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1 **Reverse left ventricular remodelling – effect of cardiac rehabilitation exercise training in**
2 **myocardial infarction patients with preserved ejection fraction**

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19 **Word count:** 3351
20

21 **Conflicts of interest and sources of funding**

22 We have no conflicts related to this work.
23

24 **Keywords:** Left ventricular remodelling, exercise training, cardiac rehabilitation, myocardial
25 infarction, NT-pro-BNP.
26
27

27 **Structured Abstract**

28 **Purpose:** In post-myocardial infarction (MI) patients with preserved LV ejection fraction
29 (>45%), the effect of cardiac rehabilitation (CR) exercise training on left ventricular (LV)
30 structure and function is unknown. We therefore sought to examine the reverse LV
31 remodelling effect of CR exercise training in this increasingly prevalent population.

32 **Methods:** Within 3-6 weeks of MI, and 10 weeks later, echocardiography and cardiopulmonary
33 exercise testing were performed in a cohort of asymptomatic, non-ischemic patients with LV
34 ejection fraction >45%. An exercise training group (n=33) completed twice weekly gym based
35 cardiovascular exercise at 60-80% VO₂ peak, and a standardised resistance training
36 programme, whilst a non-exercise group (n=17) did not. NT-pro-BNP was measured in a
37 subgroup of exercise training participants at baseline and at the end of the 10 week
38 programme.

39 **Results:** In comparison to the non-exercise group, in which there was no change, 10 weeks of
40 exercise training increased VO_{2peak} and reduced LV end diastolic and systolic volumes (all
41 $P<0.05$ vs non-exercise group). Resting NT-pro-BNP was reduced in the sub-group of exercise
42 training participants ($P<0.01$) and correlated positively with the change in LV end diastolic
43 volume ($r = 0.58$, $P<0.01$, $r^2 = 0.33$).

44 **Conclusion:** In post-MI patients with preserved LV ejection fraction (>45%), CR exercise
45 training is effective in improving functional capacity and reducing LV volumes. In this
46 previously unstudied population, the measurement of reverse LV volumetric remodelling may
47 prove useful as an indicator of CR exercise programme efficacy. To maximise the potential
48 clinical benefit from reverse LV remodelling, this patient group should be actively encouraged
49 to engage in CR exercise training.

50 **Condensed abstract**

51 Following 10 weeks of Cardiac Rehabilitation (CR) exercise training in a cohort of post-MI
52 patients with preserved LVEF (>45%), exercise capacity was improved and LV volumes reduced.

53 For potential prognostic gain, this increasingly prevalent and often overlooked post-MI
54 population should be encouraged to attend structured CR exercise training programmes.

55

56

56 **Introduction**

57 Myocardial infarction (MI) is associated with molecular disarray, myocyte hypertrophy and
58 extra-cellular matrix degradation, resulting in pathologically increased left ventricular (LV)
59 mass and volume and altered LV geometry¹. The process of LV remodelling, characterised by
60 structural maladaptation and functional decline, begins with the onset of acute MI and is
61 chronically driven by systemic neurohormonal activation². Mortality is closely linked to the
62 nature and extent of LV remodelling and also to the degree of concurrent neurohormonal
63 activation^{3,4}. Specifically, increased LV volumes and reduced LV ejection fraction (LVEF) are
64 exponentially associated with poor prognosis⁵, presenting clinicians with a clear rationale for
65 attenuating or reversing this process. In post-MI patients, pharmacological and
66 electrophysiological interventions improve cardiovascular and all-cause mortality^{6,7}. Despite
67 this, in the first two years after MI, mortality of greater than 25% can be expected in patients
68 with baseline LVEF of 31-40%, compared to less than 15% when LVEF exceeds 50%⁵. It is
69 important therefore to consider adjunctive therapeutic strategies, such as cardiac
70 rehabilitation (CR) exercise training that may enhance the reverse LV remodelling process
71 beyond that seen with medical treatment.

