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Effectiveness of low-load resistance training with blood flow restriction vs. conventional high-intensity resistance training in older people diagnosed with sarcopenia: a randomized controlled trial

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Low-load resistance training with blood flow restriction (LRT-BFR) has shown potential to improve muscle strength and mass in different populations; however, there remains limited evidence in sarcopenic people diagnosed with sarcopenia criteria. This study systematically compared the effectiveness of LRT-BFR and conventional high-intensity resistance training (CRT) on clinical muscle outcomes (muscle mass, strength and performance), cardiovascular disease (CVD) risk factors and sarcopenia-related biomarkers of older people with sarcopenia. Twenty-one older individuals (aged 65 years and older) diagnosed with sarcopenia were randomly assigned to the LRT-BFR (20%–30% one-repetition maximum (1RM), n = 10) or CRT (60%–70% 1RM, n = 11) group. Both groups underwent a supervised exercise program three times a week for 12 weeks. The primary outcome was knee extensor strength (KES), and the secondary outcomes included body composition (body mass, body mass index and body fat percentage), muscle mass [appendicular skeletal muscle mass index (ASMI)], handgrip strength, physical performance [short physical performance battery (SPPB) and 6-m walk], CVD risk factors [hemodynamic parameters (systolic and diastolic blood pressure and heart rate (SBP, DBP and HR)) and lipid parameters (total cholesterol, triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein)], sarcopenia-related blood biomarkers [inflammatory biomarkers, hormones (growth hormone (GH) and insulin-like growth factor 1) and growth factors (myostatin and follistatin)] and quality of life [Short Form 36 Health Survey (SF-36)]. Both interventions remarkably improved the body composition, KES, 6-m walk, SBP, HDL, TG, GH, FST and SF-36 scores. CRT significantly improved the ASMI ($p < 0.05$) and SPPB ($p < 0.05$). A significant improvement in HR was observed only after LRT-BFR. No significant between-group differences were found before and after the interventions. This study suggested that LRT-BFR and CRT are beneficial to the clinical muscle outcomes, CVD risk factors and certain sarcopenia-related biomarkers of older people with sarcopenia. By comparison, CRT seems more effective in improving muscle mass, while LRT-BFR may be more beneficial for improving cardiovascular health in this population. Therefore, LRT-BFR is a potential alternative to CRT for aging sarcopenia.

Keywords Sarcopenia, Blood flow restriction, Resistance training, Muscle mass, Cardiovascular disease risk, Biomarker

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Sarcopenia is an age-related musculoskeletal condition characterised by progressive loss in muscle mass and performance, as well as muscle strength, and is often associated with some adverse health consequences, such as falls, fractures, function decline, long hospital stays, decreased quality of life and even all-cause mortality[1]. Owing to the aging population, the global prevalence of sarcopenia has recently increased from 10 to 27% and is expected to rise further[2]. Its high prevalence and associated negative outcomes may result in considerable challenges to healthcare systems[3]. Therefore, exploring a safe and effective treatment for counteracting and reversing sarcopenia in older people is urgent.

Conventional high-intensity resistance training (CRT) [i.e. > 70% one-repetition maximum (1RM)] is strongly recommended as the most effective approach for preventing and managing sarcopenia in older people[4]. However, its high mechanical load may be unsuitable for frail older people as it may increase the risk of exercise-induced injuries[5]. In contrast, low-load resistance exercise (LRT, 20%–50% 1RM) has been shown to be inadequate for improving muscle mass and strength[6]. Recently, many researchers have shifted their focus to a promising training approach known as blood flow restriction (BFR) training[7]. By applying pneumatic cuffs or elastic wraps at the proximal limbs, restricting arterial inflow and blocking venous outflow during LRT[8], LRT combined with BFR (LRT-BFR) has shown significant potential in promoting muscle hypertrophy and strength gains across various populations, such as athletes, patients with musculoskeletal disorders[9], healthy young and older people[10]. Due to its low intensity and comparable effects on muscle growth, a growing body of studies recommends LRT-BFR as an alternative to CRT, particularly for populations unable to perform high-intensity exercise[11]. However, clinical studies specifically targeting older people diagnosed with the latest sarcopenia criteria—who typically have weaker physical conditions and a greater need for muscle function improvement—are still lacking[12]. Since CRT is the current gold standard for sarcopenia treatment, comparing the outcomes of LRT-BFR and CRT in this population is crucial to determine whether LRT-BFR can be recommended as a viable alternative.

In addition to the effectiveness of LRT-BFR, its safety has also been a critical research focus, particularly in populations at high risk for CVD, as the occlusion of blood vessels may trigger blood pressure reflexes that impair cardiovascular function in older people[13]. Although the pathogenesis of sarcopenia is not fully understood, it is associated with chronic low-grade inflammation, insulin resistance and metabolic imbalances caused by intramuscular fat accumulation—factors also linked with CVD[14]. Therefore, individuals with sarcopenia may have an elevated risk of developing CVD than their peers[15]. Furthermore, LRT-BFR can lead to several adverse events such as ecchymosis, haemorrhages, numbness and venous thrombosis[16], highlighting the importance of investigating its effects on CVD risk factors in sarcopenic older people. In addition, most studies have primarily focused on clinical outcomes such as muscle mass, strength and performance, while evidence regarding sarcopenia-related blood biomarkers remains limited. This gap in research may hinder a comprehensive understanding of the mechanisms underlying exercise-induced changes in older people with sarcopenia. To address this, the present study included CVD risk factors and sarcopenia-related blood biomarkers as key outcomes to investigate the potential mechanisms of these exercise-induced changes.

This study aimed to systematically compare the effects of LRT-BFR and CRT on body composition, muscle mass, strength and performance, CVD risk factors, sarcopenia-related blood biomarkers and health-related quality of life in older people with sarcopenia. Additionally, the safety of the cardiovascular health of LRT-BFR in this population was also investigated.

Materials and methods

Study design

This study is a single-blinded, two-arm, randomised controlled trial conducted from December 2022 to May 2023. It was approved by the Ethical Committee of Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences in China (approval number: CMEC-2020-KT-42) and registered in the Chinese Clinical Trial Registry (ChiCTR2100042803, registration date: 28/01/2021). The flowchart is presented in Fig. 1.

