Effect of low-intensity resistance training with blood flow restriction on functional status in knee osteoarthritis

Alvita Sari¹, I Putu Alit Pawana*, Ditaruni Asrina Utami¹, Soenarnatalina Melaniani²

ABSTRACT

Background: Knee osteoarthritis is a joint pathology with high prevalence, resulting from the increase of aging and obesity in the world population. Articular cartilage destruction can cause pain and eventually reduces activities of daily living and affects functional status in subjects with knee osteoarthritis. Exercise interventions in knee-OA aimed at increasing knee extensor muscle strength involve high-intensity resistance training but may result in joint pain due to high-compressive forces. Other alternative method includes low-intensity resistance training performed with blood flow restriction, a potential intervention for a patient who does not tolerate high loads due to lower mechanical stress. This study aims to determine the effects of blood flow restriction with low-intensity resistance training on the quadriceps for six weeks on functional status in knee-OA patients.

Methods: Twenty-eight patients aged 50-70 years old with knee-OA in Physical Medicine and Rehabilitation Outpatient Clinic Soetomo Hospital Surabaya were randomized into control and treatment groups. Both groups underwent a 6-week supervised training program consisting of LI-RT (30% 1-RM) two sessions/week. The treatment group received an additional application of blood flow restriction using a cuff on 1/3 of the upper thighs with 50 mmHg occlusion pressure. Both groups were assessed for functional status by self-reported WOMAC questionnaire before and after the protocol.

Results: Both training methods were able to reduce WOMAC pain and improve physical function subscales significantly, but WOMAC stiffness subscales only reduced significantly in low-intensity resistance training with blood flow restriction. There were no significant differences between groups for any domain from WOMAC, nor any significant differences between delta scores (all P > 0.05).

Conclusion: Low-intensity resistance training with and without blood flow restriction was similarly effective in enhancing functional status in subjects with knee osteoarthritis.

Keywords: blood flow restriction, functional status, knee osteoarthritis, quadriceps strength, resistance training, WOMAC score.

INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis. Pathologic processes of osteoarthritis are changes in joint structures and surrounding structures.¹ Osteoarthritis is a pathological condition affecting all joints with cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation.² The number of OA cases continues to increase along with increasing life expectancy and the prevalence of obesity in the world's population.³ Globally, the prevalence of knee OA reaches 16%, with an incidence of 203 per 10,000 individuals per year.⁴ OA cases occupy the second highest number of visits, around 6.6% or 720 patients in the Physical Medicine and Rehabilitation Outpatient Clinic at Dr. Soetomo Hospital in 2021.

OA based on radiological Kellgren Lawrence (KL) grade 2 represents definitive OA that is of clinical importance despite minimal severity. A cohort study from Muraki et al. on 2,282 subjects aged >60 years in Japan showed that grade 2 KL knee OA was significantly associated with knee pain in both men and women in the population. However, grade 3–4 KL showed a stronger relationship with knee pain, not only in men and women in all populations but also in all age strata.⁵,⁶,⁷

One factor that plays a significant role in the incidence of knee OA and the progression of joint cartilage damage is quadriceps muscle weakness. In patients with OA of the knee, there is a 15–38% quadriceps muscle strength deficit, which results in dynamic knee instability and physical disability.⁸ The presence of cartilage damage, inflammatory processes, and other tissue injuries around the joints in knee OA will trigger activation of Arthrogenic Muscle Inhibition, which will reduce the maximum activation ability of the quadriceps through neural inhibition.⁹ The quadriceps muscles are needed to bear the load on the knee joint and maintain stability while walking. The strength of the quadriceps muscles will decrease as people get old, and proprioception function will be disturbed so that the knee joint will work harder and become unstable, which results in more susceptibility to injury.¹⁰,¹¹

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¹Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
²Department of Epidemiology, Biostatistics, Population Studies, and Health Promotion, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia.

*Corresponding author: I Putu Alit Pawana; Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia; i.putu-ai@fk.unair.ac.id


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Until now, the ideal therapy for knee OA is still unclear, but interventions aim to reduce symptoms and risk factors to prevent disease progression and improve quality of life. One conservative approach to knee OA is exercise. The American College of Sports Medicine recommends high-intensity resistance training of 60–80% 1-RM so that good recruitment of type II muscle fibers occurs. Progressive resistance training positively stimulates intracellular anabolic signals due to mechanical tension, muscle damage, inflammatory response, and metabolic stress. These intracellular anabolic signals further increase protein synthesis and reduce protein degradation. However, knee OA patients who undergo high-intensity resistance training often report discomfort and pain during exercise, which can hamper the rehabilitation process.