72

73 Evidence of reverse LV remodelling, following CR exercise training in post-MI patients is
74 currently equivocal⁸. A number of longitudinal studies have shown a positive effect⁹⁻¹¹,
75 reporting reduced LV end diastolic volume (LVEDV), LV end systolic volume (LVESV), improved
76 LVEF and reduced N-terminal-pro-B-type natriuretic peptide (NT-pro-BNP). However,
77 conflicting data also exist^{12,13}, and the conclusions of a recent meta-analysis which showed an
78 overall beneficial effect of CR exercise training on LV remodelling, were limited by the poor

79 methodological quality of some of the included studies⁸. To date, CR exercise training studies
80 have focused almost exclusively on patients with moderate to severe impairment of LV systolic
81 function (LVEF \leq 45%). This group of patients are commonly limited by their condition and are
82 thus obvious candidates for CR exercise training. However, advancement in percutaneous
83 coronary artery revascularisation technology with rapid 24 hr access, greater sensitivity of
84 cardiac biomarkers and increased public awareness of chest pain management have led to an
85 increasingly prevalent population of asymptomatic MI survivors with preserved LV systolic
86 function (LVEF $>$ 45%)^{14, 15}. In the absence of significant functional limitation, these patients can
87 be quickly reintegrated into daily life, making their attendance on CR exercise programmes less
88 likely. This may be ill advised given that 15% of these patients will die or be hospitalised with
89 heart failure within 20 months of MI¹⁶. Exercise training may be an effective preventative
90 strategy, ameliorating the negative effects of chronic LV remodelling. Yet, the impact of CR
91 exercise training on LV structure and function has not been studied in this group of patients.
92 Therefore, the purpose of the current study was to investigate the effect of CR exercise
93 training on LV structure and function in post-MI patients with preserved LVEF ($>$ 45%). It was
94 hypothesised that 10 weeks of CR exercise training would reduce LV volumes and increase
95 LVEF in addition to improving functional capacity.

96

96 Methods**97 *Study population and protocol***

98 A total of 58 consecutive male participants were recruited to the study. An exercise training
99 group was populated by those who attended CR (n=36) and a non-exercise group by those who
100 were demographically and clinically similar to the exercise group but were unable to attend
101 structured CR due to work or personal commitments (n=20) (table 1). Participants were
102 clinically stable (in accordance with guidelines¹⁷) following treatment for an acute MI at least
103 three, but not more than six weeks previously. All participants had LVEF >45% and were non-
104 ischemic and asymptomatic following successful percutaneous coronary intervention.
105 Participants who did not meet guidelines for inclusion in exercise training,¹⁷ or who had
106 significant limiting comorbidities were excluded. Both groups were advised on a cardio-
107 protective lifestyle including general physical activity. Approval was gained from the local
108 Research and Ethics Committee and informed consent was obtained. Prior to and on
109 completion of a 10-week supervised exercise training programme or non-exercise control
110 period, transthoracic echocardiography and cardiopulmonary exercise testing were
111 undertaken in all study participants. In addition, resting whole blood samples for the
112 assessment of NT-pro-BNP were obtained in a sub-group (n=21) of exercise training
113 participants at the start and the end of the 10 week programme.

114

115 *Cardiopulmonary exercise testing*

116 Cardiopulmonary exercise testing was performed in accordance with the American Thoracic
117 Society guidelines¹⁸. Briefly, a standard ramp protocol was conducted on an electronically
118 braked, upright cycle ergometer and continuous respiratory gas exchange measurements of

119 oxygen uptake (VO_2), carbon dioxide production (VCO_2) and minute ventilation (V_E) were
120 recorded (Oxycon Pro, Care Fusion Corp., San Diego, California, USA). Electrocardiogram, blood
121 pressure and rating of perceived exertion (RPE) were monitored throughout and participants
122 were encouraged to continue until symptom limited volitional fatigue, with a respiratory
123 exchange ratio of >1.15 indicating maximal effort.

124

125 ***Echocardiography***

126 Resting echocardiographic images were acquired in accordance with British Society of
127 Echocardiography guidelines¹⁹ by a single cardiac sonographer, blinded to group allocation. A
128 commercially available ultrasound system (Vivid 7, GE Medical Systems, Horten, Norway) was
129 used to obtain and store images for subsequent off-line analysis (Echo-pac, GE Medical
130 Systems, Horten, Norway, version 7.0.0). Left ventricular internal dimensions and wall
131 thicknesses were measured from the parasternal long axis view, and LV volumes calculated
132 using the Simpson's bi-plane method from apical two and apical four-chamber images. Peak
133 early (E) and late (A) mitral inflow velocity, and the E-wave deceleration time (DT) were
134 measured with pulse wave Doppler in the apical four-chamber view, and the E/A ratio
135 calculated. Finally, tissue Doppler imaging of the septal and lateral mitral annuli in the apical
136 four-chamber view was employed to quantify systolic (s'), early diastolic (e') and late diastolic
137 (a') peak mitral annulus tissue velocities.

