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1 **Acute impact of conventional and eccentric cycling on platelet**
2 **and vascular function in patients with chronic heart failure**

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39 **Running Head:** Cycling, platelets and endothelial function in heart failure

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48

49 **Abstract**

50 Evidence-based guidelines recommend exercise therapy for patients with chronic heart failure
51 (CHF). Such patients have increased atherothrombotic risk. Exercise can transiently increase
52 platelet activation and reactivity and decrease vascular function in healthy participants,
53 although data in CHF is scant. Eccentric (ECC) cycling is a novel exercise modality which
54 may be particularly suited to patients with CHF, but the acute impacts of ECC on platelet and
55 vascular function are currently unknown. Our null hypothesis was that ECC and concentric
56 (CON) cycling, performed at matched external workloads, would not induce changes in
57 platelet or vascular function in patients with CHF. Eleven patients with heart failure with
58 reduced ejection fraction (HFrEF) took part in discrete bouts of ECC and CON cycling.
59 Before and immediately after exercise, vascular function was assessed by measuring diameter
60 and flow mediated dilation (FMD) of the brachial artery. Platelet function was measured by
61 the flow cytometric determination of glycoprotein IIb/IIIa activation and granule exocytosis
62 in the presence and absence of platelet agonists. ECC increased baseline artery diameter (pre:
63 $4.0\pm 0.8\text{mm}$ vs post: $4.2\pm 0.7\text{mm}$, $P=0.04$) and decreased FMD%. When changes in baseline
64 artery diameter were accounted for the decrease in FMD post-ECC was no longer significant.
65 No changes were apparent after CON. Neither ECC nor CON resulted in changes to any
66 platelet function measures (all $P>0.05$). These results suggest both ECC and CON cycling at
67 a moderate intensity and short duration can be performed by patients with HFrEF, without
68 detrimental impacts on vascular or platelet function.

69

70 **New and Noteworthy**

71 This is the first evidence to indicate that eccentric cycling can be performed relatively safely
72 by patients with chronic heart failure, as it did not result in impaired vascular or platelet
73 function compared to conventional cycling. This is important, as acute exercise can
74 transiently increase atherothrombotic risk and eccentric cycling is a novel exercise modality
75 that may be particularly suited to patients with chronic heart failure.

76

77 **Key words**

78 Eccentric exercise, platelets, vascular function, chronic heart failure

79

80 **Introduction**

81 Chronic heart failure (CHF) occurs in approximately 10% of individuals aged over 65 years
82 and is expected to rise significantly over the next decade (27). Chronic heart failure is
83 characterized by abnormalities in cardiac structure and/or function, resulting in the inability
84 of the heart to deliver sufficient blood and therefore oxygen to meet the metabolic demands
85 of the body. Individuals with CHF experience impaired physical function (18) and have a
86 greater risk of sudden thrombotic related events compared to healthy individuals (25). Such
87 events include acute coronary syndromes and stroke, which occur in association with
88 compromised vascular function and platelet mediated thrombosis (10, 22). Indeed, impaired
89 vascular function (9, 26), increased platelet activation (39), and a hypercoagulable state (13)
90 have been documented in patients with CHF.

91

92 Exercise training is recommended as part of the management of CHF, to alleviate decline in
93 health and physical function and to maintain quality of life (8, 32, 40). Whilst exercise is
94 generally safe and regular exercise training decreases long term risk of cardiovascular events,
95 acute coronary risk is increased during and immediately after participation in a bout of
96 exercise (35). This may relate, in part, to the impact of some forms of exercise on vascular
97 and/or platelet function. Some studies that have tested vascular function before and after
98 acute exercise in healthy participants have revealed transient decreases after exercise (3, 7).
99 The majority of such studies have been performed in healthy volunteers and involved
100 conventional forms of aerobic exercise, with assessments of the brachial artery providing a
101 surrogate for systemic vascular function. Platelet activation and reactivity to agonist exposure
102 have also been reported to be elevated immediately following both moderate and high

103 intensity exercise in healthy participants (15, 19, 36). Currently there is little evidence
104 regarding the impacts of distinct types of exercise on platelet or vascular function in CHF.

