ORIGINAL REPORT

BLOOD FLOW RESTRICTED WALKING IN ELDERLY INDIVIDUALS WITH KNEE OSTEOARTHRITIS: A FEASIBILITY STUDY

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Objective: To investigate whether blood flow restricted walking exercise is feasible in patients with knee osteoarthritis, and to examine changes in functional performance and self-reported function.

Design: Feasibility study.

Patients and methods: Fourteen elderly individuals diagnosed with knee osteoarthritis participated in 8–10 weeks of outdoor walking (4 km/h, 20 min/session, 4 times/week) with partial blood flow restriction applied to the affected leg. Adherence, dropouts and adverse events were registered. Timed Up and Go test, 30-s sit-to-stand performance, 40-m fast-paced walk speed, stair-climbing and Knee Osteoarthritis Outcome Score were assessed pre- and post-training.

Results: Nine participants completed the intervention, while 5 participants withdrew (4 due to intervention-related reasons). In non-completing participants baseline body mass index (BMI) ($p=0.05$) and knee pain ($p=0.06$) were higher, while gait ($p=0.04$) was lower. Considering completed case data, the training-adherence rate was 93%, while mean knee pain in the affected leg was 0.7 on a numerical rating scale of 0–10. Functional performance improved, while self-reported function remained unchanged.

Conclusion: Blood flow restricted walking exercise appeared feasible in patients with knee osteoarthritis. Participants who completed the intervention protocol demonstrated improvements in functional performance, with no changes in self-reported function.

Key words: knee osteoarthritis; blood flow restriction exercise; physical functional performance; knee osteoarthritis outcome score; walking; ischaemia; occlusion; rehabilitation.

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Knee osteoarthritis (OA) is among the 10 most prevalent chronic conditions in Denmark (1). Patients with knee OA experience joint pain, stiffness and functional disability (2). Typically, knee extensor muscle atrophy and strength deficits (3, 4) occur in patients with knee OA, which has been associated with reduced functional performance (5, 6). Consequently, the loss of functional performance with knee OA may reduce patients’ quality of life (QOL) (7–9). To increase or maintain functional performance and QOL, it becomes important to engage individuals with knee OA in exercise programmes that they can tolerate.

Heavy-load resistance training (HRT) (>70% of 1 repetition maximum) has been shown previously to improve lower limb muscle strength and functional performance in individuals with knee OA (10–12). However, the heavy exercise loads applied in HRT may be contraindicated in some individuals with knee OA due to exacerbated knee pain, which can limit adherence.
to HRT intervention (10, 13). Thus, more tolerable, yet effective, exercise regimes are warranted for this particular population.

Low-load resistance exercise performed with concurrent blood flow restriction (BFR) typically achieved by means of pneumatic cuff compression applied proximally around the exercising limb has repeatedly demonstrated significant improvements in skeletal muscle mass, strength, and functional performance in both healthy, elderly individuals, and clinical populations (10, 14–19). BFR training is known to create a hypoxic myocellular environment in the working limb, which is suggested to give rise to elevated levels of metabolic stress that may lead to increased type I muscle fibre recruitment (20), myocellular swelling (21), and elevated intramuscular concentrations of metabolites (22) accompanied by increased synthesis of muscle protein. Furthermore, BFR-training has been observed to stimulate the proliferation of myogenic stem cells (satellite cells), which potentially improves the regenerative capacity of the muscle tissue and contributes to the marked muscle hypertrophy observed with this type of training (23). Concurrent cuff compression during walking (BFR-walking) has been shown to be a feasible exercise regime in healthy elderly individuals (19, 24). Furthermore, BFR exercise has been reported to cause substantial increases in lower limb muscle strength (6–22%) and muscle mass (3–5%) in response to 6–10 weeks intervention (14, 19). BFR exercise may also lead to marked increases in physical function in individuals over the age of 60 years (24).

