

TITLE

Comparison of the acute perceptual and blood pressure response to heavy load and light load blood flow restriction resistance exercise in anterior cruciate ligament reconstruction patients and non-injured populations

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VERSIONS

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ABSTRACT

Objectives

To compare the acute perceptual and blood pressure responses to: 1) light load blood flow restriction resistance exercise (BFR-RE) in non-injured individuals and anterior cruciate ligament reconstruction (ACLR) patients; and 2) light load BFR-RE and heavy load RE (HL-RE) in ACLR patients.

Design

Between-subjects, partially-randomised.

Methods

This study comprised 3 groups: non-injured BFR-RE (NI-BFR); ACLR patients BFR-RE (ACLR-BFR); ACLR patients HL-RE (ACLR-HL). NI-BFR and ACLR-BFR performed 4 sets (30, 15, 15, 15 reps, total=75 reps, 30s inter-set rest) of unilateral leg press exercise at 30% 1RM with continuous BFR at 80% limb occlusive pressure. ACLR-HL performed 3 x 10 reps (Total=30 reps, 30s inter-set rest) of unilateral leg press exercise at 70% 1RM. Perceived exertion (RPE), muscle pain, knee pain and pre- and 5-min post-exercise blood pressure were measured.

Results

RPE was higher in ACLR-BFR compared to NI-BFR ($p<0.05$). Muscle pain was higher in NI-BFR and ACLR-BFR compared to ACLR-HL ($p<0.05$). Knee pain was lower in ACLR-BFR compared to ACLR-HL ($p<0.01$). There were no differences in blood pressure.

Conclusion

These responses to BFR exercise may not limit application and favourably influence knee pain throughout ACLR rehabilitation training programmes. These findings can help inform practitioners' decisions to utilise this tool.

28

29 Key words: rehabilitation; strength, surgery, blood flow restriction.

INTRODUCTION

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3 Light load blood flow restriction (BFR) exercise involves partial restriction of arterial inflow and
4 full restriction of venous outflow from the working muscle during exercise (Scott, Loenneke,
5 Slattery, & Dascombe, 2015). BFR is typically achieved using a pneumatic BFR system,
6 comprised of a cuff connected to an inflation device (Hughes, Rosenblatt, Gissane, Paton, &
7 Patterson, 2018). BFR is commonly applied in combination with light load resistance exercise
8 (RE) using loads corresponding to 20-30% of the individual's one repetition maximum (1RM)
9 (Loenneke, Wilson, Marín, Zourdos, & Bemben, 2012). Light load BFR-RE can stimulate greater
10 increases in skeletal muscle strength and hypertrophy compared to light load RE alone (Loenneke
11 *et al.*, 2012), with some studies reporting adaptations that are similar in magnitude to heavy load
12 RE (Bryk *et al.*, 2016; Kim *et al.*, 2017; Laurentino *et al.*, 2012). A recent meta-analysis
13 demonstrated that light load BFR-RE is equally effective at increasing muscle mass as heavy load
14 RE, and may provide an effective approach for increasing muscle strength in the absence of heavy
15 load RE (Lixandrão *et al.*, 2018). Light load BFR-RE is utilised as a rehabilitation tool in load
16 compromised populations, such as pre-sarcopenic older adults (Libardi *et al.*, 2015), knee
17 osteoarthritis patients (Bryk *et al.*, 2016; Segal, Williams, Davis, Wallace, & Mikesky, 2015;
18 Segal, Davis, & Mikesky, 2015) and anterior cruciate ligament reconstruction (ACLR) patients
19 (Ohta *et al.*, 2003). BFR is reportedly used by practitioners for ACLR rehabilitation in particular
20 (Patterson & Brandner, 2017). One focus of ACLR rehabilitation is attenuating atrophy and
21 regaining muscle mass and strength to restore knee joint stability (Saka, 2014), which typically
22 requires resistance loads of >65% 1RM (Folland & Williams, 2007; Garber *et al.*, 2011). It has
23 been demonstrated that light load BFR-RE is effective for increasing strength in populations with
24 clinical muscle weakness (Hughes, Paton, Rosenblatt, Gissane, & Patterson, 2017), and may be
25 used as an alternative to heavy load RE in the early post-surgery phases of ACLR rehabilitation
26 (Hughes, Rosenblatt, Paton, & Patterson, 2018).

