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Effect of Blood Flow Restriction in Low-Intensity Resistance Training of the Quadriceps Femoris Muscle on Joint Position Sense and Threshold to Detect Passive Motion in Patients with Knee Osteoarthritis

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ABSTRACT

Backgrounds: The functional ability of knee OA (KOA) patients is mainly affected by muscle weakness and poor proprioception function. Quadriceps femoris strengthening exercises can improve proprioceptive function in patients with KOA, whereas low-intensity resistance exercises with Blood Flow Restriction have been shown to produce hypertrophy and increase muscle strength equivalent to high-intensity resistance exercises. However, prescriptions for exercise with BFR are still very diverse, and only a few studies show the effects of BFR training on proprioceptive function in patients with KOA. This study aims to determine the impact of BFR in LI-RT of the quadriceps femoris muscle on joint position sense and threshold to detect passive motion in patients with KOA.

Methods: This randomized control trial study designed a clinical experiment with a before and after test. The research enrolled 28 people with KOA grades 2 and 3. The JPS and TTDPM, which reflect proprioceptive function, were measured before and after 6 weeks of exercise. This study's statistical analysis utilized the Monte Carlo test, independent t-test, and paired t-test. The effect size was noticed using Cohen's-d calculation to investigate the statistical influence of alterations further. The significance level was less than 0.05.

Results: The mean age of the control group was 61.43 ± 5.70 years old, and the treatment group was 57.71 ± 5.25 years old. There were significant improvements in JPS and TTDPM results before and after training in each group ($p < 0,05$). There was no significant difference in JPS and TTDPM results between the two groups on the post-test on delta values ($p > 0,05$).

Conclusions: The addition of BFR in LI-RT for 6 weeks did not affect JPS and TTDPM in patients with KOA.

Keywords: knee osteoarthritis, blood flow restriction, low-intensity resistance training, joint position sense, proprioception.

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INTRODUCTION

The most prevalent form of arthritis is osteoarthritis (OA) of the knee, which is a major cause of musculoskeletal pain, functional impairment, and decreased independence in older individuals worldwide. Osteoarthritis is a chronic disease that affects cartilage, subchondral bone, ligaments, muscles, and periarticular soft tissues such as the synovium and meniscus.[1] Muscle weakening and impaired proprioceptive function mostly influence the functional abilities of people with knee OA.[2] The proprioceptive system is essentially obtained from nerve input via mechanoreceptors in the related joints, muscles, tendons, and tissues. To offer proper neuromuscular control, joint mechanoreceptors detect joint position and movement. When proprioceptive function declines, functional ability can be maintained only if enough muscular strength compensates for reduced muscle modulation and activation precision.[2,3]

Several types of specific proprioception tests can be performed to assess joint proprioception. Still, those routinely used to evaluate knee joint proprioception are the joint position sense (JPS) and threshold to detect passive motion (TTDPM). The JPS test aims to check the accuracy of joint repositioning at a certain angle, while the TTDPM is a kinesthesia test to check the ability to feel joint movement.[4] A previous study found that quadriceps muscle-strengthening activities can enhance proprioception, balance, and physical function in KOA patients.[5]

The resistance training load recommended by the American College of Sports Medicine (ACSM) to produce muscle hypertrophy and increase strength is at least 70% of 1 repetition maximum (1 RM). On the other hand, patients with KOA are often unable to exercise at such intensity.[6] Low-intensity resistance training (30-40% 1-RM) for fewer than four weeks can enhance muscular strength through neural adaptation, but no changes in muscle morphology (hypertrophy) have been seen. It is also safer and more appropriate for persons unable to execute HI-RT or have a limited range of motion.[7]

LI-RT paired with BFR has recently gained popularity due to its similar to HI-RT effect on growing muscle mass and strength. This is an alternative to exercise treatment for persons unable to practice HI-RT.[8,9] Exercise with BFR is a type of exercise that involves temporarily occluding arterial and venous blood flow. The basic mechanism underlying BFR effects is metabolic accumulation, which causes higher growth factors, fast twitch muscle fiber activation, and protein synthesis via the mammalian target rapamycin (mTOR) pathway. In addition, increased NOS-1, heat shock protein (HSP), and decreased Myostatin gene expression were found to have a role in muscle development after BFR training. When paired with BFR, low-intensity resistance training can induce hypertrophic outcomes and build muscular strength equivalent to high-intensity strengthening activities.[8]

LI-RT combined with BFR are still very diverse, and only a few researchers have studied the effects of BFR training on proprioceptive function in patients with KOA. Therefore, this study aimed to evaluate the impact of exercise with LI-RT on the quadriceps femoris combined with BFR on proprioceptive function in patients with KOA measured by JPS and TTDPM. This study is to determine the effect of BFR in LI-RT of the quadriceps femoris on JPS) and TTDPM in patients with knee OA.