Recruitment of subjects

Participants were recruited via regular community medical examinations, health education lectures and home follow-ups. A total of 353 subjects were screened using the SARC-F, a reliable tool for screening sarcopenia, to determine their eligibility for participation. SARC-F encompasses five elements rated as 0–10: slow walking, walking assistance, rising from a chair, stair climbing and falls[17]. The participants with a SARC-F score of 4 points or higher (indicative of sarcopenia risk) were subjected to the Asian Working Group for Sarcopenia (AWGS) screening, which involved assessments of appendicular skeletal muscle mass index (ASMI) and handgrip strength (HGS) and a 6-m walk (6-MW) test. Those who met the screening and eligibility criteria and volunteered to participate in the study were asked to provide an informed consent form and received familiarisation courses regarding study procedures, experimental equipment and exercise protocol. Finally, 21 individuals (13 males, 8 females; Table 1) who met the eligibility criteria volunteered to participate in this study.

Inclusion criteria

a) Aged 65 years and older.
b) Diagnosed with sarcopenia according to the AWGS 2019 guidelines, sarcopenia was characterized by ASMI of less than 7 kg/m^2 in males and less than 5.7 kg/m^2 in females, determined through a bioelectrical impedance analyzer; a 6-MW test with a speed under 1 m/s; and/or HGS below 28 kg for men and below 18 kg for women)[18].
c) Without regular physical activity over the past three months (performing exercise > 2 times per week)[19].

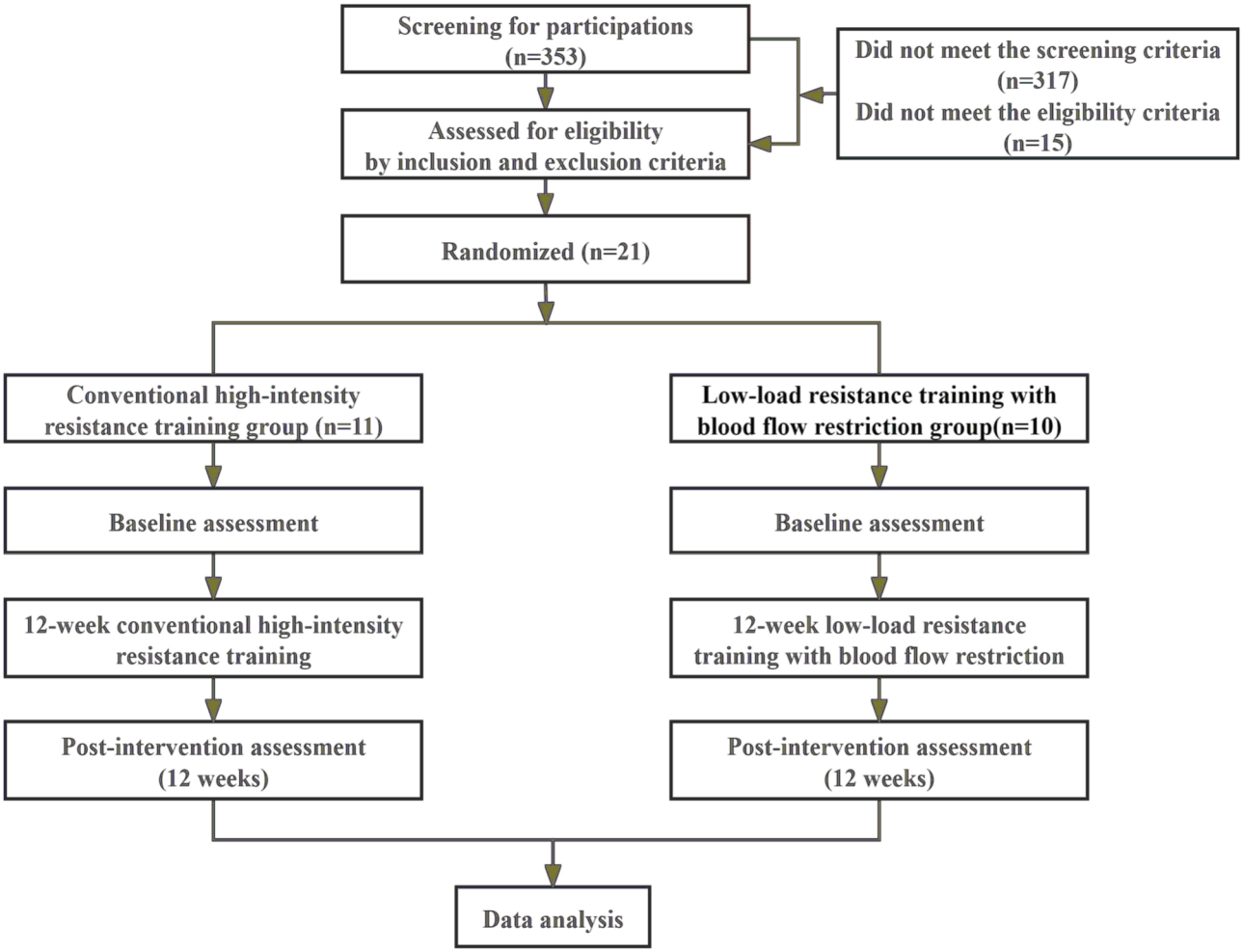

Fig. 1. Experimental flow chart.

d) No cognitive impairment and are able to follow exercise and assessment commands assessed using the Mini-Mental State Examination (MMSE). A score below 18 suggests cognitive impairment, leading to exclusion from the study[20].

Exclusion criteria

a) With contraindications to exercise, such as severe musculoskeletal complications, deep venous thrombosis or coagulation disorder.
b) With co-morbidities such as stroke diagnosed by a neurologist, diabetes with severe complications such as retinopathy, and cardiovascular diseases, including heart failure, coronary ischemia or/and arrhythmias.
c) Having high-risk factors for exercise such as uncontrolled hypertension (systolic blood pressure (SBP) > 150 / diastolic blood pressure (DBP) > 90 mmHg) and deep venous thrombosis.
d) With a history of hematological disorders or taking hematological drugs (hormones, anticoagulants, etc.)
e) Scheduled to relocate out of the community in the next three months.
f) Did not sign the informed consent form.

Randomisation and blinding

All the participants who signed informed consent forms from four communities in Chongming, Shanghai, China, were recruited and assigned randomly into the LRT-BFR (n = 10) or CRT (n = 11) group at an equal ratio. The randomised sequences stratified by sex and age were generated with SPSS software (version 27.0) by an independent biological statistician. The generated grouping information was delivered as an encrypted electronic file to the research staff responsible for implementing the intervention and the only researcher who knew the group information. This study used a single-blind design, wherein the researchers responsible for random group assignments were unaware of the specific intervention plans and the assessors conducting pre- and post-intervention evaluations were also blinded to the group allocations.

