University of South Australia

Staying strong: Improving health for Rheumatoid Arthritis using Blood Flow Restriction.

Arthritis Australia Grant in Aid: Scientific report.

Title:

An evaluation of the effect of blood flow restricted resistance training and exercise preferences in individuals with Rheumatoid Arthritis.

Authors:

Dr. Hunter Bennett [a,b] (ORCID ID: 0000-0002-8541-9104)

Associate Professor Kade Davison [a,b] (ORCID ID: 0000-0002-7101-7729)

Affiliations:

[a] Allied Health and Human Performance, University of South Australia, Adelaide, Australia

[b] Alliance for Research in Exercise, Nutrition, and Activity (ARENA), University of South Australia, Adelaide, Australia

Abstract:

The aim of this two-part study was to examine the attitudes and preferences towards blood flow restriction resistance exercise (BFR-RT) in individuals diagnosed with Rheumatoid Arthritis (RA), and then assess the efficacy and acceptability of an upper and lower body progressive BFR-RT intervention in a small subset of RA patients. Part one was a cross-sectional survey (N=97) examining the exercise preferences of RA patients, and their openness to conducting a BFR-RT intervention. Part two was a small proof-of-concept single group trial (N=12) examining the effects of a low load BFR-RT on muscle strength, muscle size, functional capacity, quality of life, and pain in RA patients. The acceptability of the intervention via exit surveys was also examined. Survey results indicated most RA patients would prefer to conduct BFR-RT if it was under the supervision of an exercise professional in a one-on-one environment, comprised of a combination of aerobic and resistance exercise, be no more than three sessions per week, and commence at a low or moderate intensity. The intervention in study two was based upon recommendations from study one, and demonstrated BFR-RT is both an effective and acceptable way to improve upper and lower body strength, functional capacity, and pain in this population. No improvements, however, in self-reported quality of life measures were observed. Future research should compare such an intervention to more traditional resistance training methods to assess differences in effectiveness and acceptability.

Keywords:

Rheumatology; blood flow occlusion; exercise; vascular occlusion; strength training; function.

Introduction:

Rheumatoid Arthritis (RA) is the second most common form of arthritis in Australia impacting approximately 2% of the total adult population.[1] Typified by gradual joint degradation, RA is known to lead to progressive reductions in activities of daily living and a marked loss of muscle mass and strength, with functional deficits as high as 70% in patients with severe RA.[2] Loss of muscle size and quality leads to complications including metabolic disease, loss of independence, and an increased risk of falls and fractures, all of which contribute to the risk of premature mortality.[3] Importantly, the number of people with RA in Australia is projected to increase from 422,309 in 2015 to 579,915 in 2030,[4] highlighting the need for practical ways for improving health and function in this population.

While advancements in RA medication have done much to assist with pain and symptom management, they do not address the loss of strength and function associated with RA. Resistance training is considered the most effective mode of exercise to increase strength and counteract muscle loss,[5] which is optimized with relatively heavy loads to maximize improvements in strength and stimulate the development of muscle tissue.[6] However, this can be problematic for some RA patients due to pain, fatigue, and the risk of joint injury.[7] Blood flow restriction resistance training (BFR-RT) has recently emerged as an alternative to traditional high-load resistance training (HRT). BFR-RT involves performing resistance training with very low loads while wearing an inflatable pneumatic cuff on the proximal portion of the working limb.[8] This cuff is inflated to a pressure that allows blood flow *into* the limb but delays its exit *from* the limb. BFR-RT creates a metabolic environment within the muscle that contributes to the development of muscle strength and size without the need for heavy loads, suggesting suitability for RA.

Low-load BFR-RT has been shown to be a safe and effective method for improving strength and function across a myriad of clinical populations, including patients with osteoarthritis.[9] To date, two studies have examined the effects of BFR-RT in RA, with promising results. The first study compared a BFR-RT intervention to a traditional HRT intervention, each comprising 2 sessions per week for 12-

weeks, in post-menopausal women diagnosed with RA.[10] Both interventions resulted in equivalent increases in lower limb strength, muscle size, and functional performance. Interestingly, the BFR-RT intervention led to significant improvements in self-reported pain and quality of life, which were not observed in the HRT group. The second study compared a BFR-RT intervention to a low-load traditional resistance training intervention in women diagnosed with RA. Both interventions involved three sessions per week for 4-weeks and resulted in equivalent improvements in several of measures of lower limb strength and endurance, however, knee extensor strength increases were significantly larger in the BFR-RT group.[11] Neither groups reported any improvements in self-reported measures pain, and quality of life was not assessed. Importantly, this study also briefly assessed the acceptability of the program. Almost one third of participants considered three sessions per week to be "too many", although ~80% of participants were satisfied with the benefits of the training, and ~10% considered the training to be "too hard." While these studies support the use of BFR-RT in patients with RA, they do have some limitations. Firstly, the interventions used were not designed based upon feedback from RA patients, which could have impacted upon their perceived acceptability. Secondly, both interventions only included lower limb exercises, and assessments of lower limb strength. As such, it is unclear whether upper limb BFR-RT would be suitable and effective in those with RA. Lastly, the exercise interventions did not increase the load used across the intervention periods. Given that progressive resistance training that gradually increases load is thought to promote better long-term training adaptations,[12] this is an important factor to consider.