A new strategy, namely Blood Flow Restriction (BFR), can improve physical function and reduce pain in patients with knee OA. With this technique, the individual wears the cuff over the upper 1/3 of the lower extremity and then develops pressure as tolerated during training. This exercise will cause an increase in the concentration of metabolic substances, including cellular and hormonal changes related to muscle ischemia, thereby inducing the recruitment of more muscle fibers.

Giving BFR to low-intensity resistance training (LI-RT) can increase muscle strength by stimulating the activation of type 2 muscle fibers due to the anaerobic environment in the muscles, increased growth hormone secretion and activation of the protein synthesis pathway. The main benefit of this exercise is that there is a physiological adaptation similar to the response to high-intensity resistance training, with shorter time, as well as lower-intensity training loads.

Knee OA patients will experience pain, joint stiffness, proprioception deficits, and muscle weakness. The complex biomechanics of the knee will impact the quadriceps muscles, causing muscle weakness, which impacts the quality of life and increases functional disability in carrying out daily activities. The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) is a specific questionnaire for knee OA patients with 24 questions assessing pain, joint stiffness, and physical function, with the higher score indicating a lower functional status. Ferraz et al. reported improvements in the WOMAC pain subscale in the LI-RT group with BFR and the LI-RT only group (45% and 39%, p < 0.05) and increases in the WOMAC physical function subscale in the BFR and HI-RT groups (49% and 42%).

The response to increasing strength and muscle mass is higher than low-intensity exercise, and a lower pain scale than high-intensity exercise makes this combination of exercises an alternative therapy for knee OA patients. There is no standard for prescribing this BFR exercise method, especially in Indonesia, so research is needed to determine safe and effective prescribing to improve functional status as assessed by the Indonesian validation version of the WOMAC score in the knee OA population. This study aims to determine the effects of blood flow restriction with low-intensity resistance training on quadriceps for six weeks on functional status in knee-OA patients.

**METHODS**

**Participants**

This study was a randomized pre-test and post-test group experimental design. The inclusion criteria are patients with unilateral or bilateral knee OA with Kellgren and Lawrence (KL) grade II-III (if the patient had both knee OA, the knee that has higher VAS will be included in this study); 50-70 years old knee OA; the knee with higher VAS will be included in this study); 50-70 years old knee OA; the knee with higher VAS will be included in this study). The exclusion criteria are blood clotting disorder; deep vein thrombosis, peripheral arterial disease on the legs; neuropathy on the lower extremity; cardiorespiratory disorder; uncontrolled hypertension or diabetes mellitus; history of stroke or transient ischemic attack; severe pain on the knee or surrounding connective tissue (VAS >60mm); participate in regular lower extremity strengthening program the last one month; history of injury, fracture, surgery, or other musculoskeletal disorder on the lower extremity in the last 6 months; balance disorder (e.g. impaired standing balance, fear of fall); consuming statin drugs, oral contraceptive, or receive chemotherapy, and visual or hearing problem. The dropout criteria of this study are if they refused to continue exercise, could not do the exercise for 2 consecutive sessions, have complications such as angina, dyspnea, syncope, joint pain (VAS >60 mm), swelling, cramp, skin discolorization, warm on the trained leg, nerve injury (paresthesia after the cuff was released and muscle weakness), muscle soreness until >72 hours post-exercise, and muscle weakness that cause the patient unable to do the exercise.

The Research Ethics Committee of Dr. Soetomo General Academic Hospital approved this study (No. 0554/KEPK/XII/2022). Prior to the study, written informed consent was obtained from all participants.