105

106 It has been demonstrated in healthy participants, that eccentric (ECC) cycling can be carried
107 out requiring less oxygen uptake compared to conventional concentric (CON) cycling (30).
108 Recently, we provided evidence to suggest that ECC cycling may be a novel and beneficial
109 exercise modality for patients with CHF, as matched exercise workloads can be performed at
110 a lower metabolic demand than CON cycling (4). Few studies have addressed the acute
111 impact of ECC exercise on either platelet or vascular function (31, 33). These studies,
112 performed in separate groups of apparently healthy participants, have reported that ECC based
113 resistance exercise did not increase platelet activation post-exercise (31), but did reduce flow
114 mediated dilation (FMD) 1 hour post-exercise (33). To our knowledge, no previous study has
115 investigated the acute impact of CON or ECC cycling on either platelets or vascular function
116 in patients with CHF. The aim of this study was to therefore compare the impact of short
117 bouts of ECC and CON cycling, matched for external workload, on platelets and vascular
118 function in patients with CHF. Our null hypothesis was that both modalities would have no
119 effects on either platelet or vascular function.

120

121 **Materials and Methods**

122 A comprehensive account of the recruitment and exercise protocols used in the present study
123 can be found in our recently published paper, which focused on metabolic and hemodynamic
124 outcomes (4). Briefly, patients with reduced left ventricular systolic function (ejection
125 fraction <45%), New York Heart Association class I to III were recruited from the Advanced

126 Heart Failure and Cardiac Transplantation Unit at Fiona Stanley Hospital, Perth, Western
127 Australia. Ethics approval for the study was provided by the Metro South Health Human
128 Research Ethics Committee (HREC 14-160) and the Human Research Ethics Committee at
129 The University of Western Australia. Exclusion criteria included: resting hypertension
130 (>165/95 mmHg), severe obstructive aortic stenosis, severe rhythm disorders that would
131 exclude safe participation in exercise, severe pulmonary hypertension (systolic >70 mmHg),
132 venous thromboembolic history within the past three months, musculoskeletal comorbidity
133 limiting functional capacity beyond the effect of CHF. Patients continued their routine
134 medical therapy throughout the study period.

135

136 A power calculation was conducted *a priori* using (G* Power 3.1.9.2 Software) using data
137 from platelet function assays conducted in our lab, indicating that based on power of 80% and
138 a standard deviation of 5%, 10 participants would be sufficient to detect a change of 5% at a
139 significance level of $P = <0.05$ (11). This was supported by a previously published study
140 (31).

141

142 *Maximal Exercise Test*

143 In an initial session, participants performed a maximal graded exercise test on a recumbent
144 bicycle ergometer (Corival, Lode BV, Groningen, Netherlands), with power output increasing
145 20 watts (W) every 3 minutes until volitional exhaustion. The maximal power output (W)
146 achieved during this test was used to prescribe the exercise intensity of subsequent sessions.

147

148 *General Protocol*

149 To ensure no recent changes were made in relation to participants symptoms, medications,
150 alcohol use and physical activity habits, participants were asked a series of questions relating
151 to this on arrival to the laboratory of each session. The participant sat on the recumbent
152 cycling ergometer that was to be used on that particular day (i.e., ECC or CON) and rested
153 for 10 minutes, after which a venous blood sample was collected. Following another 5
154 minutes of seated rest, baseline brachial artery diameter and an FMD test were performed on
155 the left arm. The participant then began the exercise protocol (see protocol below).
156 Immediately following the brief cool-down aspect of cycling, a blood sample was taken from
157 the right arm, and vascular tests were performed simultaneously on the left arm. Both the
158 CON and ECC bicycle ergometers were recumbent based apparatus, ensuring body positions
159 were identical for both modalities. Whilst the time of day at which the laboratory visits were
160 conducted varied between participants, it was maintained at the same time within
161 participants.

