SHORT REPORT: Effect of ~~cardiac rehabilitation~~ exercise training on left ventricular mechanics after acute myocardial infarction – an exploratory study

Gordon McGregor PhD [1,2*], Eric J. Stöhr PhD [1], David Oxborough PhD [3], Peter Kimani PhD [4], and Rob Shave PhD [1]

[1]Cardiff Metropolitan University, Cardiff, UK.

[2]Coventry University, Coventry, UK.

[3]Liverpool John Moore's University, Liverpool, UK.

[4]University of Warwick, Warwick, UK.

***Corresponding author:**
Dr Gordon McGregor
Cardiac Rehabilitation
University Hospitals Coventry & Warwickshire NHS Trust
Centre for Exercise & Health
Watch Close
Coventry CV1 3LN
Tel: 02476 234 570
Email: Gordon.mcgregor@uhcw.nhs.uk

Grant support, conflicts of interest

None.

Abstract

Background: cardiac rehabilitation (CR) exercise training is beneficial after myocardial infarction (MI). Whilst the peripheral adaptations to training are well defined, little is known regarding the effect on left ventricular (LV) remodelling, particularly LV function. Efficient LV ejection and filling is achieved through deformation and rotation of the myocardium in systole and diastole - LV mechanics. The response of LV mechanics to CR exercise training in MI patients is unknown.

Methods: in this observational exploratory study, 36 (of 40 enrolled) male, MI patients completed either 10-weeks of twice-weekly gym based cardiovascular exercise at 60-80% VO_{2peak} (n=18), or a non-exercise control period (n=18). Cardiopulmonary exercise testing and speckle tracking echocardiography were performed at baseline and 10 weeks.

Results: compared to the non-exercise group, VO_{2peak} improved with CR exercise training (Difference: +4.28 [95% CI, 1.34 to 7.23] $ml.kg^{-1}.min^{-1}$, *P*=0.01). Neither conventional LV structural or functional indices, nor LV global longitudinal strain, significantly changed in either group. In contrast, LV twist and twist velocity decreased in the exercise group and increased in the non-exercise group (Difference: -3.95° [95% CI, -7.92 to 0.03°], *P*=0.05 and -19.2°.sec^{-1} [95% CI, -35.9 to -2.7°.sec^{-1}], *P*=0.02, respectively).

Conclusion: in MI patients who completed CR exercise training, LV twist and twist velocity decreased, whereas these parameters increased in patients who did not exercise. These preliminary data may indicate reverse LV functional remodelling and improved functional reserve. The assessment of LV twist may serve as an indicator of the therapeutic benefit of CR exercise training and should be investigated in larger trials.

Keywords: longitudinal strain, left ventricular twist, left ventricular remodelling

Introduction

Pathologic left ventricular (LV) remodelling is a significant problem after myocardial infarction (MI) (1). In MI patients, cardiac rehabilitation (CR) exercise training improves functional capacity (2). Whilst the contribution of peripheral adaptation to this improvement is relatively well understood (3), little is known about LV remodelling, particularly in relation to function. Recent data support exercise induced reverse LV remodelling, characterised by reduced LV volumes and increased ejection fraction (4). However, LV systolic function is not well defined by ejection fraction alone. Rather, the motion of the LV during systole and diastole is a complex pattern of multi-directional deformation and rotation (LV mechanics) that underpins efficient systolic ejection and diastolic filling. Obliquely and opposingly wound endocardial and epicardial myofibres are electrically and mechanically activated, in sequence, from apex to base (5) resulting in longitudinal shortening (LV strain) (6) and LV twist i.e. clockwise basal rotation and anticlockwise apical rotation (7). During diastolic untwist, rapid recoil sucks blood into the LV, utilising energy stored in the preceding twist.

Left ventricular mechanics are compromised by ischemic heart disease (8) and are known to predict pathologic remodelling after MI (9, 10). Specifically, LV longitudinal strain and twist are acutely impaired immediately following MI, and progressively decline with chronic pathologic remodelling (9, 11). In contrast, LV mechanics are likely to be preserved in the presence of reverse LV remodelling (9, 11). Given the association between LV mechanics and remodelling, the assessment of LV longitudinal strain and

twist may help determine the effect of CR exercise training on functional LV remodelling after MI.

By assessing patients with 2D speckle tracking echocardiography (STE), before and after a CR programme, the main objective of this exploratory study was to examine the effect of exercise training on LV longitudinal strain and twist in MI patients.