	CRT group (N = 11)	LRT-BFR group (N = 10)	P
Demographic variables			
Age (years) (M ± SD)	73.15 ± 4.22	71.25 ± 3.15	0.325
Sex (M/F)	6 / 5	7 / 3	0.659
Anthropometric variables			
Mass (kg) (M ± SD)	60.87 ± 15.00	53.31 ± 6.49	0.291
Height (cm) (M ± SD)	159.77 ± 7.01	162.88 ± 6.53	0.325
BMI (kg/m^2) (M ± SD)	23.59 ± 5.83	20.16 ± 1.75	0.102
Education, n (%)			
None	3 (27)	1 (10)	0.095
Elementary school	3 (27)	7 (70)	
Middle school	5 (45)	1 (10)	
High school and above	0 (0)	1 (10)	
Smoking status, n (%)			
Never	6 (55)	4 (40)	0.417
Previous	1 (9)	3 (30)	
Current	4 (36)	3 (30)	
Alcohol status, n (%)			
Never	9 (82)	5 (50)	0.192
Previous	2 (18)	2 (20)	
Current	0 (0)	3 (30)	
Live alone, n (%)	5 (45)	3 (30)	0.392

Table 1. Baseline Characteristics of Participants. CRT, conventional high-intensity resistance training; LRT-BFR, low-load resistance training with blood flow restriction; M ± SD: mean ± standard deviation; BMI: body mass index.

Intervention program

The exercise program was conducted in the community of China under the supervision of a certified physical therapist. Before the intervention, the subjects were asked to participate in a familiarisation session (two–three pre-intervention sessions). Face-to-face exercise was performed three times a week for 12 weeks during the intervention. Both groups underwent resistance training using Thera-Band elastic bands, with the intensity tailored to the intervention protocols for each group. A 1RM test was also conducted to determine the resistance training intensity for each participant. During the training period, the research staff responsible for intervention delivery recorded the adherence rate of all participants.

All participants performed the following movements with different resistance intensities and numbers of repetitions in two groups: shoulder external rotation, elbow extension, elbow flexion, leg squat abduction, lunge and bend, shoulder abduction and half-squat stand-up.

CRT group

The participants in the CRT group performed three sets of 15 repetitions with 60% 1RM for the initial four-week period, then progressed to three sets of 12 repetitions with 65% 1RM for the next four weeks and finally completed three sets of 10 repetitions with 70% 1RM during the last four weeks. A 60-s interval was between sets.

LRT-BFR group

Determination of limb occlusion pressure (LOP) Individualized occlusion pressure was used for BFR. The patients were asked to lie supine, and a Doppler ultrasound probe (Doppler probe: DV-600, Marted, São Paulo, Brazil) was placed at the radial and carotid arteries to measure their auscultated pulses in the upper and lower extremities, respectively. The subjects were kept in the supine position to calculate their individual LOP. A nylon cuff (wide: 14 cm, H + Cuff Curved Cuffs, USA) attached to a cuff pump (H + Cuff Pump, USA) was positioned on the inguinal fold area for the resistance of the lower limbs and the armpit area for the resistance of the upper limbs to the point at which the blood pulse was interrupted, establishing the LOP. The cuff pressure was set at 50% LOP and inflated throughout each exercise session, including the intervals between sets. The percentage of LOP was determined based on previous studies. Relatively BFR with low pressure can induce comparable increases in muscle mass to those achieved with high pressure[21,22]. Moreover, older people with sarcopenia typically have reduced physical fitness and may be less tolerant of higher pressure. This consideration is important for minimizing discomfort caused by the compression of active muscles while maintaining the technique's effectiveness. Therefore, a low LOP (50%) was selected to enhance participants' comfort during the exercises[22].

Resistance training The resistance training program in LRT-BFR comprised three sets of 30–15–15 repetitions for each exercise. These repetitions were performed with increasing intensity from 20 to 30% 1RM using various colours of Thera-Band elastic bands. The subjects would rest for 20 s between sets and 30 s between exercises.

Progression program The exercise intensity was raised every four weeks by reevaluating the 1RM of each participant during the training period.

Outcomes

The primary outcome was lower extremity muscle strength, and the secondary outcomes included clinical outcomes (body composition, HGS and physical performance), CVD risk factors and sarcopenia-related blood biomarkers. Assessments were conducted at two time points: baseline (0 weeks) and post-intervention (12 weeks). The researchers responsible for the evaluation did not know the grouping information.

Primary outcome

Lower extremity muscle strength (knee extensor strength, KES): 1RM test is one of the most common methods for assessing KES in individuals with sarcopenia. Considering that the potential risk of skeletal muscle injury is associated with standard 1RM tests in older individuals, KES was evaluated using an estimated 1RM[23]. Following the measurement protocol reported by Brzycki et al.[24], the subjects underwent a test whilst seated on an extensor chair equipped with a weight plate measured in kilograms. Initially, the weight plate load was adjusted at 45% BM for females and 64% for males[25]. A high weight was applied for testing if the subjects could perform more than 10 repetitions; otherwise, a submaximal weight was used. The 1RM value was estimated using the following formula: estimated 1RM (kg) = submaximal weight (kg) / $(1.0278 - 0.0278 \times$ maximal number of repetitions$)$[24].

Secondary outcomes

Clinical outcomes

1. Body composition. BM, body mass index (BMI), body fat percentage (BFP) and ASMI were measured using a bioelectrical impedance analyzer (Inbody S10, Korean). ASMI was calculated as appendicular skeletal muscle mass / height^2.[26]
2. HGS. HGS was assessed using a hand dynamometer (Jamar Plus + Digital Hand Dynamometer; IL, USA) following the manufacturer's instructions. The measurement was performed three times, and the maximum value was recorded.
3. Physical performance. Physical performance was assessed via SPPB and 6-MW test. The SPPB has three components: a balance test, a 4-m walk test and a chair sit–stand test[27]. During the standing balance test, the subjects were asked to stand in three positions (side-by-side, semi-tandem and full tandem) and maintain them for 10 s. During the walking test, a 4-m walking at a desired stride speed was repeated twice, and the shortest duration was recorded. During the chair sit–stand test, the participants were tasked with five consecutive chair sit–stand cycles as quickly as possible, keeping their arms folded across their chests. Finally, the duration was recorded. Each task was rated on a scale of 0–4. The SPPB score consisted of the total score of the three items ranging from 0–12, where 0 represents the lowest lower extremity function and 12 represents the highest lower extremity function[27]. During the 6-MW test, the participants were asked to walk 6 m at their usual pace, the duration of which was recorded.