138

139 ***Measurement of cardiac biomarkers***

140 Serum was obtained from whole blood samples collected into ethylene diamine teracetic acid
141 tubes via peripheral venepuncture. Clotted samples were centrifuged at 3000rpm for 10 min

142 and stored at -80 deg C. NT-pro-BNP was determined using the Immulite 2500
143 electrochemiluminescent immunoassay (Siemens Healthcare Diagnostics, Frimley, UK) with a
144 linear calibration range of 20 to 35,000 pg/mL.

145

146 ***Exercise training***

147 Participants attended University Hospital, Coventry twice weekly for 10 weeks with an
148 adherence rate of 85% (17 of 20 sessions) designated as the required standard for inclusion.
149 Cardiovascular exercise was split equally between treadmill, cycle ergometer, rowing machine
150 and cross-trainer. A 10 min treadmill or cycle warm up was followed initially by 25 min of
151 continuous cardiovascular exercise. A 5 min cool down walk was performed prior to and on
152 completion of a standardised resistance training programme as previously described¹⁷. Aerobic
153 exercise intensity was initially set at a heart rate corresponding to 60-80% peak oxygen uptake
154 ($VO_{2\text{ peak}}$) from cardiopulmonary exercise test and after two sessions the supervisory team
155 ensured that participants were exercising at a heart rate equivalent to 80% $VO_{2\text{ peak}}$. Exercise
156 intensity and training heart rate range were re-prescribed every two weeks based on RPE. The
157 duration of exercise was progressively increased from 25 to 40 min by the fifth week and was
158 maintained thereafter until the end of the study.

159

160 ***Statistical analyses***

161 Baseline characteristics and continuous variables are presented as mean \pm standard deviation
162 (SD). Differences between the exercise training and non-exercise group at baseline were
163 determined using unpaired Student's *t*-tests. Further to confirmation of normality with the
164 Kolmogorov-Smirnov test, the change in outcome variables by group over time was assessed

165 with either a two-way mixed model analysis of variance (ANOVA) or paired Student's *t*-tests.
166 Pearson's product-moment correlation coefficient was used to determine relationships
167 between the relative change (Δ) in NT-pro-BNP and the absolute change (Δ) in LV volumetric
168 parameters over the 10 week period.
169

169 **Results**170 ***Recruitment***

171 Of the 36 participants in the exercise training group, 33 completed ≥ 17 of 20 sessions during
172 the training period with an average attendance of 88.3%. Two participants were lost to follow-
173 up and one failed to meet the minimum adherence target. In the non-exercise group, a
174 further three participants were lost to follow up. Accordingly, data from 50 participants
175 (exercise training, $n=33$ and non-exercise, $n=17$) was analysed to assess the effects of CR
176 exercise training on LV structure and function. Baseline demographic and clinical
177 characteristics were similar between groups (table 1), medication remained unchanged during
178 the study period, and no cardiovascular complications or other adverse effects were
179 experienced by the participants.

180

181 ***Cardiopulmonary Exercise Testing***

182 In comparison to the non-exercise group, maximum workload (W_{\max}), $VO_{2\text{ peak}}$, ventilatory
183 threshold (VT) and exercise time increased in response to exercise training (all $P<0.05$) (table
184 2). In the exercise training group, $VO_{2\text{ peak}}$ increased by 16%, W_{\max} by 19%, VT by 18%, and
185 exercise time by 16% (all $P<0.0001$) (table 2). In the non-exercise group, no changes were
186 noted. Furthermore, there were no statistical differences in body mass index (BMI), resting
187 heart rate (HR_{rest}), systolic blood pressure (BP_{sys}) or diastolic blood pressure (BP_{dia}) in either
188 group between baseline and post-study measures (table 2).

189

190

191

192 Effect of cardiac rehabilitation exercise training on left ventricular structure and function

193 On completion of the exercise training programme, LVEDV and LVEDV/BSA (both $P<0.05$), and
194 LVESV and LVESV/BSA (both $P<0.01$) were decreased in comparison to the non-exercise group.
195 As depicted in figure 1, 10 weeks of exercise training resulted in a 5% reduction in LVEDV and
196 LVEDV/BSA (both $P<0.001$) and a 9% reduction in LVESV and LVESV/BSA (both $P<0.001$),
197 whereas volumetric parameters remained unchanged in the non-exercise group ($P>0.05$). No
198 changes in either group were observed in LV linear dimensions, mass or geometry during the
199 study period ($P>0.05$). Furthermore, the exercise training programme had no impact on
200 systolic or diastolic function (table 3).

