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The effect of intermittent lower limb occlusion on recovery following exercise-induced muscle damage: a randomized controlled trial

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1 **Abstract**

2 **Objectives:** The purpose of this investigation was to examine the effectiveness of intermittent lower
3 limb occlusion in augmenting recovery from exercise induced muscle damage (EIMD) in physically
4 active males.

5 **Design:** Randomized Controlled Trial, double blind

6 **Methods:** Sixteen healthy recreationally active male participants were randomly assigned to an
7 intermittent occlusion (OCC; n = 8) or control (SHAM; n = 8) group. The EIMD protocol comprised of
8 100 drop-jumps, from a 0.6m box. Indices of muscle damage were creatine kinase (CK), thigh-
9 circumference (TC), muscle soreness (DOMS), counter-movement jump (CMJ) and maximal isometric
10 voluntary contraction (MIVC). Measurements were assessed pre, 24h, 48h and 72h following exercise.

11 **Results:** There was a significant time effect for all indices of muscle damage suggesting EIMD was
12 present following the exercise protocol. The decrease in MIVC was significantly attenuated in the OCC
13 group compared to the SHAM group at 24 (90.4 ± 10.7 vs $81.5 \pm 6.7\%$), 48 (96.2 ± 6.1 vs. $84.5 \pm 7.1\%$)
14 and 72h (101.1 ± 4.2 vs. $89.7 \pm 7.5\%$). The CK response was reduced in the OCC group at 24 ($335 \pm$
15 87 vs. 636 ± 300 IU) and 48h (244 ± 70 vs. 393 ± 248 IU), compared to the SHAM group. DOMS was
16 significantly lower in the OCC compared to the SHAM group at 24, 48 and 72h post EIMD. There was
17 no effect of OCC on CMJ or TC.

18 **Conclusions:** This investigation shows that intermittent lower limb occlusion administered after a
19 damaging bout of exercise reduces indices of muscle damage and accelerates the recovery in physically
20 active males.

21 **Key Words:** muscle function, ischemia, vascular occlusion, delayed onset muscle soreness,
22 eccentric exercise.

23

24 **Introduction**

25 Strenuous or unaccustomed exercise involving eccentric muscle contractions leads to exercise induced
26 muscle damage (EIMD)¹. Typically EIMD manifests as structural damage within the muscle including
27 disruption to sarcomeres and dysfunction of excitation-contraction coupling². EIMD also results in
28 reduced ability for muscle force production, decreased ability to produce explosive muscle contractions,
29 increased muscle swelling, pain and an increase in appearance of muscle proteins in the blood such as
30 creatine kinase (CK) in the days following exercise¹. Various strategies have been investigated as a
31 methods to attenuate the negative effects of eccentric contractions, including reduced physical function.
32 Therapies attempting to reduce EIMD include antioxidants³, non-steroidal anti-inflammatory drugs⁴,
33 cryotherapy⁵ and compression garments⁶. The effectiveness of these therapeutic strategies in reducing
34 signs and symptoms of EIMD is unclear.

35 Recently, the use of intermittent vascular occlusion (OCC) has come to attention in aiding the recovery
36 process⁹. This involves periods of intermittent vascular occlusion of a limb for short periods of time
37 (2-5 minutes), followed by reperfusion. This process also known as ischemic pre- or post-conditioning
38 has been used to protect cardiac and skeletal tissue against ischemic reperfusion (IR) injury¹⁰. IR injury
39 is the damage that occurs when blood supply returns to the tissue after a period of prolonged ischemia,
40 causing metabolic and contractile damage¹¹. This metabolic and contractile damage observed following
41 IR injury, is similar to that seen in EIMD, namely increased intracellular calcium concentrations¹² and
42 an increase in appearance of muscle proteins in the blood and cytokine markers such as CK, lactate
43 dehydrogenase and IL-6^{11; 13}. OCC can attenuate IR injury and thus may potentially be used to speed
44 up the recovery process following EIMD, via increased blood flow due to its effects on activating ATP-
45 sensitive potassium channels¹⁴, elevating adenosine levels¹⁵ and / or reducing the inflammatory
46 response¹⁶, yet the exact mechanisms are currently unknown.