CVD risk factors

1. Hemodynamic parameters. Hemodynamic responses were monitored by measuring the SBP, DBP and heart rate (HR) using a general sphygmomanometer (model HEM-705CP; OMROM).
2. Serum lipid parameters. Serum lipid markers [high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC) and triglyceride (TG)] were detected in a fasting state 48 h before the intervention and seven days after the intervention.

Blood biomarkers related to sarcopenia Hormones [growth hormone (GH) and insulin-like growth factor 1 (IGF-1)], inflammatory factors [interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α) and C-reactive protein (CRP)] and growth factors [follistatin (FST) and myostatin (MSTN)] were detected by enzyme-linked immunoassay in a fasting state 48 h before the intervention and seven days after the intervention.

Health-related quality of life (HRQoL) HRQoL was assessed using the Mandarin version of the Short Form 36 Health Survey (SF-36), which has been proved as a reliable and validated assessment tool for HRQoL among populations in Shanghai, China[28]. SF-36 includes eight dimensions: physical function (PF), role-physical (RP), body pain (BP), social function (SF), role-emotional (RE), vitality, general health, and mental health (MH)[29]. Each dimension was assessed on a scale of 0 to 100, with high scores representing a good quality of life[29].

Safety measures

1. All exercise sessions were supervised by a certified physiotherapist, with adjustments made to the exercise program if any discomfort was reported.
2. To minimize cardiovascular risks associated with the two exercise modalities in participants, subjects were equipped with fitness trackers (Xiaomi Mi Band 6, Xiaomi Corporation, Beijing, China) during sessions to continuously monitor HR, ensuring their safety throughout the intervention. Additionally, a cardiologist

monitored the subject's blood pressure and HR before and after exercise, ensuring that timely medical assistance was available for patients who experienced any discomfort.

Program for dealing with absences or withdrawals

For training absences, we scheduled remedial sessions during the week. For those unable to attend the remedial sessions, we would calculate the compliance rates based on the total sessions attended for participants who missed individual classes. If a participant's compliance rate fell below a predefined threshold (80%), their data were classified as incomplete and treated accordingly in the statistical analysis. For participants who withdrew from the study entirely, we employed an intention-to-treat (ITT) analysis to include as much baseline data as possible in the outcome assessments. Additionally, we conducted sensitivity analyses to evaluate the impact of excluding dropouts on the results.

Sample size calculation

The sample size was calculated with R software on the basis of an effect size of 1.26 for KES in older people from a previous meta-analysis on CRT[30]. With a power of 0.8 and an α level of 0.05, the required sample size was estimated to be 10 participants per group, totalling 20. Given the intention-to-treat principle, dropout rates were not taken into account. Ultimately, 10 participants were included in the experimental group and 11 in the control group due to practical considerations.

Statistical analysis

All data were analyzed following the principle of intent with statistical software SPSS software (version 27.0) and expressed as mean ± standard (M ± SD). The normality distribution of data was analyzed via the Shapiro–Wilk test. Baseline data were compared by paired-sample t-test (continuous data) or chi-square test (categorical data). A within-group comparison of post-intervention values was performed using a paired-sample t-test or Mann–Whitney U test (when the data did not match the normal distribution). The between-group post-intervention comparison was also conducted using covariance analysis with pre-test data as covariates. A post hoc Bonferroni adjustment was applied for multiple comparisons. Effect size (ES) was calculated to measure the difference between the two groups. The level of significance was set at 0.05.

Statement

All methods were carried out in accordance with the relevant guidelines and regulations.

Results

Participant characteristics

Amongst the 353 older people with sarcopenia who underwent screening, 21 met the screening and eligibility criteria and were randomly assigned to the LRT-BFR (n = 10, 71.25 ± 3.15 years) or CRT (n = 11, 73.15 ± 4.22 years) group. As shown in Table 1, no significant differences in all demographic characteristics were found between the two groups. The adherence rate to the exercise program was 98.1% and 95.5% for the LRT-BFR and CRT groups, respectively, with no between-group difference.

Changes in clinical outcome

Body composition

As depicted in Table 2, both groups showed a significant reduction in BM (LRT-BFR: $\Delta = -2.28$, 95%CI ($-3.74, -0.81$), $p = 0.007$; CRT: $\Delta = -3.52$, 95%CI ($-5.30, -1.74$), $p < 0.001$), BMI (LRT-BFR: $\Delta = -0.84$, 95%CI ($-1.39, -0.29$), $p = 0.007$; CRT: $\Delta = -1.36$, 95%CI ($-2.01, -0.72$), $p < 0.001$) and BFP (LRT-BFR: $\Delta = -2.33$, 95%CI ($0.78, -4.09$), $p = 0.009$; CRT: $\Delta = -4.15$, 95%CI ($-5.58, -2.72$), $p = 0.003$) compared with baseline (Fig. 2). Only the CRT group show a significant increase in ASMI ($\Delta = 0.30$, 95%CI (0.00, 0.59), $p = 0.021$) (Fig. 2). No significant between-group differences in these changes were observed.

Muscle strength

As depicted in Table 2, KES was significantly improved in the LRT-BFR ($\Delta = 4.18$, 95%CI (0.51, 7.85), $p = 0.030$) and CRT ($\Delta = 4.39$, 95%CI (1.19, 7.59), $p = 0.012$) groups (Fig. 2). Meanwhile, the HGS showed no significant change following LRT-BFR or CRT. The differences in KES between the two groups were not statistically significant.

Muscle performance

As shown in Table 2, a significant improvement in the 6-MW test was observed in the LRT-BFR ($\Delta = 0.18$, 95%CI (0.07, 0.30), $p = 0.005$) and CRT ($\Delta = 0.24$, 95%CI (0.16, 0.31), $p < 0.001$) groups (Fig. 2). The SPPB significantly increased in the CRT group ($\Delta = 2.09$, 95%CI (1.39, 2.79), $p = 0.004$) showed a trend towards a significant increase in the LRT-BFR group ($\Delta = 0.60$, 95%CI (-0.09, 1.29), $p = 0.059$) (Fig. 2). No statistically significant differences were observed between the two groups.

Changes in CVD risk factors

Hemodynamic parameters

As shown in Table 3, SBP significantly decreased following LRT-BFR ($\Delta = -24.30$, 95%CI ($-41.26, -7.34$), $p = 0.010$) and CRT ($\Delta = -16.09$, 95%CI ($-30.93, -1.25$), $p = 0.036$) (Fig. 3). Significant reductions in HR were observed only in the LRT-BFR group ($\Delta = -15.00$, 95%CI ($-27.86, -2.14$), $p = 0.027$) (Fig. 3). No significant between-group differences in these changes were found.