28 In clinical BFR application patients must be monitored for pain and hypertension (Hughes et al.,
29 2017). Research in non-injured populations demonstrates amplified exercise-induced increases in
30 heart rate, systolic/diastolic blood pressure and mean arterial pressure in light load BFR-RE
31 compared to matched workloads without BFR (Takano *et al.*, 2005; Hollander *et al.*, 2010; Kacin
32 and Strazar, 2011; Vieira *et al.*, 2013; Araújo *et al.*, 2014; Downs *et al.*, 2014). Additionally,
33 perceptual responses to light load RE appear to be augmented with BFR (Loenneke *et al.*, 2011;
34 Loenneke *et al.*, 2012; Staunton *et al.*, 2015). However these responses are not necessarily high;
35 research comparing the cardiovascular and perceptual responses to light load BFR-RE and heavy
36 load RE suggests such responses are similar in magnitude (Brandner, Kidgell, & Warmington,
37 2015; Hollander et al., 2010; Neto, Santos, et al., 2014; Poton & Polito, 2016). Thus, in non-
38 injured populations light load BFR-RE may provide no greater risk than an equivalent form of
39 exercise at a higher intensity (Jessee et al., 2017).

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41 Much of the research to date comprises heterogeneous protocols and is almost exclusively
42 conducted in non-injured populations. It is unclear if the acute perceptual and blood pressure
43 responses to light load BFR-RE are similar in injured populations, such as ACLR patients, and
44 non-injured populations. It has been hypothesised that the physiological responses to BFR
45 exercise may dictate work volume and patient adherence (Martín-Hernández et al., 2017). Thus,
46 it is important to understand how the acute responses compare to non-injured populations, as this
47 may have implications for decisions regarding application in rehabilitation. Moreover, it is
48 unknown if the acute physiological responses to light load BFR-RE and heavy load RE are similar
49 in ACLR patients, as reported in non-injured populations. If BFR-RE is to be considered as an
50 alternative to heavy load RE for strength rehabilitation in ACLR patients, it is important to
51 examine and compare the acute physiological responses to these exercise modalities, including
52 injury specific aspects such as knee pain (Aglietti, Buzzi, D'Andria, & Zaccherotti, 1993;
53 Shelbourne & Trumper, 1997). Therefore, the aims of this study are to compare the acute
54 physiological responses to 1) light load BFR-RE in non-injured individuals vs. ACLR patients,

55 and 2) light load BFR-RE vs. heavy load RE in ACLR patients. We hypothesised that the acute
56 perceptual response to light load BFR-RE would be 1) higher in ACLR patients compared to non-
57 injured individuals; and 2) similar to HL-RE in ACLR patients, with no differences in post-
58 exercise blood pressure.

METHODOLOGY

Participant information

A total of 30 participants were recruited for this study, which comprised 3 groups: 1) Non-injured individuals performing light load RE with BFR (NI-BFR); 2) ACLR patients performing light load RE with BFR (ACLR-BFR); and 3) ACLR patients performing heavy load RE (ACLR-HL). Participant characteristics for each group are detailed in Table 1. Non-injured participants were active non-smokers free from cardiovascular, pulmonary and metabolic diseases and musculoskeletal injuries in the past 12 months. These aspects also applied to the ACLR patients with the exception that they had undergone ACLR surgery for a unilateral ACL tear. All ACLR surgeries were performed using hamstring autografts (n=20) (Table 1). In the ACLR groups, all participants were assessed to determine they met the criteria required to perform leg press exercise in the early post-surgery phases (weeks 2-3), including minimal swelling, a range of motion of 0-90°, the ability to perform a single leg raise without knee extensor lag and the ability to unilaterally weight bear without pain (Cavanaugh & Powers, 2017). Recent research highlights that early and accelerated post-surgery rehabilitation may improve patient outcomes (Grant, 2013; Tennent et al., 2017), and may begin in the first 2-3 weeks post-surgery when following a criteria-driven approach (Cavanaugh & Powers, 2017; Hughes, Rosenblatt, Paton, et al., 2018). On average, patients in the ACLR-BFR and ACLR-HL groups were 22 ± 2 and 21 ± 3 days post-surgery, respectively, at the time of the familiarisation. Additionally, patients were free from: multiple reconstructive procedures (i.e. multiple ligaments), rheumatoid arthritis, history of deep vein thrombosis or vascular pathology in any lower limb, and the use of anticoagulant medications. All participants refrained from strenuous exercise, caffeine and alcohol in the 24 h prior to testing, and maintained normal dietary habits. All participants provided signed informed consent, in compliance with the Declaration of Helsinki, 7th version, October 2013 (World

27 Medical Association, 2013). All protocols were approved via the relevant NHS (REC reference:
 28 16/YH/0066) and University ethical committees (SMEC-2015-16-118).

