Journal of Medicinal and Chemical Sciences 6 (2023) 3004-3011

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

The Effect of Blood Flow Restriction in Low-Intensity Load Exercise on Visual Analog Scales in Knee Osteoarthritis Patients at Dr. Soetomo General Hospital Surabaya

Priscilla Anastasia Fitriany Dugis[1,*], Damayanti Tinduh[2], Ditaruni Asrina Utami[2], Soenarnatalina Melaniani[3]

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

ARTICLE INFO

Article history

Receive: 2023-06-19
Received in revised: 2023-08-06
Accepted: 2023-08-07
Manuscript ID: JMCS-2307-2179
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Yogesh Tripathi

DOI:10.26655/JMCHEMSCI.2023.12.15

KEYWORDS

Blood flow restriction
Knee osteoarthritis
Knee extensor strength
Low intensity resistance exercise
Visual analog scale

ABSTRACT

Purpose: Pain in knee osteoarthritis (KOA) causes life quality decrease and is the common complaint of patient with KOA. Cartilage destruction in KOA induced inflammation process that caused pain. Pain and tissue injury around the knee joint caused quadriceps weakness due to neural inhibition on quadriceps activation (Arthrogenic Muscle Inhibition (AMI)). Combination of blood flow restriction (BFR) and low intensity resistance training (LIRT) significantly showed improvement of visual analog scale (VAS), but the prescription is so variative and limited in Indonesia.

Patients and methods: This was clinical experimental study with randomized control trial with pre-test and post-test design. Subjects were 28 KOA patient (50-70 years old). Intervention group (n=14) received combination of LIRT (30% 1-RM; 75 repetitions) and BFR (50 mmHg). Control group (n=14) received LIRT (30% 1-RM; 75 repetitions). Both groups received training twice a week with q-bench machine for 6 weeks. Visual analog scale was assessed before and after the training program.

Results: There was the significant improvement of VAS before and after training program in both groups (intervention group, p=0.000; control group, p=0.000). There was the significant improvement of delta VAS between both groups (p=0.000) and post-test between both groups (p=0.000). The effect size value of intervention group was 10.08 (very large) and control group was 3.42 (very large).

Conclusions: BFR addition to LIRT quadriceps muscle for 6 weeks can improve visual analog scale more than LIRT alone in patient with knee osteoarthritis.

* Corresponding author: Priscilla Anastasia Fitriany Dugis
✉ E-mail: paf.dugis@gmail.com

G R A P H I C A L A B S T R A C T

Introduction

Pain in osteoarthritis (OA) of the knee causes a decrease in quality of life in the form of impaired mobility and independence of sufferers [1]. Pain is the main complaint of OA patient to seek intervention [2, 3]. This pain caused by damage of cartilage and tissue around the joint and the inflammatory process. Inflammatory mediators such as bradykinins and prostaglandins stimulate the Aδ and C fibers. This stimulus will be transmitted to the spinal cord, thalamus, and somatosensory cortex to be perceived as pain. Pain and joint tissue damage will trigger the process of Arthrogenic muscle inhibition (AMI) which inhibits full activation of the quadriceps muscles through neural inhibition, causing this muscle weakness [4, 5]. Pain, in addition to making patients less active, can lead to a reduction in muscle mass. This decrease in muscle strength in the quadriceps can increase strain on the knee joint and worsen cartilage damage, ultimately resulting in higher levels of osteoarthritis and pain [6]. Furthermore, pain is a highly subjective symptom that varies depending on the circumstances and a person's psychological state. The perception of pain is further influenced by cognitive and emotional factors that affect brain processes involved in pain regulation [7].