	CRT group (N = 11)			LRT-BFR group (N = 10)			Mean change (95% CI)		Between-group differences	
	Pre (M ± SD)	Post (M ± SD)	P	Pre (M ± SD)	Post (M ± SD)	P	Δ (CRT group)	Δ (LRT-BFR group)	P	ES
Body composition										
BM (kg)	60.87 ± 15.00	57.35 ± 13.32	< 0.001***	53.31 ± 6.49	51.03 ± 6.14	0.007**	-3.52 (-5.30, -1.74)	-2.28 (-3.74, -0.81)	0.696	0.009
BMI (kg/m^2)	23.90 ± 5.99	22.54 ± 5.43	< 0.001***	20.17 ± 1.73	19.32 ± 1.81	0.007**	-1.36 (-2.01, -0.72)	-0.84 (-1.39, -0.29)	0.679	0.010
BFP (%)	31.18 ± 8.75	27.03 ± 8.46	0.003**	23.44 ± 4.30	21.12 ± 5.77	0.009**	-4.15 (-5.58, -2.72)	-2.33 (0.78, -4.09)	0.058	0.195
Muscle mass										
ASMI (kg/m^2)	6.33 ± 0.84	6.63 ± 0.97	0.021*	6.16 ± 0.73	6.28 ± 0.81	0.169	0.30 (0.00, 0.59)	0.13 (-0.10, 0.36)	0.349	0.049
Muscle strength										
KES (kg)	42.02 ± 8.41	46.41 ± 5.37	0.012*	47.30 ± 6.17	51.48 ± 5.28	0.030*	4.39 (1.19, 7.59)	4.18 (0.51, 7.85)	0.203	0.089
HGS (kg)	21.92 ± 5.45	24.22 ± 8.19	0.722	28.61 ± 6.89	27.47 ± 4.66	0.610	2.30 (-2.08, 6.68)	-1.14 (-5.99, 3.71)	0.942	0.000
Muscle performance										
SPPB (score)	9.55 ± 1.21	11.64 ± 0.67	0.004**	11.20 ± 0.92	11.80 ± 0.42	0.059	2.09 (1.39, 2.79)	0.60 (-0.09, 1.29)	0.341	0.566
6-MW test (m/s)	0.66 ± 0.10	0.90 ± 0.12	< 0.001***	0.87 ± 0.10	1.05 ± 0.16	0.005*	0.24 (0.16, 0.31)	0.18 (0.07, 0.30)	0.779	0.005
Quality of life										
SF-36										
PF	65.91 ± 23.65	77.27 ± 21.61	0.005**	79.00 ± 20.79	94.00 ± 9.66	0.016*	11.36 (4.30—18.42)	15.00 (3.56—26.44)	0.085	0.008
RP	56.82 ± 37.23	72.73 ± 34.38	0.020*	70.00 ± 38.73	72.50 ± 32.17	0.564	15.91 (4.59—27.23)	2.50 (-7.65—12.65)	0.102	0.142
BP	100.00 ± 0.00	100.00 ± 0.00		100.00 ± 0.00	100.00 ± 0.00		0	0		0
General health	50.45 ± 28.41	67.73 ± 19.28	0.033*	64.50 ± 24.99	76.00 ± 14.10	0.043*	17.27 (1.71—32.84)	11.50 (0.44—22.56)	0.702	0.008
Vitality	73.18 ± 20.65	81.36 ± 14.51	0.018*	80.00 ± 14.91	90.00 ± 10.27	0.039*	8.18 (1.76—14.60)	10.00 (0.61—19.39)	0.190	0.093
SF	82.83 ± 26.93	81.36 ± 14.51	0.084	81.11 ± 25.69	83.34 ± 13.09	1.00	12.12 (-4.39—28.63)	2.22 (-13.14—17.58)	0.010*	0.319
MH	70.55 ± 11.63	79.55 ± 11.57	0.046*	72.40 ± 19.27	89.60 ± 8.26	0.014*	9.00 (0.184—17.82)	17.20 (4.33—30.07)	0.038*	0.219
RE	72.73 ± 29.13	78.79 ± 34.23	0.441	70.00 ± 39.91	93.33 ± 14.05	0.089	6.06 (-10.75—22.87)	23.33 (-4.32—50.98)	0.158	0.108

Table 2. Comparison of clinical outcomes within and between groups before and after the intervention. CRT, conventional high-intensity resistance training; LRT-BFR, low-load resistance training with blood flow restriction; Pre, pre-invention; Post, post-intervention; ES: effect size; BM, body mass; BMI, body mass index; ASMI, appendicular skeletal muscle mass index; BFP, body fat percentage; KES, knee extensor strength; HGS, handgrip strength; SPPB, short physical performance battery; 6-MW test, 6-m walk test; SF-36, Short Form 36 Health Survey; PF, physical function; RP, role-physical; BP, body pain; SF, social function; MH, mental health; RE, role-emotional.

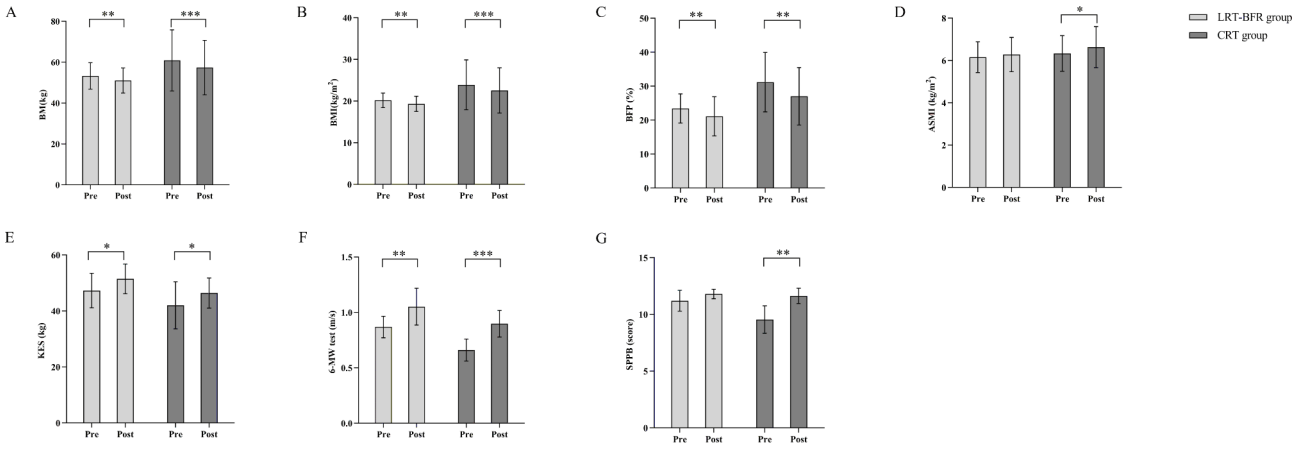

Fig. 2. Comparison of clinical outcomes within and between groups before and after the intervention. Note: (**A**) BM: body mass (**B**) BMI: body mass index (**C**) BFP: body fat percentage (**D**) ASMI: appendicular skeletal muscle mass index (**E**) KES: knee extensor strength (**F**) 6-MW test: 6-m walk test (**G**) SPPB: short physical performance battery. * Significance < 0.05; ** Significance < 0.01; *** Significance < 0.001. CRT, conventional high-intensity resistance training; LRT-BFR, low-load resistance training with blood flow restriction; Pre, pre-invention; Post, post-intervention.