Materials and methods

Ethical considerations

This study was conducted in line with the principles of Good Clinical Practice, and complied fully with the Declaration of Helsinki. Research and Ethics Committee approval was gained (Coventry & Warwickshire (08/H1210/56) and informed consent obtained from all participants.

Study design

A prospective, non-randomised observational study was conducted. Forty male participants were allocated to an exercise (n=20) or non-exercise group (n=20) (figure 1). Ethical constraints and institutional policy prevented randomisation, however, groups did not differ demographically or clinically at baseline.

Participants and procedures

Conventional echocardiography, STE and cardiopulmonary exercise testing (CPET) were performed at baseline and after a 10-week exercise programme or non-exercise control period. ~~. Forty male participants were allocated to an exercise (n=20) or non-exercise group (n=20). Ethical constraints and institutional policy prevented randomisation, however, groups did not differ demographically or clinically at baseline.~~ Participants were optimally treated with percutaneous coronary intervention for acute MI. Complete revascularisation was undertaken and no clinically significant atherosclerotic lesions remained untreated. Clinical stability (12) was medically certified and further confirmed by the absence of exercise induced angina and/or ischemic ECG changes during cardiopulmonary exercise testing. Patients were excluded if comorbidities prevented full participation. ~~Research and Ethics Committee approval was gained and informed consent obtained.~~

Exercise training

Gym based, continuous, moderate intensity cardiovascular exercise training (i.e. treadmill, cycle, rower, cross-trainer) was completed for 25-40 mins, twice weekly for 10 weeks. A 10-min progressive treadmill or cycle warm-up preceded the cardiovascular exercise. A standardised resistance machine training programme (1 set, 12 reps, 5 upper and 2 lower body exercises) (12) followed a five-minute cool down walk. Cardiovascular exercise workload was equivalent to 60-80% peak oxygen uptake

($VO_{2\ peak}$) from CPET, and after two sessions, the supervising Exercise Physiologist ensured that participants were exercising at a heart rate equivalent to 80% $VO_{2\ peak}$. Individualised exercise intensity was systematically re-prescribed every two weeks based on perceived exertion, and duration was incrementally increased to 40 minutes by week-five. Adherence of ≥17 of 20 sessions was required for inclusion in the analysis. The non-exercise group did not complete supervised CR exercise training but were advised on a cardio-protective lifestyle.

Cardiopulmonary exercise test (CPET)

In accordance with guidelines (13), a ramp CPET was performed on a cycle ergometer. Respired gas was analysed for oxygen uptake (VO_2), carbon dioxide production (VCO_2) and minute ventilation (V_E) (Oxycon Pro, Care Fusion Corp, San Diego, California, USA). ECG was continuously recorded and blood pressure measured at two-minute intervals. Tests were continued until symptom-limited volitional fatigue. A respiratory exchange ratio of >1.15 was considered representative of maximal effort. Peak oxygen uptake ($VO_{2\ peak}$) was taken to be the mean O_2 uptake in the final 20 seconds of the test, whilst O_2 uptake at the anaerobic threshold ($VO_{2\ AT}$) was confirmed with the V-slope method and analysis of the ventilatory equivalents and end-tidal gas tension data (21).

Transthoracic echocardiography

A single cardiac sonographer, blinded to group allocation, acquired resting echocardiographic images in accordance with current guidelines (14). A commercially available ultrasound system (Vivid 7, GE Medical Systems, Horten, Norway) was used

to obtain and store images from 3 consecutive cardiac cycles for subsequent off-line analysis (Echo-pac, GE Medical Systems, Horten, Norway, version 7.0.0). From the parasternal long axis view, LV internal dimensions/wall thicknesses and atrial diameter were measured. Left ventricular volumes were calculated by the Simpson's bi-plane method from apical two and four-chamber (A4C) images, and relative wall thickness and LV mass derived according to Lang et al., (2015) (15). Standard mitral inflow parameters were assessed with pulse wave Doppler imaging in the A4C view and mitral annulus tissue velocities were determined with tissue Doppler imaging of the septal and lateral mitral annuli.