201

202 Relationship between NT-pro-BNP and left ventricular volumetric parameters

203 In the sub group of exercise training participants ($n=21$), resting NT-pro-BNP was significantly
204 reduced further to completion of the 10 week programme (267 ± 232 vs 158 ± 121 pg/mL,
205 $P<0.01$). Additionally, the relative change in resting NT-pro-BNP (%) from baseline to 10 weeks
206 correlated positively with the absolute change in LVEDV (ml) ($r = 0.58$, $P<0.01$, $r^2 = 0.33$) (figure
207 2). There was no significant relationship between the relative change in NT-pro-BNP and the
208 absolute change in either LVESV ($r = 0.10$, $P>0.05$, $r^2 = 0.01$) or LVEF ($r = 0.17$, $P>0.05$, $r^2 = 0.03$)
209 (figure 2).

210

211

211 Discussion

212 The aim of the present study was to evaluate the reverse remodelling effect of CR exercise
213 training in a cohort of post-MI patients with preserved LVEF (>45%). We hypothesised that, in
214 addition to an improvement in functional capacity, LV volumes would be reduced and LVEF
215 increased. The primary findings, which allow our hypotheses to be partially accepted, were an
216 improvement in exercise capacity and a reduction in LV volumes in response to CR exercise
217 training. Specifically, VO₂ peak improved by 16%, with a concurrent 5% and 9% reduction in
218 LVEDV and LVESV respectively. Given the association between reduced LV volumes and
219 improved clinical outcome⁶ these data provide additional impetus to recommend CR exercise
220 training to post-MI patients with preserved EF.

221

222 Reverse volumetric remodelling with CR exercise training

223 In patients with significant LV systolic dysfunction, a reduction in LV volumes is highly
224 desirable, demonstrating a clear relationship with improved survival¹⁶. Whilst data confirming
225 this association are primarily derived from pharmacological rather than exercise trials, CR
226 exercise training has consistently been shown to reduce cardiovascular and all-cause mortality
227 in patients with MI²⁰. The mechanisms responsible for this remain to be fully confirmed, but
228 are likely to include both structural and functional cardiac adaptation. The reduction in LV
229 volumes observed in the current study confirm findings from a recent meta-analysis which,
230 although not providing a causative link between reverse LV remodelling and mortality,
231 reported a positive effect of exercise training on LV volumes in post-MI patients with impaired
232 LVEF⁸. Unique to the current study is evidence of reverse LV remodelling in post-MI patients
233 with preserved LVEF (>45%). In this population, where LV volumes are within normal limits, the

234 significance of reverse volumetric LV remodelling, whether it be medically mediated or
235 exercise-induced, is yet to be fully evaluated. However, it is possible that improved prognosis
236 as a result of reduced LV volumes may not be exclusive to those with pronounced LV systolic
237 dysfunction, rather, it may also extend to less compromised patients. Abnormal
238 hemodynamics following MI are a product of the pathological imbalance between LV
239 pressures, cavity dimensions and wall thicknesses and can result in functional impairment²¹.
240 Ultimately, left untreated, this may lead to a progressive decline in cardiac function and
241 exercise capacity, with resultant prognostic implications⁶. Recent reports have indicated that,
242 despite preserved function, 15% of post-MI patients with LVEF >45% will die or be admitted to
243 hospital with heart failure within 20 months of their event¹⁶. For these patients, a reduction in
244 LV volumes may provide the environment for the maintenance, or restoration, of more
245 'normal' LV hemodynamics and may prevent a progressive decline in LV function. On this basis,
246 asymptomatic patients with normal LV volumes and preserved LVEF, who are likely to return
247 relatively quickly and seamlessly to activities of daily living and work, should be encouraged to
248 participate fully in supervised CR exercise training.

249

250 **NT-pro-BNP as an indicator of reverse volumetric remodelling**

251 The higher concentration of NT-pro-BNP observed prior to exercise training in the current
252 study likely reflects a degree of hemodynamic compromise and increased LV wall stress²².
253 Raised NT-pro-BNP is related to a worse prognosis throughout the spectrum of cardiac
254 disease¹⁴. The significant decrease in NT-pro-BNP observed following CR exercise training is
255 indicative of an improvement in the overall neurohormonal and hemodynamic environment.
256 The positive correlation of this change in NT-pro-BNP with a reduction in LV volumes may