Knee joint loading forces during horizontal walking are lower and thus potentially more tolerable to some OA patients than the loads applied with HRT. Consequently, the application of BFR-walking may represent a feasible and effective training modality for individuals with knee OA. Previous investigations have reported BFR exercise as safe when correctly and cautiously implemented (18, 25–29). However, only a single case study has investigated functional performance following BFR-walking in an individual with knee OA (30). Therefore, the aim of the current study was to investigate whether BFR-walking exercise is feasible in patients with knee OA in terms of adherence, drop-outs, adverse events, and knee pain responses to the training intervention. A secondary purpose was to examine changes in functional performance and self-reported knee joint function following BFR-walking exercise.

**MATERIALS AND METHODS**

**Participants**
Fourteen elderly individuals (70.4 ± 6.3 years of age) diagnosed with knee OA volunteered to participate in the feasibility study. The participants were recruited from a senior centre between 27 January 2020 and 30 January 2020. Individuals were considered eligible for participation if they were at least 60 years old, clinically diagnosed with knee OA, and radiographically verified. Exclusion criteria included: (i) previous knee replacement surgery (both knees), (ii) musculoskeletal or neurological diseases or impairments that could potentially be expected to hamper the execution of outdoor walking (4 km/h), (iii) previously experienced thrombosis events, (iv) cardiovascular problems without using prescribed medication for regulation of their conditions.

All participants were informed about the study procedures and signed a written informed consent in accordance with the Declaration of Helsinki. The Central Denmark Region Committee on Biomedical Research Ethics concluded that the study was exempt from ethical notification and approval (case number 1-10-72-148-19). The project was registered at the Danish Data Protection Agency (case number 1-16-02-51-20).

Baseline characteristics of the study participants are listed in Table I.

**Intervention**
BFR-walking exercise was completed 4 times/week, with 1 supervised session and 3 non-supervised sessions each week. Training sessions consisted of 20-min outdoor walking performed at moderate walking speed (~4 km/h) with concurrent BFR applied to the affected leg (BFR-leg). In case of bilateral OA, the leg most severely affected by knee OA (based on the participant’s experience with OA symptoms and disability) was chosen as the affected leg. Participants used either (i) the Endomondo App (Under Armour, Baltimore, Maryland) for smartphones to track time, speed and distance covered during exercise, or (ii) completed a predefined walking-route planned by the principal author (NP). Walking speed and session duration remained constant throughout the training period. In addition, the participants were instructed to continue their regular and habitual physical activities during the intervention period.

Before each training session, the participant placed the cuff around the most proximal portion of the thigh and inflated the cuff in a neutral standing position. During exercise the cuff pressure remained constant. BFR to the exercising limb was maintained during the entire 20-min walk. The pressure was released immediately after cessation of exercise. To ensure constant cuff pressure during walking, the participants were instructed to evaluate and adjust the occlusion pressure after 10 min of walking.

Due to restrictions during the COVID-19 pandemic, the supervised training sessions ceased early into the initiation of BFR-walking. A route diagram
Blood flow restricted walking