**Exercise intervention**

Knee OA patients in the Physical Medicine and Rehabilitation Outpatient Clinic at Dr. Soetomo Hospital Surabaya, who met the inclusion criteria and were not included in the exclusion criteria, were given information about the objectives of the study and the probable side effects that could occur. When they are willing to become research subjects, they will be asked to sign an informed consent form. The sample size was calculated based on the Lwanga and Lemeshow Formula and obtained a minimum of 24 research subjects. Research subjects were randomized into two groups: treatment group (TG) and control group (CG), using consecutive proportional random sampling. Both groups underwent a 6-week supervised training program consisting of low-intensity resistance training (LI-RT) two sessions/week with a minimum interval of 48 hours between sessions with the intensity of 20% 1-RM on weeks 1-2 and 30% 1-RM on weeks 3-6. The training program was conducted for 4 sets x 15 reps in week 1 and 5 sets x 15 reps in weeks 2-6, with 60 second rest period between each set using a quadriiceps bench machine. The maximum exercise time in one practice session was 10 minutes. The treatment group received an additional application of BFR using a sphygmonanometer cuff placed on 1/3
upper thigh with 50 mmHg occlusion pressure and maintained throughout the training session.

After initial data collection, the subjects were evaluated for vital signs and explained about the Borg scale and Visual Analog Scale (VAS) before administration of the exercises according to the group's division. The subject then warmed up using a static cycle for 5 minutes and stretched the hamstring, quadriceps, triceps surae, and tibialis anterior muscles for 5 minutes. During the exercise (the rest period between sets 2 and 3), evaluate the Borg scale to assess fatigue, VAS to assess pain levels elicited by cuff pressure, and oxygen saturation and pulse using a pulse oximeter. After the exercise, recheck the vital signs, then continue to cool down with a static cycle and stretching for 5 minutes each. All subjects were given icing with cold packs on the thigh and knee muscles for 10 minutes and 100 Hz TENS therapy to the quadriceps muscles for 15-20 minutes at an intensity according to the subject's tolerance. Safety and emergency kits are also prepared, and if an emergency occurs, the action will follow the existing protocol.

Data collection
Before starting the exercise program, the WOMAC score data was collected. The post-intervention evaluation was conducted at the end of the sixth week of training (96 hours after the last exercise), and the re-measurement of the WOMAC score was conducted. This study compared the WOMAC score differences before and after 6 weeks of exercise in the control group and the BFR group, respectively. After that, a comparison of the delta WOMAC score between the control and BFR groups was made.

Statistical analysis
The data obtained would be processed using the SPSS 27.0 version. A descriptive presentation of the data was carried out to determine the characteristics of all the data to determine the average and standard deviation. The data normality test was carried out using the Monte Carlo test. Normal data distribution if $p > 0.05$. Data homogeneity test was analyzed by independent t-test and called homogenous if $p > 0.05$.

The data comparison between before and after treatment in each group using paired t-test (if the data was normally distributed) and The Wilcoxon sign rank test (if the data was not normally distributed). The difference is significant if $p < 0.05$.

The data comparison between the control and treatment groups, before and after treatment, was tested using an independent t-test (if the data was normally distributed) and The Mann-Whitney test (if the data was not normally distributed). The difference was significant if $p < 0.05$. The effect size (Cohen's d) was calculated to compare the effect of WOMAC score improvement between the treatment and control groups.

RESULTS

Participant characteristics
A total of 28 knee OA subjects participated in this study, allocated to TG and CG, each group consisting of 14 subjects (see Table 1). There were no statistical differences between the groups in the characteristic of age, gender, weight, height, IMT, the site of the affected knee, the severity of the knee OA, physical activity, and mean of isometric peak torque. The normality test results were all the variables in both groups had a normal distribution ($p$-value $> 0.05$).

Table 2 shows a significant decrease in the WOMAC pain subscale in the TG ($p$-value $= 0.000$) and CG ($p$-value $= 0.000$) before and after the intervention. There was a significant decrease in the WOMAC stiffness subscale in the treatment group ($p$-value $= 0.045$) but no significant decrease in the WOMAC stiffness subscale in the control group ($p$-value $= 0.365$).

There was a significant improvement in the WOMAC physical function subscale in the TG ($p$-value $= 0.000$) and the CG ($p$-value $= 0.000$) before and after the intervention. There was a significant decrease in the WOMAC total score in the TG ($p$-value $= 0.000$) and the CG ($p$-value $= 0.000$) before and after the intervention.

WOMAC subscale score differences between the two groups
Table 3 shows no significant difference between groups in the WOMAC pain subscale ($p$-value $= 0.437$), WOMAC stiffness subscale ($p$-value $= 0.651$), WOMAC physical function subscale ($p$-value $= 0.385$) and WOMAC total score ($p$-value $= 0.175$).