Taking this into consideration, we believed it important to first assess the attitudes and preferences toward BFR-RT in those with RA, and then assess the efficacy and acceptability of an upper and lower body progressive BFR-RT intervention in a small subset of RA patients. Therefore, there were two key aims for this body of research, addressed through two parts. Part one aimed to assess beliefs about, and practices around, exercise in individuals with RA, while also surveying their willingness to engage in BFR-RT. Part two aimed to examine the effect of progressive BFR-RT on

measures of upper and lower body strength, pain, and function, in a small sample of individuals diagnosed with RA, while also investigating its acceptability.

Materials and Methods:

Part One:

Study design

A cross-sectional observational design was used to examine the exercise preferences and characteristics of pain in individuals diagnosed with RA using an online survey (Qualtrics, Provo, UT). The study was granted ethical approval by the University of South Australia Human Research Ethics Committee (Protocol Number 205828).

Participants

Participants were eligible for inclusion in this study if they were aged 18 years or older and currently diagnosed with RA. Participants were recruited between August 2023 and June 2024 through social media advertising, RA support groups, and word of mouth. All participants provided informed consent via the online survey platform prior to completing the survey. A total of 132 individuals viewed the survey, with 97 consenting to participate.

Outcome Measures

Participant demographics

Participants were asked to provide information pertaining to their age, gender, country of residence, employment status, duration since RA diagnosis, current medication regime, and exercise habits. With respect to exercise habits, participants were asked to detail how many times per week on average they engaged in moderate to vigorous exercise or physical activity, the average length of time they completed each bout of exercise or physical activity, whether any of that physical activity

or exercise involved resistance training, and if so, how many sessions per week on average involved resistance training.

Rheumatoid Arthritis Pain Scale (RAPS)

Participants completed the Rheumatoid Arthritis Pain Scale (RAPS), a self-reported pain assessment scale comprised of 24-items designed to measure several aspects of pain in adults with RA.[13] Items are scored on a 7-point Likert scale (0=never, 6=always) and summed to provide an overall RAPS score (higher scores are indicative of greater pain). The RAPS also has a single question pertaining to overall general pain, where participants are required to answer the following question on a 10-point visual analogue (VAS) scale (0=never, 10=severe): "When looking at the scale below, overall I would rate my pain as…".

Exercise Preferences

To evaluate preferences towards exercise, participants were asked questions regarding their willingness to engage with an exercise program, preferred type, frequency, intensity, and duration of exercise, preferred exercise location and delivery method, whether they prefer to exercise alone or with others, and how far they would be willing to travel to participate in an exercise program.

Willingness to engage in BFR-RT

Lastly, participants were asked to watch a short video depicting BFR-RT (https://tinyurl.com/BFRRTvideo). This video provided a brief overview of BFR-RT, with a visual demonstration of its application. Participants were then asked questions regarding their level of interest and concern associated with engaging in a BFR-RT intervention as well as the extent to which they perceived it to be effective for individuals with RA.

Part Two:

Study design

A small single group pre-post study was conducted to pilot the effects of a low load BFR-RT on muscle strength, muscle size, functional capacity, quality of life, and pain in women and men with RA. The acceptability and feasibility of the intervention via exit surveys was also examined.

Participants

Women and men, aged 45-75 years, diagnosed with RA in accordance with the 2010 Rheumatoid Arthritis Classification Criteria,[14] and under stable medication regime for 3 months (minimum) before starting the study were included. Participants were excluded if they had participated in resistance training regularly in the last 12 months, had been diagnosed with cardiovascular disease or fibromyalgia, had a musculoskeletal issue preventing them from exercising, were pregnant, or had previously undergone a joint replacement surgery. A combination of self-selection, network, and purposive non-probability sampling methods were used to recruit participants. To reach potential participants, the survey was advertised through Arthritis SA, UniSA media, and the professional networks of the research team via social media, newsletters, and flyers. Ethical approval was initially provided by the University of South Australia Human Research Ethics Committee (protocol number: 205066). However, due to lower than anticipated recruitment rates, additional ethical approval was sought to recruit through the Royal Adelaide Hospital (Adelaide, 5000, South Australia) from the Central Adelaide Local Health Network Research Services (protocol number: 1823). Recruitment was conducted between June 2023 and April 2024.

Primary Outcome Measures

Primary outcome measures were completed the week prior to starting the intervention (baseline), and the week following the completion of the intervention (post-intervention). These measures align with the 2019 revised European consensus for the diagnosis on sarcopenia,[15] with the inclusion of RA specific measures related to functional capacity, pain, and quality of life. This is based on evidence indicating that individuals with RA are at a high risk of developing sarcopenia after

diagnosis,[16, 17] a disease typified by a loss of muscle mass and strength, which are also key contributors to the functional declines observed in RA.

Muscle Strength

Grip strength was measured using handgrip dynamometer as an indicator of whole-body strength (strongly associated with functional disability in RA).[18] One repetition maximum (1RM) strength was estimated for the following exercises to assess strength and guide the intensity of the intervention: leg press, machine hamstring curl, machine knee extension, cable tricep extension, and cable bicep curl. 1RM strength was estimated using the Brzycki formula (weight in kg ÷ [1.0278 - 0.0278 × number of repetitions]).[19] To obtain this estimation, participants conducted repetition maximum testing on the above exercises with the intent to reach volitional failure (i.e., they felt they could no longer complete another rep) within 3 to 10 repetitions. All participants completed a minimum of one warmup set of 10 repetitions on each exercise to allow the research team to approximate an appropriate load for repetition maximum testing. Due to differences in baseline strength levels, some participants required multiple warmup sets that increased in load.