Intervention of knee OA aims to relieve pain and increase quadriceps muscle strength. It consists of pharmacological and non-pharmacological as well as surgery. According to the American College of Rheumatology, exercise therapy, weight loss, and use of canes and braces are highly recommended. Exercise therapy itself consists of aerobic exercises, strengthening exercises, stretching exercises, and balance exercises [8]. Strengthening exercise with blood flow resistance (BFR) is a muscle strengthening technique using a combination of low-intensity loads (20-40% 1-RM) and providing blood flow restriction using an air-filled cuff in the proximal area of the limb being trained [9]. The restricted blood flow in the BFR leads to tissue ischemia, resulting in a significant physiological metabolic stress. This stress prompts the body to produce growth hormone and enhances the recruitment of type II muscle fibers. In addition, the buildup of lactic acid as a metabolic byproduct triggers the activation of Aδ nerves and C fibers, causing pain. Interestingly, this pain acts as a form of conditioned pain modulation (CPM), in which pain inhibits the perception of pain. Moreover, lactic acid stimulates the sympathetic nervous system and baroreceptors. The location of pain perception and baroreceptors in the brain cortex are adjacent so that the inhibition that occurs in the baroreceptors as compensation to maintain the stability of the cardiovascular system will also inhibit the descending pathway of pain.

In the same vein, the use of low-intensity loads on BFR is expected to reduce the burden on the joints thereby reducing pain during exercise and increasing exercise tolerance [10]. Until now, the standard prescribing of BFR exercises in patients with knee OA is very diverse and is still rare in Indonesia, so researchers believe that research is needed with effective, fast, safe, and comfortable prescribing using 50 mmHg pressure to restrict blood flow in low-intensity weight training quadriceps muscle for six weeks to assess the effect of BFR on knee pain in OA patients.

Materials and Methods

This is a clinical experimental study with a randomized control trial, pre-test and post-test design. The research was carried out starting in September 2022 until May 2023 at the Medical Rehabilitation Outpatient Clinic at Dr. Soetomo General Hospital Surabaya. Ethical clearance obtained from the Ethics Committee for research and basic/clinical science at Dr. Soetomo General Hospital Surabaya no. 0554/KEPK/XII/2022. The inclusion criteria for this study are: (1) Patients with knee OA confirmed by the clinical criteria of the American College of Rheumatology and radiology according to Kellgren and Lawrence grade II-III criteria both unilaterally and bilaterally. If bilateral, then the leg with the higher pain score (VAS) will be included in the study assessment. (2) Male or female aged 50-70 years old. (3) Do not have cognitive impairment (MoCA-Ina score or the Indonesian version of the Montreal Cognitive Assessment ≥ 26). 4) Willing to participate in this study by signing an informed consent form. Exclusion criteria for this study are: (1) History of blood coagulation disorder. (2) History or increased risk of deep vein thrombosis in both legs. (3) Peripheral arterial disease in both legs. (4) Peripheral neuropathy and/or polyneuropathy in the leg. (5) Cardiorespiratory disease. (6) Uncontrolled hypertension (systolic > 140 mmHg or < 100 mmHg and/or diastolic > 100 mmHg). (7) Uncontrolled Diabetes Mellitus (HbA1c > 6.5). (8) History of thrombotic stroke, haemorrhagic stroke, and transient ischemic attack. (9) Pain in the knee joint and/or the surrounding tissue with a VAS score > 60 (mm), with or without inflammation and there is a limitation of the range of motion of the knee joint in the leg to be trained. (10) Currently undergoing or have undergone a lower limb muscle strengthening exercise program within last month. (11) History of injuries, fractures, surgery, or other musculoskeletal diseases in the lower extremities that will be trained in the last 6 months. (12) Impaired vision and hearing. (13) Currently taking statin class drugs, in chemotherapy intervention, or oral contraceptives. (14) Balance disorder. The criteria for Drop Out in this study include: (1) Subjects are not willing to continue research for any reason. (2) Subject cannot complete the intervention according to research protocol (missed > 2 sessions). (3) Subject experienced complications during the intervention which makes it impossible to continue.

