

Blood Flow Restricted Low-Load Resistance Exercise in Patients with Knee Pain: A Pilot Cohort Study.

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Abstract

Background: Blood flow restricted low-load exercise (LL-BFR) has been shown to elicit beneficial adaptations in muscle size and strength. The aim was to investigate if LL-BFR was feasible in patients with knee pain in a rehabilitation setting. A secondary objective was to investigate functional performance, knee muscle strength and patient-reported outcomes.

Methods: Data were collected from April-June 2018. Patients with knee Osteoarthritis or knee pain/functional loss after previous knee surgery were included. LL-BFR was performed twice weekly for 4-8 weeks as unilateral leg press with an individualized pressure (40% LOP) at 30% of one repetition maximum. Two protocols were tested (3-4 rounds, 30 second pauses). Patients were assessed by a 30-second chair-stand-test, Timed Up & Go, thigh circumference (TC), knee extensor strength (MVC) by handheld dynamometer, and completed the Knee Osteoarthritis Outcome Score (KOOS) score at baseline and follow-up.

Results: Adherence to training was 95.6%. Few and minor adverse events were observed. One patient dropped out due to pain aggravation in relation to baseline testing. Scores on three out of five KOOS subscales improved more than 10 points. Also, functional tests and MVC of the affected limb improved ($p \leq 0.05$).

Conclusion: The study indicates that supervised LL-BFR is feasible in patients with knee pain. At follow-up, the patients experienced subjective and functional gains.

Trial registration: Danish Data Protection Agency (Journal No 1-16-02-90-18).

Introduction

Patients suffering from knee pain related to orthopedic disorders often suffer from skeletal muscle disuse atrophy and weakness due to either pain-related alteration in their habitual activity level and/or postsurgical load restrictions. These degenerative muscular adaptations can affect the patient's ability to recover to their pre-injury physical activity levels. Thus, interventions targeting skeletal muscle hypertrophy and strength are warranted for these patients.

The effectiveness of heavy load resistance strength training (HRST) (training load $\geq 70\%$ of 1 repetition maximum: RM) to promote muscle hypertrophy and increase muscle strength is well documented (1, 2). Despite the evidence favoring HRST, it can be contraindicated in some patients due to postsurgical load restrictions and/or pain restrictions. To increase muscle mass and strength in these patients, alternative methods for promoting hypertrophy and increasing strength is required.

Resistance training with low loads (LL) ($\sim 30\%$ of 1 RM) performed with concurrent partial blood flow restriction (BFR) of the working limb (LL-BFR) has demonstrated to promote muscle hypertrophy and increase strength in both healthy- and patient populations (3, 4). Several mechanisms have been

suggested to be involved in the muscular adaptations seen with LL-BFR (5). The restrictive pressure applied to the limb during LL-BFR creates a hypoxic environment distal to the cuff. This hypoxic environment seems to cause a metabolic stress in working muscles that may lead to increased type II muscle fiber recruitment, increased inflammatory and endocrine response, cellular swelling, and elevated intramuscular inorganic phosphate, all of which have been demonstrated to mediate protein synthesis and satellite cell proliferation (4–6). Therefore, the combination of exercising with low loads and concurrent BFR seems attractive to apply in clinical settings in patients where HRST is contraindicated.

The main purpose of the project was to determine the feasibility of LL-BFR in patients suffering from knee pain due to orthopedic knee disorders in terms of adherence. Secondly, we investigated changes in functional performance, knee muscle strength and patient-reported outcomes.

Materials And Methods

Participants

The study was conducted at the Department of Physical and Occupational Therapy, and the Department of Orthopedic Surgery, Horsens Regional Hospital (HRH), Denmark.

The study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Central Denmark Region Committee on Biomedical Research Ethics (journal number 1-10-72-166-18). Approval from the Danish Data Protection Agency (Journal number 1-16-02-90-18) was obtained and all patients gave written informed consent prior to inclusion.

Data were collected from April-July 2018.

Inclusion criteria were: Knee pain due to an orthopedic disorder, age ≥ 18 years, and ability to adhere for ≥ 4 weeks of twice-weekly LL-BFR.

Exclusion criteria were: cardiovascular diseases, former stroke, unregulated hypertension (systolic > 180 mmHg and/or diastolic > 110 mmHg), wound healing dysfunctions, former thrombosis, traumatic nerve injuries, renal insufficiency, varicose veins, diabetes, smoking, spinal cord injuries and pregnancy.