257 suggest that this biomarker could be used as a simple, cheap and effective measure of reverse
258 LV remodelling following CR exercise training. Similar associations have been previously
259 reported. Giallauria and colleagues demonstrated a positive correlation between changes in
260 NT-pro-BNP and LVEDVI ($r=0.86$, $P<0.001$) in patients with significant LV systolic dysfunction
261 ($LVEF<45\%$)¹¹. Furthermore, reduced NT-pro-BNP was shown to correlate with improved early
262 diastolic filling (E-wave) ($r= -0.44$, $P<0.001$)¹¹, E/A ratio ($r= -0.59$, $P<0.001$)²³ and LV elastance
263 ($r= -0.58$, $P<0.01$)²⁴. The direct and indirect molecular and cellular adaptations associated with
264 exercise training likely reduce LV wall stress and, therefore, NT-pro-BNP. Although we did not
265 witness an improvement in diastolic filling as demonstrated previously^{11,23}, this may be
266 explained by the fact that diastolic function was relatively well preserved in our patients
267 following MI. Unlike LVEDV, there was no association between the changes in NT-pro-BNP and
268 either LVESV or LVEF. This is a reflection of the mechanism of NT-pro-BNP secretion, for which
269 the predominant stimulus is cardiac myocyte 'stretch'²². Further to MI, regional and global LV
270 dysfunction can lead to increased LV diastolic filling pressures and volume overload, promoting
271 the release of NT-pro-BNP²⁶. The very nature of this biomarker, therefore, means it is better
272 suited to evaluating changes in LVEDV. Rather than diminish the utility of NT-pro-BNP in the
273 CR setting, this observation may allow targeted evaluation of a specific and important marker
274 of LV remodelling.

275

276 **Reverse functional remodelling with CR exercise training**

277 The positive change in LV volumes in the present study was not accompanied by a change in
278 functional parameters, i.e. SV and LVEF. These data do not, therefore, corroborate previous
279 findings of the coexistence of volumetric and functional adaptation⁸. Haykowsky et al

280 reported improvements in both LV volumes (LVEDV and LVESV) and LVEF with CR exercise
281 training. In the current study, however, within group analysis did indicate an improvement in
282 LVEF in the exercise training group ($P=0.011$), whilst there was no change in the non-exercise
283 group. It is likely that with greater statistical power the between groups comparison of LVEF
284 may have proved significant. Alternatively, the mild impairment of LVEF in this cohort, as
285 opposed to the marked dysfunction in previous studies may, by definition, dictate limited
286 scope for improvement.

287

288 **Mechanisms facilitating reverse LV remodelling**

289 Current knowledge of the underpinning mechanisms promoting reverse LV remodelling with
290 medical therapy and exercise training is limited, although recent animal and human
291 investigation has provided some insight into molecular and cellular adaptation. There is good
292 evidence, however, of the counteractive effect of exercise training on the associated
293 compensatory neurohormonal mechanisms²⁷. It is well known from pharmacological trials that
294 suppression of these mechanisms can reduce their destructive effects²⁸⁻³⁰. This appears to be
295 important in preventing the progression of maladaptive LV remodelling. In addition, in
296 combination with specific vascular adaptation to exercise i.e. improved endothelial function,
297 reduced neurohormonal activation contributes to the normalisation of LV afterload^{31, 32}. It is
298 likely that this helps restore normal LV loading conditions and thus facilitates the process of
299 reverse LV remodelling. The magnitude of this effect, however, may prove less significant than
300 originally thought, in light of findings from recent animal investigations³³. The direct effect of
301 exercise training on the myocardium has been demonstrated in a number of animal models
302 and is increasingly verified as a key contributor to the process of reverse LV remodelling³⁴⁻³⁷. A

303 plethora of exercise induced, biomolecular adaptations interfere with maladaptive signalling
304 pathways which results in attenuation of hypertrophy, fibrosis and apoptosis. It is, therefore,
305 likely that the reverse remodelling effect attributed to CR exercise training in the current
306 study, is a result of the combined influence of these and as of yet unidentified processes.

307

308 Limitations of the current study warrant discussion. Firstly, due to ethical constraints,
309 participants were not assigned randomly to exercise training or non-exercise. Secondly, sample
310 size was relatively small, particularly in the non-exercise group. Finally, the study population
311 was exclusively male reflecting a very small percentage of female patients in this CR population
312 as a whole. Future randomised studies to confirm our results are recommended.