Subjects were given information about the objectives of the research and signed the informed consent. Daily physical activity was assessed using the IPAQ-SF questionnaire. Subjects randomly divided into two groups intervention group and control group. Intervention group received low intensity weight training combined with blood flow restriction using a blood pressure cuff (50 mmHg pressure applied). Control group received low intensity weight training. Pre-intervention visual analog scale was measured.

Before and after the exercise intervention, vital sign examination was performed. Subject also explained about Borg scale and Visual Analog Scale. The subject were warmed up using a static cycle for 5 minutes and stretched the hamstring, quadriceps, triceps surae, and tibialis anterior muscles for 5 minutes. In the middle of the exercise intervention (rest period between sets 2 and 3), fatigue levels were assessed using the Borg scale, pain levels elicited by cuff pressure using the Visual Analog Scale, as well as oxygen saturation. After the exercise intervention, the subjects cooled down with a static cycle for 5 minutes and stretched the hamstring, quadriceps, triceps surae, and tibialis anterior muscles for 5 minutes. Safety and emergency kits prepared in case of an emergency according to the protocol. At the end of the 6th week of training (96 hours after the last exercise), a Visual Analog Scale assessment performed to asses the trained knee joint. The VAS score of knee joint extension before and after intervention compared in each group and between group.

Results and Discussion

In this study, total 28 subjects included with 14 subjects for each group. Characteristics of data subject are listed in Table 1. This study was dominated by female subjects similar with study by Susanti A. *et al.* in Dr. Soetomo general hospital also [11]. Study by Neogi T. *et al.* and Tschon M. *et al.* stated that women have a greater risk of osteoarthritis after the age of over 50 and menopausal period. This is influenced by hormonal, genetic, anatomical differences, and a history of previous trauma [12]. Decreased of oestrogen in postmenopausal women will reduce muscle mass and inhibit the repair process of muscle damage and the presence of pro-inflammatory agents including interleukins, which are greater than men, causing more severe pain in women [13, 14].

The age range of the subjects included in the inclusion criteria was 50 to 70 with an average age in the intervention group 57.71 ± 5.25 and in the control group 61.42 ± 5.70. This data is similar to that of Ferraz *et al.* with an average age of 50 to 65 [15, 16].

Table 1: Characteristics of the subject

	Control Group (n = 14)	Intervention Group (n = 14)	P-value
Sex			0.622
Male	2 (14.3%)	3 (21.4%)	
Female	12 (85.7%)	11 (78.6%)	
Age (Years)	61.42 ± 5.70	57.71 ± 5.25	0.085
Category			0.127
Elderly	4 (28.6%)	8 (57.1%)	
Pre-Elderly	10 (71.4%)	6 (42.9%)	
Body Weight (Kilograms)	64.71 ± 8.65	66.78 ± 13.00	0.624
Body Height (Centimetre)	152.57 ± 8.73	158.78 ± 7.84	0.058
BMI $(kg/m^2)^2$	27.85 ± 2.80	26.30 ± 3.99	0.243
BMI Category			0.964
Normal	2 (14.3%)	3 (21.4%)	
Overweight	4 (28.6%)	4 (28.6%)	
Obese Grade I	7 (50%)	6 (42.9%)	
Obese Grade II	1 (7.1%)	1 (7.1%)	
Affected Knee			0.699
Right	9 (64.3%)	8 (57.1%)	
Left	5 (35.7%)	6 (42.9%)	
Grade OA			0.430
Grade 2	8 (57.1%)	10 (71.4%)	
Grade 3	6 (42.9%)	4 (28.6%)	
IPAQ Pre Intervention			0.430
Low	8 (57.1%)	10 (71.4%)	
Moderate	6 (42.9%)	4 (28.6%)	
Comorbid			0.313
No Comorbid	8 (57.1%)	9 (64.3%)	
Hypertension	5 (35.7%)	3 (21.4%)	
Diabetes Type II	0 (0%)	2 (14.3%)	
Visual Analog Scale (VAS)	53.07 ± 4.44	53.78 ± 5.46	0.708