	CRT group (N = 11)			LRT-BFR group (N = 10)			Mean change (95% CI)		Between-group differences	
	Pre (M ± SD)	Post (M ± SD)	P	Pre (M ± SD)	Post (M ± SD)	P	Δ (CRT group)	Δ (LRT-BFR group)	p	ES
CVD risk factors										
SBP (mmHg)	154.55 ± 13.60	138.45 ± 18.04	0.036*	148.70 ± 21.35	124.40 ± 19.70	0.010*	-16.09 (-30.93, -1.25)	-24.30 (-41.26, -7.34)	0.147	0.113
DBP (mmHg)	84.55 ± 6.71	78.00 ± 7.27	0.083	77.20 ± 14.13	73.60 ± 8.00	0.313	-6.55 (-14.11, -1.02)	-3.60 (-14.22, 4.02)	0.446	0.033
HR (bpm)	90.18 ± 17.03	81.82 ± 9.45	0.144	87.50 ± 15.33	72.50 ± 13.24	0.027*	-8.36 (-20.12, 3.39)	-15.00 (-27.86, -2.14)	0.093	0.149
LDL (mmol/L)	7.53 ± 6.10	2.75 ± 0.61	0.155	9.01 ± 7.38	2.96 ± 0.86	0.074	-4.78 (-9.01, -0.56)	-6.05 (-11.14, -0.96)	0.576	0.018
HDL (mmol/L)	1.81 ± 0.45	3.15 ± 1.46	0.018*	2.12 ± 0.49	3.64 ± 1.75	0.012*	1.34 (2.40, 0.28)	1.53 (2.63, 0.42)	0.194	0.097
TC (mmol/L)	4.79 ± 0.69	5.05 ± 0.96	0.258	5.71 ± 1.13	5.52 ± 1.24	0.573	0.26 (-0.23, 0.75)	-0.19 (-0.93, 0.55)	0.611	0.015
TG (mmol/L)	2.02 ± 1.26	1.16 ± 0.60	0.006**	2.09 ± 0.90	1.08 ± 0.33	0.028*	-0.86 (-1.55, -0.18)	-1.01 (-1.77, -0.25)	0.656	0.011
Sarcopenia-related blood biomarkers										
IL-6 (pg/ml)	55.72 ± 9.88	50.36 ± 4.75	0.110	51.17 ± 5.84	53.57 ± 12.93	0.566	-5.35 (-12.19, 1.48)	2.40 (-6.71, 11.50)	0.350	0.051
TNF-α (pg/ml)	85.48 ± 13.20	84.56 ± 13.98	0.845	81.98 ± 5.32	94.86 ± 16.65	0.068	-0.91 (-11.06, 9.23)	12.89 (-1.20, 26.97)	0.133	0.121
CRP (pg/ml)	9.52 ± 17.71	2.29 ± 2.17	0.374	1.63 ± 1.89	4.37 ± 10.04	0.594	-7.23 (-21.18, 6.73)	2.74 (-3.93, 9.41)	0.546	0.025
IGF-1(pg/ml)	180.46 ± 31.07	193.34 ± 45.87	0.367	168.39 ± 14.61	188.62 ± 52.20	0.244	12.87 (-17.51, 43.26)	20.24 (-16.52, 57.00)	0.927	0.000
GH (pg/ml)	18.06 ± 2.92	25.55 ± 2.99	< 0.001***	16.92 ± 1.12	25.32 ± 3.95	< 0.000***	7.49 (5.01, 9.97)	8.40 (5.16, 11.64)	0.906	0.001
FST (pg/ml)	12.89 ± 1.66	9.80 ± 1.35	< 0.001***	12.81 ± 1.43	10.39 ± 1.31	0.003**	-3.10 (-1.99, -4.21)	-2.42 (-1.06, -3.78)	0.713	0.008
MSTN (pg/ml)	8.46 ± 0.79	8.04 ± 1.36	0.297	8.00 ± 0.79	8.77 ± 2.01	0.310	-0.42 (-1.28, 0.44)	0.77 (-0.85, 2.38)	0.247	0.078

Table 3. Comparison of CVD risk factors and sarcopenia-related blood biomarkers within and between groups before and after the intervention. CRT, conventional high-intensity resistance training; LRT-BFR, low-load resistance training with blood flow restriction; Pre, pre-invention; Post, post-intervention; ES: effect size; CVD, cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TC, total cholesterol; TG, triglycerides; IL-6, interleukin-6; TNF-α, tumor necrosis factor-alpha; CRP, C-reactive protein; IGF-1, insulin-like growth factor 1; GH, growth hormone; FST, follistatin; MSTN, myostatin.* Significance < 0.05; ** Significance < 0.01; *** Significance < 0.001.