Table I. Baseline characteristics of study participants

| Characteristics        | All participants (n = 14) | Intervention group (n = 9) | Withdrawals (n = 5) | p-value |
|------------------------|---------------------------|---------------------------|---------------------|---------|
| Sex, women, n          | 12                        | 7                         | 5                   | 0.505   |
| Age (yrs)              | 70.4 ± 6.3                | 70.4 ± 6.0                | 70.4 ± 7.4          | 0.990   |
| Height (cm)            | 167 ± 9                   | 170 ± 9                   | 161 ± 6             | 0.075   |
| Body mass (kg)         | 85.8 ± 16.2               | 83.7 ± 18.1               | 89.7 ± 13.0         | 0.527   |
| BMI (kg/m²)            | 31 ± 5                    | 29 ± 5                    | 34 ± 4              | 0.051   |
| Disease duration (yrs) | 6.1 ± 5.2                 | 5.9 ± 6.0                 | 6.5 ± 4.0           | 0.836   |
| Bilateral knee OA, n   | 10                        | 6                         | 1                   | 1.000   |
| AOP (mmHg)             | 240 ± 38                  | 229 ± 38                  | 260 ± 32            | 0.149   |
| 60% AOP (mmHg)         | 151 ± 39                  | 138 ± 23                  | 176 ± 51            | 0.075   |
| Physiological function |                           |                           |                     |         |
| 30STS (reps)           | 10 ± 2                    | 10 ± 2                    | 10 ± 3              | 0.875   |
| TUG (s)                | 9.7 ± 1.3                 | 9.3 ± 1.4                 | 10.2 ± 1.1          | 0.237   |
| 40MWT (m/s)            | 1.48 ± 0.18               | 1.55 ± 0.13               | 1.36 ± 0.19         | 0.044   |
| 11-step SCT (s)        | 16.3 ± 6.5                | 13.9 ± 2.4                | 20.8 ± 9.4          | 0.181   |
| KOOS (score 0–100)     |                           |                           |                     |         |
| Pain                   | 65 ± 19                   | 72 ± 15                   | 53 ± 19             | 0.057   |
| Symptoms               | 77 ± 17                   | 80 ± 19                   | 73 ± 14             | 0.500   |
| ADL                    | 67 ± 20                   | 76 ± 12                   | 50 ± 22             | 0.053   |
| Sport                  | 28 ± 24                   | 34 ± 26                   | 15 ± 13             | 0.149   |
| QOL                    | 44 ± 17                   | 49 ± 10                   | 33 ± 23             | 0.179   |

BMI: body mass index; Yrs: years since diagnosis; AOP: Arterial occlusion pressure; 30STS: 30 seconds chair-stand test; TUG: Timed Up and Go; 40MWT: 40m fast-paced walk test; 11-step SCT: 11-step stair-climb test; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: activities of daily living; QOL: quality of life. *p-values represent comparisons between the Intervention group and the Withdrawal group. *p < 0.05, **p < 0.10.

Blood flow occlusion

Arterial occlusion pressure (AOP) of the affected leg was determined with participants seated on an examination table in a resting state. An 11-cm wide pneumatic cuff depicting the individual intervention activities is shown in Fig. 1.

Baseline testing & Initiation of BFR-walking

- Group 1 (n = 5): 10 weeks of BFR-walking incl. 5 weeks with supervised sessions
- Group 2 (n = 9): 9 weeks of BFR-walking incl. 4 weeks with supervised sessions
- Group 3 (n = 1): 6 weeks of BFR-walking incl. 2 weeks with supervised sessions

One participant completed eight weeks followed by two weeks without training

Outcome measures

All participants underwent baseline testing 1 week prior to the first exercise session. Participants were re-tested (post-testing) after 8–10 weeks of BFR-walking exercise (4 times weekly), in the week following completion of their final training session. Test procedures are elaborated below.

Feasibility and adherence

After each training session, participants registered total walking-time into a designated training diary, along with distance covered, cuff pressure, knee pain in the BFR-leg during walking (numerical rating scale (NRS) 0–10, scores of 10 representing maximal intolerable pain), and perceived exertion in the BFR-leg during walking (NRS 0–10, score of 10 representing maximal and complete exertion). Also, the participants were instructed to report any adverse events or complica-
tions related to the cuff application during training. Adherence was calculated as:

\[
\text{Adherence} = \frac{\text{Total training sessions completed (number of sessions)}}{\text{Total weeks completed (number of weeks)}} \times 100
\]

**Functional performance**

Physical performance was assessed before and after the intervention period using the 30-s chair sit-to-stand test (30STS), Timed Up and Go (TUG), 40-m fast-paced walking (40MWT) and stair-climbing (11-step SCT) (Fig. 2). All tests are characterized as reliable and valid performance tests (5, 34). A description of each test including equipment and procedures are described by Tolk et al. and Dobson et al. (34, 35). The tests were intended to assess functional and balance performance and lower body strength, and have all been extensively used to test individuals with knee OA (5, 6, 24).

**Self-reported knee function**

Knee joint pain, knee-related symptoms, function in daily living (ADL), function in sport and recreation and QOL were assessed using the Knee Injury and Osteoarthritis Outcome Score survey (KOOS). The KOOS questionnaire has been demonstrated as a reliable and valid tool for evaluating perceived knee function and associated problems in persons with knee OA (36, 37).