47 Whilst OCC may attenuate the functional and metabolic damage associated with EIMD, few studies
48 have studied the efficacy of this intervention on recovery. Unilateral OCC applied following a training
49 session resulted in beneficial effects on functional measures of athletic performance, including repeated

50 sprint ability and jump height, 24 hs following the intervention⁹. This was the first study to demonstrate
51 a potential use of OCC in the recovery process from athletic efforts. More recently Northey and
52 colleagues¹⁷ applied OCC following a heavy strength training session and found that it did not improve
53 recovery at 1 and 24 h post exercise, when compared to a passive recovery. Therefore evidence for
54 OCC as a recovery tool is conflicting.

55 To summarize, OCC is recognized as an effective and reliable protective strategy in human cardiac and
56 skeletal muscle, reducing the negative side effects of IR injury. The mechanisms by which damage
57 occurs following ischemia are comparable to those seen following EIMD¹. Therefore the aim of this
58 investigation was to determine if OCC could enhance the recovery process following EIMD. It was
59 hypothesised that OCC would attenuate the markers of EIMD during recovery in healthy recreational
60 males.

61 **METHODS**

62 Sixteen healthy recreationally active male participants (age, 22.6 ± 2.8 yr; height, 179.6 ± 5.8
63 cm; mass, 75.5 ± 8.1 kg; mean \pm SD) volunteered to take part in the study. The design, implementation
64 and reporting of this study conforms to the Consolidated Standards of Reporting Trials (CONSORT)
65 guidelines for randomized trials. Participants were fully informed of all procedures and associated risks
66 before giving their written informed consent. Participants were randomly assigned to one of two
67 independent groups, OCC or SHAM, in a double blind fashion. Inclusion criteria included an ability
68 and willingness to abstain from strenuous exercise, caffeine, alcohol and anti-inflammatory medication
69 for 72 hours before and for the duration of the study. Exclusion criteria included recent use of other
70 pain management methods, previous history of cardiovascular disease and any lower limb
71 musculoskeletal injuries in the past 6 months. All experimental procedures were approved by the ethics
72 committee of St Mary's University, London, which conformed to the Declaration of Helsinki.

73 The participants were required to attend the laboratory on five separate occasions based around
74 a 10 day testing period. All trials were performed at the same time of day. In the initial trial, participants
75 were required to attend a familiarization session of all the performance tests. Seven days later,

76 participants reported to the laboratory for four consecutive days. The first day involved baseline
77 performance tests and completing the EIMD protocol; immediately followed by post exercise tests and
78 the intervention or placebo protocols. The indices of EIMD (muscle soreness [DOMS], maximum
79 voluntary contraction [MIVC], thigh circumference [TC] and vertical jump height [CMJ]) were taken
80 pre and post exercise and at 24 h intervals post exercise up to 72 h. CK was measured at all the same
81 time points except immediately post exercise. The rating of recovery intervention (RORI) was only
82 administered and collected immediately post-intervention.

83 Muscle damage was induced via repeated drop jumps from a box 0.6m in height and has previously
84 been demonstrated to result in EIMD ¹⁸. Prior to commencing the protocol, participants, had to
85 demonstrate the correct technique; coaching was used to ensure safe practice. Participants conducted
86 five sets of 20 repetitions separated by a two minutes of recovery to ensure maximal intensity was
87 maintained throughout. Participants stepped off the box with their dominant leg, hands on hips and upon
88 landing jumped maximally landing on the same surface.