Table 2: Visual analog scale comparison for each group

Variable	Control Group (n = 14)			Intervention Group (n = 14)		
	Before	After	P-value	Before	After	P-value
Visual Analog Scale (VAS)	53.07 ± 4.44	34.85 ± 6.58	0.000	53.78 ± 5.46	22.64 ± 5.98	0.000

Table 3: Visual analog scale after six weeks intervention

	Control Group (n = 14)	Intervention Group (n = 14)	P-value
Visual Analog Scale (VAS)	34.85 ± 6.58	22.64 ± 5.98	0.000

Table 4: Delta of visual analog scale for each group

	Control Group (n = 14)	Intervention Group (n = 14)	P-value
Δ Visual Analog Scale (VAS)	-18.21 ± 5.32	-31.14 ± 3.08	0.000

The aging process result in replacement of skeletal muscles by fat tissue and it will reduce muscle strength. Fat tissue secretes inflammatory cytokines and adipokines which play a role in the OA pathogenesis.

Biomechanically, patients with overweight and even obesity will increase the load on the knee joint 3-5 times the body weight during ambulation [17].

Most subjects are being obese grade I followed by overweight, normal weight, and obese grade II based on Asia-Pacific BMI criteria. Pain is supported by pro-inflammatory agents produced from fat tissue that will cause a person to tend to be inactive and further aggravate weight gain and muscle weakness, especially the quadriceps. These things will continue to influence each other to form a chain of negative effects. This is also consistent with the profile of knee OA patients studied by Zamri *et al.* who examined the prevalence and risk factors for OA patients in Asia, one of which is obesity [18]. Patient with normal weight also could has KOA since it was not affected by BMI only, but also other risk factors as well [19].

Daily physical activity in each subject was assessed with an IPAQ score where the results of low and moderate physical activity were the same for each group. Low physical activity or tending to immobilize will reduce the myokines production which consist of cytokines, peptides, and growth factors which play a role in metabolic processes. Myokines are regulated by muscle contractions so that decline a person's physical activity and the myokines produced, and also weaken the muscles. Muscle weakness around the joints and increased fatty tissue will exacerbate joint damage and produce more pro-inflammatory agents that will increase pain [20].

At baseline, the mean visual analog scale in the intervention group was 53.78 ± 5.46 and the control group was 53.07 ± 4.44. There was no significant difference in the visual analog scale between two groups at baseline (p-value = 0.708). The visual analog scale after six weeks intervention in the intervention group was 22.64 ± 5.98 and in the control group was 34.85 ± 6.58. There is a significant improvement of visual analog scale in both groups (p-value = 0.000 and 0.000) (Table 2) and significant difference in the visual analog scale in the intervention group compared to control groups (p-value = 0.000) after 6 weeks intervention (Table 3).

Delta of the visual analog scale of the intervention group was -31.14 ± 3.08 and the control group was -18.21 ± 5.32. There was a significant difference in the improvement of visual analog scale between groups (p-value = 0.000) (Table 4).

The results of this study showed significant improvement pain in both groups. Research by Mahmoud *et al.* assessed the relationship between increased muscle strength and VAS values in patients with knee OA and obtained the results, an increase in muscle strength by 1 Newton meter would reduce the VAS value to 0.05. This is consistent with the results of this study where a decrease in VAS values was found in both groups after receiving strengthening exercises with or without BFR [21].