Physical performance

Physical performance was assessed using the Four-Meter Gait Speed Test,[20] which required participants to perform two trials walking a distance of 4 meters, at two speeds: their usual walking speed, and as fast as possible, with the mean speed (m/s) for each walking speed the measures of interest.

Functional Capacity

Functional capacity was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI), based on self-reported activity limitations.[21] This 20-item questionnaire assesses the ability to perform fine motor movements of the upper extremities, and large motor activities of the lower limbs across eight domains: reach, grip, eating, dressing, hygiene, walking, arising, and activities.

Each response is scored on a four-point scale in which higher scores indicated more disability (0 = “without any difficulty” to 3 = “unable to do”). There are also questions pertaining to the use of an aid or assistance device within each domain. The highest score reported for any item in each domain determines the score for that domain unless aids or devices are required. If aids or devices are required for support in a specific domain, the score of that domain is automatically raised from 0 or 1, to a 2 (remains unadjusted if already scored as a 2 or 3). The final HAQ-DI score is calculated as the average of the eight domains scores ranging between 0 and 3, with higher scores indicating lower functional capacity.

Quality of Life

Quality of life was assessed using The Rheumatoid Arthritis Quality of Life Questionnaire (RAQoL), which is a 30-item questionnaire evaluating the effect that RA has on an individual’s quality of life.[21] Each questionnaire is responded to with a yes (1 point) or a no (0 points), higher scores indicating lower quality of life (highest possible score is 30).

Pain

Pain was measured using the RAPS.[13] A detailed overview of the RAPS is provided in above.

Secondary Outcome Measures

Acceptability and Feasibility of the Intervention

At the completion of the intervention a questionnaire with both open- and closed-questions was provided to each participant to gain insight into the acceptability of the intervention. Close ended questions used Likert scales (1-5) to explore the level of agreement regarding different statements on the acceptability of the intervention. Open ended questions sought to obtain information regarding specific aspects of the intervention that participants liked and disliked. The perceived difficulty of each training session was also obtained using the Borg CR10 ratings of perceived exertion scale, to examine the perceived difficulty of the intervention.[22] Intervention adherence was

also monitored to provide an indication of the feasibility of the intervention. The intervention was considered acceptable if more than 80% of participants responded with a 4 or 5 (1 = completely unacceptable, 3 = no opinion, 5 = completely acceptable) in response to the question "How acceptable was the exercise program to you? ?" The exercise intervention was considered feasible if at least 90% of enrolled participants completed the study, and if they attended an average of 80% or more of the sessions within the intervention.

Exercise intervention:

The exercise interventions were performed in a gym located at the University of South Australia city east campus (Adelaide, 5000, South Australia), and consisted of two sessions per week, for 8-weeks (16 total sessions). All sessions commenced with a 5-minute warmup, and finished with a 5-minute cool down, consisting of low intensity aerobic exercise performed using a self-selected modality at a self-selected pace. All sessions were conducted one-on-one under direct guidance by third year Clinical Exercise Physiology students under the supervision of an Exercise and Sport Science Australia (ESSA) Accredited Clinical Exercise Physiologist.

The BFR-RT intervention was comprised of the same five exercises conducted during baseline testing. Exercises commenced in the first week using loads corresponding to 20% of the participant's one repetition maximum (1RM), estimated from baseline testing. Load was progressed over the 8-week duration, as depicted in Table 1. Each exercise was performed for four sets. The first set was performed for 30 repetitions, and the remaining three sets for 15 repetitions, with 60 seconds rest between sets. Each lower body exercise was performed with a pneumatic inflatable air cuff placed at the proximal of the thigh, and each upper body exercise with a cuff at the proximal portion of the arm. The cuff was inflated to 70% of arterial occlusion pressure (AOP) for lower body exercises and 40% of AOP for upper body exercises (please see section titled "Determination of arterial occlusion pressure"). The cuff remained inflated during the rest periods of each exercise, but deflated for 3-5 minutes between exercises.[8] Session time including warm up and cool down was ~60 minutes.

Table 1: Weekly load progression for the BFR exercise intervention.

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Intensity (%1RM)	20%	25%	30%	30%	35%	35%	40%	40%

Determination of arterial occlusion pressure (AOP)

The intervention required participants to perform lower body resistance training exercises with a pneumatic cuff inflated to 70% of the pressure required to completely occlude blood flow into the limb (i.e., AOP), and upper body exercises with the cuff inflated to 40% of AOP for the upper limbs. AOP (mmHg) was measured during baseline testing and determined using the same device used during the training intervention (Smart Tools, USA) and a vascular doppler ultrasound (Smart Tools, USA). To determine lower body AOP participants were required to lie supine. The cuff was placed on the proximal region of the thigh and inflated to the point at which the auscultatory pulse of the tibial artery was completely interrupted (measured via doppler ultrasound). The pressure at which this occurs was deemed AOP. Using the same equipment, to determine AOP of the arm, the cuff was applied to the most proximal portion of the arm and inflated to the point at which the auscultatory pulse of the radial artery was completely interrupted.

