An Update from the American Society
36 of Echocardiography and the European Association of Cardiovascular Imaging. *Eur*
37 *Heart J – Cardiovasc Imaging*. 2015;16:233–271.
- 38 24. van Dalen BM, Vletter WB, Soliman OII, ten Cate FJ, Geleijnse ML. Importance of
39 Transducer Position in the Assessment of Apical Rotation by Speckle Tracking
40 Echocardiography. *J Am Soc Echocardiogr*. 2008;21:895–898.

- 1 25. Matsui K, Takahashi K, Tanaka N, Kobayashi M, Yamada M, Kishiro M, Itatani K,
2 Miyaji K, Shimizu T. Relationship Between Left Ventricular Deformation and Early
3 Diastolic Intraventricular Pressure Difference During Rest and Exercise. *順天堂醫事雜*
4 *誌*. 2016;62:26–33.
- 5 26. Rademakers FE, Rogers WJ, Guier WH, Hutchins GM, Siu CO, Weisfeldt ML, Weiss
6 JL, Shapiro EP. Relation of regional cross-fiber shortening to wall thickening in the
7 intact heart. Three-dimensional strain analysis by NMR tagging. *Circulation*.
8 1994;89:1174–1182.
- 9 27. Stöhr EJ, Stembridge M, Esformes JI. In vivo human cardiac shortening and
10 lengthening velocity is region dependent and not coupled with heart rate: 'longitudinal'
11 strain rate markedly underestimates apical contribution. *Exp Physiol*. 2015;100:507–
12 518.
- 13 28. Beaumont A, Grace F, Richards J, Hough J, Oxborough D, Sculthorpe N. Left
14 Ventricular Speckle Tracking-Derived Cardiac Strain and Cardiac Twist Mechanics in
15 Athletes: A Systematic Review and Meta-Analysis of Controlled Studies. *Sports Med*.
16 2016;
- 17 29. Szauder I, Kovács A, Pavlik G. Comparison of left ventricular mechanics in runners
18 versus bodybuilders using speckle tracking echocardiography. *Cardiovasc Ultrasound*
19 [Internet]. 2015 [cited 2016 Dec 7];13. Available from:
20 <http://cardiovascularultrasound.biomedcentral.com/articles/10.1186/s12947-015-0002-y>
- 21 30. Nelson MD, Altamirano-Diaz LA, Petersen SR, DeLorey DS, Stickland MK, Thompson
22 RB, Haykowsky MJ. Left ventricular systolic and diastolic function during tilt-table
23 positioning and passive heat stress in humans. *Am J Physiol Heart Circ Physiol*.
24 2011;301:H599-608.
- 25 31. Oxborough D, George K, Birch KM. Intraobserver Reliability of Two-Dimensional
26 Ultrasound Derived Strain Imaging in the Assessment of the Left Ventricle, Right
27 Ventricle, and Left Atrium of Healthy Human Hearts: Intraobserver Reliability of 2D
28 Derived ϵ . *Echocardiography*. 2012;29:793–802.

Tables

Table 1 Reproducibility of apical, basal and global circumferential strain at rest and during submaximal cycling and isometric knee extension exercise

Measure	Rest		Submaximal cycling				Isometric knee extension			
			70 watts		170 watts		40% MVC		75% MVC	
	n	CV (%)	n	CV (%)	n	CV (%)	n	CV (%)	n	CV (%)
Basal circumferential strain	13	6.31	11	11.07	8	10.84	9	15.4	10	17.28
Apical circumferential strain	12	7.93	11	8.90	8	14.35	9	11.74	9	8.71
Global circumferential strain	11	3.64	11	8.86	7	10.21	9	9.75	8	6.05

CV: coefficient of variation.

Table 2 Haemodynamic measures at rest and during both intensities of the cycling and isometric knee extension exercises

Variable	Cycling (% W_{\max})			Knee extension (% MVC)		
	Rest	30%	60%	Rest	40%	75%
HR (beats·min ⁻¹)	57 (14)	96 (11) †	128 (14) †‡	57 (14)	81 (24) †	97 (29) †‡
SBP (mmHg) ^a	118 ± 9	141 ± 9 †	172 ± 21 †‡	118 ± 9	130 ± 10 †	146 ± 18 †‡
DBP (mmHg) ^{b c}	77 (9)	81 (4) †	82 (6) †‡	77 (9)	79 (9) †	82 (9) †‡
MAP (mmHg) ^{b c}	89 ± 6	101 ± 5 †	114 ± 8 †‡	89 (11)	94 (5) †	104 (10) †‡
RPP ^a	6867.00	13100.00	22862.00	6867.00	10664.00	13774.00
(beats·min ⁻¹ · mmHg)	(1652.00)	(2617.50) †	(3540.50) †‡	(1652.00)	(3897.50) †	(4577.50) †‡

Normally distributed data presented as mean ± standard deviation, non-normally distributed data presented as median (interquartile range)

HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; RPP: rate pressure product; W_{\max} : work rate maximum; MVC: maximal voluntary isometric contraction.

† $p < 0.01$ compared to rest.

‡ $p < 0.01$ compared to previous intensity.

^a $n = 25$ during cycling and knee extension ^b $n = 25$ during cycling, ^c $n = 24$ during knee extension.

All data except RPP have been reported previously ¹⁵.

Figure captions

Figure 1 Circumferential strain during incremental cycling ($n= 22$) (**a**) and during incremental isometric knee extension ($n=23$) (**b**).

ACS: apical circumferential strain; BCS: basal circumferential strain; GCS: global circumferential strain; W_{\max} : work rate maximum; MVC: maximum voluntary contraction.

† $p < 0.05$ compared with rest

‡ $p < 0.05$ compared with previous intensity

See text for exact p values. Data are presented as means \pm standard deviation