WOMAC subscale score after intervention
Table 4 shows no significant difference after the intervention between the two groups in the WOMAC pain subscale ($p$-value $= 0.146$), WOMAC stiffness subscale ($p$-value $= 0.849$), WOMAC physical function subscale ($p$-value $= 0.589$), and WOMAC total score ($p$-value $= 0.882$).

DISCUSSION

WOMAC pain subscale
There was a significant decrease in the WOMAC pain subscale in the TG and CG ($p$-value $= 0.000$) before and after the intervention. This study is in line with a study by Ferraz et al., which assessed 48 women with knee OA aged 50-65 years and compared the effects of LI-RT (30% 1-RM), a combination of LI-RT (30% 1-RM) and BFR, and HI-RT (80% 1-RM) and then assessed functional status with the WOMAC questionnaire pre and post-intervention for 12 weeks. There was a significant decrease in the WOMAC pain subscale in the LI-RT and LI-RT + BFR groups but not in HI-RT. In addition, 25% of subjects in the HI-RT group dropped out of the study due to complaints of exercise-related knee pain. 21

This research is not in line with a study from Harper et al. on 36 subjects with knee OA aged >60 years divided into 2 groups, namely the low-intensity resistance training group 20% 1-RM with BFR and moderate intensity resistance training 60% 1-RM who underwent exercise 3 times a week for 12 weeks. 22 It could be due to the use of different intensities; in this study, the two groups used a LI-RT of 30% 1-RM with and without BFR, whereas Harper et al. used a LI-RT of 20% 1-RM and a moderate intensity of 60% 1-RM. 23 Complex biopsychosocial factors, such as nociceptive and central sensitization pathways, and psychological factors, including self-efficacy, pain perception, depression, and social support, influence complaints of pain in knee OA. 24
## Table 1. Basic characteristics of participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention Group (n = 14)</th>
<th>Control Group (n = 14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)¹</td>
<td>57.71 ± 5.25</td>
<td>61.42 ± 5.70</td>
<td>0.085</td>
</tr>
<tr>
<td>Age category¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Pre-elderly</td>
<td>8 (57.1%)</td>
<td>3 (28.6%)</td>
<td>0.127</td>
</tr>
<tr>
<td>2. Elderly</td>
<td>6 (42.9%)</td>
<td>10 (71.4%)</td>
<td></td>
</tr>
<tr>
<td>Gender¹</td>
<td></td>
<td></td>
<td>0.622</td>
</tr>
<tr>
<td>1. Male</td>
<td>3 (21.4%)</td>
<td>2 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>2. Female</td>
<td>11 (78.6%)</td>
<td>12 (85.7%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)²</td>
<td>66.78 ± 13.00</td>
<td>64.71 ± 8.65</td>
<td>0.624</td>
</tr>
<tr>
<td>Height (cm)²</td>
<td>158.78 ± 7.84</td>
<td>152.57 ± 8.73</td>
<td>0.058</td>
</tr>
<tr>
<td>IMT (kg/m²)²</td>
<td>26.30 ± 3.99</td>
<td>27.85 ± 2.80</td>
<td>0.243</td>
</tr>
<tr>
<td>IMT category¹</td>
<td></td>
<td></td>
<td>0.964</td>
</tr>
<tr>
<td>1. Normoweight</td>
<td>3 (21.4%)</td>
<td>1 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>2. Overweight</td>
<td>4 (28.6%)</td>
<td>4 (28.6%)</td>
<td></td>
</tr>
<tr>
<td>3. Obese Grade I</td>
<td>6 (42.9%)</td>
<td>7 (50%)</td>
<td></td>
</tr>
<tr>
<td>4. Obese Grade II</td>
<td>1 (7.1%)</td>
<td>1 (7.1%)</td>
<td></td>
</tr>
<tr>
<td>Kellgren-Lawrence¹</td>
<td></td>
<td></td>
<td>0.430</td>
</tr>
<tr>
<td>1. Grade 2</td>
<td>10 (71.4%)</td>
<td>8 (57.1%)</td>
<td></td>
</tr>
<tr>
<td>2. Grade 3</td>
<td>4 (28.6%)</td>
<td>6 (42.9%)</td>
<td></td>
</tr>
<tr>
<td>Affected knee¹</td>
<td></td>
<td></td>
<td>0.699</td>
</tr>
<tr>
<td>1. Right</td>
<td>8 (57.1%)</td>
<td>9 (64.3%)</td>
<td></td>
</tr>
<tr>
<td>2. Left</td>
<td>6 (42.9%)</td>
<td>5 (35.7%)</td>
<td></td>
</tr>
<tr>
<td>Comorbid¹</td>
<td></td>
<td></td>
<td>0.313</td>
</tr>
<tr>
<td>1. No comorbid</td>
<td>9 (64.3%)</td>
<td>8 (57.1%)</td>
<td></td>
</tr>
<tr>
<td>2. HT</td>
<td>3 (21.4%)</td>
<td>5 (35.7%)</td>
<td></td>
</tr>
<tr>
<td>3. DM</td>
<td>2 (14.3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>4. Lung TBC</td>
<td>0 (0%)</td>
<td>1 (7.1%)</td>
<td></td>
</tr>
<tr>
<td>Physical activity¹</td>
<td></td>
<td></td>
<td>0.430</td>
</tr>
<tr>
<td>1. Inactive</td>
<td>10 (71.4%)</td>
<td>8 (57.1%)</td>
<td></td>
</tr>
<tr>
<td>2. Minimally active</td>
<td>4 (28.6%)</td>
<td>6 (42.9%)</td>
<td></td>
</tr>
<tr>
<td>WOMAC Pre²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Pain subscale</td>
<td>5.85 ± 1.29</td>
<td>5.92 ± 1.20</td>
<td>0.881</td>
</tr>
<tr>
<td>2. Stiffness subscale</td>
<td>2.85 ± 0.94</td>
<td>2.57 ± 0.75</td>
<td>0.386</td>
</tr>
<tr>
<td>3. Function subscale</td>
<td>25 ± 4.55</td>
<td>22.85 ± 2.68</td>
<td>0.142</td>
</tr>
<tr>
<td>4. Total score</td>
<td>33.71 ± 4.90</td>
<td>31.35 ± 3.07</td>
<td>0.140</td>
</tr>
</tbody>
</table>