<u>Statistical analysis:</u>

Part one:

Participant characteristics and survey scores were summarised and described descriptively, whereby descriptive statistics for categorial data were reported using frequency counts and percentages, and for numerical data, medians and interquartile ranges as the data were not normally distributed. While no restrictions were placed on sample size, it was determined that a minimum of 71 participants would be required to achieve a 95% confidence interval with a margin of 4 points, based on prior research reporting RAPS scores in exercising individuals with RA, where the standard deviation of the outcome was 17.2 points.[23]

Part two:

Data were presented descriptively where appropriate (mean, standard deviation). All primary outcome measures (dependent variable) were compared statistically using a linear mixed effects model, with the time (pre and post) input as the independent variable. Pre and post change were also presented using standardized mean differences, and interpreted as trivial (<0.20), small (0.20 – 0.49), moderate (0.50 – 0.79), and large (>0.79)[24] to provide insight into the practical relevance of the change. Secondary outcome measures are presented descriptively, while open ended responses to the exit survey questions were analyzed thematically to identify relevant themes pertaining to what participants did and did not like about the intervention. All formal analysis was conducted in Stata statistical software version 18.0 (College station, TX), and statistical significance was set to $P<0.05$.

Results:

A total of 97 participants (female = 85 [88%], male = 9 [9%], non-binary = 3 [3%]) with a mean age of 50.1 (SD 15.5; range 22-83) years completed the survey. The mean time since RA diagnosis was 114.1 (SD 123.8; range 1-600) months. A total of 35 participants were from Australia, 31 from America, six from the United Kingdom, five from Canada, two from New Zealand, and one each from Cambodia, Netherlands, Lithuania, Norway, Spain, and South Africa, while 12 did not report their primary country of residence. Within the sample, 89 participants were currently taking prescribed medication for their RA. Thirty-two participants were currently employed full-time, 26 were retired, 13 worked part-time, eight were employed on a casual basis, while 17 were currently unemployed. The mean RAPS and VAS scores were 74.4 (SD 35.4; range 0-144) and 5.0 (SD 2.3; range 1-10) respectively.

Table 2 outlines the current exercise habits of those diagnosed with RA. 72% of participants reported that they participated in at least two sessions of physical activity per week and the most common duration of physical activity session was 31 – 40 minutes.

Table 2: Exercise habits of individuals diagnosed with RA (presented as frequency (percentage)).

Question / Response	**n (%)**
On average, how many days per week do you engage in moderate to vigorous physical activity (e.g., a brisk walk or something of equal or greater effort than that)?	
None	8 (8%)
One	6 (6%)
Two	20 (21%)
Three	22 (23%)
Four	9 (9%)
Five	7 (7%)
Six	4 (4%)
Seven	8 (8%)
No response	11 (11%)
On average, how many minutes do you engage in physical activity at this level?	
None	2 (2%)
0 – 5 minutes	4 (4%)
6 – 10 minutes	3 (3%)
11 – 15 minutes	12 (12%)
16 – 20 minutes	1 (1%)
21 – 25 minutes	6 (6%)
26 – 30 minutes	10 (10%)
31 – 40 minutes	14 (14%)
41 – 50 minutes	7 (7%)
51 – 60 minutes	10 (10%)
More than 60 minutes	7 (7%)
No response	23 (24%)
Do any of these sessions involve any resistance exercise that requires you to lift or push your own bodyweight or an external load (e.g., squatting, push ups, lifting weights)?	
Yes	56 (58%)
No	38 (39%)
No response	3 (3%)
If yes. how many sessions of this do you do each week?	
One	13 (13%)
Two	25 (26%)
Three	10 (10%)
Four	3 (3%)
Five	3 (3%)
Six	3 (3%)
Seven	1 (1%)
No response	39 (40%)

Table 3 outlines the exercise preferences for those diagnosed with RA. Most participants indicated that three or fewer sessions per week of exercise would be achievable (58%), with only 6% stating they would be willing to travel more than 30 minutes to participate in an exercise program.

Table 3: Exercise preferences of individuals diagnosed with RA (presented as frequency (percentage)).

Question / Response	**n (%)**
Are you interested in taking part in an exercise program?	
Yes	59 (61%)
No	9 (9%)
Not sure	18 (19%)
No response	11 (11%)
Do you feel you could take part in an exercise program?	
Yes	58 (60%)

No	6 (6%)
Not sure	22 (23%)
No response	11 (11%)
Would you be willing to engage in an exercise program if it could reduce the use of medication and other treatments?	
Yes	80 (82%)
No	6 (6%)
No response	11 (11%)
Would you be willing to engage in an exercise program if it could improve your quality of life?	
Yes	84 (87%)
No	2 (2%)
No response	11 (11%)
Which of the following would you prefer most?	
Exercise at a gym facility with supervision	16 (17%)
Exercise at a gym with guidance from a program	9 (9%)
Exercise at home with in-person supervision	4 (4%)
Exercise at home with remote (i.e., skype, zoom, etc.) supervision	4 (4%)
Exercise at home with the guidance from a program	18 (19%)
Other	3 (3%)
No response	43 (44%)
What is your preferred type of exercise?	
Cardiovascular exercise (constant movement that makes you breath more – e.g., walking, jogging, cycling)	14 (14%)
Resistance exercise (e.g., lifting weights or using machines to work your muscles against a load)	13 (13%)
A combination of the two	49 (51%)
Playing sport (e.g., tennis, soccer, etc.)	2 (25)
No preference	8 (8%)
No response	11 (11%)
What is you preferred intensity of exercise?	
Low (feels like about a 30-40% effort – able to talk comfortably)	34 (35%)
Moderate (feels like about a 50-70% effort – can still talk but have a few pauses for breath or effort)	44 (45%)
High (feels like about a 70-90% effort – can't really hold a conversation due to breathing or effort)	7 (7%)
No preference	1 (1%)
No response	11 (11%)
How long would you be willing to exercise for per session?	
15 – 30 minutes	31 (32%)
31 – 45 minutes	26 (27%)
46 – 60 minutes	25 (26%)
Other	4 (4%)
No response	15 (15%)
Would you prefer to exercise:	
By yourself	46 (47%)
With one other person	3 (3%)
In a group	12 (12%)
No preference	25 (26%)
No response	11 (11%)
Would you prefer to exercise:	
In a gym	28 (29%)
Outside	32 (33%)
No preference	26 (27%)
No response	11 (11%)
How many times per week of exercise do you think would be achievable for you?	
None	1 (1%)
One	2 (2%)
Two	21 (22%)
Three	33 (34%)