89 Upon completion of the EIMD protocol, participants adopted a supine position to allow bilateral arterial
90 occlusion cuffs to be placed on the proximal portion of the thigh (14.5 cm width; Delfi Medical
91 Innovations, Vancouver, Canada). The inflatable cuffs were connected to a pressure gauge and were
92 automatically inflated to either 220mmHg (OCC) or 20mmHg (SHAM) for five minutes followed by
93 five minutes reperfusion. This was repeated three times totalling 30 minutes (15 minutes ischemia and
94 15 minutes of reperfusion). The pressures chosen have previously been used in similar studies
95 investigating vascular occlusion for recovery ⁹. Participants were not informed about the rationale of
96 the study to reduce any placebo effect.

97 Performance measures for MIVC and CMJ followed a standardised warm-up consisting of five
98 incremental sub-maximal efforts before commencing three maximal efforts separated with 60 seconds
99 recovery. The maximal value was recorded and used for evaluation. This has been quantified to reduce
100 the CV to < 5% ¹⁹.

101 Knee extension peak torque of the dominant leg was measured via a digital strain gauge (MIE Digital
102 Myometer; MIE Medical Research Ltd. Leeds). Participants were seated in a standardised position with
103 arms folded across their shoulders and both hips and knees flexed at 90°, measured prior to each
104 contraction via a goniometer to minimise error (Bodycare Products, Warwickshire, UK). Participants
105 were required to extend as hard as possible for three seconds²⁰. Participants performed a CMJ with
106 hands on hips to assess lower limb muscular power. Participants stood on a portable electronic matt
107 (FLS Electronics Ltd. Jump matt. Ireland) and dropped to a self-selected level (approximately a 90°
108 knee angle) before jumping maximally, jump height, in cm, was used for evaluation. Jump height was
109 calculated from the formula: $h = g \cdot t^2 / 8$ (where h is the jump height in metres; g is gravitation acceleration
110 [9.81 m·s⁻²]; t is the flight time in seconds).

111 Plasma CK was determined from fingertip capillary blood samples. Approximately 300 µl of capillary
112 whole blood was collected ((Microcuvette® CB300, Sarstedt, Numbrecht, Germany) and was
113 immediately placed in a refrigerated centrifuge (Mikro 220R D-78532, Tuttlingen, Germany) and spun
114 at 3,500 rpm for 10 minutes at 4°C. The sample was immediately stored at -80°C for analysis at a later
115 date. All samples were analysed using a semi-automated clinical chemistry analyser (Randox RX
116 Monza Randox, Crumlin, United Kingdom). The normal ranges for plasma CK for this assay are 24-
117 195 IU and the intra sample CV was 2.3%. Muscle swelling was measured on the dominant leg midway
118 between the greater trochanter and the lateral epicondyle of the femur. TC was measured in an
119 anatomical position using an anthropometric tape measure (HaB Direct Southam Warwickshire). To
120 ensure consistent measurements between testing days, TC was marked with a semi-permanent pen²⁰.
121 DOMS was assessed via a 200mm visual analogue scale. Participants stood in anatomical position with
122 hands on hips and were asked to hold a half squat (90° knee angle). The far-left of the 200mm line
123 represented 'no pain' while the far-right represents 'extremely painful'. Participants were asked to mark
124 their perceived soreness on the scale²⁰.

125 Five minutes post intervention, participants were asked to rate the intervention they received on how
126 they perceived and expected the recovery intervention to encourage the recovery process. This was

127 measured on a 1–5 Likert scale with one represented ‘Like Very Much’ and five represented ‘Dislike
128 Very Much’⁷.

129 All data are reported as means \pm SD. To account for inter individual variation, CMJ and MIVC were
130 expressed as a percentage change relative to baseline. CK, TC, DOMS and RORI data were expressed
131 as absolute values. RORI was analysed using an independent t-test. Differences in the other measured
132 variables were analysed with a mixed factorial two-way repeated measures ANOVA, using treatment
133 as the between subject factor and time as the within subject factor. Where a significant effect was
134 observed, interaction effects were further examined using Fishers least significant difference (LSD)
135 post hoc analysis. All data were analysed using SPSS for Windows (v. 21.0 software package) with the
136 level of significance set at $P < 0.05$.