Left ventricular mechanics: strain, rotation and twist

A rigorous methodology was employed to optimise and standardise image acquisition and analysis. Speckle tracking echocardiography at frame rates between 70 and 100 frames/s was used to derive indices of LV mechanics from the A4C view and the basal and apical parasternal short axis (PSAX) views. Care was taken to ensure that basal images were recorded at the tips of the mitral valve leaflets, apical images recorded just proximal to the level of LV luminal closure at end-systole, and that the LV cross-section was as circular as possible. Inter-individual basal and apical images were acquired at the same frame rates, as were pre- and post-study measurements. Prior to STE analysis, the research team, blinded to group allocation and time point, examined all images to validate quality. Those that did not meet the required level of optimisation and standardisation were excluded. The endocardium was manually traced and a 6-segment region of interest automatically applied by the STE software (Echo-pac, GE Medical Systems, Horten, Norway, version

7.0.0). The motion of the region of interest was automatically tracked frame-by-frame throughout the cardiac cycle, and segmental tracking quality was improved manually where necessary. Segments with inadequate tracking were excluded at baseline and from repeat measurements. Participants were excluded from statistical analysis where more than two segments were deemed to have insufficient tracking quality (16). Data were exported as the average of all segments to bespoke software (2D Strain Analysis Tool, Stuttgart, Germany) for further automated and operator processing. To accommodate inter and intra-individual variations in heart rate, data were normalised to the percentage of systolic and diastolic duration using cubic spline interpolation (17). Mean global longitudinal strain (GLS) was defined as the highest absolute value of peak negative strain attained during systole (18). Systolic rotation was measured at the base and apex and represented as positive (anti-clockwise) and negative (clockwise) values respectively. Systolic twist was calculated by subtracting peak basal rotation from peak apical rotation, thus defining the variable as the net apex-base difference in rotation angle along the longitudinal axis of the LV (8). The magnitude of movement over time was reported as velocity for rotation, twist and untwist (19).

~~Research and Ethics Committee approval was gained and informed consent obtained.~~

Statistical analyses

Baseline characteristics and continuous variables were summarised as mean ± standard deviation (SD), with independent *t*-tests used to compare group means at baseline. Mean differences at week 10 were compared by fitting either 1) a repeated measures model that included main effect terms and interaction terms for ‘group’ and ‘visit’, or 2) a

linear model for outcome values at week 10 with terms for ‘group’ and ‘baseline value’. A linear model was only used if the t-test comparing outcomes at baseline, and visualisation of raw data suggested that mean outcomes for exercise and non-exercise at baseline were different. From the fitted model, the estimated mean difference at week 10, corresponding 95% confidence interval (CI), and p-values were reported. Statistical significance was considered as $P<0.05$. A formal sample size calculation was not performed as this was an exploratory study to generate future hypotheses.

Results

Recruitment

Of the 40 male patients, four dropped out and five were excluded as reliable STE analysis was not possible due to sub-optimal image acquisition (primarily at the LV apex). Ultimately, the study population consisted of an exercise group (n=15) and a non-exercise group (n=16). Exercise adherence was 88.7% (17.7 ± 0.9 sessions). At baseline, groups did not differ in demographic, clinical or echocardiographic characteristics (tables 1-3), were optimally pharmacologically treated, and there were no notable changes in cardiovascular or other relevant medication during the study period.

Cardiopulmonary exercise testing and echocardiography

Compared to the non-exercise group, VO_{2peak} and VT improved significantly in the exercise training group; (Difference: +4.28 [95% CI, 1.34 to 7.23] mL/kg/min, $P<0.01$ and +2.37 [95% CI, 0.85 to 3.89] mL/kg/min, $P<0.01$, respectively) (table 2). There were no significant changes in LV structure, conventional measures of LV function, or GLS (table 3). However, exercise training did result in a tendency towards a reduction in LV twist and a significant reduction in LV twist velocity in comparison to the non-exercise group (Difference: -3.95° [95% CI, -7.92 to 0.03°], $P=0.05$ and -19.2°.sec^{-1} [95% CI, -35.9 to -2.7°.sec^{-1}], $P=0.02$, respectively, table 3 and figure 2~~1~~). Exercise training also appeared to have more of an effect than non-exercise control on LVEDV/BSA (Difference: -4.80 [95% CI, -10.8 to 1.20] mL/m^2, $P=0.11$) and diastolic untwist velocity (Difference: +13.3°.sec^{-1} [95% CI, -4.7 to 31.2°.sec^{-1}], $P=0.14$), but neither difference reached statistical significance.

Discussion

The principal finding from this exploratory study was that patients with recent MI undertaking a CR exercise-training programme, demonstrated a reduction in LV twist and twist velocity compared to non-exercise control. We also observed an improved exercise capacity further to training.