162

163 *Eccentric Cycling (ECC)*

164 Seven days following the maximal bicycle ergometer test, participants underwent the ECC
165 protocol. This was performed on a recumbent ergometer (Eccentric Trainer, Metitur, Ltd,
166 Jyväskylä, Finland) with a 1.5 kW motor that powered the cranks in reverse. Participants then
167 performed 11 minutes of continuous ECC cycling, maintaining a cadence of 40 rpm
168 throughout. This was composed of a 3 minute warm-up aiming to achieve 30% W_{max} , 5
169 minutes at 70% W_{max} and 3 minutes of active recovery with no resistance. As external
170 workload during ECC cycling is difficult to maintain constant, the watts performed was
171 documented every 10 seconds, and this was used to match the intensity for CON cycling.

172

173 *Concentric Cycling (CON)*

174 After a further seven days, participants underwent the CON protocol, which was performed at
175 the same time of day as the ECC protocol. CON cycling was performed on the same
176 recumbent bicycle as the maximal exercise test. The total exercise duration, warm-up, main
177 component, active recovery and cadence were identical to that described above for ECC.
178 However, the intensity (watts) of CON was changed manually by a researcher every 30
179 seconds to match the intensity performed during ECC for each individual subject.

180

181 *Blood Samples*

182 A venous blood sample was collected from the antecubital fossa with no stasis using a 21G
183 winged needle set (Greiner bio-one, Kremsmuenster, Austria). The first 2 mL was collected
184 into a non-additive discard tube, followed by a 4 mL 3.2% sodium citrate tube (Vacuette by
185 Greiner bio-one, Kremsmuenster, Austria).

186

187 *Platelet Function Tests*

188 Platelet function was measured by flow cytometric determination of glycoprotein IIb/IIIa
189 activation (measured by PAC-1 binding) and granule exocytosis (measured by surface
190 CD62P expression), in the presence and absence of platelet agonists according to recent
191 recommendations (23). Within ten minutes of collection, whole blood from the sodium citrate
192 tube was diluted 1:5 with HEPES saline buffer and incubated for exactly 15 minutes in a
193 cocktail of three fluorescent conjugated antibodies. These included: CD42b PE-Cy5 (platelet

194 identifier), PAC-1 fluorescein (FITC) and anti-CD62P phycoerythrin (PE), or isotype control
195 IgG1K PE (all BD Pharmingen, San Diego, CA). Seven reaction tubes (1.5 mL Protein
196 LoBind, Eppendorf, Germany) were used for platelet immunophenotyping which included:
197 isotype control, positive control (250 μ M thrombin receptor activating peptide-6, TRAP
198 [SFLLRN, Sigma-Aldrich, MO]), no agonist, TRAP 2 μ M, adenosine diphosphate (ADP) 1.5
199 μ M (Chrono-Log Corp., PA), arachidonic acid AA 10 μ g/mL (Sodium arachidonate,
200 Bio/Data Corp., PA) and collagen 1.5 μ g/mL (Chrono-Log Corp., PA). Samples were
201 incubated at room temperature with the exception of tubes containing AA and collagen,
202 which were incubated at 37°C using a dry block heater (Ratek DBH20D, Victoria, Australia).
203 Following 15 minutes of incubation, samples were fixed with stabilizing fixative (Becton
204 Dickinson), stored at 4°C and were analyzed within 24 hours by flow cytometry (BD
205 FACSCanto II) at a low flow rate. For each reaction tube, 10,000 platelet positive events
206 were counted and single stained compensation beads were utilized to account for spectral
207 overlap between the three fluorophores (BD Biosciences). ADP at the concentration used (1.5
208 μ M) caused maximal PAC-1 binding in all participants, so was not included in statistical
209 analysis.

210

211 *Vascular function tests*

212 The vascular assessments were conducted in a quiet, temperature-controlled room in
213 accordance to recent guidelines (34). In brief, to examine baseline brachial artery diameter
214 and FMD, the non-dominant arm was extended and positioned at an angle of ~80° from the
215 torso. A rapid inflation and deflation pneumatic cuff (D.E. Hokanson, Bellevue, WA, USA)
216 was positioned on the forearm, immediately distal to the olecranon process to provide a
217 forearm ischemia stimulus. A 10-MHz multi-frequency linear array probe, attached to a high-