Eligible patients were referred to the study by orthopedic surgeons and collaborating physiotherapists at HRH. Also, patients diagnosed with knee Osteoarthritis (OA) not eligible for knee prosthesis were recruited at two OA seminars held at HRH.

Intervention

The training protocols applied in this project were designed based on available evidence and in collaboration with strength and conditioning coaches with practical experience in applying LL-BFR. In this study, supervised LL-BFR was performed twice weekly, with a minimum of one day between each session,

for 4–8 weeks. Limb occlusion pressure (LOP) was determined as described by Ferraz et al. (7). LOP of the affected limb was determined at baseline for each patient.

Training Protocol

After 5 minutes of warm up on a stationary bike, patients performed one of two LL-BFR protocols (Table 1). Patients started each session on the affected limb. Subsequently, the non-affected limb performed the same amount of work as the affected limb (i.e. same cuff pressure, load). All sessions were supervised by a physiotherapist (SLJ) to ensure sufficient loading and progression.

Table 1: Exercise variables for the two BRFE protocols

Exercise variable	Description of the exercise variables		
PROTOCOL 1	All sessions		
Level of LOP	40%		
Sets	4		
Load intensity	30% 1RM		
Repetitions 1 st set	30		
Repetitions 2 nd set	15		
Repetitions 3 rd set	15		
Repetitions 4 th set	To volitional failure		
Contraction modes per repetition			
Concentric	No restrictions		
Isometric	0 seconds		
Eccentric	No restrictions		
Rest between repetitions	0 seconds		
Range of movement	maximum		
Rest between sets	30 seconds		
Rest between sessions	≥36 hours		
PROTOCOL 2	Session 1-3	Session 4-7	Session 8-X
Level of LOP	40%	40%	40%
Sets	3	4	4
Load intensity	30% 1RM	30% 1RM	30% 1RM
Repetitions 1 st set	20	20	30
Repetitions 2 nd set	10	10	15
Repetitions 3 rd set	To failure	10	15
Repetitions 4 th set	-	To failure	To failure
Contraction modes per repetition	No restrictions	No restrictions	No restrictions
Concentric	0 seconds	0 seconds	0 seconds
Isometric	No restrictions	No restrictions	No restrictions
Eccentric	0 seconds	0 seconds	0 seconds
Rest between repetitions	Maximum	Maximum	Maximum
Range of movement	30 seconds	30 seconds	30 seconds
Rest between sets	≥36 hours	≥36 hours	≥36 hours
Rest between sessions	The minimal possible load (10 kilo) is added when patients perform >15 repetitions in 3 rd set	The minimal possible load (10 kilo) is added when patients perform >15 repetitions in 4 th set	The minimal possible load (10 kilo) is added when patients perform >15 repetitions in 4 th set
Progression			

Table 1. Overview of the protocols used in the present study. A: no progression during the exercise period. B: Gradually progressing the training volume per session. Every third session, the volume was increased until reaching session number 8. From session 8, the training volume was kept constant.. LOP: Limb

occlusion pressure; RM: Repetitions Maximum. The load was increased if the patients were able to perform more than 15 repetitions in the last set.

Outcomes

Adherence

At the first visit, the patients declared how many weeks they intended to participate which were used to calculate the adherence. Acceptable adherence to training was not defined *a priori*.

Descriptive measurements

Bodyweight, age, gender, and referring diagnosis were registered.

Baseline and follow-up tests

Prior to the physical tests at baseline and follow-up, patients completed the Knee Osteoarthritis Outcome Score (KOOS). KOOS is a patient-administered, knee-specific questionnaire comprising five subscales; Pain, Symptoms, activities of daily living (ADL), Sport & Recreation, and Knee-Related QoL (8). KOOS is responsive to change following non-surgical and surgical treatments of the knee (8).

Baseline tests were performed on the same day as the first LL-BFR session. Follow-up tests were performed on a separate day (~ 3 days after) after the last LL-BFR session.

The physical tests were executed chronologically as listed below:

Thigh circumference (TC) was measured with tape measure 10 cm above apex patella in supine on both limbs (9).

30-Seconds Chair Stand Test (30 s-CST) was used to determine the number of sit-to-stand repetitions a patient was able to complete within 30 seconds (10). The 30 s-CST was used to indicate lower limb strength and functional performance (10).