Pathologic post-MI remodelling is characterised by increased LV volumes. These measures are clinically and prognostically significant (20). As such, reverse LV remodelling is an objective of both pharmacological and exercise therapy. In the current study, volumetric parameters did not change significantly in either group. However, previous studies, from our group and others, have demonstrated reverse volumetric remodelling in MI patients undertaking CR exercise training (4, 21). To complement these conventional measures, the assessment of LV mechanics may help quantify reverse remodelling. Whilst GLS was unaltered in the present study, there was a striking differential response, in LV twist and twist velocity, between the two study groups. Exercise training resulted in a 23% and 18% reduction in LV twist and twist velocity respectively, whereas an increase of 22% and 17% was observed in the non-exercise group. Reduced LV twist has been reported in highly trained individuals (22) and may indicate increased systolic efficiency and a greater 'twist reserve' (23, 24). An increase in twist reserve, and subsequent functional capacity, would be a favourable adaptation in an LV compromised by MI. Measurement of LV twist during exercise, however, is required to confirm greater twist reserve. The magnitude of change we observed in LV twist, in the

absence of any meaningful change in conventional functional indices or GLS, may indicate twist to be particularly sensitive to exercise training, as proposed in previous studies (17). As such, LV twist could be a useful tool for evaluating exercise-induced reverse remodelling in patients with MI.

In marked contrast to the exercise group, LV twist increased following the control period. Volumetric parameters, which were within normal range at baseline, remained unchanged, indicating the absence of gross LV remodelling. The increase in LV twist could therefore be interpreted negatively as a compensatory adaptation preceding pathologic remodelling and functional decline. Equally, it could be viewed as part of the LV recovery process following MI in response to medical therapy. Compared to healthy age matched controls, reduced LV twist has been reported immediately following revascularisation for MI (9). Subsequently, at six-months and two-years, LV twist increased in patients without adverse remodelling, whilst continued suppression and/or deterioration of LV twist was observed in pathologic LV dilation (9, 11). Essentially, patients without pathologic structural remodelling at six-months, were more likely to demonstrate an increase in LV twist, secondary to medical therapy. This is the most likely explanation for the increased twist in our data. Therefore, whilst on initial examination, the decrease in LV twist in the exercise group and the increase in the control group could be viewed as adaptive in the former, and maladaptive in the latter, it is plausible that both responses are representative of myocardial recovery. The differential response may be a product of the physiological, neurohormonal and biomolecular adaptation associated with exercise training (3, 25), but this requires further work to clarify.

A number of potential confounders should be the subject of future investigation. In accordance with local CR policy, exercise training was performed twice weekly for 10 weeks. In comparison to previous studies, typically three times a week for 12 weeks, the overall volume of exercise in this study was relatively low. Similarly, the training protocol adopted was a moderate intensity and steady-state prescription. It is possible that both training volume and intensity may differentially effect LV mechanics, as might exercise modality (26). Although difficult to draw parallels to healthy populations, it is possible that there is a phasic response to training by which short-term LV functional responses precede chronic structural adaptations, as has been shown in athletic individuals (22). Given that haemodynamic load is also known to greatly influence LV mechanics (26), the effect that cardiovascular medication has on training induced LV functional remodelling in post-MI patients is also of interest and needs to be studied further. It is important to acknowledge that this exploratory study was not randomised and was conducted in a small, heterogeneous population of male participants. Accordingly, these data are not conclusive or generalizable but have identified viable hypotheses for future trials.

In summary, ten weeks of CR exercise training altered LV mechanics. Whilst GLS was unaffected by exercise training, LV twist was reduced. Conversely, LV twist increased in non-exercise control patients. The measurement of LV twist may therefore offer valuable insight into exercise-induced reverse remodelling, and help characterise the therapeutic

benefit of CR exercise training. The clinical significance of these findings should be investigated in larger randomised trials.

Conflict of interest

We have no conflict of interest

Acknowledgements

We would like to extend our thanks to the cardiac rehabilitation team for their expertise in exercise programming and prescription.