Four	11 (11%)
Five	8 (8%)
More than five	9 (9%)
Not sure	1 (1%)
No response	11 (11%)
How long would you be willing to travel to participate in an exercise program?	
0 – 5 minutes	12 (12%)
6 – 10 minutes	12 (12%)
11 – 15 minutes	17 (18%)
16 – 20 minutes	24 (25%)
21 – 25 minutes	3 (3%)
26 – 30 minutes	12 (12%)
31 – 40 minutes	2 (2%)
41 – 50 minutes	1 (1%)
51 – 60 minutes	1 (1%)
More than 60 minutes	2 (2%)
No response	11 (11%)

Table 4 outlines the participants openness to participating in BFR specific exercise. Results indicate high interested in conducting an exercise intervention that used this mode of training (median score = 4). However, there were concerns that it may cause pain or make symptoms worse (median score = 3).

Table 4: Openness to participating in BFR exercise interventions.

Question	**Median (IQR)**
How interested would you be in conducting an exercise program using the above method of exercise (0 = not at all, 5 = extremely interested)	4 (3)
I am concerned blood flow restricted exercise will cause me pain (0 = strongly disagree, 5 = strongly agree)	3 (2.75)
I am concerned blood flow restricted exercise will make my symptoms worse (0 = strongly disagree, 5 = strongly agree)	3 (3)
Blood flow restricted exercise isn't safe for me (0 = strongly disagree, 5 = strongly agree)	1 (3)
I would only perform blood flow restricted exercise under supervision from a professional (0 = strongly disagree, 5 = strongly agree)	4 (3.75)
I would be happy to perform blood flow restricted exercise on my own (0 = strongly disagree, 5 = strongly agree)	3 (3.5)
Blood flow restricted exercise would improve my quality of life (0 = strongly disagree, 5 = strongly agree)	3 (2)
Blood flow restricted exercise looks scary (0 = strongly disagree, 5 = strongly agree)	1 (3.5)
I am not fit enough to complete blood flow restricted exercise (0 = strongly disagree, 5 = strongly agree)	1 (3)
Blood flow restricted exercise looks fun (0 = strongly disagree, 5 = strongly agree)	3 (2)

IQR = interquartile range

Part Two:

A total of 12 participants completed the intervention (female = 11; age = mean 58.3 [SD 5.7] years; height = mean 165.5 [SD 7.3] cm; mass = mean 81.0 [SD 20.4] kg; BMI = mean 29.6 [SD 7.3] kg/m^2).

Mean AOP was 120.0 (SD 16.9) mmHg for the upper limb, and 180.4 (SD 28.6) mmHg for the lower limb.

Primary outcome measures

All measures of strength increased significantly across the intervention period, with moderate and large effect sizes suggesting meaningful changes from baseline (Table 5; Figure 1). There was a significant and large improvement in walking speed when performed at a normal speed, but no change observed when walking as fast as possible. Of the perceptual measures, participants reported a significant reduction in perceived pain as indicated by the RAPS (Figure 1), and improved perceptions in wellness as indicated by the HAG-DI wellness question (Table 5). There were no changes in self-reported quality of life or functional capacity.