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31 **Table 1.** Participant group characteristics (Mean \pm SD)

	NI-BFR	ACLR-BFR	ACLR-HL
Number of participants (M/F)	10 (10/0)	10 (6/4)	10 (7/3)
Age (y)	28 \pm 5	29 \pm 5	31 \pm 7
Body mass (kg)	82.6 \pm 13.4	76.5 \pm 15.7	80.7 \pm 12.3
Height (cm)	180.55 \pm 6.83	172.18 \pm 7.67	177.68 \pm 7.57
Body mass index (kg.m ²)	25.25 \pm 3.20	25.69 \pm 4.16	23.51 \pm 3.38
Blood pressure (Systolic/diastolic mmHg)	126 \pm 10/76 \pm 8	125 \pm 3/80 \pm 2	122 \pm 3/81 \pm 4
Mean arterial pressure (mmHg)	93 \pm 5	95 \pm 2	95 \pm 3
Time from surgery to familiarisation (days)	-	22 \pm 2	21 \pm 3
Graft type, <i>n</i>			
Hamstring autograft (%)	-	10 (100%)	10 (100%)

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34 Study design and randomisation

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36 This study was a between-subjects, partially randomised design. At a post-surgery consultant
 37 surgeon appointment, ACLR participants were block randomised to either heavy load RE (n=10)
 38 or light load BFR-RE (n=10) by an independent member of the research team using 5 x opaque
 39 envelopes each with 4 folded slips inside (2 x heavy load RE, 2 x light load BFR-RE).

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42 Experimental procedures

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44 *Familiarisation and medical screening*

45 All participants attended a familiarisation session and health screening, followed by one
46 experimental session, separated by a minimum of 48 h. During the familiarisation, body mass and
47 height were recorded to the nearest 0.1 kg and 0.01 cm, respectively; blood pressure was measured
48 in a supine position at the brachial artery; unilateral concentric 10RM was recorded; and
49 participants were familiarised to the RE protocols. Due to the nature of ACLR surgery, 10RM
50 was calculated and used to predict each individual's 1RM (Wathan, 1994) to prescribe RE load
51 for a safer approach to strength testing.

52

53 *Exercise protocols*

54 All participants performed a warm-up of 5 min of unloaded cycling at a free cadence followed by
55 10 repetitions of unilateral leg press exercise at a self-selected weight, with a subsequent 5 min
56 rest period. ACLR participants performed the exercise on their injured limb, and non-injured
57 participants on their dominant limb. RE protocols were designed consistent with standard
58 protocols for each type of RE (Fahs, Loenneke, Rossow, Tiebaud, & Bembem, 2012), which is in
59 line with previous studies examining the perceptual and hemodynamic responses to BFR-RE
60 (Brandner & Warmington, 2017; Pinto & Polito, 2016). Participants in the NI-BFR and ACLR-
61 BFR groups then performed 4 sets (30, 15, 15 and 15 repetitions, respectively, with 30 s inter-set
62 rest periods) of unilateral leg press exercise at 30% 1RM throughout 0-90° ROM and a contraction
63 cycle of 1 s concentric/1 s eccentric with BFR applied continuously at 80% limb occlusive
64 pressure (LOP). This set/repetition scheme is common in the BFR literature (Yasuda *et al.*, 2006,
65 2010, 2012; Loenneke *et al.*, 2012, 2016) and doubling the volume does not appear to augment
66 any adaptations (Loenneke, Fahs, Wilson, & Bembem, 2011; Martín-Hernández *et al.*, 2013).
67 Moreover, completing BFR-RE to volitional failure (Loenneke *et al.*, 2014; Fahs *et al.*, 2015)
68 may not be practical in an early post-surgery setting. The rest period duration of 30 s was selected

69 as strength gains occur with 30 s inter-set rest periods (Loenneke, Wilson, et al., 2012) and this
70 reflects recommendations for achieving skeletal muscle hypertrophy (Kraemer & Ratamess,
71 2004). The pressure of 80% LOP was selected based on research suggesting higher pressures
72 maximise fast twitch fibre recruitment and strength adaptations to BFR-RE (Lixandrão et al.,
73 2015; Suga et al., 2012). Participants in the ACLR-HL group performed unilateral leg press
74 exercise (3 x 10 repetitions with 30 s inter-set rest periods) throughout a 0-90° ROM at 70% 1RM,
75 which is a recommended protocol design for improving muscle strength (Garber et al., 2011).
76 Previous research has also suggested that heavy loading following ACLR surgery may not
77 negatively affect knee joint laxity (Bieler et al., 2014) and may be required to increase muscle
78 strength to a satisfactory level (Thomeé et al., 2011).