The difference in the visual analog scale before and after intervention between two groups in this study showed a significant difference which was greater in the intervention group. Tubach *et al.* states that the minimum clinically important improvement (MCII) value of the pain scale using the VAS is 19.9 mm [22]. The improvement in the VAS value in the intervention group exceeded the MCII value, while the control group had not yet reached the MCII value. Strengthening exercises will produce endogenous morphine (endorphins) which function to reduce pain. This hormone is produced and released from the anterior pituitary gland which is stimulated by a stressor such as lactic acid which begins to be produced 10 minutes from the onset of exercise and peaks 30 minutes from the onset of BFR exercise with a load of 20% 1 RM and 40 minutes at 80% intensity weight training 1 RM. The accumulation of lactic acid is achieved faster with BFR than conventional exercise, the duration of exercise per session in this study is a maximum of 10 minutes so that lactic acid has been formed even though it has not yet reached its peak, but this level is higher than exercise without BFR. The accumulation of lactic acid will further stimulate the Aδ nerves and C fibers and cause pain, where this pain acts as conditioned pain modulation (CPM), namely the process of "pain inhibits pain". The presence of lactic acid in the body can activate both the sympathetic and baroreceptors. It has been observed that the regions in brain cortex responsible for detecting pain and the baroreceptors are located close to each other. As a result, when the baroreceptors are inhibited to maintain cardiovascular stability, it also leads to the suppression of pain signals that travel down from the brain [23].

The VAS score after 6 weeks of intervention between the two groups showed a significant difference. Furthermore, the magnitude of the effect size in both groups showed a very large effect on improving VAS values, with the effect size value in the intervention group was 3 times greater. These results are consistent with the study of Bryk *et al.* where both the intervention and control groups had a positive effect on improving pain in knee OA patients [18]. VAS improvement in both groups was due to quadriceps muscle strengthening exercises that could restore joint kinematics and knee joint stability thereby reducing joint damage. Fat reduction will reduce inflammatory mediators that play a role in pain complaints. Strengthening exercises will also increase the production of adrenaline, growth factors, and endogenous morphine (endorphins) which function to reduce pain, calm the brain and cause a feeling of happiness. Study by Pitsillides shows that at least 6 weeks of exercise sessions are needed with a frequency of 2-3 times per week and varying BFR pressures (200 mmHg; 70% total arterial pressure; BFR pressure formula = 0.5 (systolic blood pressure) + 2 (thigh circumference) + 5), but these studies use Kaatsu as a standardized tool for BFR training and Doppler ultrasound to monitor blood flow [20]. Another study by Sumide *et al.* showed that a pressure of 50 mmHg can provide a significant increase in isokinetic peak torque in the knee extensor muscles without pain as at other higher pressures (100 mmHg, 150 mmHg, and 200 mmHg), but the subjects of this study are healthy people [21]. In this study, it is proved that there was a significant improvement in visual analog scale (VAS) values in patients with knee OA with the addition of 50 mmHg pressure placed proximal to the quadriceps muscle in low-intensity weight training (30% 1-RM), 2-3 sessions per week for 6 weeks without any side effects such as joint pain that has been monitored before, during, and immediately after exercise (before 30 minutes after exercise) subjectively using VAS with results, there was no difference in VAS values before, during, and immediately after exercise. This occurs due to the process of immediate pain inhibition by BFR through the mechanism of conditioned pain modulation (CPM) where this pathway is not only activated through the accumulation of lactic acid, but also the given amount of pain stimulus. The first pain stimulus by cuff pressure on the BFR, should exceed the second pain stimulus, in this case knee pain, to produce a greater descending inhibition process so that it covers the second painful stimulus [9].

The cuff pressure in this study was only 50 mmHg whereas a study by Korakakis *et al.* proved the CPM mechanism used a cuff pressure of 80% of total arterial occlusion or around 200 mmHg [22]. This improvement of pain is expected to improve the function and quality of life of subjects with knee OA. This study has limitation because it is not measuring the thigh circumference of the trained leg which can affect the amount of cuff pressure for blood flow restriction.

Conclusion

Low-intensity weight training with or without additional blood flow restriction in the quadriceps muscles of knee osteoarthritis patients for six weeks reduced the visual analog scale. However, the addition of Blood Flow Restriction can reduce the visual analog scale of the knee better than low-intensity weight training alone.

Acknowledgments

The authors would like to present their sincere gratitude to all respondent at Dr. Soetomo General Hospital.

Conflict of Interest

No potential conflict of interest was reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the article and agreed to be responsible for all the aspects of this work.