Timed Up & Go (TUG) was used to determine functional mobility and assess the time required for patients to stand from a chair (seat height 43 cm), walk around a tape mark 3 meters away, and sit onto the chair at return (11).

Maximum isometric contraction of the knee extensors (MVC Knee) was measured on both limbs with a hand-held dynamometer (HHD) (JTech Commander PowerTrack Muscle Dynamometer MMT, USA) as previously described in detail by Koblbauer et al. (12). Measurements were performed with the patient sitting on an examination table with knees and hips positioned at 90° flexion, and the HDD fixed with a rigid belt to the examination table (12).

1 Repetition maximum (1RM) leg press strength was estimated from a 5RM leg press test on the injured limb (13). The load was increased with 10–20 kilo until the patient could perform ≤ 5 repetitions. Two minutes rest was given between trials.

1RM was calculated as: $1RM \text{ leg press (kg)} = (1,1307 \cdot [5RM \text{ leg press (kg)}]) + 0,66998$ (14).

If a patient failed to perform a 5RM leg press test, the initial exercise loads was set to 20 kg.

Statistical analysis

Descriptive statistics are presented as means (standard deviation: SD) or medians with range. Normality was evaluated by plotting the data. Changes from pre- to post-intervention were evaluated using paired *t*-tests provided the assumption of normally distributed data was fulfilled. The Wilcoxon signed-rank test was used in cases where data did not follow normal distribution. If the result of parametric and non-parametric tests gave the same results, the results of parametric tests were presented. The level of significance was set at 5% ($p \leq 0.05$). All statistics were performed in Stata (Stata/MP 16.1 for Windows). The purpose of the project was mainly to determine the feasibility of LL-BFR in patients suffering from lower limb injuries. Therefore, no power calculations for treatment effects were performed.

Results

Eligible patients

Twelve patients (six women) with a median age 50.3 (range 25–81) and a mean body mass of 79 ± 15 kg were included in the study. Eight (five women) patients completed the intervention (Fig. 1). Five patients completed protocol 1 and three patients completed protocol 2.

The average LOP was 192 ± 43 mmHg. The patients were diagnosed with knee OA ($n = 3$), conservative treated Anterior Cruciate Ligament (ACL) rupture ($n = 2$), ACL reconstruction ($n = 2$), patellar tendinopathy ($n = 2$), non-specific knee pain ($n = 1$), several unsuccessful knee surgeries due to meniscus resection ($n = 1$), and total knee arthroplasty ($n = 1$).

Adherence

Training adherence for the eight patients who completed their planned training period was 95.6% (8%). When related to the *a priori* adherence, eight of the 12 patients participated in $\geq 90\%$ of the planned exercise sessions. On average, each patient completed 11 sessions (range: 8–16).

Four patients dropped out (Fig. 1).

Patient-reported Outcomes

All KOOS subscales improved from baseline to follow-up. Statistically significant improvements after the intervention were seen in one KOOS subscale (Sport & Recreation), while trends towards a significant change were observed in two subscales (“Pain” and “Symptoms”) (Table 2).

Table 2
Outcomes

Outcome	n	Pre			Post			Mean Change	95% CI mean change			P
Thigh circumference: Affected limb (cm)	6	45.3	±	3.9	46.3	±	5.0	1	[-0.2	-	2.2]	0.08
Non-affected limb (cm)	5	47.5	±	4.6	47.5	±	5.1	0	[-1.0	-	1.0]	1.0
Timed Up & Go (sec):	7	11.4	±	16.4	9.4	±	13.1	-2	[-5.0	-	1.0]	0.02
30 seconds sit-to-stand test (repetitions):	7	15	±	4.0	17	±	4.0	3	[0.5	-	5.0]	0.03
Knee extension MVC: Affected limb (N/kg)	5	2.4	±	0.4	3.9	±	1.2	1.5	[0.5	-	3.0]	0.05
Non-affected limb (Nm/kg)	5	3.8	±	1.0	4.4	±	0.6	0.6	[-0.4	-	1.7]	0.2
5RM leg press: Affected limb (kg)	2	70.5	±	6.4	88.5	±	6.4	18	[18	-	18.0]	< 0.01
KOOS : Pain	6	66	±	19	77	±	20	11	[-1.5	-	23.9]	0.07
Symptoms	6	62	±	15	71	±	13	10	[-0.3	-	20.0]	0.06
Activities of Daily Living	6	68	±	28	74	±	23	6	[-3.7	-	16.4]	0.2
Sport & Recreation	6	23	±	20	43	±	26	19	[1.2	-	37.2]	0.04
Quality of Life	6	40	±	13	47	±	26	7	[-15.0	-	28.6]	0.1