218 resolution ultrasound machine (T3200; Terason, Burlington, MA, USA) was used to image
219 the brachial artery in the distal 1/3rd of the upper arm. When an optimal image was obtained,
220 the probe was held stable and the ultrasound parameters were set to optimize the longitudinal,
221 B-mode images of lumen–arterial wall interface. Continuous Doppler velocity assessments
222 were also obtained using the ultrasound, and were collected using the lowest possible
223 insonation angle (always $<60^\circ$). Following a 1 minute baseline recording of brachial artery
224 diameter and velocity (Camtasia Studio 8, TechSmith, Okemos, MI), the forearm cuff was
225 inflated (220 mmHg) for 5 min. Diameter and flow recordings resumed 30 seconds prior to
226 cuff deflation and continued for 3 minutes thereafter. Post-test analysis of brachial artery
227 diameter was performed using custom-designed edge-detection and wall-tracking software,
228 which is largely independent of investigator bias (38). Brachial artery FMD is presented as
229 relative (%) rise from the preceding baseline diameter. We have shown that the
230 reproducibility of diameter measurements using this semi-automated software is significantly
231 better than manual methods, reduces observer error significantly, and possesses an intra-
232 observer CV of 6.7% (37).

233

234 **Statistics**

235 Statistical analyses were performed using SPSS 22 (IBM, Armonk, NY) software. For data
236 meeting the assumptions of parametric statistical tests, paired *t*-tests were conducted to
237 determine if significant changes occurred within each session over time. For data failing the
238 assumptions of parametric tests, Wilcoxon signed rank tests were conducted. Subsequently,
239 for results revealing a significant change in FMD% post-exercise, a linear mixed model
240 analysis was conducted with logarithmically transformed artery diameter. This procedure
241 accounts for changes in baseline diameter and is appropriate under such circumstances (1).

242

243 **Results**

244 Eleven participants (9 male) (mean \pm SD) age: 52.0 ± 9.3 yrs, height 178.5 ± 9.3 cm, body
245 mass 91.6 ± 19.6 kg, $\dot{V}O_{2\text{ peak}}$ 19.9 ± 4.0 ml.kg.min⁻¹ completed the study. The medication use
246 of participants is presented in Table 1. Due to complications with the vascular data files of
247 one participant, ten participants were included in the analysis of peripheral vascular function.
248 Most of these participants were the same as those included in our recent manuscript related to
249 oxygen consumption and hemodynamic variables (4). Briefly, this paper revealed that ECC
250 cycling can be performed at matched external workloads, but lower $\dot{V}O_2$, minute ventilation
251 and respiratory exchange ratio compared to CON cycling.

252

253 *Vascular function*

254 ECC cycling resulted in a significant ($P = 0.04$) increase in baseline artery diameter from pre-
255 (4.0 ± 0.8 mm) to post-exercise (4.2 ± 0.7 mm) (see Figure 1). No change ($P = 0.43$) was
256 observed in baseline artery diameter after CON (pre 4.0 ± 0.7 mm vs post 4.0 ± 0.7 mm). No
257 significant difference ($P = 0.18$) in peak artery diameter was observed between pre- (4.4 ± 0.8
258 mm) and post-exercise (4.5 ± 0.7 mm) for ECC, as well as CON ($P = 0.53$, pre 4.3 ± 0.7 mm
259 vs post 4.4 ± 0.7 mm).

260

261 ECC cycling resulted in a significant ($P = 0.05$) decrease in FMD% from pre- (9.0 ± 2.9 %)
262 to post-exercise (6.0 ± 4.0 %) when changes in baseline diameter (ie changes in the baseline
263 pre to post ECC bout) were not accounted for (Figure 2A). CON cycling did not result in any
264 change ($P = 0.94$) in FMD% (pre: 8.8 ± 2.8 % vs post: 8.8 ± 3.9 %). When the FMD response

265 was corrected to account for changes in baseline diameter as a result of the exercise bout
266 (Figure 1), the change in FMD post-ECC was no longer significant ($P = 0.26$), as shown in
267 Figure 2 (panel B). This suggests the decrease in FMD following ECC was due, at least in
268 part, to the increase in baseline artery diameter following ECC. No significant change was
269 found for time to peak brachial artery diameter for ECC (pre: 68.9 ± 34.0 sec vs post: $77.5 \pm$
270 23.3 sec, $P = 0.55$) or CON (pre: 68.4 ± 26.1 sec vs post: 66.6 ± 27.9 sec, $P = 0.64$).