Notes: significant if p-value < 0.05.

The value is described as amount (percentage) and mean ± standard deviation. P-value based on ¹Chi-square test and ²Independent t-test.

## Table 2. WOMAC subscale results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exercise Group (n = 14)</th>
<th>Control Group (n = 14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td>WOMAC Pain Subscale</td>
<td>5.85 ± 1.29</td>
<td>2.07 ± 0.61</td>
<td>0.000</td>
</tr>
<tr>
<td>WOMAC Stiffness Subscale</td>
<td>2.85 ± 0.94</td>
<td>2.21 ± 0.80</td>
<td>0.045</td>
</tr>
<tr>
<td>WOMAC Physical Function Subscale</td>
<td>25 ± 4.55</td>
<td>9.71 ± 5.63</td>
<td>0.000</td>
</tr>
<tr>
<td>Total WOMAC Score</td>
<td>33.71 ± 4.90</td>
<td>13.42 ± 6.09</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Notes: significant if p < 0.05.

Low-intensity resistance training with BFR is said to have a hypoalgesia-stimulating effect. Increased metabolite concentrations due to BFR will stimulate chemoreceptors in muscles and then activate group III and IV afferent fibers, which can change afferent feedback to the central nervous system to trigger activation of the opioid system and modulate pain via spinal or supraspinal inhibition mechanisms and release of endocannabinoids in response to physical stress that occurs.²⁵ Data from the Osteoarthritis Initiative show that as knee OA disease progresses, every 1/20 point increase on the WOMAC pain subscale is linearly related to a 2% decrease in isometric strength of the knee extensors and flexors in men and women.²⁶ An article on knee OA states that in order to detect a decrease in pain or improvement...
Table 3. WOMAC subscale score differences between the two groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exercise Group (n = 14)</th>
<th>Control Group (n = 14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ WOMAC Pain Subscale</td>
<td>-3.78 ± 1.12</td>
<td>-3.50 ± 0.75</td>
<td>0.437</td>
</tr>
<tr>
<td>Δ WOMAC Stiffness Subscale</td>
<td>-1.00 ± 0.87</td>
<td>-0.85 ± 0.77</td>
<td>0.651</td>
</tr>
<tr>
<td>Δ WOMAC Physical Function Subscale</td>
<td>-15.28 ± 3.91</td>
<td>-14.07 ± 3.33</td>
<td>0.385</td>
</tr>
<tr>
<td>Δ Total WOMAC Score</td>
<td>-20.28 ± 4.19</td>
<td>-18.21 ± 3.64</td>
<td>0.175</td>
</tr>
</tbody>
</table>