313

314 **Conclusions**

315 Ten weeks of CR exercise training improved functional capacity and had a reverse LV
316 remodelling effect in the previously unstudied population of post-MI patients with relatively
317 preserved LVEF (>45%). Not only does this serve to confirm the general therapeutic benefit of
318 CR exercise training, but may also indicate the potential contribution of cardiac adaptation to
319 the well documented reductions in cardiovascular and all-cause mortality. To date, these
320 improvements can be only partially explained by data relating to ventilatory, skeletal muscle
321 and vascular endothelial adaptation. The measurement of reverse LV remodelling, which may
322 be adequately quantified with NT-pro-BNP, may prove useful as an indicator of CR exercise
323 programme efficacy and may aid in the long-term management of the post-MI population.
324 Patients with normal LV volumes and preserved LVEF, who may otherwise resume normal daily

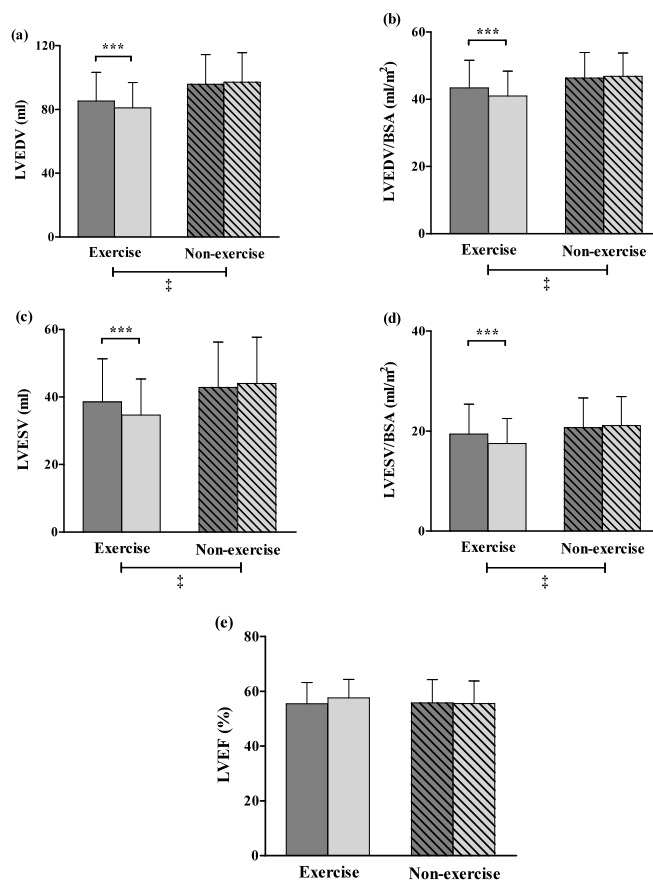
325 activities at the expense of CR, should be actively encouraged to attend structured CR exercise
326 programmes to maximise the potential clinical gains from reverse LV remodelling.

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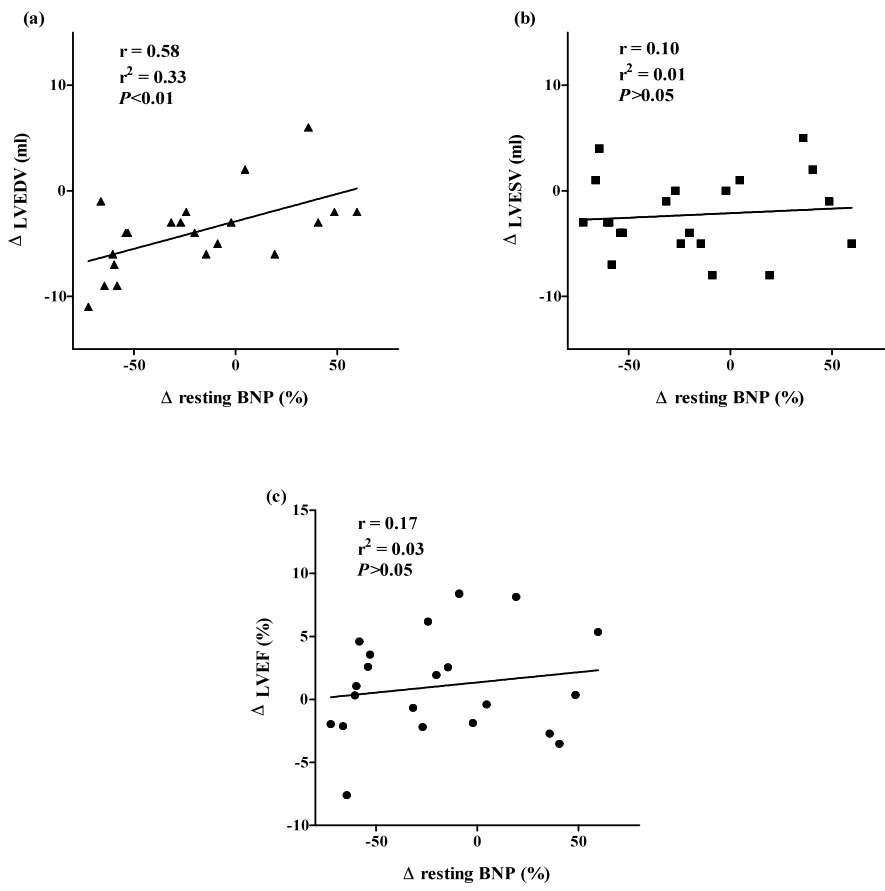
331 **Figure 1.** Left ventricular (LV) volumetric parameters at baseline (dark grey bars) and at 10 weeks (light
 332 grey bars) in the exercise training group (solid bars) and non-exercise group (striped bars) (a) LV end