79

80 *10RM testing*

81 Participants' isotonic 10RM strength was tested on a spring-loaded leg press (Technogym,
82 Bracknell, UK). Prior to testing participants performed a warm-up of 5 min light cycling followed
83 by 10 repetitions of unilateral leg press at a self-selected weight, separated by 1 min of rest.
84 Concentric 10RM was defined as the maximum load that could be lifted through controlled, full
85 ROM (0-90°) with correct form. Beginning at 80% of predicted 10RM, 10RMs were achieved
86 within 5 attempts, with 3 min of rest between attempts to ensure full muscle recovery (Tobalina,
87 Calleja-González, De Santos, Fernández-López, & Arteaga-Ayarza, 2013).

88

89 *Blood flow restriction*

90 BFR was achieved using an automatic personalised tourniquet system (PTS) for BFR (Delfi
91 Medical, Vancouver, BC, Canada), comprised of a dual-purpose easy-fit variable contour nylon
92 cuff (11.5 cm x 86 cm, 5 mm thick) connected by airtight hose tubing to a PTS device with LOP
93 calculation sensors and software. The PTS automatically adjusts pressure around the set pressure
94 (McEwen, Jeyasurya, & Owens, 2016) and effectively regulates interface pressure within
95 acceptable limits during BFR-RE (Hughes, Rosenblatt, Gissane, et al., 2018). The Delfi PTS

96 system automatically calculates LOP by increasing the cuff pressure in stepwise increments,
97 analysing the pneumatic pressure pulsations in the cuff bladder by the arterial pressure pulsations
98 at each cuff pressure increment, and uses these characteristics to determine LOP (McEwen, Masri,
99 Day, & Younger, 2015). Previous research demonstrates that measurement of lower limb LOP
100 with this system concurs with the gold standard doppler technique of calculating LOP (McEwen
101 et al., 2015). LOP was calculated with the participants in the position for exercise to ensure
102 accurate calculation of LOP (Hughes, Jeffries, Waldron, et al., 2018).

103

104 *Perceptual responses*

105 Perceptual responses were assessed following each set using Borg's ratings of perceived exertion
106 (RPE) and pain (RPP) scales (Borg & Løllgen, 1998). Participants received verbal instructions
107 on rating both during the familiarisation visit and were reminded at the experimental session. The
108 pain scale ranges from 0 to 11; for muscle pain, participants were instructed that 10 was their
109 reference point representing their previous worst felt pain, and a score of 11 represented worse
110 pain than any they had ever felt before, similar to previous research examining discomfort during
111 BFR (Dankel et al., 2017; Jessee et al., 2017). This same explanation was used to instruct patients
112 on how to rate knee pain. Muscle pain was assessed in all 3 groups. Participants in the ACLR-
113 BFR and ACLR-HL groups were also asked to provide a score for knee pain; participants were
114 instructed that this score represented any pain felt within the knee joint capsule. ACLR
115 participants were also contacted 24 hr post-exercise to provide a knee pain score. Knee pain was
116 not assessed in the NI-BFR group as any knee pain during the familiarisation session likely
117 indicated a musculoskeletal problem that was grounds for exclusion from the study. For RPE,
118 participants were instructed that a rating of 6 meant they felt no exertion, and 20 meant they were
119 giving maximal effort and could not exert themselves any further (Dankel et al., 2017). For both
120 pain and RPE the final exercising values were used for analysis to provide session ratings, which
121 is line with previous studies (Brandner & Warmington, 2017; Neto, Sousa, et al., 2014; Vieira et
122 al., 2014).

123 *Blood pressure*

124 Systolic and diastolic blood pressure (mmHg) was measured at the brachial artery at pre-exercise
125 and 5 min post-exercise using a Mobil-O-Graph ambulatory blood pressure monitor connected to
126 a laptop with Hypertension Management software (IEM, Cockerillstrasse, Stolberg, Germany).
127 This system measures peripheral blood pressure and records the systolic and diastolic data.