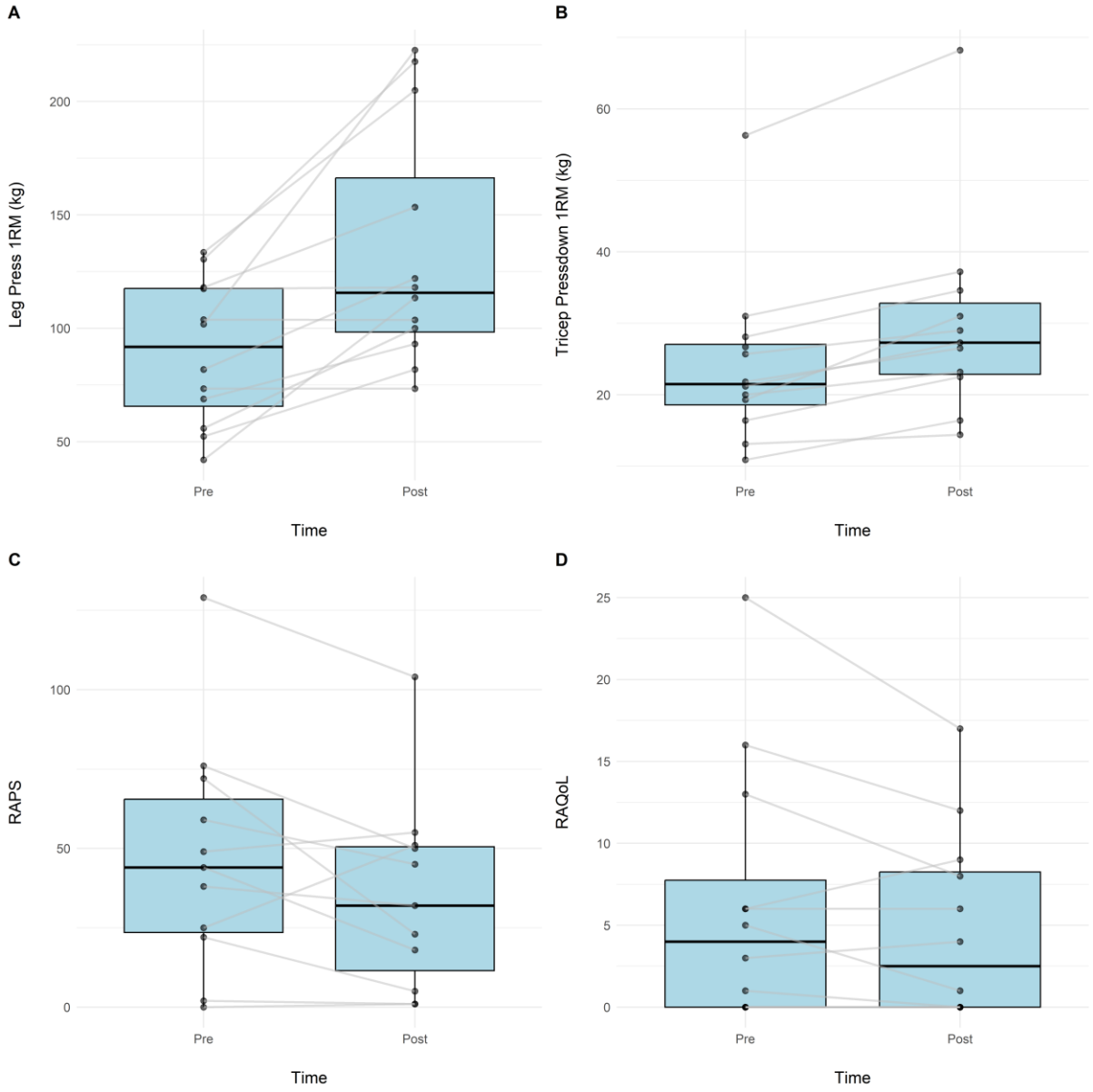

Figure 1: Pre and post intervention changes in A) Leg press strength, B) Tricep pressdown strength, C) rheumatoid arthritis pain scale (RAPS) score, and D) rheumatoid Arthritis Quality of Life (RAQoL) questionnaire.

Table 1: Changes in primary outcomes pre- and post- intervention (pre and post measures presented as mean (SD); change score presented as mean difference (95% CI); effect size estimate presented as *d* (95% CI)).

Outcome	**Pre**	**Post**	**Change**	**P=**	***d*=**	**Effect size descriptor**
Mass (kg)	81.0 (20.4)	80.9 (20.7)	-0.1 (-1.2, 1.1)	0.931	0.0 (0.0, 0.0)	*Trivial*
Arm circumference (mm)	338.3 (46.0)	338.2 (46.1)	-0.1 (-2.4, 2.0)	0.883	0.0 (0.0, 0.0)	*Trivial*
Thigh circumference (mm)	597.9 (94.8)	595.4 (94.6)	-2.5 (-8.2, 3.2)	0.391	0.0 (-0.1, 0.0)	*Trivial*
Handgrip right (kg)	28.6 (6.2)	30.2 (6.7)	1.6 (-0.0, 3.3)	0.057	0.3 (-0.3, 0.8)	*Small*
Handgrip left (kg)	24.8 (5.9)	26.5 (6.7)	1.7 (0.1, 3.4)	0.042*	0.3 (-0.3, 0.9)	*Small*

Leg press 1RM (kg)	89.9 (31.7)	133.7 (53.3)	43.7 (23.3, 64.2)	<0.001*	1.4 (-1.4, 4.2)	*Large*
Hamstring curl 1RM (kg)	33.2 (12.0)	43.5 (15.3)	10.3 (6.3, 14.3)	<0.001*	0.9 (-0.9, 2.6)	*Large*
Knee extension 1RM (kg)	32.8 (15.2)	48.5 (20.4)	14.7 (10.4, 18.9)	<0.001*	1.0 (-1.0, 2.9)	*Large*
Tricep pressdown 1RM (kg)	24.2 (11.7)	30.0 (14.4)	5.8 (4.2, 7.9)	<0.001*	0.5 (-0.5, 1.5)	*Moderate*
Bicep curl 1RM (kg)	22.5 (6.4)	29.9 (9.6)	7.4 (3.9, 11.0)	<0.001*	1.2 (-1.2, 3.5)	*Large*
Normal gait speed (s)	3.48 (0.42)	3.11 (0.37)	-0.36 (-0.58, -0.15)	0.001*	-0.9 (-2.6, 0.9)	*Large*
Fast gait speed (s)	2.45 (0.26)	2.40 (0.28)	-0.05 (-0.17, 0.07)	0.414	-0.2 (-0.6, 0.2)	*Trivial*
HAQ-DI	0.27 (0.43)	0.26 (0.47)	-0.01 (-0.11, 0.08)	0.823	0.0 (-0.1, 0.0)	*Trivial*
HAQ-DI pain	24.25 (23.20)	21.91 (21.28)	-1.73 (-13.76, 10.31)	0.778	-0.1 (-0.2, 0.1)	*Trivial*
HAQ-DI wellness	37.6 (36.5)	18.7 (25.7)	-18.9 (-35.9, -1.9)	0.029*	-0.5 (-1.6, 0.5)	*Moderate*
RAQol	6.3 (7.9)	4.8 (5.7)	-1.5 (-3.2, 0.2)	0.079	-0.2 (-0.6, 0.2)	*Trivial*
RAPS	46.9 (37.1)	35.0 (30.7)	-11.9 (-23.3, -0.6)	0.040*	-0.3 (-1.0, 0.3)	*Small*
RAPS pain	3.0 (2.3)	2.5 (2.2)	-0.5 (-1.6, 0.6)	0.371	-0.2 (-0.7, 0.2)	*Trivial*