**Statistical analysis**

Microsoft Excel (version 16.36, Microsoft Corporation, USA) and SPSS statistics (version 26, IBM Corporation, USA) were used to compute the data. The Shapiro–Wilk test was performed to assess if data were normally distributed. Descriptive statistics are presented as group means ± SD and 95% confidence interval (95% CI) unless otherwise stated.

To examine any changes in baseline data between the group of participants who completed the intervention period (n=9) and the withdrawals (n=5) an independent t-test or the Mann–Whitney U test was applied, depending on whether the data was normally distributed. Furthermore, changes from pre- to post-intervention, as well as development in knee joint pain, and perceived exertion during BFR-walking exercise, were examined using paired t-testing. Wilcoxon signed-ranked testing was used in cases where data did not follow a normal distribution.

**RESULTS**

**Baseline characteristics**

Nine participants completed the BFR-walking training protocol and were evaluated at post-testing, while 5 participants withdrew from the study during the intervention period. A number of differences were noted between the 2 groups (Table I). Baseline measurements demonstrated that participants who withdrew from the study showed: (i) slower walking speed during the 40MWT (p = 0.044), (ii) a tendency to elevated perceived knee pain (p = 0.057), (iii) a tendency to higher body mass index (BMI) (p = 0.051), and (iv) a tendency to worse self-reported ADL (p = 0.053) in comparison with participants who completed the intervention protocol.
Feasibility and adherence
In total, 8–10 weeks of BFR-walking exercise was performed by 9 participants. Six participants completed 9 weeks training, 2 participants completed 10 weeks of training, and only 1 participant completed 8 weeks of BFR-walking training. They completed a mean of 34±4 training sessions per participant, and the mean±SD adherence to the training sessions was 92.8±9.2 % considering completed case data.

The mean±SD (min–max range) cuff pressure during BFR-walking was 137±23 (96–173) mmHg. Target cuff-pressures were maintained throughout the study period in 7 of the 9 participants, but had to be reduced in 2 participants (to reach levels corresponding to ~ 50% AOP) due to lower limb discomfort during BFR-walking. The first participant experienced discomfort in the lower leg due to varicose veins, which, according to a consultant vascular surgeon assessment, was not deemed dangerous or harmful to the person. However, discomfort in the lower leg did occur, and thus the cuff pressure was reduced for the final 2 weeks of exercise. The second participant experienced a leg discomfort of unknown cause in the last 2 weeks of exercise, which could not be related directly to the BFR-walking training. Despite 2 participants experiencing discomfort from the cuff pressure during BFR-walking, the mean±SD perceived exertion in the BFR-leg was rated 3.4±2.1 on the 0–10 point NRS.

The mean±SD knee joint pain during BFR-walking was 0.7±0.9 on the 0–10 point NRS.

Drop-outs
Five participants withdrew from the study during the intervention period due to; (i) exercise-induced discomfort when using the cuff (n = 3), (ii) exacerbated knee pain during the BFR-intervention period (n = 1), (iii) pain in the contra-lateral knee joint (n = 1) (unknown relation to BFR-walking exercise). It should be noted that 1 of the participants who withdrew from the study due to limb discomfort was excluded from the study, since she could not manage to safely apply the cuff at home according to the desired method in the current study.

Functional performance
Signs of improved functional performance were observed after the period of BFR training (Fig. 3) (p < 0.05) for 30STS (+16%), TUG (−8%) and 40MWT (+5%) (Table II). In contrast, the 11-step SCT test remained unchanged (+0.7% n.s.) (Table II).

Self-reported knee function
KOOS subscale scores remained unchanged following the period of BFR-walking (Table II).

DISCUSSION
This is the first study to examine the feasibility of BFR-walking exercise in elderly individuals with knee OA. The main findings were that participants who completed 8–10 weeks of BFR-walking exercise demonstrated; (i) high adherence to training, (ii) minimal knee pain and exertion during BFR-exercise, (iii) significant improvements in functional performance (30STS, TUG and 40MWT); however, (iv) without demonstrating any changes in KOOS subscale scores. Notably, 5 participants withdrew from the study, of which 4 participants experienced intervention-related adverse events, such as exacerbated knee pain in the BFR-leg or discomfort from the cuff during BFR-walking.