METHODS

This clinical experiment with a randomized control trial research design includes a before and post-test. This research included 28 people (5 males and 23 females) with Kellgren Lawrence grade 2 and 3 unilateral or bilateral KOA. All participants were split into two groups of 14 each. Based on the medical history, clinical symptoms, physical examination, and radiological findings, patients were diagnosed with KOA. 1) Patients with unilateral or bilateral knee OA as defined by the American College of Rheumatology clinical criteria and radiologically grade II-III as defined by Kellgren and Lawrence criteria. If the pain affects both legs, the leg with the higher pain rating on the Visual Analogue Scale (VAS) will be considered for evaluation in the study. Participants should meet the following inclusion criteria: 1) Male or female aged between 50 and 70 years old; 2) No cognitive impairment (a MoCA-Ina score of 26 or above); and 3) Willingness to sign the research agreement form. Exclusion criteria include 1) Blood clotting disorders; 2) Deep vein thrombosis; 3) Peripheral arterial disease; and 4) Peripheral neuropathy and/or polyneuropathy affecting the lower extremities. 5) Cardiorespiratory disease, including ischemic heart disease, heart rhythm disturbances, heart failure, valvular disorders, chronic obstructive pulmonary disease, and asthma; 6) Uncontrolled hypertension; 7) Uncontrolled diabetes mellitus; 8) Thrombotic stroke, hemorrhagic stroke, and transient ischemic attack. 9) Pain in a specific knee joint and/or surrounding soft tissue exceeding a VAS score of 60 mm. 10) Currently participating in a lower limb strengthening exercise program within the last 3 months. 11) Lower limb injuries, fractures, surgeries, or other musculoskeletal disorders within the last 6 months. 12) Currently receiving therapy with statins, chemotherapy, or oral contraceptives. 13) Impaired balance. 14) Hearing and visual impairments.

Dropout Criteria: 1. The research subject is unwilling to continue the study for any reason; 2. The subject could not complete the exercise according to the predetermined research protocol (did not do two consecutive training sessions); 3. Subjects experienced complications during the exercise program, such as symptoms of chest pain, dyspnea, syncope, pain (VAS > 60 mm), signs of inflammation in the trained limb, nerve injury (paresthesia that did not disappear after the cuff was removed), prolonged muscle soreness (>72 hours post-exercise) and did not improve with the provision of TENS and icing modalities, muscle weakness during or after exercise, which did not allow for continued training.

The LI-RT (30% 1-RM) was administered to the intervention group with BFR, while the control group underwent only LI-RT. BFR was applied to the most proximal region of the thigh in the targeted extremity of the intervention group using a 21 cm wide thigh cuff at 50 mmHg pressure. The cuff remained inflated throughout the workout, and each session was limited to a maximum of 10 minutes. LI-RT using a Quadriceps Bench Machine at 30% 1-RM, with 75 repetitions per session (split into 5 sets of 15 repetitions with a 1-minute rest between sets) for 6 weeks, was implemented on both groups. The JPS and TTDPM were assessed via a Cybex NORM TM Isokinetic Dynamometer Machine before and after the intervention (96 hours after the last session). The obtained data was analyzed using several tests, such as the Monte Carlo test, independent t-test, and paired t-test, through SPSS statistic 26 (IBM, USA). The statistical effect of changes was quantified using Cohen's d formula. The significance level was established as below 0.05.

This study was conducted at the Medical Rehabilitation Installation of Dr. Soetomo Surabaya Hospital outpatient clinic from January to March 2023. Ethical approval was granted by the Health Research Ethics Committee of Dr. Soetomo Surabaya Hospital/Universitas Airlangga with certificate number 0544/KEPK/XII/2023.