ORCID

Priscilla Anastasia Fitriany Dugis
https://orcid.org/0009-0002-2562-1711
Damayanti Tinduh
https://orcid.org/0000-0001-6604-8152
Ditaruni Asrina Utami
https://orcid.org/0000-0001-7935-5987
Soenarnatalina Melaniani
https://orcid.org/0000-0002-4449-153X

References

[1]. Ferraz R.B., Gualano B.R.U.N.O., Rodrigues R.E.Y.N.A.L.D.O., Kurimori C.O., Fuller R., Lima F.R., De Sa-Pinto A.L., Roschel H., Benefits of Resistance Training with Blood Flow Restriction in Knee Osteoarthritis, *Medicine & Science in Sports & Exercise*, 2018, **50**:897 [Crossref], [Google Scholar], [Publisher]

[2]. Prajoko Y.W., Pramono S., Hartanto A., Prakoso M.A., The Effect of Moringa Oleifera Extract on CPK and Quality of Life of Breast Cancer Hpatinnts Reseiving Aromatase Inhibitor Therapy, *Journal of Medicinal and Chemical Sciences*, 2023, **6**:2750 [Crossref], [Publisher]

[3]. AL-Mashhadani F.A., Abdulrasol Albayati S., haidary S.M., The Protective Effect of Powdered Tart Cherry Supplements or Eating Local Iraqi Tart Cherry Fruit on Moderate to Border Level of Uric Acid and Lipid Profile in Human Serum, *Journal of Medicinal and Chemical Sciences*, 2021, 4:333 [Crossref], [Google Scholar], [Publisher]

[4]. Hidayat S., Arief Y.S., Effendi F., Hannan M., Huzaimah N., The Context of Nursing Intervention of Sand Bed Culture in Reducing Osteoarthritis Pain Scale, *Journal of Medicinal and Chemical Sciences*, 2023, **6**:2387 [Crossref], [Google Scholar], [Publisher]

[5]. Zhang Y., Jordan J.M., Epidemiology of Osteoarthritis, *Clinics in geriatric medicine*, 2010, **26**:355 [Crossref], [Google Scholar], [Publisher]

[6]. Bazgir N., Bonyadi M., Shafiei E., Survey rheumatic diseases in ILAM Province, Iran (2018-2019), *Journal of Medicinal and Chemical Sciences*, 2021, **4**:586 [Crossref], [Google Scholar], [Publisher]

[7]. Kozyk M., Strubchevska K., Yuzkiv V., Bezkorovayna U., Nedilko R., Symptoms of Acute and Chronic Viral Hepatitis: Effects on Human Body, *Journal of Medicinal and Chemical Sciences*, 2023, **6**:2580 [Crossref], [Google Scholar], [Publisher]

[8]. Neogi T., The epidemiology and impact of pain in osteoarthritis, *Osteoarthritis Cartilage*,

2013, **21**:1145 [Crossref], [Google Scholar], [Publisher]

[9]. Rice D.A., McNair P.J., Quadriceps Arthrogenic Muscle Inhibition: Neural Mechanisms and Treatment Perspectives, *Seminars in arthritis and rheumatism*, 2010, **40**:250 [Crossref], [Google Scholar], [Publisher]

[10]. O'Neill T.W., Felson D.T., Mechanisms of Osteoarthritis (OA) Pain, *Current osteoporosis reports*, 2018, **16**:611 [Crossref], [Google Scholar], [Publisher]

[11]. Susanti, A., Wardhani, R. I. L., Pawana, I. P. A. The Relationship Between Quadriceps Muscle Atrophy and Proprioception Function in Knee Osteoarthritis Patients. *Surabaya Physical Medicine and Rehabilitation Journal*, 2019, 1 [Crossref], [Publisher]

[12]. Ikeda S., Tsumura H., Torisu T., Age-related quadriceps-dominant muscle atrophy and incident radiographic knee osteoarthritis, *Journal of Orthopaedic Science*, 2005, **10**:121 [Crossref], [Google Scholar], [Publisher]