Table 2. Baseline and follow-up outcomes are presented.; n/m: newton divided by body mass, strength is expressed as kilo; *: p<0.05

Functional performance and muscle strength tests

Data are presented in Table 2. Only five patients volunteered to perform pre- and post- testing of the knee extensor muscle strength (MVC knee) and only two patients were able to perform both baseline and follow-up assessment of the 5RM leg press strength without stopping prematurely due to fear of pain exacerbation (Table 2).

Discussion

The main finding of this study was that LL-BFR exercise twice weekly for 4–8 weeks was feasible in patients suffering from knee pain due to various orthopedic knee disorders. The mean adherence rate was on average 95.6% for the eight participants, when related to the *a priori* adherence calculation. All eight participants completed $\geq 90\%$ of the planned exercise sessions. Training adherence in the present study is comparable to Ferraz et al. (7) and Segal et al. (15) both reporting excellent adherence to LL-BFR in patients with knee OA. Additionally, we found that performing LL-BFR twice weekly without reaching concentric contraction failure, as done by the non-affected limb (work matched to the affected limb), was inferior to increase thigh circumference and knee extensor strength.

In the present study, one of the five KOOS subscales showed a significant improvement. However, a change of + 10 points was seen in three subscales (“pain”, “symptoms”, and “sport & recreation”). In general, the minimal important change is considered to be 8–10 points in each KOOS subscale (16), suggesting that the patients experienced a meaningful change from baseline to follow-up. Ferraz et al. (11) also demonstrated significant changes in patient-reported outcomes (WOMAC pain, stiffness and Physical activity) after 12 weeks of LL-BFR, suggesting that longer and more intensive training periods seem necessary to further improve patient reported outcomes.

The association between quadriceps muscle strength and functional performance is well-documented (17–19). Hence, it is crucial for elderly and patients suffering from disuse atrophy and strength deficits to increase knee extensor strength (17–19). In the present study, MVC knee increased for both legs. However, the strength increment of the affected limb (62%, $p = 0.05$) was higher than the non-affected limb (15%, $p = 0.2$), suggesting that LL-BFR protocols performed to volitional failure add strength gains. Increments in MVC knee after a period of LL-BFR have been demonstrated in several studies (20, 21).

In line with strength increments, functional performance assessed by 30-sec CST and TUG tests improved significantly in this present study. Improvements in 30-sec CST after 36 sessions LL-BFR was shown by Ferraz et al.(7), while Ozaki et al. demonstrated a faster TUG performance in old adults after 10 weeks of BFR walk training (4/weekly) (20). Thus, our results, combined with findings from other studies utilizing BFR exercise methods, indicate that functional performance can be improved with a minimal mechanical stress on the musculoskeletal system.

Strengths and limitations

This study is limited by the heterogeneous group of patients, the lack of a control group and the small sample size. The small sample size resulted in insufficient statistical power to detect changes. We cannot conclude if changes reflect the efficacy of LL-BFR or a result of participating in a physiotherapy-supervised training program. Also, we did not predetermine an acceptable adherence before starting the pilot project, hence, limiting our interpretation of the adherence. However, when comparing the adherence rate to other LL-BFR studies (7, 15), it seems that our patient population exhibited a high adherence to LL-BFR. Additionally, two different protocols were tested resulting in some variations in the total amount of work performed by the patients. However, all patients performed the exercise to failure, making the endpoint for each protocol identical. A strength of the present study was that all patients trained with an individualized restrictive pressure, hence increasing the safety and unifying the exercise stimulus to all participants.

Assessment of pain exacerbation during training was not included in this study. Thus, the amount of knee discomfort during training remains unknown. We did, however, not register any dropouts due to LL-BFR-related pain aggravation which suggests that LL-BFR was tolerable for patients involved in this project. At baseline, seven patients were able to perform the 5RM test while only two patients performed the test at follow-up. This might reflect a fear of pain aggravation and suggest that the patients included in the present study may not have been able to perform HRST.