RESULTS

The entire amount of patients examined in this study was 28, divided into two groups of 14 each. The intervention group received LI-RT in conjunction with BFR on the quadriceps femoris, whereas the control group received only LI-RT. Both groups got exercise twice per week for six weeks. According to the research protocol, subjects were measured for JPS 30^{o}, JPS 60^{o} and TTDPM before and after exercise, and 28 subjects were able to complete the

Table 1. Characteristics of the subjects in both groups before treatment

Variables	Treatment Group (n = 14)	Control Group (n = 14)	p-values
Gender			0.622
Man	3 (21.4%)	2 (14.3%)	
Woman	11 (78.6%)	12 (85.7%)	
Age (years)	57.71 ± 5.25	61.43 ± 5.70	0.085
Age Category			0.127
Elderly	8 (57.1%)	4 (28.6%)	
Pre-Elderly	6 (42.9%)	10 (71.4%)	
Body Weight (Kilograms)	66.78 ± 13.00	64.71 ± 8.65	0.624
Height (Centimeters)	158.78 ± 7.84	152.57 ± 8.73	0.058
BMI (kg/m^2)	26.30 ± 3.99	27.85 ± 2.80	0.243
BMI category			0.964
Normoweight	3 (21.4%)	2 (14.3%)	
Overweight	4 (28.6%)	4 (28.6%)	
Obese Grade I	6 (42.9%)	7 (50%)	
Obese GradeII	1 (7.1%)	1 (7.1%)	
Location of the OA			0.699
Right	8 (57.1%)	9 (64.3%)	
Left	6 (42.9%)	5 (35.7%)	
Grade OA			0.430
Grade 2	10 (71.4%)	8 (57.1%)	
Grade 3	4 (28.6%)	6 (42.9%)	
IPAQ Pre			0.430
Low	10 (71.4%)	8 (57.1%)	
Moderate	4 (28.6%)	6 (42.9%)	
Comorbid			0.313
No Comorbid	9 (64.3%)	8 (57.1%)	
Hypertension	3 (21.4%)	5 (35.7%)	
Diabetes Mellitus	2 (14.3%)	0 (0%)	
Joint Position Sense(JPS) Pre at 30^o (Degree)	25.10 ± 6.84	22.70 ± 5.98	0.331
Joint Position Sense(JPS) Pre at 60^o (Degree)	50.08 ± 9.94	49.65 ± 9.66	0.907
Time to Detect Passive Motion (TTDPM) Pre (Second)	16.56 ± 19.51	11.16 ± 4.45	0.972

IPAQ: International Physical Activity Questionnaire (IPAQ); BMI: Body Mass Index; OA: Osteoarthritis; *Significant p-vslue < 0.05

exercise protocol without any adverse effects. Result analysis assessed the JPS 30o, JPS 60o and TTDPM before and after exercise and compared changes in the values of JPS 30^o, JPS 60^o and TTDPM after exercise between groups.

Regarding the subject's characteristics, the most common gender in both groups was women. The mean age of the control group was 61.43 ± 5.70 years old, and the treatment group was 57.71 ± 5.25 years old. The majority of the treatment group was elderly (57.1%), in contrast with the control group, the majority of pre-elderly (71.4%). Regarding the nutrition status of the treatment group, it found that most of the subjects had obese grade I (42.9%), with the average BMI from all of the subjects in the treatment groups was 26.30 ± 3.99 kg/m^2, body weight was 66.78 ± 13.00 kg. Nonetheless, the nutrition status of the control group is quite different. The BMI average of all subjects in the control groups was 64.71 ± 8.65 kilograms, and the BMI was 27.85 ± 2.80, which was higher than the treatment group, and most of them belonged to obese grade I. Both groups showed that the most common OA grading was grade 2. The mean before TTDPM exercise of JPS at 30^o, 60^o and the TTDPM pre-exercise was higher in the treatment groups than in the control group. There was no significant association of the characteristic subjects with each group (p>0.05). The detail characteristics of the research subjects are detailed in Table 1.

In the table below, we reported the changes of JPS at 300 and 600, TTDPM before and after exercise. In general, there was an enhancement of JPS at 300 and 600 in the treatment and control groups. Nonetheless, the TTDPM in both groups decreased. We found a significant difference in both group of JPS at 300 and 600 TTDPM before and after exercise (p<0.05). Differences in JPS 30^o, 60^o and Time to Detect Passive Motion Values Before and After Exercise in TTDPM were explained in detail in Table 2.