128

129 *Statistical analysis*

130 All data was stored on the password protected servers at the NHS hospital and university. All data
131 were analysed using IBM SPSS Statistics Version 24.0 (IBM Corp, Chicago IL, United States of
132 America). Data are presented as mean \pm standard deviation with 95% confidence intervals (CIs)
133 unless otherwise stated. Normal distribution of data was assessed using Shapiro-Wilks test
134 ($p>0.05$), and homogeneity of variances (where appropriate) was assessed using Levene's Test of
135 Homogeneity of variances ($p>0.05$). Pearson's r correlation test was used to examine any
136 relationship between total exercise volume and each perceptual measure. Final RPE and muscle
137 pain scores were assessed using one-way between subjects' ANOVAs. Data for 24 h post-exercise
138 knee pain was non-normally distributed; a logarithmic transformation was applied and the
139 normally distributed ($p>0.05$) data for knee pain was assessed using a two-way between subjects'
140 ANOVA. LOP, 1RM, exercise load and volume were assessed using independent samples' t-
141 tests. Blood pressure was assessed using one-way between subject's ANOVAs. For any
142 statistically significant interaction determined by ANOVA, Bonferroni post-hoc analysis was
143 performed to examine the differences. Alpha significance was set *a priori* $p<0.05$.

RESULTS

Participants

All 30 participants completed the study with no adverse events. Correlation analysis found no significant relationship between total exercise volume and perceptual measures. Mean \pm SD for RE loads, volume and BFR pressures are detailed in Table 2.

Table 2. Exercise load, volume and BFR pressures (mean \pm SD).

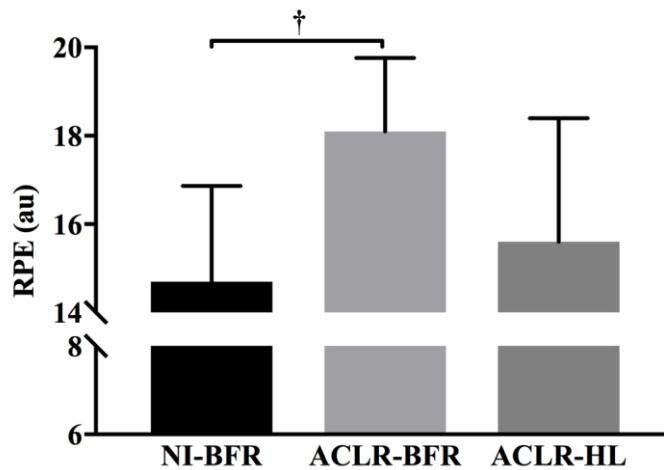
	NI-BFR	ACL-R-BFR	ACL-R heavy
1RM (kg)	161 \pm 44	61 \pm 28*	57 \pm 17*
Exercise load (kg)	48 \pm 13	16 \pm 9*	38 \pm 11*
Exercise volume (Reps)	75 \pm 0	64 \pm 13*	30 \pm 0**
LOP (mmHg)	173 \pm 22	186 \pm 28	-
80% LOP (mmHg)	138 \pm 18	148 \pm 22	-

*=significantly lower than NI-BFR group ($p < 0.05$); †=significantly lower than ACL-R-BFR group ($p < 0.05$)

RPE

RPE was statistically significantly different between the groups, $F_{(2, 27)} = 6.098$, $p < 0.01$. RPE was higher in the ACL-R-BFR group compared to the NI-BFR group, a mean difference of 3.4 ± 1 (95% CI: 0.825 to 5.975, $p < 0.01$). There were no differences in RPE between the ACL-R-BFR group and the ACL-R-HL (mean difference of 2.5 ± 1 , 95% CI: -0.075 to 5.075, $p > 0.05$). There were no differences in RPE between the ACL-R-HL and NI-BFR groups (mean difference of 0.9 ± 1 (95% CI: -1.675 to 3.475, $p > 0.05$) (Figure 1).

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30 **Figure 1.** Session rating of perceived exertion in the three groups (mean \pm SD). † indicates a significant difference ($p < 0.01$).

31 Muscle pain

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33 Muscle pain was statistically significantly different between the groups, $F_{(2, 27)} = 16.084$, $p < 0.01$.

34 Muscle pain was higher in the ACLR-BFR group compared to the NI-BFR group, a mean
35 difference of 2.7 ± 1 (95% CI: 0.292 to 5.058, $p < 0.05$). Muscle pain was higher in the ACLR-

36 BFR group compared to the ACLR-HL group, a mean difference of 5 ± 1 (95% CI: 2.942 to
37 7.758, $p < 0.01$). Muscle pain was higher in the NI-BFR group compared to the ACLR-HL group,

38 a mean difference of 3 ± 1 (95% CI: 0.242 to 5.058, $p < 0.05$) (Figure 2).