Notes: significant if p < 0.05

Table 4. WOMAC subscale score after intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exercise Group (n = 14)</th>
<th>Control Group (n = 14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC Pain Subscale</td>
<td>2.07 ± 0.61</td>
<td>2.42 ± 0.62</td>
<td>0.146</td>
</tr>
<tr>
<td>WOMAC Stiffness Subscale</td>
<td>2.21 ± 0.80</td>
<td>2.28 ± 1.13</td>
<td>0.849</td>
</tr>
<tr>
<td>WOMAC Physical Function Subscale</td>
<td>9.71 ± 5.63</td>
<td>8.78 ± 2.91</td>
<td>0.589</td>
</tr>
<tr>
<td>Total WOMAC Score</td>
<td>13.42 ± 6.09</td>
<td>13.14 ± 3.67</td>
<td>0.882</td>
</tr>
</tbody>
</table>

Notes: significant if p < 0.05

in knee function, an increase in muscle strength is required by ≥ 30% of the initial pre-exercise value.27

A study from Gandek in 2015 stated that the WOMAC pain subscale assesses pain during physical activity more than assessing the pain itself in real terms. The assessment of pain during physical activity does not have more diverse items, such as assessing pain during more strenuous activities.28-30

WOMAC stiffness subscale

There was a significant decrease in the WOMAC stiffness subscale before and after the intervention in the TG (p-value = 0.045). However, there was no significant decrease in the CG (p-value = 0.365). This study is in line with Ferraz et al., who assessed the WOMAC stiffness subscale and found a significant decrease in stiffness in the LI-RT + BFR group but not in the HI-RT and LI-RT groups.21

The WOMAC stiffness subscale has a negative correlation with quadriceps muscle strength, which means that the lower muscle strength, the higher the degree of joint stiffness experienced by the subject. Epidemiological studies of joint damage in knee OA suggest that quadriceps weakness may precede radiologically detectable joint damage. Articular incongruence is a predictor of joint stiffness because the degree of incongruence between the condylar surfaces can vary depending on the position of the condyles. Differences in the degree of cartilage degeneration will cause incongruence between loads due to changes in the mechanical axis of weight bearing, where joint kinematic changes will persist over time and cause abnormal stress, which results in gradual cartilage damage, causing joint stiffness.29-30

Chronic synovitis in OA triggers cell proliferation and increases the synthesis of matrix proteins (collagen types I, III, and IV), causing adhesions, arthrofibrosis, and joint dysfunction and ending with joint stiffness. The limitation of joint range of motion is also caused by joint stiffness and narrowing of the joint space, which results in muscle contractions around the joints that are not optimal, causing muscle weakness. Joint stiffness in knee OA is a compensatory mechanism for joint instability so that muscle-strengthening exercises can increase joint stability. Kim et al. stated that the WOMAC pain and physical function subscale at K/L grade ≥ 2 correlated with age, nutritional status, and knee extensor muscle strength, while the WOMAC stiffness subscale at K/L grade ≥ 2 only correlated with knee extensor muscle strength.30

WOMAC physical function subscale

There was a significant improvement in the WOMAC physical function subscale in the treatment and control groups (p-value = 0.000) before and after intervention. It was in line with a study by Ferraz et al., which assessed the WOMAC physical function subscale and experienced significant improvements in the LI-RT + BFR and HI-RT groups but not in the LI-RT group. Impaired physical function is related to restrictions on physical performance in daily activities to achieve independence and is a predictor of disability, so maintaining functional status is one of the main goals in the management of OA.31

The WOMAC physical function subscale is specific to the knee but can be affected by the pain status of the contralateral knee. Assessment of general activity level and objective functional performance tests is highly dependent on each knee’s interaction and functional status. Objective functional performance tests such as the chair stand test are considered more suitable for assessing the effect of therapy on differences in changes in unilateral knee pain and more sensitive in assessing differences between groups with different knee pain conditions.31

Some question points related to the WOMAC physical function subscale indicate cultural differences and can cause misunderstandings when completing the questionnaire. Getting in/out of the bathtub is the most subjective question in this questionnaire because most Indonesians do not have a bathtub. So, for this question, points are given to additional information, namely stepping +50cm high, but it is still challenging to make the subject understand the question’s meaning.20