271

272 *Platelet Function*

273 No significant differences (all $P = >0.05$) were found in either PAC-1 (see Table 2) or anti-
274 CD62P binding (see Table 3) in the absence or presence of canonical platelet agonists
275 following CON or ECC cycling.

276

277 **Discussion**

278 Acute bouts of exercise involve a transient elevation in the risk of an acute cardiovascular
279 event (35). This may be associated with evidence suggesting that some forms of acute
280 exercise can reduce indices of vascular function (7) and increase platelet activation and
281 sensitivity to agonists (15, 19). This is the first study, to our knowledge, to investigate the
282 acute effect of discrete bouts of CON and ECC cycling, matched for duration and external
283 workload, on platelet and brachial artery vascular function in patients with HFrEF. We
284 assessed the impacts of ECC exercise because it may be particularly relevant in HFrEF, since
285 it requires less oxygen uptake to sustain matched workloads of exercise (30). We found that
286 ECC cycling significantly increased conduit artery diameter, with no such change observed
287 following CON cycling. The decrease in brachial FMD observed following ECC may, at least

288 partly, have been caused by this significant increase in baseline artery diameter post-exercise,
289 as FMD corrected for changes in baseline diameter was not significantly altered by exercise.
290 This does not exclude the possibility that the changes in FMD% were attributable to the
291 impact of ECC on vasodilator function, but it is appropriate to consider baseline diameter
292 effects on the interpretation of FMD% responses (1).

293

294 The vasodilator impact of ECC on baseline arterial diameter occurred despite the workload
295 being matched to the CON condition, with the ECC session performed with ~13% lower $\dot{V}O_2$
296 requirement (4). Participation in short bouts of CON and ECC cycling at a moderate intensity
297 did not result in any significant change in platelet activation, as measured by PAC-1 or anti-
298 CD62P binding, both of which are sensitive and specific markers of platelet function
299 associated with acute coronary risk (24). These findings suggest that short bouts of moderate
300 intensity ECC or CON cycling have no significant detrimental impacts on vascular or platelet
301 function in patients with HFrEF.

302

303 Eccentric exercise is an appealing modality of exercise for patients with impaired cardiac and
304 hemodynamic function, and we have recently demonstrated that ECC cycling is associated
305 with a lower oxygen demand than conventional CON cycling in patients with HFrEF (4).
306 Exercise prescription in heart failure is often challenging, given the extreme deconditioning
307 that characterizes the disease. A form of exercise, such as ECC, which allows greater
308 intensities of exercise to be undertaken at a lower relative systemic burden, should
309 theoretically enhance the benefits of training. However, the acute effects of ECC cycling on
310 peripheral vascular and platelet function, both of which may have implications relating to
311 acute atherothrombotic risk, have not previously been explored in HFrEF. Indeed, acute ECC

312 exercise data in patients with CHF are sparse, but one study suggests that eccentric resistance
313 exercise decreased brachial FMD post-exercise, even after adjustment for baseline diameter
314 changes (33). This contrasts somewhat with our findings which suggest an increase in arterial
315 function post-ECC, characterized by baseline vasodilation which impacted upon the FMD
316 result. Decreases in FMD need to be considered with caution in cases where significant
317 changes in the baseline diameter have occurred, as we have previously explained (1). It has
318 also been demonstrated that post-exercise changes in FMD are dependent on exercise
319 intensity, with higher intensities conferring greater reduction (3), and we cannot rule out the
320 possibility that exercise performed at a different intensity or for longer duration, may have
321 resulted in a different outcome.

322

323 The primary difference in brachial artery response between the cycling modalities was an
324 increase in resting vessel diameter following ECC. No such change was evident following
325 CON. The underlying mechanisms behind this are unknown, but may be linked to differences
326 in hemodynamics, neural and hormonal responses between these contrasting exercise
327 modalities (2). We recently reported that heart rate, mean arterial pressure and rate pressure
328 product are similar between the ECC and CON cycling (4), implying that differences in
329 hemodynamics are not likely to account for the vasodilator effect of ECC. It is well
330 established that hemodynamic effects such as those associated with increased shear stress,
331 transmural wall pressure and heart rate can directly modify artery function (14). Whilst the
332 mechanisms responsible for the dilator effect of ECC are not currently known, our findings
333 suggest that moderate intensity, short duration ECC exercise does not adversely impact on
334 vascular function in HFrEF.