Feasibility and adherence
Participants who completed the intervention period demonstrated an exercise adherence of 93% to the scheduled training sessions, which is in line with previous study reports in comparable populations (OA) and exercise conditions (resistance training intervention with and without BFR) (10). Furthermore, perceived knee pain-scores and exertion in the BFR-leg were low (NRS 0.7 and 3.4, respectively). These results indicate that the application of a pneumatic cuff during the exercise was tolerable for the majority of the present group of OA patients and did not contribute to exacerbated knee pain nor lead to increased levels of discomfort.

However, 4 participants experienced adverse events during the BFR-walking intervention period, which led to withdrawal from the current study. A number of differences existed between the participants who completed the intervention period and participants withdrawing from the study (cf. Table I). These differences might have been, at least in part, contributing to the observed withdrawal of participants. Thus, it could be speculated that the extent of knee pain may have negatively affected the adherence to exercise. Furthermore, differences such as slower 40-m walking speed and a tendency to lower self-reported ADL were found in withdrawing compared with completing participants, which may have affected at least some participants’ ability to complete the intervention period. Thus, walking continuously for 20 min may be difficult for some patients with knee OA. Alternatively, BFR-walking, performed as either interval-based training or simply reducing the walking time to 10 min have previously been demonstrated to improve functional performance (24). These BFR-walking exercise protocols would perhaps increase the overall adherence to the study.

As reported by Gomes-Neto et al. (2015) obese elderly people with knee OA demonstrate reduced functional
performance, higher levels of knee pain and greater difficulty in performing everyday tasks compared with non-obese age-matched elderly people with knee OA (38). Thus, it is possible that a higher BMI, as seen in the current group of withdrawing participants, might have complicated their ability to complete the BFR-walking exercise.

Notably however, a majority of the current participants experienced BFR-walking as a tolerable and feasible exercise paradigm, which could be performed with a relatively high exercise adherence and with minimal knee pain and discomfort. Nonetheless, the current data suggest that individuals with high BMI and high degrees of perceived knee pain and low ADL function may benefit less from this type of exercise, as manifested by events of exacerbated knee pain and discomfort from the occlusion cuff.

### Table II. Functional performance and Knee Injury and Osteoarthritis Outcome Score (KOOS) subscale scores pre-and-post 8–10 weeks of blood flow restricted (BFR)-walking exercise

|                     | Pre-test Mean | [95% CI]   | Post-test Mean | [95% CI]   | Change Mean | [95% CI] | p-value |
|---------------------|---------------|------------|----------------|------------|-------------|----------|---------|
| **Functional performance tests** |               |            |                |            |             |          |         |
| 30STS (reps)       | 10            | [8.4, 11.1] | 11             | [10.2, 12.5]| 1.6         | [0.5, 2.6]| 0.008*  |
| TUG (s)            | 9.3           | [8.4, 10.3] | 8.6            | [8.0, 9.3] | -0.7        | [-1.3, -0.1]| 0.032*  |
| 40MWT (m/s)        | 1.55          | [1.47, 1.64]| 1.63           | [1.53, 1.73]| 0.07        | [0.03, 0.11]| 0.003*  |
| 11-step SCT (s)    | 13.8          | [12.3, 15.4]| 13.9           | [12.5, 15.4]| 0.10        | [-1.10, 1.31]| 0.847   |
| **KOOS subscales** |               |            |                |            |             |          |         |
| Pain               | 72            | [62, 82]   | 77             | [70, 85]   | 5.3         | [-3.2, 13.9]| 0.218   |
| Symptoms           | 80            | [67, 92]   | 81             | [73, 89]   | 1.2         | [-7.8, 10.2]| 0.778   |
| ADL                | 76            | [68, 84]   | 78             | [72, 85]   | 2.2         | [-5.0, 9.5]| 0.528   |
| Sport/Recreation   | 37            | [21, 52]   | 45             | [32, 58]   | 10.6        | [-6.0, 27.1]| 0.310   |
| QOL                | 49            | [43, 56]   | 48             | [38, 58]   | -1.4        | [-5.0, 7.9]| 0.642   |