Secondary outcome measures

Participants attended an average of 81.3% (SD 16.6%) of training sessions, and the mean RPE across the intervention was 5.1 (SD 1.6). Closed ended responses to the exit survey indicated that 100% of participants liked the program, 92% perceived it to be acceptable for them as an individual, and 83% perceived it to be suitable for individuals with RA. In conjunction with high measures of acceptability, 50% believed the program improved their RA, and 66% indicated that it required high effort to complete.

Table 2: Acceptability of BFR exercise intervention.

Question	**1**	**2**	**3**	**4**	**5**
Did you like or dislike the exercise program? (1= strongly dislike, 3 = no opinion, 5 = strongly liked)	0 (0%)	0 (0%)	0 (0%)	6 (50%)	6 (50%)
How much effort did it take to perform the exercise program? (1 = no effort at all, 3 = no opinion, 5 = huge effort)	0 (0%)	4 (33%)	0 (0%)	7 (58%)	1 (8%)
How fair is the exercise program for people with Rheumatoid Arthritis? (1 = very unfair, 3 = no opinion, 5 = very fair)	0 (0%)	0 (0%)	2 (17%)	6 (50%)	4 (33%)
The exercise program has improved my Rheumatoid Arthritis. (1 = strongly disagree, 3 = no opinion, 5 = strongly agree)	0 (0%)	1 (8%)	5 (42%)	3 (25%)	3 (25%)

It is clear to me how the exercise program will help improve my Rheumatoid Arthritis. (1 = strongly disagree, 3 = no opinion, 5 = strongly agree)	0 (0%)	1 (8%)	3 (25%)	5 (42%)	3 (25%)
How confident did you feel about performing the exercise program? (1 = very unconfident, 3 = no opinion, 5 = very confident)	0 (0%)	1 (8%)	1 (8%)	7 (58%)	3 (25%)
Performing in the exercise program interfered with my other priorities. (1 = strongly disagree, 3 = no opinion, 5 = strongly agree)	2 (17%)	8 (67%)	1 (8%)	1 (8%)	0 (0%)
How acceptable was the exercise program to you? (1 = completely unacceptable, 3 = no opinion, 5 = completely acceptable)	0 (0%)	0 (0%)	1 (8%)	5 (42%)	6 (50%)

Thematic analysis identified two main themes with respect to what participants enjoyed about the program. The first theme related to “strength progress”, with participants clearly stating that they enjoyed (and in some cases were motivated by) seeing their strength improve across the intervention period. The second related to “service”, with several participants stating that they enjoyed contributing to research that could help other individuals diagnosed with RA in the future.

Conversely, “inconvenience” was the only negative theme identified. Participants noted that attending exercise sessions around work and life commitments were at times challenging. Within this, two participants noted that more flexible training times would have been desirable to make attending sessions easier.

Discussion:

Part one of this study assessed beliefs about, and practices around, exercise in individuals with RA, while reporting on their willingness to engage in BFR-RT for the first time in the scientific literature. The second study examined the effects of BFR-RT on measures of upper and lower body strength, pain, and function, in a small sample of individuals diagnosed with RA, while also evaluating its acceptability.

Results from the survey indicated that more than two thirds of participants performed at least two sessions of physical activity per week. The most common duration of physical activity session was 31 – 40 minutes. Over half of those who exercised regularly included resistance training as part of their

normal exercise routine. Contrary, Sokka et al.[25] investigated physical inactivity in a large sample (N=5235) of RA patients and reported that only 29% engaged in regular physical activity. One possible explanation for this disparity may be related to selection bias.[24] The present study investigated exercise preferences as opposed to levels of physical activity in people with RA, and therefore, individuals that already undertake exercise were more likely to participant in our study. Another explanation may be that there has been a shift in exercise habits over time in the RA population. Data from the study by Sokka et al.,[25] was collected almost 20 years ago.