Table 1. Baseline demographic and clinical parameters

	Baseline		
	No exercise (n=16)	**Exercise (n=15)**	**p**
Demographics			
Age (yrs)	54.1 ± 10.6	57.0 ± 10.7	0.45
Height (cm)	175 ± 7.0	173 ± 4.4	0.38
Body mass (kg)	88.9 ± 13.2	84.2 ± 9.5	0.27
BMI (kg/m^2)	28.7 ± 3.8	28.0 ± 2.7	0.52
Clinical			
STEMI (n, %)	10 (67)	12 (75)	0.70
Anterior (n, %)	4 (40)	7 (58)	0.67
Inferior (n, %)	6 (60)	5 (42)	0.67
NSTEMI (n, %)	5 (33)	4 (25)	0.70
PCI (n, %)	16 (100)	15 (100)	0.91
Time post MI (days)	35.8 ± 6.2	35.6 ± 7.9	0.95
CV medication **(n, %)**			
Beta-blockers	13 (81)	13 (87)	
ACE inhibitors	15 (94)	14 (93)	
Diuretics	3 (19)	2 (13)	
Statin	16 (100)	15 (100)	
Anti-platelet	16 (100)	15 (100)	
Hypoglycaemic	2 (13)	4 (27)	
CV disease risk factors **(n, %)**			
Smoking history	9 (56)	5 (33)	
Sedentary behaviour	13 (81)	12 (80)	
Diabetes mellitus (type II)	2 (13)	4 (27)	
Dyslipidaemia	10 (63)	7(47)	
Hypertension	8 (50)	7 (47)	

Data for continuous variables as Mean ± SD; BMI, body mass index; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; CV, cardiovascular

Table 2. Clinical and exercise test parameters at baseline and 10 weeks

	Baseline			Week 10		Difference	
	No exercise	Exercise	p	No exercise	Exercise	95% CI	p
Body mass (kg)	88.9 ± 13.2	84.2 ± 9.5	0.27	89.0 ± 13.3	84.3 ± 10.3	-4.65 (-13.29, 4.00)	0.28
BMI (kg/m^2)	28.7 ± 3.8	28.0 ± 2.7	0.52	28.8 ± 3.9	28.0 ± 3.0	-0.76 (-3.25, 1.72)	0.54
HR_{rest} (bpm)	55.6 ± 6.6	55.9 ± 6.7	0.89	55.3 ± 6.6	56.8 ± 7.9	1.55 (-3.50, 6.60)	0.54
BP_{sys} (mmHg)	118 ± 13	110 ± 15	0.15	116 ± 12	108 ± 16	-0.75 (-11.28, 9.78)	0.88
BP_{dia} (mmHg)	70 ± 9	69 ± 6	0.66	69 ± 9	71 ± 8	0.77 (-5.77, 7.31)	0.81
W_{max} (watts)	144 ± 27	153 ± 27	0.33	148 ± 30	180 ± 32	31.4 (10.1, 52.7)	0.01
$VO_{2\ peak}$	20.8 ± 3.2	24.9 ± 4.3	0.01	20.2 ± 4.2	28.2 ± 5.4	4.28 (1.34, 7.23)	0.01
VT (ml/kg/min)	11.1 ± 1.7	12.8 ± 3.0	0.07	10.9 ± 2.3	14.7 ± 3.2	2.37 (0.85, 3.89)	<0.01

Data for continuous variables as Mean ± SD; difference, no exercise – exercise at 10 weeks; CI, confidence interval; BMI, body mass index; HR, heart rate; BP_{sys}, resting systolic blood pressure; BP_{dys}, resting diastolic blood pressure; W_{max}, maximum workload; $VO_{2\ peak}$, peak oxygen uptake; VT, ventilatory threshold