335

336 There were no significant changes in circulating activated platelets, or platelet reactivity to
337 physiologically relevant agonists, following either exercise protocol. A previous study in
338 healthy, untrained participants observed that the acute effect of exercise on platelets is
339 intensity dependent (16), and it is possible that the intensity and/or duration of exercise used
340 in the present study were insufficient to induce significant changes in platelet function. This
341 may also explain why our findings contrast with a previous study that reported increased
342 platelet activation following a maximal CON cycling exercise test in CHF (5). ECC exercise
343 is not commonly prescribed to patients with CHF and the acute impacts of ECC on platelets
344 have not previously been reported in such participants. Whilst the exercise protocols included
345 in the present study were somewhat conservative, in part to reduce the risk of skeletal muscle
346 damage and soreness (20, 29), our findings suggest that ECC cycling can be conducted
347 acutely in patients with HFrEF, without the risk of inducing significant platelet activation.
348 We cannot comment on the possible detrimental effects of ECC performed at higher
349 intensities than those used in the present experiment.

350

351 Participants were undergoing treatment for HFrEF throughout the study period, and were
352 instructed to maintain their normal regimen of medication, so not to impact upon their
353 therapy. As such, ~63% of participants were prescribed some form of anti-
354 platelet/coagulation medication, and it is possible this may have masked any effect of
355 exercise on platelets in the present study. However, there is evidence to suggest this may not
356 be the case, as aspirin and warfarin use have previously shown to be incapable of inhibiting
357 the effects of maximal exercise on platelets and coagulation markers (6, 17, 21). Another
358 important limitation of this study was that the ECC session had to precede the CON session
359 in all cases, so that we could closely and accurately match the exercise intensities. Because
360 these sessions were not randomized, we cannot exclude the possibility of an order effect, but

361 the sessions were separated by a minimum of 7 days in an attempt to avoid this problem.
362 Finally, it is germane to emphasize that our study of the acute effect of exercise cannot not be
363 directly extrapolated to a chronic adaptation. Although, logically, repetition of acute
364 responses should lead to adaptation, the nature and direction of such training-induced
365 adaptation may differ from changes seen in response to acute bouts of exercise. This concept
366 been captured in the term “hormesis” (12, 28), taken in this context to indicate that repetitive
367 episodic exposure to stimuli that challenge and compromise function, may lead to
368 upregulation and enhancement in chronic responses. In the present study, we did not observe
369 large responses, either positive or negative, in terms of platelet function, but that does not
370 necessarily mean that training studies will not reveal adaptation.

371

372 In summary, we observed a relative vasodilator impact of ECC cycling, but not after CON
373 cycling in patients with HFrEF, however platelet function was unaffected after both
374 exercises. Given that both platelet and vascular function are involved in acute coronary
375 syndromes, our findings provide novel data relating to the impact of ECC cycling in patients
376 with HFrEF, and do not suggest that ECC cycling has greater acute impacts on patients with
377 HFrEF than conventional cycling, when matched for external workload and duration. While
378 the acute effects on vascular function of the brachial artery and platelet activation of ECC
379 exercise do not differ from concentric cycling, future studies will be required before
380 recommendations can emerge regarding the adoption of ECC cycling in routine HFrEF
381 training programs.

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395

396 **Disclosures**

397 None.

398

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529 **Figure Caption**

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531 **Figure 1.** Changes in brachial artery diameter before and immediately after concentric
532 (CON) and eccentric (ECC) cycling (A), delta change in artery diameter from pre- to post-
533 exercise time-points (B), individual response changes in baseline diameter during CON (C)
534 and ECC cycling (D). N=10. Data in Panels A and B are mean \pm SE, * indicates significant
535 difference from pre-exercise ($P = 0.04$).