333 diastolic volume (ml) (b) LV end diastolic volume/BSA (ml/cm²), (c) LV end systolic volume (ml), (d) LV

334 end systolic volume/BSA (ml/cm²), (e) LV ejection fraction (%). Data as mean \pm SD. ‡ $P < 0.05$ group \times time

335 interaction effect (ANOVA), *** $P < 0.001$

336



336

337 **Figure 2.** Correlation between the relative change (Δ) in NT-pro-BNP (%) and the absolute change (Δ) in

338 left ventricular (LV) (a) end diastolic volume (EDV) (ml), (b) end systolic volume (ESV) (ml) and (c)

339 ejection fraction (EF) (%) in the exercise training group

340 **Table 1 Demographic, clinical and exercise test parameters at baseline and 10 weeks**

	Exercise training (n=33)		Non-exercise (n=17)	
	Baseline	Week 10	Baseline	Week 10
Demographics				
Male gender (%)	100	-	100	-
Age (yrs)	55.8 ± 9.2	-	56.2 ± 10.8	-
Height (m)	1.7 ± 0.1	-	1.8 ± 0.1	-
Body mass (kg)	82.7 ± 10.2	83.1 ± 10.5	90.4 ± 14.2	90.5 ± 14.3
BMI (kg/m ²)	27.4 ± 2.6	27.6 ± 2.7	29.2 ± 4.1	27.6 ± 2.7
BSA (m ²)	2.0 ± 0.1	2.0 ± 0.1	2.1 ± 0.2	2.1 ± 0.2
Clinical				
STEMI (n)	20	-	13	-
NSTEMI (n)	13	-	4	-
Time post MI (days)	33.7 ± 8.9	-	35.7 ± 7.7	-
HR _{rest} (bpm)	59 ± 8	58 ± 7	56 ± 7	56 ± 7
BP _{sys} (mmHg)	113 ± 17	110 ± 16	118 ± 12	117 ± 12
BP _{dia} (mmHg)	71 ± 8	71 ± 8	70 ± 9	70 ± 9
Exercise test				
VO _{2 peak} (L.min ⁻¹) † ‡	2.0 ± 0.4	2.3 ± 0.4****	1.9 ± 0.4	1.8 ± 0.5
VO _{2 peak} (ml.kg ⁻¹ .min ⁻¹) † ‡	24.0 ± 4.1 §	27.5 ± 4.6****	20.8 ± 3.1	20.2 ± 4.1
W _{max} (watts) † ‡	148 ± 27	175 ± 30****	146 ± 28	150 ± 31
VT (ml.kg ⁻¹ .min ⁻¹) † ‡	12.5 ± 2.8	14.6 ± 3.5****	11.2 ± 1.7	10.8 ± 2.3
Exercise time (mins) † ‡	8.6 ± 1.0	9.9 ± 1.2****	8.3 ± 1.4	8.2 ± 2.7

341

342 Data as mean ± SD. BMI, body mass index; BSA, body surface area; STEMI, ST elevation myocardial
343 infarction; NSTEMI, non ST elevation myocardial infarction; MI, myocardial infarction; HR_{rest}, resting
344 heart rate; BP_{sys}, systolic blood pressure; BP_{dia}, diastolic blood pressure; VO_{2 peak}, peak oxygen uptake;
345 W_{max}, maximum workload; VT, ventilatory threshold. § P<0.05 vs. non-exercise at baseline, † P<0.05
346 time effect (ANOVA), ‡ P<0.05 group × time interaction effect (ANOVA), ****P<0.0001 vs. baseline