After inter-group exercises, we found that the JPS at 30o and 60o and also the TTDPM after inter-group exercise were higher in the treatment group rather than the control group. Meanwhile, the mean

Table 2. Differences in JPS 30º, 60º and Time to Detect Passive Motion Values Before and After Exercise in TTDPM

Variables	Treatment Group (n = 14)			Control Group (n = 14)		
	Before	After	p-values	Before	After	p-values
Joint Position Senseat 30º (degrees)	25.10 ± 6.84	29.05 ± 2.69	0.033	22.70 ± 5.98	27.84 ± 3.58	0.000*
Joint Position Senseat 60º (degrees)	50.08 ± 9.94	57.42 ± 2.00	0.012	49.65 ± 9.66	55.57 ± 4.08	0.010*
Time to Detect Passive Motion (second)	16.56 ± 19.51	8.25 ± 2.80	0.002	11.16 ± 4.45	7.80 ± 2.90	0.000*

*Significant p-vslue < 0.05

Table 3. Value of Joint Position Sense at 30º and 60º and Threshold to Detect Passive Motion after inter-group exercises

Variables	Treatment Group After Training (n = 14)	Control Group After Training (n = 14)	p-values
Joint Position Sense at 30º (degrees)	29.05 ± 2.69	27.84 ± 3.58	0.323
Joint Position Senseat 60º (degrees)	57.42 ± 2.00	55.57 ± 4.08	0.143
Time to Detect Passive Motion (second)	8.25 ± 2.80	7.80 ± 2.90	0.679

*Significant p-vslue < 0.05

Table 4. Differences in Joint Position Sense Values at 30º and 60º and Time to Detect Passive Motion in both groups

Variables	Treatment Group (n = 14)	Control Group (n = 14)	p-values
Δ Joint Position Sense at 30º (degrees)	3.94 ± 6.17	5.14 ± 4.93	0.575
Δ Joint Position Sense at 60º (degrees)	7.34 ± 9.47	5.92 ± 7.41	0.662
Δ Time to Detect Passive Motion (seconds)	-8.30 ± 19.80	-3.35 ± 2.50	0.702

*Significant p-vslue < 0.05

difference of the variables measured in both groups was insignificant (p>0.05). The value of JPS 30º, JPS a60º and TTDPM Motion after inter-group exercises in Table 3

Even though we found a significant difference between the before and after exercise intra- group, the mean difference intergroup was not significant in JPS 300, 600, and TTDPM. The difference (delta) in the value of JPS 30º, JPS a60º and TTDPM before and after exercise between the intervention group and the control group is shown in Table 4.

DISCUSSION

Regarding subject characteristics, most subjects were female, 78.6% in the treatment group and 85.7% in the control group. The mean age of the treatment group was 57.71 5.25 years, whereas the mean age of the control group was 61.42 5.70 years. This is in line with the incidence of knee OA, which is higher in women than in men, particularly in women over the age of 55.[10] Patients in the study had an average BMI of 23-34 kg/m2, with the largest distribution in obesity class I, with 6 subjects in the treatment group and 7 subjects in the control group. According to a 2014 meta-analysis by Zheng and Chen, obesity is a significant risk factor for knee OA.[11] The IPAQ was used to measure the activity level of the research subjects before treatment, revealing a majority of subjects with low physical activity. According to a 2018 study by Shim et al., persons with knee OA engage in less physical activity than people without knee OA.[12]

Controlled type 2 diabetes mellitus impacted 14.3% of the treatment group participants, whereas controlled hypertension affected 21.4% of the treatment group and 35.7% of the control group (p-value 0.313). This is connected to the hypothesis that the severity and risk of knee OA are determined not only by age and excess load on the knee joint but also by metabolic variables like diabetes and hypertension, which alter vascularization and the inflammatory response in the knee joint.[13,14]

This study showed significant improvement in JPS 30º and 60º and TTDPM in the intervention and control groups after training for 6 weeks. The JPS measurements at 30º and 60º are considered two angles with the most extreme knee joint movement. The most activated muscle spindles are in the most difficult and extreme joint positions, so the angles of 30º and 60º are considered the two angles that best represent the assessment of knee joint proprioception.[14,15]