30STS: 30 seconds chair-stand test; TUG: Timed Up and Go; 40MWT: 40-m fast-paced walk test; 11-step SCT: 11-step stair-climb test; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: activities of daily living; QOL: quality of life; 95% CI: 95% confidence interval. KOOS score 0 = extreme knee problems. Score 100 = no knee problems. *p < 0.05, Pre vs Post.
In the current study 8–10 weeks of BFR-walking exercise was accompanied by significant improvements in functional performance, assessed as 30STS (+16%), TUG (−8%) and 40MWT (+5%) in elderly individuals with knee OA. In contrast, stair walking performance remained unaltered following the period of training.

Improvements in functional performance have consistently been reported following BFR-walking exercise, which are in line with the current study data (14, 19, 24). Clarkson et al. (2017) demonstrated that 6 weeks of outdoor BFR-walking exercise (10-min sessions, 4km/h, 4 times a week) improved performance in 30STS (+28±6%), TUG (−12±2%), 6MWT (−9±1%) and the modified Queen’s College Step Test (+80±11%) in healthy elderly individuals (60–80 years). Likewise, Ozaki et al. (2011) demonstrated that 10 weeks of BFR treadmill walking exercise (20-min, 4.5km/h, 1.6°, 4 times a week) improved the performance in The Up & Go test (11%) and 30STS (21%) in healthy elderly individuals (57–73 years), while control subjects who performed regular walking without BFR experienced improvements only in the 30STS (8%).

The current study results combined with Clarkson et al. (2017) and Ozaki et al. (2011) indicate that BFR-walking exercise may represent an effective training modality to improve functional performance in elderly people, including individuals with knee OA.

Unsurprisingly, no changes in KOOS subscale scores were observed in the current study in response to 8–10 weeks of BFR-walking exercise, despite consistent improvements in functional performance. The lack of changes might be due to a ceiling effect of the KOOS scores. That is, a study by Steven-Lapsley et al. (2011) found a strong correlation between KOOS-Pain and KOOS-ADL scores in a group of patients undergoing total knee arthroplasty (39). KOOS was measured 2 weeks prior to surgery and 1-, 3- and 6-months post-surgery. KOOS-ADL and KOOS-Pain were continuously inter-related (r = 0.766–0.826), indicating a strong relationship between pain intensity and ability to perform ADL. These data suggest that participants’ perceived ability to perform given ADL-related activities may depend on perceived knee pain intensity. Therefore, given the relatively low levels of perceived knee pain observed at baseline, a ceiling effect on KOOS-ADL might have occurred in the present study. In line with this notion, the baseline KOOS subscale scores observed in the current study appeared to be higher compared with reference data reported previously in individuals with knee OA (40). Accordingly, the participants in this study might have difficulty improving their KOOS scores in general, due to already high levels of perceived knee function.

This study has a number of potential limitations. The absence of a non-exercising control group hinders determination of whether the BFR intervention was the direct cause of the concurrent improvements in functional performance. Furthermore, the small sample size gives rise to low statistical power in the pre-to-post comparisons. In addition, only 1 of 4 weekly training sessions were supervised and, during the period of COVID-19 restrictions, no on-site supervision was possible. Lastly, despite thorough education in applying the cuff proximally at the thigh, some participants experienced difficulties reproducing this procedure accurately, which could have influenced the effective occlusion pressure applied during BFR-walking.

There is a lack of evidence regarding the mechanisms behind increases in functional performance (including measures of muscle strength, hypertrophy and/ or neural drive) in response to BFR-walking exercise in patients with OA. Therefore, future studies examining the effect of BFR-walking on lower limb muscle strength, morphology and neuromuscular function in patients with knee OA seem highly relevant.
evidence on the effect of BFR-walking exercise in patients with knee OA.

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