When considering general exercise preferences, more than 60% were both willing, and believed themselves capable, of conducting a formalized exercise program. Interestingly, this number increased to 87% if that exercise program was likely to improve their quality of life. This may highlight the importance of education when prescribing exercise to individuals with RA to improve uptake and adherence.[26] While less than half of the participants reported a preference for exercise location and supervision, the majority of those who did, indicated that exercising either at home with the guidance of a program, or at a gym facility under supervision, was preferable. Additionally, more than half indicated that they would prefer to conduct a combination of aerobic and resistance exercise that is of a low or moderate intensity. This may add support for the use of BFR-RT rather than traditional high load RT in this population, as it most commonly involves loads of less than 50% of an individual's 1RM,[8] and may be perceived as a more approachable form of exercise. Lastly, most participants suggested that exercising alone was preferred rather than in a group, and that performing three or fewer sessions per week would be desirable, which aligns with previous research reporting on the acceptability of a three day per week BFR-RT intervention in RA.[11]

Participants in the present study also indicated they were interested in conducting an exercise intervention that used BFR-RT, despite some concerns that it may cause pain or worsen RA symptoms. Importantly, most participants did not perceive BFR-RT to be unsafe, scary, or beyond their current levels of fitness, but would prefer if it was conducted under the supervision of an

exercise professional. These findings may suggest that BFR-RT will be a suitable method of exercise in those diagnosed with RA if it is delivered by a trained professional. It is also likely that BFR-RT interventions in RA are likely to be more well-received if they also consider the general exercise preferences described above.

The BFR-RT intervention in the present body of work was guided by the results of the survey in part one. As hypothesized, measures of strength increased significantly across the intervention period, a finding which has been observed previously in older adults at risk of mobility limitations,[27] and individuals diagnosed with osteoarthritis.[28] Importantly, these findings also align with two previous studies investigating the effects of BFR-RT in individuals with RA, which reported significant increases in lower limb strength after a four-[11] and 12-week[10] intervention. It is important to note that this is the first study to examine the effects of BFR resistance exercise on upper limb strength in individuals with RA, and include males diagnosed with RA (albeit only one was included). Results indicated small improvements in grip strength, in conjunction with moderate-to-large improvements in measures of upper limb strength. Considering the association between upper limb and grip strength, and functional capacity and quality of life in individuals with RA,[29, 30] this is a noteworthy finding, and may suggest that BFR-RT offers a suitable means of improving function in this population.

Improvements were also observed in participants normal gait speed. This aligns with previous research examining improvements in functional gait speed tests after BFR resistance exercise interventions in patients with knee osteoarthritis,[31, 32] myositis,[33] and older adults.[34] However, it is important to note that despite observing a large improvement in this test of function, there was no significant increase in self-reported functional capacity or quality of life. While the exact reason for this is unclear, it is important to note that the current cohort had notably high levels of function and life quality, and as such, simply may not have had much capacity to improve. If similar changes were seen in individual that were sarcopenic, it could have significant implications on their risk profile for

falling and other frailty related morbidity. It may also be that while the intervention was long enough to elicit improvements in strength and functional performance, it may not have been long enough to allow these to translate into improvements in perceived quality of life and function.

One important finding from this work is that BFR-RT caused a significant reduction in perceived daily pain, as measured by the RAPS. There is a large body of research indicating that both aerobic and resistance exercise can improve perceived pain in individuals with RA.[35] Furthermore, prior studies examining the effect of BFR resistance exercise in RA patients also reported significant improvements in self-reported measures of daily pain.[10, 11] This is noteworthy, as reductions in pain may contribute to increased physical activity levels, reducing disease burden, and leading to long-term improvements in health and quality of life.

Importantly, the BFR-RT intervention implemented in the present study was well received by participants, with 100% reporting they liked the program, and more than 80% believed it was suitable for other individuals with RA. This is supported by the high session adherence (>80%) observed across the intervention, which is comparable to other non-BFR[36, 37] and BFR[10, 11] resistance training interventions in people with RA. Despite this, it is important to note that two thirds of the participants reported that the program required high effort to complete, and the average RPE across the intervention was ~5 on the 10-point RPE scale, which aligns with the verbal descriptor "hard".[22] As such, it is possible that BFR-RT may not be suitable for all RA patients and may be best suited to those who have undergone a period of light exercise first to ensure they can tolerate the associated exercise demands.

A consistent theme reported by participants related to "strength progress," with participants stating that they enjoyed seeing their strength improve. Prior research examining progressive resistance exercise (i.e., resistance exercise with regular increases in load) have demonstrated considerable improvements in strength and function.[5, 38, 39] While this highlights the importance of gradually increasing exercise intensity to ensure continued improvements in strength, the results of the

present study also suggest that progressively increasing load may improve enjoyment, sensations of success, and potentially adherence, and should be a key component of any RA-specific exercise intervention.

Limitations

The results from part one was from a modest cohort of individuals with RA that presented with higher activity levels than observed in previous research. As such, it is unclear if these results pertaining to exercise preferences would generalize to less physically active individuals with RA. Similarly, most of the participants included in the sample were from Australia and America, who may not have exercise preferences that align with other countries. While results from part two supported the use of BFR-RT to improve strength and function in RA patients, the sample size was small and it was not compared to another intervention, either control or standard resistance training. It is therefore unclear as to whether BFR exercise is more effective, or more acceptable than other methods of training. Furthermore, the individuals within this cohort reported considerably better scores for quality of life and pain than observed in many prior research studies. It is unknown whether individuals more heavily affected by RA symptoms would find this intervention acceptable.

Conclusions:

The results of the present study indicate that BFR-RT is viewed positively as a health promoting intervention for individuals diagnosed with RA, and when delivered in a way that aligns with their preferences is acceptable, has high adherence, and has the capacity to improve strength and function and reduce perceived pain. Future research should consider examining the effects of such an intervention in people with RA who are sarcopenic and compare it to other more common modes of exercise.

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Declaration of interests:

The authors have no conflicts of interest to declare.

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