The increase in proprioceptive function after resistance training in this study aligns with a study conducted by Lai et al. in 2018, which stated that strengthening exercises with squats for 8 weeks in patients with knee OA improved proprioceptive function as assessed by TTDPM. This improvement in proprioception is associated with increased muscle strength, which stimulates proprioception receptors around the knee joint, especially the muscle spindles, resulting in improvements in proprioception after 6 weeks of exercise. Decreased proprioception function in patients with KOA, most elderly and pre-elderly, can occur at the central and/ or peripheral level. At the central level, declining in proprioception is related to age caused by the degeneration process, where the proprioception function will decrease because of poor sensory input integration. While the peripheral level is a decrease in proprioception that occurs due to damage to the joints and structures around it occur in patients with KOA.[16]

A study by Ribeiro and Oliveira (2010) stated that there was an improvement in knee joint proprioception in the group of patients with knee OA who received exercise compared to those who did not. The proprioceptive function is regulated at the peripheral and central system levels. In the peripheral system, after doing regular exercise, morphological adaptation occurs in the muscle spindle. Adaptation occurs at the micro level which the intrafusal muscle fibers undergo metabolic changes, and at the macro level, the latency of the stretch reflex shortens, and the amplitude increases so that the joint mechanoreceptors become more sensitive to movement. At the central level of the proprioception system, exercise can increase muscle spindle output via the γ route to increase proprioception projection on the cortex. Therefore, regular exercise can support central nervous system plasticity, such as increasing synaptic connections and/ or structural changes in the organization and number of connections between brain neurons. And at the macro level, namely, the latency of the stretch reflex shortens, and the amplitude increases so that the joint mechanoreceptors become more sensitive to movement. At the central level of the proprioception system, exercise can increase muscle spindle output via the γ route to increase proprioception projection on the cortex.[17]

Proprioception problems in KOA are caused by damage to the joint due to the ongoing degeneration process in OA and damage to the structures around the joint, such as muscles, ligaments, and meniscus. This study found no significant difference in the JPS and TTDPM values of the knee joints between the intervention and the control group after exercise for 6 weeks. However, in each group, there were significant improvements in proprioception before and after training for 6 weeks. This was contrary to the researchers' expectations, in which the improvement in knee joint proprioception was greater in the group that received the additional BFR. Proprioceptive mechanoreceptors are most commonly found in muscles and affect joint accuracy.[18] Researchers did not objectively measure muscle mass before and after the study in each group, so it cannot be known whether the increase in muscle mass in both groups after exercise for 6 weeks was significant enough to produce greater proprioception improvements in the BFR group.

In addition, a study by Vincent et al. states that age is correlated with musculoskeletal and neurological function, in which the older the age, the more musculoskeletal and neurological systems decline.[19] Relph et al. also stated that the elderly population has decreased joint accuracy as assessed by JPS and TTDPM.[14] The control group in this study was dominated by the pre-elderly age group, namely those under 60 years of age, with the highest distribution of pre-elderly in the control group (71.4%) and the treatment group was dominated by the elderly age group (57.1%). Although statistically, the distribution by age category did not differ significantly between the two groups, this could be the reason for the insignificant improvement in proprioception between the two groups after 6 weeks of exercise.

The assessment of the differences in proprioception improvement scores before and after exercise between groups in this study showed insignificant results (p-value JPS 30º 0.576; p-value JPS 60º 0.662; p-value TTDPM 0.702). Several things might be the cause behind the insignificance of the research results. First, this study was dominated by patients with low physical activity as assessed by IPAQ scores, in which the number in the intervention group was greater (10 subjects; 71.4%) compared to the control group (8 subjects; 57.4%). Statistically, the difference in the distribution of these numbers was not significant, but this is likely the reason for the insignificant results in the improvements in the two groups. According to a study by Aldosari et al. (2022), low physical activity correlated with decreased muscle mass, worsening knee OA, and reduced proprioception accuracy.[20]

This is contrary to a study conducted by Lazaridou et al. (2018), which states that there is a decrease in physical function and quality of life in patients with knee OA with high physical activity as measured by Self-administered Western Ontario and McMaster Universities index (WOMAC). And Patient Reported Measurement Information System (PROMIS).[21] Researchers only assessed the IPAQ score at the beginning of the study as primary data and did not assess it during and after the exercise was completed. The researchers of this study do not know whether there were changes in the activity level of the subjects during the study, which caused more significant loading on the knee joints, or reduced activity levels, which led to decreasing quadriceps femoris muscle mass so that knee joint proprioception was not improved.