Total WOMAC score results

There was a significant decrease in the WOMAC total score in the TG (p-value 0.000) and CG (p-value 0.000) before and after the intervention. This study is in line with Ferraz et al., who experienced a significant decrease in the total WOMAC score before and after the intervention in each group (HI-RT -39%, ES = -1.23, p = 0.016; LI-RT -42%, ES = -0.79, p = 0.005,
and LI-RT + BFR -46%, ES = -1.3, p = 0.008.21

A study from Turner et al. states that strengthening exercises can reduce pain and improve physical function in patients with knee OA, where a large effect size value is associated with a minimum total of 24 exercise sessions in 8-12 weeks.22

Comparisons of WOMAC scores between group

There were no significant differences in the difference (delta) of the pain subscale, the stiffness subscale, the physical function subscale, and the total WOMAC total between the two groups before and after the intervention. There were no significant differences in the score of pain, stiffness, physical function (p-value 0.589), and total WOMAC score after the intervention between the two groups.

Based on the data that the researchers got, there were only 2 studies that assessed the effect of resistance training with BFR on the functional status of patients with knee OA as assessed by the WOMAC questionnaire. Ferraz et al. did not include a data comparison of the WOMAC subscale score between groups. In contrast, Harper et al. only assessed the WOMAC pain subscale and did not report the score of other subscales, making it difficult to make direct comparisons with the variables of this study.

Several studies have assessed the effect of BFR training on the functional status of patients with knee OA using different questionnaires and found no significant differences between groups. Bryk et al. compared the effects of LI-RT (30% 1-RM) + BFR and HI-RT (70% 1-RM) in 34 women with knee OA, an average age of 61 years, 3 times/week for 6 weeks and an increase in functional status was assessed by the Lequesne questionnaire before and after the intervention in both groups (p-value 0.001). There was no significant difference between the groups.23 Harper et al. assessed the functional status of patients with knee OA with the Late-Life Function and Disability Questionnaire, and there were no significant differences in each group and between groups after the intervention.23

Petersson et al. assessed 14 subjects with knee OA with an average age of 70 years who were given 20 minutes of walking exercise with BFR applications 4 times/ week for 8-10 weeks and found no significant differences in all subscales Knee Injury and Osteoarthritis Outcome Score questionnaire before and after the intervention.33 The study by Segal et al. examined 40 women aged 45-65 with a risk of symptomatic knee OA who underwent LI-RT (30% 1-RM) with and without BFR 3 times/week for 4 weeks. There was no significant difference in the reduction of KOOS pain in each group and between groups.34

Another study assessed the effect of resistance training with BFR in populations other than knee OA using different questionnaires, one of which was Rodriguez et al., assessed 48 women with rheumatoid arthritis with an average age of 58 years who were divided into 3 groups: HI-RT (70% 1-RM), LI-RT (30% 1-RM) + BFR, and controls who underwent quadriceps strengthening exercises 2 times a week. The BFR group showed significant improvement on the Health Assessment Questionnaire with \( P = 0.038 \) and in the physical (\( P = 0.024 \)) and bodily pain (\( P = 0.036 \)) domains on Short Form 36 before and after 12 weeks, and there were no significant differences between groups on all variables.35

The Insignificant results between group comparisons In this study are consistent with other studies on knee OA and different populations; people with rheumatoid arthritis use different measuring instruments but still use questionnaires based on self-reporting by research subjects. The subjects of this study were aged 50-70 years, with 57.12% of the elderly, and the rest were pre-elderly. Sarcopenia is a decrease in strength and muscle mass with age that puts the elderly at high risk of various disabilities, for example, weakness of the knee extensor muscles, which is a predictor of low physical function and is associated with increased hospitalization and mortality rates. Strengthening exercises in this population are expected to increase muscle strength, which will positively impact the subject's physical function. The relationship between muscle strength and physical function usually tends to be linear. However, in the elderly who are weak, an increase in muscle strength is not always accompanied by an increase in physical function.36

The functional status of knee OA patients is strongly influenced by muscle strength. Factors that affect muscle strength in knee OA can be divided into muscle factors in the form of quality, quantity, and muscle activation; general factors in the form of physical activity, exercise, endocrine and metabolic factors, nutrition and vitamins; also factors related to OA, including joint degeneration, biomechanical factors, inflammatory markers, and pain.37

De Melo et al. studied 28 post-ACL reconstruction subjects aged 18-59 years, divided into 2 groups, namely HI-RT and LI-RT + BFR 2 times/week for 12 weeks. They assessed functional status periodically with 3 different questionnaires, and the results indicated significant differences between the two groups.38 The difference in results with this study could be due to the fact that subjects have a wider age range, and some have quadriceps deficits due to ACL injuries after reconstruction. In contrast, this study consisted of subjects aged 50-70 with degenerative diseases in the form of knee OA and other accompanying comorbidities.