[13]. Akbarnejad F., Dermatology Benefits of *Punica granatum*: A Review of the Potential Benefits of *Punica granatum* in Skin Disorders, *Asian Journal of Green Chemistry*, 2023, **7**:208 [Crossref], [Google Scholar], [Publisher]

[14]. Raja S.N., Carr D.B., Cohen M., Finnerup N.B., Flor H., Gibson S., et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises, *Pain*, 2020, **161**:1976 [Crossref], [Google Scholar], [Publisher]

[15]. Zeng C.Y., Zhang Z.R., Tang Z.M., Hua F.Z., Benefits and Mechanisms of Exercise Training for Knee Osteoarthritis, *Frontiers in physiology*, 2021, **12**:2267 [Crossref], [Google Scholar], [Publisher]

[16]. Hughes L., Patterson S.D., The effect of blood flow restriction exercise on exercise-induced hypoalgesia and endogenous opioid and endocannabinoid mechanisms of pain modulation, *Journal of Applied Physiology*, 2020, **128**:914 [Crossref], [Google Scholar], [Publisher]

[17]. Wang H.N., Chen Y., Cheng L., Wang S.T., Hu D.X., Wang L.N., Ni G.X., Effect of low-load resistance training with different degrees of blood flow restriction in patients with knee osteoarthritis: study protocol for a randomized trial, *Trials*, 2022, **23**:6 [Crossref], [Google Scholar], [Publisher]

[18]. Tschon M., Contartese D., Pagani S., Borsari V., Fini M., Gender and Sex Are Key Determinants in Osteoarthritis Not Only Confounding Variables. A Systematic Review of Clinical Data, *Journal of clinical medicine*, 2021, **10**:3178 [Crossref], [Google Scholar], [Publisher]

[19]. Widhiyanto L., Desnantyo A.T., Lilik Djuari L., Kharismansha M. Correlation between knee osteoarthritis (oa) grade and Body Mass Index (BMI) in outpatients of orthopaedic and traumatology Department RSUD Dr. Soetomo. *Journal Orthopaedi and Traumatology Surabaya*, 2017, 6 [Crossref], [Publisher]

[20]. Chidi-Ogbolu N., Baar K., Effect of Estrogen on Musculoskeletal Performance and Injury Risk, *Frontiers in physiology*, 2019, **9**:1834 [Crossref], [Google Scholar], [Publisher]

[21]. Krishnasamy P., Hall M., Robbins S.R., The role of skeletal muscle in the pathophysiology and management of knee osteoarthritis, *Rheumatology*, 2018, **57**:iv22 [Crossref], [Google Scholar], [Publisher]

[22]. Zamri N.A.A., Harith S., Yusoff N.A.M., Hassan N.M., Ong Y.Q., Prevalence, Risk Factors and Primary Prevention of Osteoarthritis in Asia: A Scoping Review, *Elderly Health Journal*, 2019, **5**:19 [Crossref], [Google Scholar], [Publisher]

[23]. Mahmoud W.S., Osailan A., Ahmed A.S., Elnaggar R.K., Radwan N.L., Optimal parameters of blood flow restriction and resistance training on quadriceps strength and cross-sectional area and pain in knee osteoarthritis, *Isokinetics and Exercise Science*, 2021, **29**:393 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE

Priscilla Anastasia Fitriany Dugis, Damayanti Tinduh, Ditaruni Asrina Utami, Soenarnatalina Melaniani. The Effect of Blood Flow Restriction in Low-Intensity Load Exercise on Visual Analog Scales in Knee Osteoarthritis Patients at Dr. Soetomo General Hospital Surabaya. *J. Med. Chem. Sci.*, 2023, 6(12) 3004-3011.

DOI: https://doi.org/10.26655/JMCHEMSCI.2023.12.15

URL: https://www.jmchemsci.com/article_177126.html