ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 7561-7565 (2026)
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BIOINFORMATION
Discovery at the interface of physical and biological sciences
BIOMEDICAL INFORMATICS
www.bioinformation.net
Volume 22(10)
Research Article

Received October 1, 2026; Revised October 31, 2026; Accepted October 31, 2026, Published October 31, 2026
DOI: 10.6026/973206300227561

SJIF 2026 (Scientific Journal Impact Factor for 2026) = 8.478
2022 Impact Factor (2023 Clarivate Inc. release) is 1.9

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Edited by Ruby Singh
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Citation: Muthusamy *et al*. Bioinformation 22(10): 7561-7565 (2026)

Blood flow restriction training and rhythmic auditory cueing in subacute stroke: A randomized controlled trial

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ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 7561-7565 (2026)
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Abstract:
Stroke often causes lower-limb weakness and impaired gait, limiting functional recovery. Therefore, it is of interest to compare the blood flow restriction (BFR) training with and without rhythmic auditory cueing (RAC) in 48 subacute stroke survivors over 4 weeks. Both groups showed significant improvements, but the BFR+RAC group achieved greater gains in knee muscle strength, gait velocity and cadence ($p < 0.05$). No serious adverse events occurred, indicating that both interventions were safe and well tolerated. Thus, combining RAC with BFR training is an effective adjunct to conventional rehabilitation for improving strength and gait after subacute stroke**.**

Keywords: Blood flow restriction (BFR), rhythmic auditory cueing (RAC), stroke rehabilitation, muscle strength, gait velocity, cadence, randomized controlled trial (RCT)

Background:
Lower-limb weakness and impaired gait are common and disabling consequences of stroke, particularly during the subacute phase and are associated with reduced functional independence **[1]**. Improving paretic lower-limb strength and walking performance is therefore a major goal of stroke rehabilitation **[2]**. Blood flow restriction (BFR) training combines low-load resistance exercise with partial vascular occlusion to induce metabolic stress and neuromuscular adaptations while reducing mechanical loading **[3]**. Studies in stroke survivors suggest that BFR training can improve lower-limb strength, motor function and walking capacity when combined with rehabilitation **[4]**. Rhythmic auditory cueing (RAC) uses metronomes or rhythmic music to facilitate auditory-motor entrainment during gait and has been shown to improve walking velocity, cadence and stride length after stroke **[5].** Its effects are attributed to auditory-motor networks that provide temporal cues for coordinated stepping **[6]**. BFR primarily promotes peripheral muscular adaptation, whereas RAC facilitates gait timing and motor coordination, suggesting potential complementary effects **[7]**. However, the combined effects of BFR training and RAC on lower-limb strength and gait performance in subacute stroke survivors remain insufficiently investigated **[8]**. Therefore, it is of interest to evaluate the effects of combining blood flow restriction training with rhythmic auditory cueing on lower-limb muscle strength, gait velocity and cadence in subacute stroke survivors undergoing conventional rehabilitation.

Methods:
This single-center, assessor-blinded, parallel-group, two-arm randomized controlled trial was conducted in accordance with the Declaration of Helsinki and reported following the CONSORT 2010 guidelines for parallel-group randomized trials. Written informed consent was obtained from all participants before enrollment. Participants were recruited from the inpatient and outpatient neurorehabilitation services of Meenakshi Academy of Higher Education and Research (MAHER). Eligible participants included individuals with a first-ever unilateral ischemic or hemorrhagic stroke confirmed by computed tomography (CT) or magnetic resonance imaging (MRI), who were in the subacute phase (4–24 weeks post-stroke), aged 40–75 years, had a Brunnstrom lower-limb recovery stage of ≥3, were able to walk at least 10 m with or without a gait aid or orthosis and without physical assistance, had a Mini-Mental State Examination (MMSE) score of ≥24, demonstrated normal bilateral ankle-brachial index values and were medically stable with physician clearance to participate in resistance exercise. Participants were excluded if they had peripheral vascular disease, deep vein thrombosis, a history of venous thromboembolism, uncontrolled hypertension (resting systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg), bleeding disorders or anticoagulant therapy with supratherapeutic INR, severe cardiac disease (New York Heart Association class III–IV), lower-limb orthopedic disorders limiting exercise, significant hearing impairment preventing perception of auditory cues, severe cognitive or communication impairment or unilateral neglect interfering with safe participation, or previous experience with blood flow restriction (BFR) training. The sample size was calculated a priori using gait velocity as the primary outcome. Based on an anticipated