Applying BFR can induce a hypoxic environment in muscles and activate metabolic cascades that stimulate protein synthesis, change gene regulation of muscle satellite cells, and increase muscle fiber recruitment, increasing muscle strength and impacting functional status. Factors related to BFR application that must be considered are individual factors, restriction pressure prescribing, and cuff width. The application of BFR is safe and effective for use as an adjunct to rehabilitation regimens for the lower limbs.39

This study did not use Doppler ultrasonography as the basis for prescribing optimal restrictive cuff pressure per individual and for screening for vascular pathologies that subjects may experience. Bryk et al. applied a restriction pressure of 200 mmHg guided by Doppler ultrasonography to ensure that total vascular occlusion did not occur in subjects with knee OA, Ferraz et al. used a restriction pressure of 70% AOP, while
Harper et al. used individual formula for determining the restriction pressure.\textsuperscript{16,21,23} The restriction pressure In this study was In accordance with Sumide et al. of 50 mmHg. Ih was applied to all research subjects. This is in accordance with a study by Brandner et al., which states that a BFR pressure of 40% AOP is equivalent to 53 ± 7 mmHg, and Kubota et al. that a pressure of 50 mmHg is said to be less than arterial blood pressure but greater than venous blood pressure so that the flow of venous blood will be blocked and cause a buildup of metabolism which is one of the primary mechanisms for increasing muscle strength in BFR.\textsuperscript{30-42} Thigh circumference is a significant predictor for prescribing optimal individual restriction pressure, where the larger thigh requires higher pressure to reach the level of occlusion equivalent to a smaller thigh.\textsuperscript{43} Studies show that thigh muscle mass correlates with muscle strength, function, and symptom progression in women with knee OA, where the higher the composition of lean muscle mass will require a lower BFR restriction pressure; conversely, the higher the percentage of body fat mass will require higher restriction pressure.\textsuperscript{44} This study did not evaluate thigh circumference and thigh muscle mass in the study subjects. The width of the lower limb cuff In the BFR literature ranges from 5-23 cm, where a wider size can provide a lower restriction pressure that is sufficient to cause an effect and reduce the risk of nerve compression, discomfort, burning, and numbness.\textsuperscript{45} Ferraz et al. used an 18 cm cuff for knee OA subjects undergoing weight training with BFR.\textsuperscript{34} This study used a special 21 cm thigh sphygmomanometer cuff.

The Osteoarthritis Research Society International (OARSI) recommends performance-based tests of physical function to reflect activity-relevant assessments for individuals with knee OA. This test supports patient-based test assessment and assists decision-making in a practical clinical context. OARSI recommends tests in the form of a 30-second chair-stand test, 40 meters fast-paced walk test, a stair-climb test, a timed up-and-go test, and a 6-minute walk test, where three initial tests are recommended as a minimum assessment of the performance-based test that must be evaluated in patients with knee OA.\textsuperscript{41-45} This research has several limitations. The subjects’ physical activity outside the exercise program and the nutritional intake could not be controlled, making it a confounding variable in this study. The differences in muscle mass and fat mass in the thighs of each subject and the determination of restrictive cuff pressure that is not based on individual arterial occlusion pressure may affect the results.

**CONCLUSION**

Administration of low-intensity resistance training alone and BFR administration in low-intensity resistance training of the quadriceps muscles affects the WOMAC score in the patients with knee OA before and after exercise for 6 weeks. There is no statistical difference in the effect of giving BFR to low-intensity resistance training and low-intensity resistance training of the quadriceps muscles alone on the WOMAC score of patients with knee OA before and after exercise for 6 weeks.

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**CONFLICT OF INTEREST**

The author reports no conflicts of interest in this work.

**AUTHOR CONTRIBUTION**

All authors have contributed equally from the conceptual framework, data acquisition, and data analysis until the study results are reported through publication.

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