Table 3. Left ventricular echocardiographic parameters at baseline and 10 weeks

	Baseline			Week 10		Difference	
	No exercise	**Exercise**	**p**	**No exercise**	**Exercise**	**95% CI**	**p**
Mass/BSA (g/m^2)	115 ± 26	111 ± 18	0.64	105 ± 20	114 ± 22	8 (-8, 24)	0.30
EDV/BSA (ml/m^2)	46.2 ± 7.9	44.6 ± 9.6	0.62	46.6 ± 7.1	41.8 ± 8.0	-4.80 (-10.80, 1.20)	0.11
ESV/BSA (ml/m^2)	20.0 ± 5.6	20.6 ± 6.8	0.81	20.5 ± 5.5	18.1 ± 5.4	-2.43 (-6.71, 1.84)	0.26
EF biplane (%)	56.9 ± 7.5	54.6 ± 6.8	0.37	56.4 ± 7.5	57.3 ± 5.7	0.90 (-4.17, 5.96)	0.72
E/A ratio	1.14 ± 0.38	1.22 ± 0.33	0.57	1.18 ± 0.37	1.08 ± 0.22	-0.09 (-0.33, 0.16)	0.49
Mean E/e' ratio	7.6 ± 1.7	8.3 ± 2.2	0.28	7.1 ± 3.0	7.8 ± 1.7	0.74 (-0.87, 2.34)	0.36
Systolic twist (°)	13.0 ± 4.2	15.6 ± 6.8	0.22	15.9 ± 5.7	11.9 ± 4.9	-3.95 (-7.92, 0.03)	0.05
Systolic twist vel. ($°.sec^{-1}$)	73.5 ± 22.5	94.3 ± 30.7	0.04	85.9 ± 24.5	77.1 ± 24.7	-19.2 (-35.9, -2.7)	0.02
Systolic basal rotation (°)	-4.4 ± 2.8	-5.4 ± 2.9	0.36	-5.3 ± 2.3	-4.6 ± 2.7	0.67 (-1.26, 2.60)	0.49
Systolic apical rotation (°)	9.3 ± 4.2	11.2 ± 4.8	0.25	11.1 ± 5.3	8.7 ± 4.1	-2.42 (-5.77, 0.93)	0.15
Diastolic untwist vel. ($°.sec^{-1}$)	-77 ± 24	-80 ± 32	0.81	-85 ± 18	-71 ± 23	13.3 (-4.7, 31.2)	0.14
GLS (%)	-17.4 ± 2.9	-17.5 ± 2.6	0.98	-17.4 ± 2.2	-17.2 ± 3.2	0.33 (-1.70, 2.37)	0.74
GLS rate (sec^{-1})	-0.89 ± 0.17	-0.90 ± 0.14	0.92	-0.86 ± 0.15	-0.86 ± 0.15	0.003 (-0.11, 0.12)	0.96

Data for continuous variables as Mean ± SD; difference, no exercise – exercise at 10 weeks; CI, confidence interval; BSA, body surface area; EDV, end diastolic volume; ESV, end systolic volume; EF, ejection fraction; E/A ratio, ratio of peak early (E) to late (A) mitral inflow velocity; E/e' ratio, ratio of peak early mitral inflow velocity to peak early diastolic mitral annulus tissue velocity; vel, velocity; GLS, global longitudinal strain. LV mechanics parameters reported as peak values.

References

1. Verma A, Meris A, Skali H, Ghali JK, Arnold JM, Bourgoun M, et al. Prognostic implications of left ventricular mass and geometry following myocardial infarction: the VALIANT (VALsartan In Acute myocardial iNfarcTion) Echocardiographic Study. JACC Cardiovasc Imaging. 2008;1(5):582-91.

2. Valkeinen H, Aaltonen S, Kujala UM. Effects of exercise training on oxygen uptake in coronary heart disease: a systematic review and meta-analysis. Scand J Med Sci Sports. 2010;20(4):545-55.

3. Gielen S, Schuler G, Adams V. Cardiovascular effects of exercise training: molecular mechanisms. Circulation. 2010;122(12):1221-38.

4. Haykowsky M, Scott J, Esch B, Schopflocher D, Myers J, Paterson I, et al. A meta-analysis of the effects of exercise training on left ventricular remodeling following myocardial infarction: start early and go longer for greatest exercise benefits on remodeling. Trials. 2011;12:92.

5. Sengupta PP, Khandheria BK, Korinek J, Wang J, Jahangir A, Seward JB, et al. Apex-to-base dispersion in regional timing of left ventricular shortening and lengthening. J Am Coll Cardiol. 2006;47(1):163-72.

6. Dandel M, Hetzer R. Echocardiographic strain and strain rate imaging--clinical applications. Int J Cardiol. 2009;132(1):11-24.

7. Buckberg G, Hoffman JI, Nanda NC, Coghlan C, Saleh S, Athanasuleas C. Ventricular torsion and untwisting: further insights into mechanics and timing interdependence: a viewpoint. Echocardiography. 2011;28(7):782-804.

8. Geyer H, Caracciolo G, Abe H, Wilansky S, Carerj S, Gentile F, et al. Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications. J Am Soc Echocardiogr. 2010;23(4):351-69; quiz 453-5.