137

138 **RESULTS**

139 MIVC was not different between groups at baseline (611 ± 51 vs. 629 ± 136 N, for OCC and SHAM
140 respectively). There was a significant time effect for MIVC, ($P < 0.05$). MIVC showed a significant
141 group ($P < 0.05$) and interaction effect ($P < 0.05$). Post-hoc analysis indicated that the decrease in MIVC
142 was significantly attenuated ($P < 0.05$) in the OCC group compared to the SHAM group at 24 ($90.4 \pm$
143 10.7 vs $81.5 \pm 6.7\%$), 48 (96.2 ± 6.1 vs. $84.5 \pm 7.1\%$) and 72h (101.1 ± 4.2 vs. $89.7 \pm 7.5\%$) post EIMD
144 (Figure 1).

145 CMJ was not different between groups at baseline (34.0 ± 4.4 vs. 38.9 ± 8.1 cm, for OCC and SHAM
146 respectively). There was a significant time effect for CMJ ($P < 0.05$) with peak loss in CMJ occurring
147 24 hours post exercise (84.3 ± 4.3 and 80.0 ± 6.5 % of baseline values for OCC and SHAM
148 respectively). There was no significant interaction ($P = 0.098$) or group effect observed ($P = 0.069$;
149 Table 1).

150 There was a significant time effect for CK ($P < 0.05$), however there was no significant main effect of
151 group observed ($P = 0.78$). There was a significant interaction between time and treatment for CK ($P <$

152 0.05), with post hoc analysis revealing CK to be lower in the OCC group at 24 (335 ± 87 vs. 636 ± 300
153 IU) and 48h (244 ± 70 vs. 393 ± 248 IU) post EIMD when compared to the SHAM group (Table 1).

154 There was a small but significant time effect for TC ($P < 0.05$), however there was no main group effect
155 observed ($P > 0.05$). TC demonstrated a significant interaction between time and treatment ($P < 0.05$;
156 Table 1), however Post-hoc analysis did not reveal were the differences in TC between OCC and SHAM
157 conditions lay.

158 There was a significant time effect for DOMS ($P < 0.05$) with peak soreness occurring 24h post EIMD.
159 DOMS demonstrated a significant interaction between time and treatment ($P < 0.05$) and group effect
160 ($P < 0.05$). Post-hoc analysis indicated that the difference in DOMS was significantly lower ($P < 0.05$)
161 in the OCC compared to the SHAM group at 24, 48 and 72h post EIMD (Figure 1).

162 There was a no difference in the RORI for post-conditioning (mean rank: 2.62 ± 0.92) and control (mean
163 rank: 2.62 ± 0.52) conditions ($P > 0.05$).

164

165 **DISCUSSION**

166 The primary aim of this study was to examine the effect of OCC on indices of muscle damage following
167 eccentric exercise. The findings confirm our hypothesis that OCC can shorten the recovery process
168 following EIMD, as evidenced by a return to pre strength levels 24 hs earlier than the SHAM condition.
169 This faster recovery of functional outcomes is likely due to a decrease in the inflammatory response
170 observed following strenuous eccentric exercise as observed by reduced creatine kinase and soreness.
171 Thus, OCC promoted a positive environment for reduced muscle soreness and functional recovery in
172 physically active males to a greater extent than a SHAM treatment.

173 The exercise protocol resulted in EIMD, as evidenced by significant time effects of all dependent
174 variables, supporting the work of others^{5,21}. In the current study we demonstrated MIVC was reduced
175 following EIMD in both conditions, yet the significant group effect indicated the drop in MIVC was
176 attenuated to a greater extent in the OCC group in comparison to the SHAM condition. Post hoc tests

177 revealed that the loss in muscle strength following EIMD was attenuated across all time points following
178 the application of OCC and returned to pre testing levels within 48 hs. In comparison strength was 90%
179 of pre testing levels in the SHAM condition 72 hs post EIMD. Despite the positive effect on strength
180 recovery, it is not possible to detect whether this was a result of improving the recovery of disrupted
181 sarcomeres in myofibrils and / or damage to the excitation-contraction coupling system.