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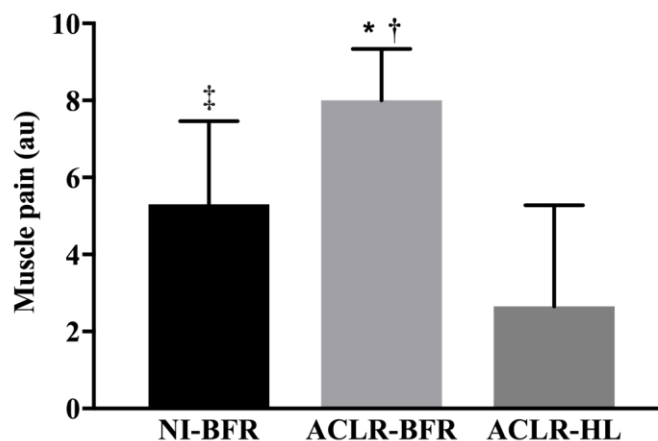
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46 **Figure 2.** Session rating of muscle pain in the 3 groups (mean \pm SD). * indicates a significant
47 difference compared to NI-BR group ($p < 0.05$); † indicates a significant difference compared to
ACLR-HL group ($p < 0.01$); ‡ indicates a significant difference compared to ACLR-HL group
($p < 0.05$)

48 Knee pain

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50 There was no statistically significant interaction between the groups and timepoints for knee pain,

51 $F_{(1, 36)} = 0.123$, $p > 0.05$. A main effect of treatment on knee pain was found, $F_{(1, 38)} = 21.992$,

52 $p < 0.001$. Knee pain was lower in the ACLR-BFR group compared to the ACLR-HL group, a

53 mean difference of 1.3 (95% CI: -1.890 to -0.750, $p < 0.01$) (Figure 3 and Figure 4).

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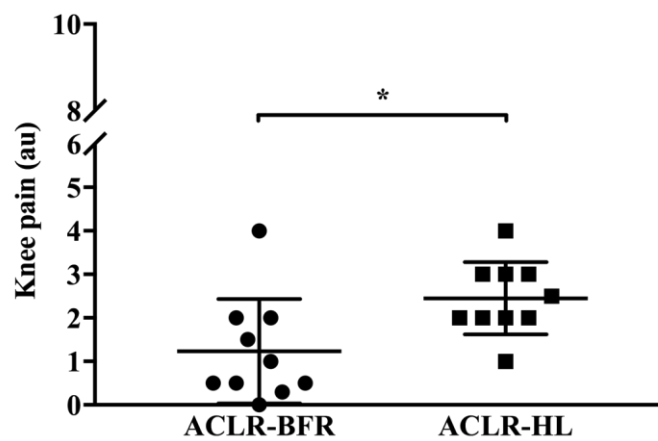
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62 **Figure 3.** Session knee pain score in the ACLR groups (mean \pm SD). * indicates a significant difference ($p < 0.05$).

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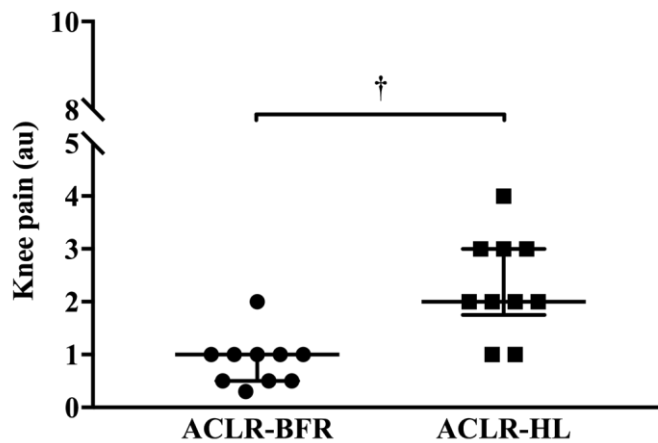
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72 **Figure 4.** 24 hr post-exercise knee pain scores in the ACLR-BFR and ACLR-HL groups (median \pm IQR). † indicates a significant difference ($p < 0.01$).

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75 Blood pressure

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77 There were no differences in pre- and post-exercise blood pressure between any groups (Table

78 3).

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80 **Table 3.** Pre- and 5 min post-exercise blood pressure in each group (mean \pm SD).