Conclusion

This pilot study indicates that supervised LL-BFR is feasible in patients with knee pain due to a variety of orthopedic knee disorders. Improvements in KOOS subscales, muscle strength and functional performance are seen, but this needs to be confirmed in a homogenous population in a well-powered future randomized controlled trial.

Abbreviations

HRST: heavy load resistance strength training

RM: repetition maximum

LL: Resistance training with low load

BFR: Blood flow restriction

LL-BFR: Resistance training with low loads and partial blood flow restriction

HRH: Horsens Regional Hospita

OA: knee osteoarthritis

LOP: limp occlusion pressure

SLJ: Stian Langgård Jørgensen

KOOS: Knee Osteoarthritis Outcome Score

ADL: Activities of daily living

TC: Thigh circumference

30s-CST: 30-Seconds Chair Stand Test

TUG: Timed Up & Go

MVC knee: Maximum isometric contraction of the knee extensor strength

HHD: Hand held dynamometer

Kg: Kilo

SD: Standard deviation

ACL: Anterior cruciate ligament

Declarations

Ethical approval and consent to participate

Ethical approval was obtained from the Central Denmark Region Committee on Biomedical Research Ethics (journal number 1-10-72-166-18). A written informed consent was obtained before enrolment of participants, and the rights of participants were protected.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Declaration of Conflicting Interests

The Authors have no conflicts of interest.

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Authors' contribution

Concept/idea/research design: all authors

Competing interests

The authors reports no competing interests

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Figures

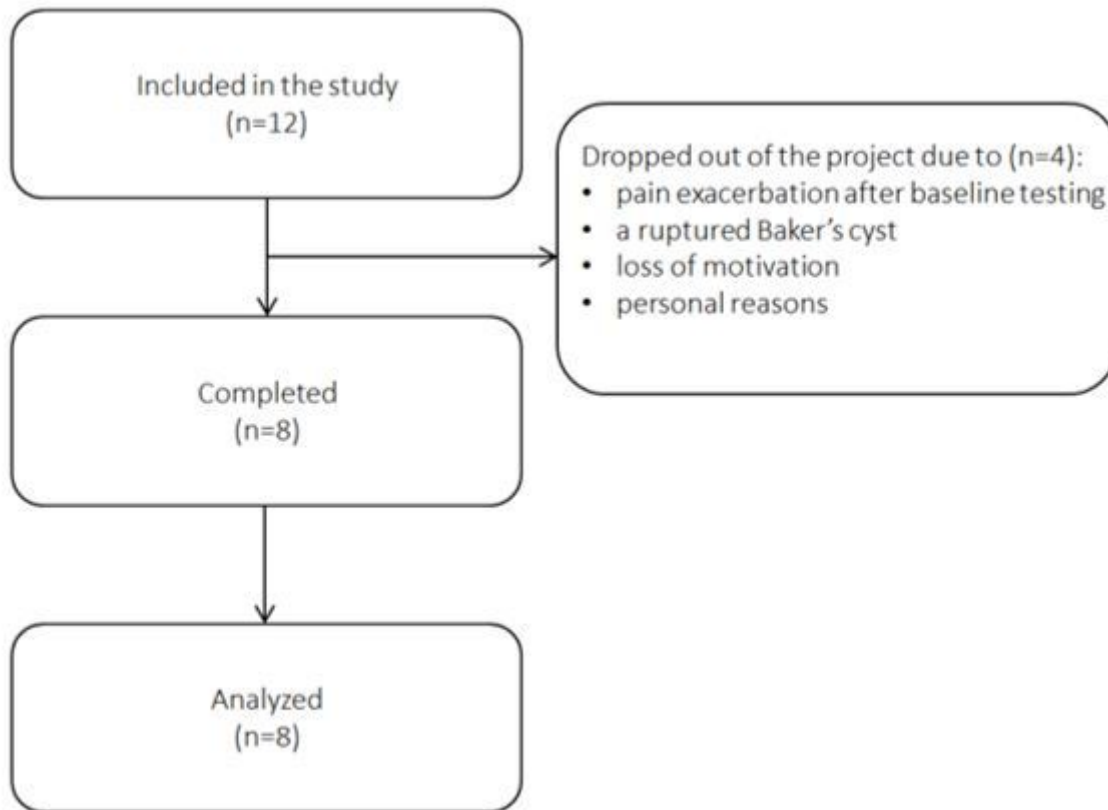


Figure 1

Flow chart of the included patients and final number of subjects available for analysis