182 In addition, the data presented supports previous work that OCC is an effective intervention to enhance
183 the rate of recovery following strenuous exercise ⁹. Beaven and colleagues ⁹ were the first to
184 demonstrate the effectiveness of OCC in the recovery process. It should be noted that whilst improved
185 recovery was observed ⁹ the exercise protocol and outcome measurements were different from our work.
186 They demonstrated improved recovery 24 hs post-intervention in power production and sprint
187 performance. One more recent study demonstrated that exercise with blood flow restriction may play a
188 role in attenuating EIMD ²² suggesting OCC may be important in preconditioning muscle tissue prior
189 to damage. In contrast we observed OCC was not able to attenuate the decline in lower limb muscular
190 power despite a trend for a group ($p = 0.069$) and interaction ($p = 0.09$) effect. Furthermore Northey
191 and colleagues ¹⁷ did not demonstrate any benefit of OCC in the recovery process following strenuous
192 resistance exercise. It is possible that the training status of the individuals may explain the differences
193 between their study and our own. For example, the participants in the current study were recreationally
194 active and therefore MIVC was reduced by 18.5% following EIMD in the SHAM group. In contrast the
195 participants in the Northey and colleagues ¹⁷ study had a history of strength training which resulted in
196 a smaller loss of force production (4%), which was likely due to the repeated bout effect ²³, suggesting
197 that OCC was less likely to play a role in the trained group.

198 Our data demonstrates OCC can attenuate the increase in CK as evidenced by reduction at 24 and 48
199 hs following exercise. CK is an indirect marker of EIMD, which displays a high degree of inter and
200 intra subject variability, mainly due to the training status of the individual ²⁴. The reduction in CK
201 following the application of OCC suggests cell membrane integrity was maintained to a greater extent
202 than the SHAM group, suggesting a reduction in the inflammatory response to EIMD. A reduction in
203 inflammatory response leads to a reduction in muscle oedema and intramuscular pressure, which

204 reduces the stimulation of nociceptors, potentially reducing pain, stiffness and muscle soreness
205 sensations ¹.

206 OCC also had a positive reduction on muscle soreness following EIMD. This is in line with previous
207 research using a similar technique (ischemic preconditioning), which reported reduced postoperative
208 pain following total knee arthroplasty ²⁵. The mechanism(s) by which OCC might lead to reduced
209 soreness / pain remains elusive. Whilst there was an increased swelling over time, the degree of change
210 was minimal, which is similar to previous studies using this mode of exercise to induce EIMD ⁸.
211 Therefore it is likely that the reduced muscle soreness observed following OCC was due to an attenuated
212 inflammatory response to EIMD. Speculatively this may be due to a downregulation of circulating
213 leukocytes ¹⁶ and / or increased nitric oxide (NO) which is up-regulated in response to OCC ²⁶, and
214 appears to be an important intracellular and intercellular regulator of muscle inflammation and muscle
215 remodelling ²⁷. It should be noted however that a reduced inflammatory response may not always be
216 sought. Whilst this may be beneficial for short term recovery, as evidenced in the current study, the
217 inflammatory response is important for adaptations to exercise and thus practitioners should take care
218 as to when they apply different recovery techniques.

219 A limitation of studies investigating strategies to improve the recovery process is the possible
220 psychological effect of recovery. In both conditions participants were blinded to the rationale of the
221 study. RORI showed no difference between interventions suggesting that the recovery process was due
222 to physiological responses and not psychological mechanisms suggested by others ^{7, 28}. This suggests
223 that the blinding procedures were successful and their expectations had no effect on other dependant
224 variables. Secondly, participants were recreationally active and therefore the damage they experienced
225 may have been greater than the elite athletic population who would be more accustomed to this type of
226 exercise ²³. Future investigations should aim to further elucidate the mechanisms for improved recovery,
227 including a greater focus on cellular and inflammatory responses. Alongside this research should aim
228 to investigate the dose, frequency and timing of the intervention including the potential impact that
229 OCC has on the adaptation process.