	Pre-exercise blood pressure (mmHg)		Post-exercise blood pressure (mmHg)	
	<i>Systolic</i>	<i>Diastolic</i>	<i>Systolic</i>	<i>Diastolic</i>
NI-BFR	127 \pm 10	80 \pm 3	129 \pm 13	78 \pm 5
ACLR-BFR	130 \pm 9	78 \pm 6	131 \pm 12	82 \pm 7
ACLR-HL	139 \pm 9	85 \pm 4	139 \pm 9	82 \pm 4

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DISCUSSION

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This study was the first to compare the acute perceptual and hemodynamic responses to heavy load RE and light load BFR-RE in clinical populations. The main findings were: 1) RPE was higher in the ACLR-BFR group compared to the non-injured BFR group, but similar to the ACLR-HL group; 2) Muscle pain was higher in both BFR groups compared to the ACLR-HL group; 3) Session knee pain and 24 hr post-exercise knee pain was lower in the ACLR-BFR group compared to the ACLR-HL group; and 4) There were no differences in pre- and post-exercise blood pressure between the groups.

Research in non-injured populations suggests the perceptual responses to light load BFR-RE are similar to, or greater than, heavy load RE (Brandner & Warmington, 2017; Hollander et al., 2010; Loenneke et al., 2015; Vieira et al., 2014). In a randomised crossover design, Hollander et al. (2010) demonstrated comparable increases in RPE response to an acute bout of light load BFR-RE (30% 1RM) and heavy load RE (70% 1RM) in non-injured populations, which is in line with the findings of Loenneke *et al.* (2015). The present study demonstrates similar findings, suggesting that the acute RPE response to light load BFR-RE is not greater than heavy load RE in ACLR patients. It has been demonstrated that proximal arterial occlusion of a limb during exercise results in overestimation of perceived force (Takarada, Nozaki, & Taira, 2006), which may explain the findings of the present study and previous research. Although the mechanisms of increased estimation of effort with light loads and BFR are not fully understood, it has been proposed that impeded conduction in peripheral nerves due to mechanical deformation during compression and inhibition of cutaneous sensory nerves may alter the response of somatic efferent neurons (Hollander et al., 2010; Takarada et al., 2006). Additionally, post-surgery volitional muscle activation failure (Perraton et al., 2017) caused by failure of the central nervous system to activate the knee extensor muscles (Mizner, Petterson, Stevens, Vandenborne, & Snyder-

28 Mackler, 2005) may contribute to a greater RPE response in the ACLR-BFR group compared to
29 the non-injured BFR group at the same relative exercise load.

30

31 In the present study, muscle pain scores were higher in both the non-injured BFR and ACLR-
32 BFR groups compared to the ACLR-HL group. There is an increase in pain perception with light
33 load BFR exercise alongside increased muscle activation (Wernbom, Järrebring, Andreasson, &
34 Augustsson, 2009) which has been attributed to metabolite accumulation due to venous occlusion
35 and hypoxia (Suga et al., 2009). It is hypothesised that this may stimulate group III and IV afferent
36 fibres, increasing sympathetic nervous system activity (Takarada et al., 2000). The observation
37 of higher pain scores in the present study is in contrast to previous work demonstrating similar
38 perceptions of pain between light load BFR-RE (30% 1RM) and heavy load (70% 1RM) exercise
39 (Hollander et al., 2010). However, the restriction pressures used in the present study (173 and 186
40 mmHg for the NI-BFR and ACLR-BFR groups, respectively) were likely higher than those used
41 by Hollander et al. (20% below systolic blood pressure). Higher pressures may cause greater
42 accumulation of metabolites (Yasuda, Abe, et al., 2010), which may increase perception of
43 discomfort (Jessee et al., 2017). Moreover, in the present study a greater total volume of work
44 was completed by the BFR groups, which may have influenced pain responses due to greater time
45 under BFR. Regarding the BFR groups only, muscle pain and strains that are observed following
46 ACLR surgery (D'Alessandro, Wake, & Annear, 2013) may contribute to the higher pain scores
47 observed in the ACLR-BFR group compared to the non-injured BFR group, particularly if the
48 ACLR-BFR group were present with some degree of muscle pain prior to exercise.