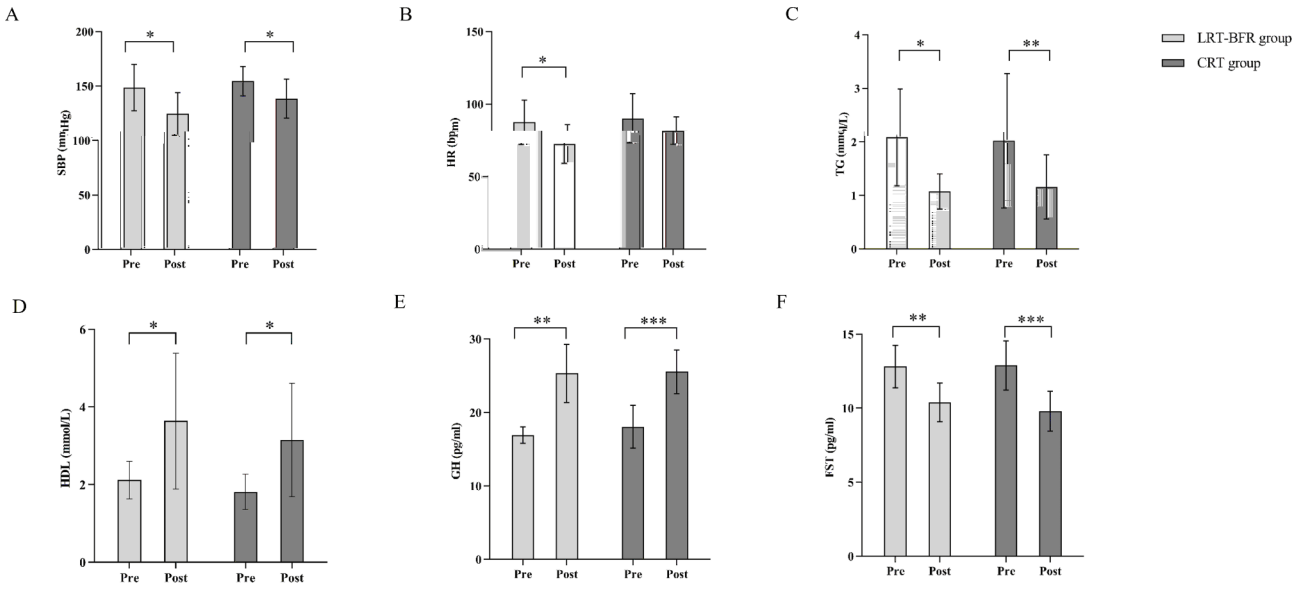

Fig. 3. Comparison of CVD risk factors and sarcopenia-related blood biomarkers within and between groups. Note: (**A**) SBP: systolic blood pressure (**B**) HR: heart rate (**C**) TG: triglycerides (**D**) HDL: high-density lipoprotein. (**E**) GH: growth hormone (**F**) FST: follistatin. * Significance < 0.05; ** Significance < 0.01; *** Significance < 0.001. CRT, conventional high-intensity resistance training; LRT-BFR, low-load resistance training with blood flow restriction; Pre, pre-invention; Post, post-intervention.

Lipid parameters

As shown in Table 3, HDL significantly elevated and TG significantly decreased in the LRT-BFR (HDL: Δ = 1.53, 95%CI (2.63, 0.42), p = 0.012; TG: Δ = −1.01, 95%CI (−1.77, −0.25), p = 0.028) and CRT (HDL: Δ = 1.34, 95%CI (2.40, 0.28), p = 0.018; TG: Δ = −0.86, 95%CI (−1.55, −0.18), p = 0.006) groups (Fig. 3). No significant between-group differences in these changes were observed.

Changes in sarcopenia-related blood biomarkers

As shown in Table 3, significant increases in GH and significant reductions in FST were observed following LRT-BFR (GH: Δ = 8.40, 95%CI (5.16, 11.64), p < 0.001; FST: Δ = −2.42, 95%CI (−1.06, 3.78), p = 0.003) and CRT (GH: Δ = 7.49, 95%CI (5.01, 9.97), p < 0.001; FST: Δ = −3.10, 95%CI (−1.99, −4.21), p < 0.001) (Fig. 3).

Changes in HRQoL

As depicted in Table 2, the LRT-BFR group exhibited significant improvement in four dimensions: PF, general health, vitality and MH (PF: Δ = 15.00, 95%CI (3.56, 26.44), p = 0.016; general health: Δ = 11.50, 95%CI (0.44, 22.56), p = 0.043; vitality: Δ = 10.00, 95%CI (0.61, 19.39), p = 0.039; MH: Δ = 17.20, 95%CI (4.33, 30.07), p = 0.014). In the CRT group, significant improvement was observed in five dimensions: PF, RP, general health, vitality and MH (PF: Δ = 11.36, 95%CI (4.30, 18.42), p = 0.005; RP: Δ = 15.91, 95%CI (4.59, 27.23), p = 0.020; general health: Δ = 17.27, 95%CI (1.71, 32.84), p = 0.033; vitality: Δ = 8.18, 95%CI (1.76, 14.60), p = 0.018; MH: Δ = 9.00, 95%CI (0.184, 17.82), p = 0.046). The significant improvement in SF favoured CRT (p < 0.05), and the significant improvement in MH favoured LRT-BFR (p < 0.05).

Adverse events and severe adverse events

No adverse events or serious adverse events were observed during the 12-week study period.

Discussion

This study is the first to systematically compare the effects of LRT-BFR and CRT on body composition, muscle strength and function, CVD risk factors, sarcopenia-related biomarkers and HRQoL in older people diagnosed with sarcopenia. The key findings were as follows (1) 12-week LRT-BFR and CRT led to significant changes in body composition (BM, BMI and BFP), muscle strength (KES), muscle function (6-MW test), CVD risk factors (rest SBP, TG and HDL), sarcopenia-related biomarkers (GH and FST) and certain dimensions of HRQoL (PF, general health, vitality and MH). (2) Only CRT produced significant changes in ASMI and SPPB, and only LRT-BFR resulted in a remarkable improvement in HR. (3) No significant differences were observed between groups.

In our study, the CRT group showed a significant improvement in ASMI, which was not observed in the LRT-BFR group. This result suggested that CRT may offer a slight advantage over LRT-BFR in enhancing muscle mass, although the difference between groups was not statistically significant. Given the limited clinical research on LRT-BFR for sarcopenia[12], comparisons were drawn primarily from studies on healthy young and older adults who underwent BFR. Our findings align with previous research on muscle mass changes[31,32], including a recent meta-analysis by Chang et al., indicating that BFR training may have limited effects on muscle mass growth[31]. Similarly, a case report by Lopez et al. on a 91-year-old man with sarcopenia observed a 2.4% muscle mass increase, comparable to our findings[33]. The similarity in participant profiles between these studies further supported this comparability, as both focused on older people with sarcopenia[33], unlike other studies that largely examined healthy or inactive older individuals. This lack of consistency in research subjects could be a crucial factor contributing to the discrepancies between this study and others that suggesting that LRT-BFR can yield similar increases in muscle mass as CRT. Moreover, differences in LOP parameters may contribute to these variations. Other studies on BFR in healthy older individuals have typically used LOP values ranging from 50 to 80%[22], whereas our study selected a low LOP value of 50% to account for sarcopenic frailty. Higher LOP values are generally associated with greater hypertrophic effects[34], which may explain the failure to achieve significant muscle mass improvement in the LRT-BFR group. Future studies should further establish the optimal LOP range for enhancing muscle mass in sarcopenia.