347 **Table 2 Left ventricular structural parameters at baseline and 10 weeks**

	Exercise training (n=33)		Non-exercise (n=17)	
	<i>Baseline</i>	<i>Week 10</i>	<i>Baseline</i>	<i>Week 10</i>
<i>LV size</i>				
LVIDd (cm)	4.8 ± 0.5	4.8 ± 0.5	4.9 ± 0.5	4.9 ± 0.5
LVIDs (cm)	3.2 ± 0.5	3.3 ± 0.5	3.4 ± 0.6	3.4 ± 0.5
LVIDd/BSA (cm/m²)	2.2 ± 0.6	2.4 ± 0.2	2.4 ± 0.6	2.4 ± 0.2
LVIDs/BSA (cm/m²)	1.7 ± 0.3	1.7 ± 0.2	1.6 ± 0.3	1.7 ± 0.2
<i>LV mass and geometry</i>				
LV mass (g)	209 ± 46	217 ± 57	234 ± 51	217 ± 45
IVSd (cm)	1.3 ± 0.2	1.3 ± 0.2	1.4 ± 0.3	1.3 ± 0.2
LVPWd (cm)	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2
IVSs (cm)	1.7 ± 0.2	1.7 ± 0.2	1.8 ± 0.3	1.8 ± 0.3
LVPWs (cm)	1.5 ± 0.3	1.5 ± 0.2	1.5 ± 0.3	1.5 ± 0.3
RWT (cm)	0.45 ± 0.08	0.45 ± 0.08	0.46 ± 0.11	0.45 ± 0.10
LV mass/BSA (g/m²)	106 ± 20	109 ± 25	115 ± 26	105 ± 19

348

349 Data as mean ± SD. LV, left ventricular; LVIDd, LV internal diameter in diastole; BSA, body surface area;
 350 LVIDs, LV internal diameter in systole; LVEDV, LV end diastolic volume; LVESV, LV end systolic volume;
 351 IVSDd, inter-ventricular septal wall in diastole; LVPWd, LV posterior wall in diastole; IVSs, inter-
 352 ventricular septum in systole; LVPWs, LV posterior wall in systole; RWT, relative wall thickness

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354 **Table 3** Left ventricular functional parameters at baseline and 10 weeks

	Exercise training (n=33)		Non-exercise (n=17)	
	Baseline	Week 10	Baseline	Week 10
LV systolic function				
Fractional shortening (%)	31.9 ± 7.2	32.1 ± 5.3	31.9 ± 7.2	31.5 ± 7.3
Stroke volume (ml)	46.8 ± 9.5	46.3 ± 8.3	52.9 ± 11.9	53.1 ± 9.8
Lateral s'(cm/s)	8.1 ± 2.9	8.3 ± 2.4	9.1 ± 2.3	8.5 ± 3.0
Mean s'(cm/s)	8.0 ± 1.9	8.0 ± 1.6	8.4 ± 1.6	8.1 ± 2.0
LV diastolic function				
E/A ratio	1.15 ± 0.33	1.06 ± 0.24	1.14 ± 0.36	1.17 ± 0.37
DT (ms)	215 ± 34	224 ± 44	217 ± 67	245 ± 67
Lateral e'(cm/s)	9.5 ± 3.3	10.0 ± 3.1	10.0 ± 3.3	9.8 ± 2.9
Lateral a'(cm/s)	8.6 ± 2.4	9.2 ± 2.4	8.9 ± 1.4	8.8 ± 2.3
Lateral e'/a' ratio	1.2 ± 0.5	1.1 ± 0.4	1.2 ± 0.4	1.2 ± 0.5
Lateral E/e' ratio	7.3 ± 2.6	6.6 ± 2.0	6.6 ± 2.0	6.2 ± 2.8
Mean e'(cm/s)	8.1 ± 2.3	8.6 ± 2.1	8.9 ± 2.4	8.8 ± 2.1
Mean a'(cm/s)	8.9 ± 1.6	9.2 ± 1.3	8.9 ± 1.2	8.6 ± 1.9
Mean e'/a' ratio	1.0 ± 0.3	1.0 ± 0.2	1.0 ± 0.3	1.1 ± 0.4
Mean E/e' ratio	8.4 ± 2.0	7.6 ± 1.6	7.5 ± 1.7	7.0 ± 2.9

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356 Data as mean ± SD. s', peak systolic mitral annulus tissue velocity; E/A ratio, ratio of peak early
357 (E) to late (A) mitral inflow velocity; DT, rate of deceleration of early mitral inflow; e' peak early
358 diastolic mitral annulus tissue velocity; a', peak late diastolic mitral annulus tissue velocity; e'a'
359 ratio, ratio of peak early to late diastolic mitral annulus tissue velocity; E/e' ratio, ratio of peak
360 early mitral inflow velocity to peak early diastolic mitral annulus tissue velocity; IVRT, iso-
361 volumic relaxation time. † P<0.05 time effect (ANOVA), **P<0.01 vs. baseline.

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