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50 Knee pain is widely reported following ACLR surgery, particularly in the anterior knee
51 compartment (Chmielewski et al., 2008), and may predict a more difficult and prolonged
52 rehabilitation process (Dunn et al., 2010). Knee pain has been linked to concomitant injuries such
53 as bone bruising and cartilage/meniscal damage (Hughes, Rosenblatt, Paton, et al., 2018), and
54 pain intensity is associated with self-reported function following surgery and successful return to

55 sport (Chmielewski et al., 2008; Czuppon, Racette, Klein, & Harris-Hayes, 2014). Thus,
56 minimising knee pain in early strength rehabilitation is important. In the present study, the ACLR-
57 BFR group experienced less knee pain during RE, likely due to the lower loads (30% vs. 70%
58 1RM) and lower knee joint forces during RE. Interestingly, the ACLR-BFR group also reported
59 less knee pain in the 24 hours following exercise. This suggests light load BFR-RE in the early
60 post-surgery phases may not exacerbate pain or inflammation within the knee joint on subsequent
61 days after training, which may positively influence exercise volume during sessions and patient
62 adherence to a rehabilitation programme (Juan Martín-Hernández et al., 2017). Therefore,
63 similarly to research in non-injured populations, light load BFR-RE may be used more frequently
64 than heavy load RE, such as twice daily (Abe, Kawamoto, *et al.*, 2005; Yasuda, Fujita, *et al.*,
65 2010). Adaptations in muscle strength and mass have been observed in short time frames such as
66 two weeks (Abe, Yasuda, *et al.*, 2005; Yasuda *et al.*, 2005) and even one week (Abe, Kawamoto,
67 *et al.*, 2005; Fujita, Brechue, Kurita, Sato, & Abe, 2008), thus the findings of the present study
68 may have important implications for the use of BFR in early ACLR rehabilitation.

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70 Collectively, the findings of the present study suggest that the perceptual responses to light load
71 BFR-RE are similar or greater than heavy load RE in ACLR patients. Previous research suggests
72 that exacerbated perceptual responses subside after a few exercise sessions with BFR (Clarkson,
73 Conway, & Warmington, 2017; Fitschen *et al.*, 2014; Weatherholt, Beekley, Greer, Urtel, &
74 Mikesky, 2013), suggesting an adaptive effect facilitating tolerance with exposure (Brandner *et al.*,
75 2018). Moreover, there appears to be a similar time course of adaptation to perceptual
76 responses between light load BFR-RE and heavy load RE (Juan Martín-Hernández *et al.*, 2017).
77 Although it is unknown if the time course of adaptation in ACLR populations is similar,
78 collectively these reports and the findings of the present study suggest that high initial perceptual
79 responses may not be a limiting factor when using BFR in an ACLR rehabilitation programme
80 (Loenneke *et al.*, 2016).

81

82 Finally, the present study found no differences in post-exercise blood pressure between the
83 groups. This is in line with previous research demonstrating similar blood pressure responses in
84 light load BFR-RE and heavy load RE (Brandner et al., 2015; Neto, Santos, et al., 2014; Poton &
85 Polito, 2016; Sardeli et al., 2017). Thus, light load BFR-RE likely provides no greater
86 hemodynamic risk than heavy load RE (Jessee et al., 2017). Moreover, these findings are in line
87 with previous work indicating return to baseline of mean arterial pressure following BFR-RE with
88 the Delfi PTS device (Hughes, Rosenblatt, Gissane, et al., 2018). However, it is of note that the
89 blood pressure response to unilateral exercise is likely lower than bilateral exercise with greater
90 muscle mass involvement (Adams, Cline, Hubbard, McCullough, & Hartman, 2006), therefore
91 the findings of the present study may be specific to unilateral exercise only.

92
93 There are several limitations to this study. Firstly, total exercise volume was heterogeneous
94 between groups, therefore a volume effect on perceptual responses cannot be disregarded;
95 however, the protocols used reflect current guidelines for light load BFR-RE and heavy load RE
96 for improving muscle strength and mass. Secondly, we could not quantify overall presence or
97 severity of any concomitant pathologies, which may also impact upon the perceptual responses
98 to RE; however, post-surgery pathologies vary in incidence and severity in ACLR patients and
99 thus are difficult to account for (Tahami & Rad, 2015). Thirdly, our NI-BFR group was composed
100 of males only. Literature suggests that the perceptual response to relative RE load is similar
101 between males and females (Pincivero, Coelho, & Campy, 2003), however at present there is a
102 lack of research concerning gender differences in the perceptual response to BFR exercise which
103 may impact the findings of the present study. Finally, the findings of the present study may be
104 specific to the RE protocols used.

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CONCLUSION

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3 Collectively, the findings of present study suggest that the hemodynamic and perceptual
4 responses to light load BFR-RE in ACLR patients may not be a limiting factor for clinician
5 concern in a rehabilitation setting, and that this mode of exercise may favourably influence knee
6 pain during and throughout a training programme. Future research should monitor these responses
7 over the course of a rehabilitation training programme.

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