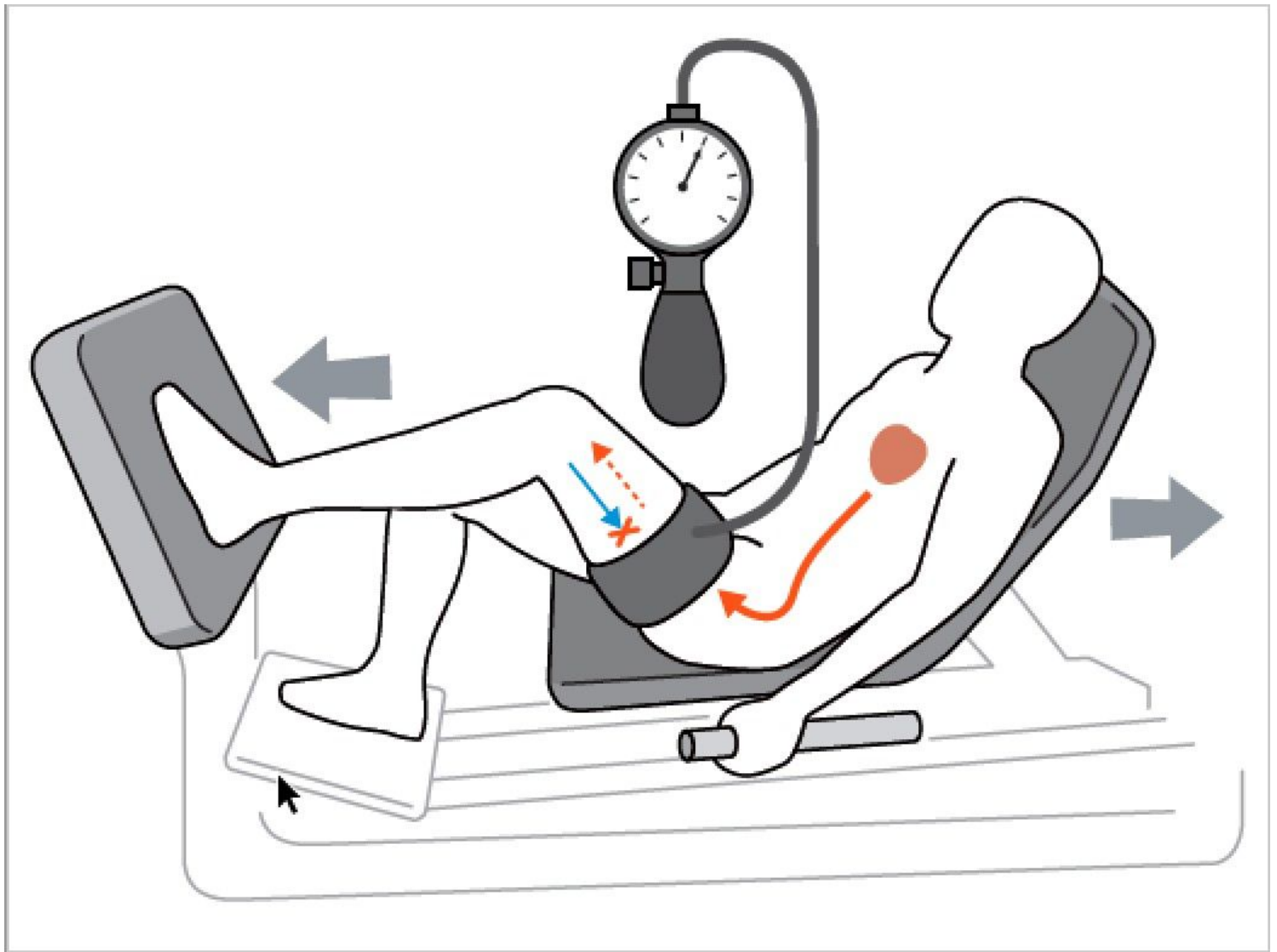


Figure 2

To accommodate a cuff pressure of 40% of LOP, the cuff was inflated while subject sat in the leg press machine with the working limb on the plate. Between rounds, the working limb rested in this same position. During exercise, the manometer was removed from the cuff.

Supplementary Files

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- [CONSORTextensionforPilotandFeasibilityTrialsChecklist.doc](#)