The second possible cause of insignificant is related to the TTDPM value. In this study, the primary data mean TTDPM values were more significant in the control group, namely 16.56 ± 19.51, while in the control group, it was 11.16 ± 4.45. Even though there was no statistically significant difference in the baseline data before the practice started, this is also suspected to be the cause of the difference in improvement that was not significant between the two groups. By the theory of TTDPM, the greater the value of TTDPM, the worse the joint's ability to feel movement.[13]

Third, improvements in proprioception can occur at the level of central and/or peripheral proprioception at the micro or macro level. Researchers did not evaluate muscle morphology or laboratory markers as markers of metabolic muscle changes at the micro or macro levels, namely latency stretch reflex or firing of the motor unit via electromyography. So it is unclear whether the improvement in JPS and TTDPM values that occurred in each group was followed by enhancements at other micro and macro levels which might indicate whether one of the two groups is superior to the other.

Fourth, the literature by Jha et al. (2017) states that warming up for 5-10 minutes before measuring proprioception has a positive correlation with the measurement results, which warms up before assessing proprioception causes the muscle spindles to be stretched constantly so that the sensitivity to joint position increases.[22] This is contrary to this study, wherein the protocol, the researchers should have done a warm-up before measuring JPS and TTDPM. This may also affect the results of the JPS and TTDPM measurements in this study.

In Indonesia, more research on the effect of adding BFR to LI-RT on patients with KOA is needed. Exercise with BFR can produce muscular hypertrophy and enhance muscle strength by stimulating increased growth factors, activation of rapid twitch muscle fibers, and increased protein synthesis via the mammalian target of rapamycin (mTOR) pathway. Furthermore, metabolic buildup increases Nitric oxide synthase 1 (NOS-1), heat shock protein (HSP), and decreases Myostatin gene expression.[8]

The improvement in the accuracy of knee joint proprioception was found in the group that received additional BFR in LI-RT and the group with LI-RT only, indicating that weight training in patients with KOA can improve knee joint proprioception. This is associated with increased muscle strength and muscle mass, the site of most proprioceptive receptors. Thus, LI-RT with the addition of BFR or LI-RT with many repetitions, such as the control group protocol used in this study, can be an alternative therapy for patients with KOA who cannot tolerate moderate or high-intensity resistance training. Until now, the prescribing of training with BFR is still very diverse, and there is no standard prescribing. To the knowledge of the researchers, this study is the first study in Indonesia to assess the effect of BFR on LI-RT in patients with KOA on knee joint proprioception function as assessed by JPS and TTDPM, so the results of this study can enrich scientific references regarding the effects of BFR administration on LI-RT of the quadriceps femoris on the proprioceptive function in patients with KOA.

This research has several limitations, including 1) Researchers did not do warm up before assessing JPS and TTDPM either before or after the exercise protocol, which could affect knee joint sensitivity in feeling motion and positioning joint; 2) Researchers did not conduct periodic assessments and monitoring of daily intake, activity levels, and other supporting examinations such as laboratory markers, evaluation of muscle mass, or electromyography studies.

CONCLUSION

Performing LI-RT with high repetitions on the quadriceps femoris for 6 weeks improves JPS and TTDPM values in patients with KOA. It can be inferred that supplementing BFR to low-intensity resistance training (LI-RT) on the quadriceps femoris for 6 weeks enhances JPS and TTDPM values in KOA patients. Performing LI-RT with high repetitions on the quadriceps femoris for 6 weeks improves JPS and TTDPM values in patients with KOA. Performing LI-RT with high repetitions on the quadriceps femoris for 6 weeks improves JPS and TTDPM values in patients with KOA. However, in comparison to LI-RT only, the addition of BFR did not significantly enhance JPS and TTDPM values in patients with KOA who underwent LI-RT for 6 weeks.

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CONFLICT OF INTEREST

This research report has no conflicts of interest.

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AUTHOR CONTRIBUTION

All of the author has been contributed in the manuscript preparation

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