230 *Conclusion*

231 In conclusion, the data presented in this investigation suggests that the application of 3 x five minutes
232 of arterial occlusion administered following eccentric damaging exercise reduces soreness and enhances
233 post-exercise muscular function. Thus, OCC accelerates the recovery post-exercise in recreational
234 active males, potentially via reduced secondary muscle damage.

235 *Practical Implications*

- 236 • The current findings contribute to our understanding of recovery from EIMD, which is
237 important for developing appropriate training strategies;
- 238 • OCC enhances the recovery process following strenuous eccentric exercise
- 239 • OCC may be used by practitioners as a simple and cost effective tool to help athletes recover
240 from exercise.

241 **Acknowledgements**

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Figure Legends

Figure 1. Consort diagram of enrolled participants

Figure 2. Maximal isometric voluntary contraction (MIVC) before and following EIMD. Values are expressed as mean \pm SD. ■OCC, □SHAM. * Indicates significantly different from SHAM, $P < 0.05$.

Table Legends

Table 1. Measures for OCC and SHAM groups; counter movement jump (CMJ), perceived muscle soreness (DOMS), plasma creatine kinase (CK) and thigh circumference (TC) assessed pre, post, 24, 48 and 72h after EIMD. Values are expressed as means \pm SD. * Indicates significantly different from SHAM, $P < 0.05$.

Table 1.

CMJ (% Baseline)	OCC	100 ± 0	85.1 ± 7.3	84.3 ± 4.3	87.0 ± 8.2	87.5 ± 3.1
	SHAM	100 ± 0	84.7 ± 5.2	79.8 ± 6.5	80.5 ± 8.7	82.3 ± 8.1
DOMS (mm)	OCC	8.9 ± 8.0	47.1 ± 25.7	57.0 ± 24.6*	51.4 ± 30.6*	24.5 ± 20.7*
	SHAM	15.6 ± 12.5	68.1 ± 31.8	106.1 ± 30.1	99.5 ± 40.4	64.5 ± 37.6
CK (I/UL)	OCC	163.5 ± 30.1		335.8 ± 87.3*	243.8 ± 69.6*	211.8 ± 68.4
	SHAM	178.4 ± 61.4		636.4 ± 300.1	393.2 ± 248.0	335.1 ± 244.1
TC (cm)	OCC	53.9 ± 3.1	54.8 ± 3.0	54.1 ± 3.1	54.0 ± 3.0	53.8 ± 2.8
	SHAM	54.1 ± 4.4	54.9 ± 4.6	54.7 ± 4.3	54.8 ± 4.2	54.6 ± 4.3

Figure 1

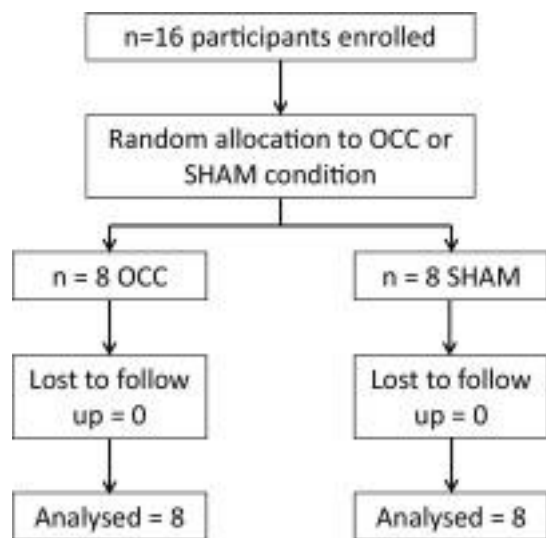


Figure 2