LRT-BFR and CRT positively impacted KES and the 6-MW test, with only CRT demonstrating additional benefits for SPPB. This finding suggested a favourable trend for muscle strength and performance associated with CRT compared with LRT-BFR, although no significant differences were observed between groups. This observation was consistent with previous research[35–37]. A recent meta-analysis by Lixandrão et al. demonstrated that CRT can yield greater improvements in muscle strength compared with LRT-BFR, even after controlling for various factors such as test specificity (dynamic versus isometric), cuff width and absolute occlusion pressure[38]. The favourable trend of CRT in muscle strength and performance may stem from its strong activation. Although the specific mechanisms behind the activation differences between CRT and LRT-BFR remain unclear, some studies suggested that CRT leads to elevated levels of central and peripheral activation. For instance, Biazon et al. reported higher EMG peak values in CRT compared with LRT-BFR regarding muscle activation[39], and Kubo et al. found significant central activation increases in the CRT group, which was not observed in the BFR group[40]. Elevated EMG peak values are associated with increased recruitment of type II muscle fibres, which are primarily responsible for hypertrophy and strength[41]. Despite trends favouring CRT for muscle growth, the lack of statistically significant differences indicates that both training modalities may be equally effective in clinical practice, consistent with findings in other populations[35,42].

The underlying mechanisms contributing to the gradual loss of muscle mass in sarcopenia may be multifactorial. Although not fully understood, this condition is characterised by an imbalance between muscle protein synthesis and degradation rates[43]. This imbalance may be associated with the progressive decline in growth factors (GH and IGF-1) occurring with aging, systemic low-grade inflammation status (IL-6, TNF-α and CRP) and myokine disbalance (MSTN and FST)[44]. These negative health conditions are closely linked to CVD,

a leading cause of mortality among older people. Consequently, several studies have indicated an increased risk of CVD in older people diagnosed with sarcopenia compared with their healthier peers[14]. However, research on the effects of LRT-BFR on CVD risk factors in older people with sarcopenia remains limited.

In our study, CRT and LRT-BFR significantly improved various health markers, including body composition (BM, BMI and BFP), blood lipid level (TG) and blood pressure (SBP). A positive effect on resting HR was observed following LRT-BFR, suggesting a superior trend in reducing CVD risk in this population compared with CRT[44,45]. The chronic improvements in haemodynamic parameters observed here were aligned with findings from previous research; a recent meta-analysis indicated that LRT-BFR has a favourable trend in lowering blood pressure compared with CRT[46]. Another similar meta-analysis also found that LRT-BFR results in a decrease in SBP and SDP post-exercise[47]. These positive outcomes may be attributed to improved autonomic function and vascular endothelial health following LRT-BFR. Research on LRT-BFR in patients with HIV also showed advantages in autonomic nervous system function and enhanced HR variability[45], supporting our findings of decreased HR. Similar conclusions have been validated in patients with hypertension[48]. Additionally, LRT-BFR may improve fat and muscle metabolism during exercise, leading to improved lipid profiles and body composition, thereby promoting cardiovascular wellness[49]. Taken together, these findings suggest that LRT-BFR may improve haemodynamic parameters, body composition and blood lipid levels through the modulation of autonomic function and the improvement of endothelial function.

In addition to comparing the effects of both training methods on clinical muscle-related outcomes and CVD risk factors, this study explored the potential mechanisms through changes in various sarcopenia-related biomarkers. Both exercise modalities significantly increased serum GH levels and decreased FST levels, while MSTN levels remained unchanged. These results were both consistent and inconsistent with existing literature. The increase in GH levels may be attributed to the GH/IGF-1 axis[50], a key physiological process in sarcopenia influenced by factors such as the MSTN/FST axis and inflammatory markers[51]. MSTN acts as a negative regulator of growth, and FST can antagonise MSTN's effects[52]. Previous research has linked elevated MSTN and reduced FST in older individuals to age-related loss of muscle mass[52]. However, the effects of exercise on MSTN and FST remain inconsistent across studies. Some research indicated post-exercise increases in FST and decreases in MSTN[53], whereas others reported no change in MSTN protein levels despite increased mRNA levels, possibly due to inhibitors affecting MSTN signalling rather than protein expression[54.] Moreover, findings by Perakakis et al. suggested that older individuals may have higher FST levels than their younger counterparts, indicating a compensatory response to preserve muscle metabolic function[55]. In our study, the decrease in FST without a change in MSTN could reflect a compensatory adjustment linked to muscle metabolic improvements from training. Additionally, differences in participant demographics and study designs, such as variations in exercise types and load prescriptions, likely accounted for the observed discrepancies across studies. This underscores the complexity of exercise effects on this pathway and highlights the need for further research in this area. The absence of significant inflammatory changes suggests that LRT-BFR may be a safe option for older people with sarcopenia.

In this study, CRT and LRT-BFR led to significant improvements in four dimensions: PF, general health, vitality and MH. This finding aligned with the results of a previous study[56]. The current work demonstrated that both exercise modalities could enhance the physical and mental well-being of individuals with sarcopenia, thereby improving their overall quality of life.

Despite these positive findings, this study had several limitations. Firstly, the relatively small sample size restricted the ability to conduct subgroup analyses by sex and age, which are clinically relevant. Secondly, this study did not explore the long-term effects of the two exercise modalities, highlighting the need for further studies to provide conclusive evidence for clinical practice in the future.

Conclusion

This study represents the first randomized controlled trial comparing the efficacy of LRT-BFR versus CRT in older people diagnosed with sarcopenia, focusing on clinical muscle-related outcomes, CVD risk factors and sarcopenia-related biomarkers. The findings suggested that CRT appeared to be more effective in improving muscle mass and strength, while LRT-BFR may be more beneficial for cardiovascular health in this population. Additionally, our preliminary findings suggest that the changes induced by the two exercise modalities are associated with growth hormone levels and fat metabolism. Further high-quality studies are necessary to explore deeper mechanisms in older people with sarcopenia and to provide a theoretical basis for clinical practice in this population.

Data availability

The data that support the findings of this study are not publicly available but are available from the corresponding author on reasonable request.

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Author contributions

M.Z. contributed to the conceptualization, study design, data collation, and completion and revision of the manuscript. Y.S. participated in the conceptualization, data analysis, writing and revision of the manuscript. J.Z. participated in study design, collation and proofreading of data, and draft and formatting of the manuscript. P.D. contributed to the conceptualization, project administration, supervision, and review and checking of the manuscript. N. C. contributed to conceptualization, study design, project administration, funding acquisition, supervision, review, and checking of manuscripts. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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