9. Jang JY, Woo JS, Kim WS, Ha SJ, Sohn IS, Kim W, et al. Serial assessment of left ventricular remodeling by measurement of left ventricular torsion using speckle tracking echocardiography in patients with acute myocardial infarction. Am J Cardiol. 2010;106(7):917-23.

10. Huttin O, Coiro S, Selton-Suty C, Juilliere Y, Donal E, Magne J, et al. Prediction of Left Ventricular Remodeling after a Myocardial Infarction: Role of Myocardial Deformation: A Systematic Review and Meta-Analysis. PLoS One. 2016;11(12):e0168349.

11. Zito C, Sengupta PP, Di Bella G, Oreto G, Cusma-Piccione M, Longordo C, et al. Myocardial deformation and rotational mechanics in revascularized single vessel disease patients 2 years after ST-elevation myocardial infarction. J Cardiovasc Med (Hagerstown). 2011;12(9):635-42.

12. ACSM. Guidelines for exercise testing and prescription. 9th ed. Riverwoods, IL: Lippincott Williams & Wilkins; 2014.

13. Guazzi M, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, et al. EACPR/AHA Scientific Statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. Circulation. 2012;126(18):2261-74.

14. British Society of Echocardiography. A minimum dataset for a standard transthoracic echocardiogram. London, UK; 2012.

15. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the american society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2015;28(1):1-39 e14.

16. Kim HK, Sohn DW, Lee SE, Choi SY, Park JS, Kim YJ, et al. Assessment of left ventricular rotation and torsion with two-dimensional speckle tracking echocardiography. J Am Soc Echocardiogr. 2007;20(1):45-53.

17. Stohr EJ, McDonnell B, Thompson J, Stone K, Bull T, Houston R, et al. Left ventricular mechanics in humans with high aerobic fitness: adaptation independent of structural remodelling, arterial haemodynamics and heart rate. J Physiol. 2012;590(Pt 9):2107-19.

18. Grenne B, Eek C, Sjoli B, Dahlslett T, Hol PK, Orn S, et al. Mean strain throughout the heart cycle by longitudinal two-dimensional speckle-tracking echocardiography enables early prediction of infarct size. J Am Soc Echocardiogr. 2011;24(10):1118-25.

19. Notomi Y, Lysyansky P, Setser RM, Shiota T, Popovic ZB, Martin-Miklovic MG, et al. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol. 2005;45(12):2034-41.

20. Solomon SD, Skali H, Anavekar NS, Bourgoun M, Barvik S, Ghali JK, et al. Changes in ventricular size and function in patients treated with valsartan, captopril, or both after myocardial infarction. Circulation. 2005;111(25):3411-9.

21. McGregor G, Gaze D, Oxborough D, O'Driscoll J, Shave R. Reverse left ventricular remodeling: effect of cardiac rehabilitation exercise training in myocardial infarction patients with preserved ejection fraction. Eur J Phys Rehabil Med. 2016;52(3):370-8.

22. Weiner RB, DeLuca JR, Wang F, Lin J, Wasfy MM, Berkstresser B, et al. Exercise-Induced Left Ventricular Remodeling Among Competitive Athletes: A Phasic Phenomenon. Circ Cardiovasc Imaging. 2015;8(12).

23. Sengupta PP, Khandheria BK, Narula J. Twist and untwist mechanics of the left ventricle. Heart Fail Clin. 2008;4(3):315-24.

24. Beladan CC, Calin A, Rosca M, Ginghina C, Popescu BA. Left ventricular twist dynamics: principles and applications. Heart. 2013.

25. Gademan MG, Swenne CA, Verwey HF, van der Laarse A, Maan AC, van de Vooren H, et al. Effect of exercise training on autonomic derangement and neurohumoral activation in chronic heart failure. J Card Fail. 2007;13(4):294-303.

26. Stohr EJ, Shave RE, Baggish AL, Weiner RB. Left ventricular twist mechanics in the context of normal physiology and cardiovascular disease: a review of studies using speckle tracking echocardiography. Am J Physiol Heart Circ Physiol. 2016;311(3):H633-44.

Figure 1. Study flowchart

Figure 2~~1~~. Group mean data over one cardiac cycle as a percentage of systole and diastole for (a) LV apical rotation (red lines), (b) LV basal rotation (blue lines) and (c) LV twist (black lines) in the exercise training group (left column) and non-exercise group (right column) at baseline (solid lines) and at 10 weeks (dashed lines). LV, left ventricular; AVC, aortic valve closure; °, degrees.