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538 **Figure 2.** Change in flow mediated dilation (FMD%) from pre- to post-concentric (CON) and
539 eccentric (ECC) cycling when not adjusted for baseline diameter changes (A), and when
540 adjusted for baseline diameter change (B). Individual responses in FMD (unadjusted for
541 baseline diameter) pre and post CON (C) and ECC cycling (D). N=10. Data in Panels A and
542 B are mean \pm SE, * indicates significant difference from pre-exercise ($P = 0.05$).

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Table 1. Medication use of participants

	Medication	N (%)
548	Anti-platelet (total)	7 (63.6)
549	Aspirin	3 (27.3)
550	Warfarin	4 (36.4)
551	Rivaroxaban	2 (18.2)
551	Prasugrel	1 (9.1)
552	ACE Inhibitors (total)	9 (81.8)
553	Ramipril	8 (72.7)
553	Perindopril	1 (9.1)
554	β -Blockers (Bisoprolol)	9 (81.8)
555	Statins (Atorvastatin)	7 (63.6)
556	Anti-arrhythmic (Amiodarone)	4 (36.4)
556	Aldosterone receptor antagonist	4 (36.4)
557	Angiotensin II receptor antagonist	1 (9.1)

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Table 6.2 Platelet PAC-1 binding before and after concentric and eccentric cycling

Variable	% PAC-1 binding		Statistics
	Pre	Post	
No Agonist			
<i>Concentric</i>	6.8 ± 5.2	5.6 ± 2.2	<i>P</i> = 0.859
<i>Eccentric</i>	4.7 ± 0.8	5.2 ± 0.9	<i>P</i> = 0.213
TRAP 2 µM			
<i>Concentric</i>	25.1 ± 3.6	22.8 ± 1.8	<i>P</i> = 0.450
<i>Eccentric</i>	23.7 ± 3.6	23.3 ± 3.5	<i>P</i> = 0.594
AA 10 µg/ml			
<i>Concentric</i>	29.0 ± 3.3	25.1 ± 3.1	<i>P</i> = 0.104
<i>Eccentric</i>	24.8 ± 3.0	22.3 ± 2.8	<i>P</i> = 0.284
Collagen 1.5 µg/ml			
<i>Concentric</i>	14.7 ± 2.0	11.4 ± 1.2	<i>P</i> = 0.091
<i>Eccentric</i>	11.7 ± 1.5	9.9 ± 1.6	<i>P</i> = 0.178
<i>Thrombin Receptor Activating Peptide-6 TRAP, Arachidonic Acid AA</i>			

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Table 6.3 Platelet anti-CD62P binding with concentric and eccentric cycling

Variable	% anti-CD62P binding		
	Pre	Post	Statistics
No Agonist			
<i>Concentric</i>	2.0 ± 0.9	2.6 ± 1.0	<i>P</i> = 0.450
<i>Eccentric</i>	1.8 ± 1.3	2.0 ± 1.4	<i>P</i> = 0.169
TRAP 2 µM			
<i>Concentric</i>	5.5 ± 3.5	5.9 ± 3.8	<i>P</i> = 0.374
<i>Eccentric</i>	5.3 ± 4.5	6.3 ± 5.1	<i>P</i> = 0.213
ADP 1.5 µM			
<i>Concentric</i>	69.1 ± 25.0	68.9 ± 27.9	<i>P</i> = 0.722
<i>Eccentric</i>	69.4 ± 26.3	71.8 ± 26.0	<i>P</i> = 0.450
AA 10 µg/ml			
<i>Concentric</i>	12.2 ± 6.1	13.7 ± 8.1	<i>P</i> = 0.398
<i>Eccentric</i>	13.2 ± 6.6	13.2 ± 6.1	<i>P</i> = 0.981
Collagen 1.5 µg/ml			
<i>Concentric</i>	5.1 ± 4.4	6.1 ± 6.6	<i>P</i> = 0.213
<i>Eccentric</i>	5.3 ± 4.8	5.1 ± 4.9	<i>P</i> = 0.712

Thrombin Receptor Activating Peptide-6 TRAP, Adenosine diphosphate ADP, Arachidonic Acid AA

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