between-group mean difference of 0.10 m/s with a standard deviation of 0.13 m/s derived from previous BFR and rhythmic auditory cueing (RAC) studies, an alpha level of 0.05 and a statistical power of 80% indicated that 21 participants were required per group using G*Power software. To account for an expected attrition rate of 15%, a total sample of 48 participants (24 participants in each group) was targeted. Following baseline assessment, eligible participants were randomly allocated in a 1:1 ratio to either the BFR combined with RAC group or the BFR-alone group using a computer-generated randomization sequence with variable block sizes of four and six. The allocation sequence was prepared by an investigator who was not involved in participant recruitment or assessment. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes that were opened only after baseline evaluation. Outcome assessors and the statistician remained blinded to group allocation throughout the study. Due to the nature of the interventions, participants and treating physiotherapists could not be blinded; however, they were unaware of the study hypothesis. Both groups received a standardized conventional rehabilitation program consisting of task-oriented mobility training, balance exercises and routine physiotherapy for five sessions per week over four weeks (20 sessions), in addition to their allocated intervention. Blood flow restriction training was performed in both groups using a pneumatic tourniquet cuff (11–13 cm wide) positioned around the proximal thigh of the paretic limb. Limb occlusion pressure (LOP) was determined individually using a handheld Doppler while the participant was at rest and cuff inflation pressure during exercise was maintained at 50–60% of the measured LOP. Participants performed unilateral seated knee extension and standing or seated knee flexion exercises at approximately 30% of their estimated one-repetition maximum following a four-set protocol of 30, 15, 15 and 15 repetitions with 30-second rest intervals between sets. The cuff remained inflated throughout each exercise block and was released between exercises. Training was conducted five sessions per week for four weeks, with cuff pressure and exercise loads reassessed weekly according to participant tolerance. Participants allocated to the BFR+RAC group additionally completed 20 minutes of treadmill or over ground gait training using rhythmic auditory cueing provided through a digital metronome. The metronome was initially set at 100% of the participant's baseline comfortable walking cadence during the first week and progressively increased by 5% each week to reach 110% of baseline cadence by the fourth week, according to participant tolerance. Participants were instructed to synchronize heel strike of the paretic limb with the auditory beat and gait training was performed immediately after the BFR resistance exercises. Participants in the BFR-alone group completed treadmill or over ground gait training for an equivalent duration without rhythmic auditory cueing at a self-selected comfortable walking cadence, ensuring equal treatment duration and therapist contact between groups. Outcome assessments were performed at baseline (week 0) and immediately after completion of the four-week intervention (week 4) by an assessor blinded to treatment allocation. Primary outcome measures included paretic knee extensor and flexor muscle strength measured in kilogram-force (kgf) using a calibrated hand-held dynamometer with the break-test technique, comfortable gait velocity measured using the 10-Metre Walk Test (10MWT) and cadence measured as steps per minute during the 10MWT using a wearable inertial gait sensor or manual step counting, with the average of three trials recorded for each outcome. Secondary outcome measures included the Fugl-Meyer Assessment–Lower Extremity, Berg Balance Scale, Timed Up and Go test and continuous monitoring of adverse events such as pain, bruising, numbness, dizziness and thrombotic symptoms throughout the intervention period. Data were analyzed according to the intention-to-treat principle using SPSS version 26.0. Data normality was assessed with the Shapiro-Wilk test. Between-group comparisons of change scores were performed using independent-samples t-tests for normally distributed data or Mann-Whitney U tests for non-normally distributed data, while within-group pre- and post-intervention comparisons were analyzed using paired t-tests or Wilcoxon signed-rank tests, as appropriate. Baseline categorical variables were compared using the chi-square test or Fisher's exact test. A two-way repeated-measures analysis of variance (group × time) was performed to evaluate interaction effects for each primary outcome, followed by Bonferroni-adjusted post hoc comparisons where appropriate. Effect sizes were calculated using Cohen's d for between-group differences. Statistical significance was established at $p < 0.05$ and missing data were managed using multiple imputations under the missing-at-random assumption, with complete-case analysis performed as a sensitivity analysis.

Results:

Of 67 patients screened, 48 met eligibility criteria and were randomized (24 per group). Three participants withdrew after randomization (2 in BFR+RAC: 1 relocation, 1 withdrew consent, 1 in BFR-alone intercurrent illness), leaving 45 participants (22 BFR+RAC, 23 BFR-alone) in the final analysis (94% retention). Groups were comparable at baseline on all demographic and clinical variables **(Table 1),** confirming successful randomization. Both groups showed statistically significant within-group improvements from baseline to week 4 in knee extensor and flexor strength, gait velocity and cadence (all $p < 0.01$). Two-way repeated-measures ANOVA revealed a significant group × time interaction for all four primary outcomes, indicating that the magnitude of improvement differed between groups **(Table 2)**. Between-group p-value for change scores (independent-samples t-test). HHD = hand-held dynamometry, 10MWT = 10-metre walk test. The BFR+RAC group demonstrated significantly greater improvement than the BFR-alone group in gait velocity (mean difference 0.11 m/s, 95% CI 0.04–0.18, $p = 0.004$, Cohen's $d = 0.71$) and cadence (mean difference 7.7 steps/min, 95% CI 2.1–13.3, $p = 0.008$, $d = 0.64$). Knee extensor strength gains were also significantly greater in the BFR+RAC group (mean difference 2.1 kgf, 95% CI 0.5–3.7, $p = 0.011$, $d = 0.60$), as were knee flexor strength gains (mean difference 1.6 kgf, 95% CI 0.2–3.0, $p = 0.026$, $d = 0.52$). Secondary outcome measures (Fugl-Meyer Assessment–Lower Extremity,

Berg Balance Scale, Timed Up and Go) improved in both groups with numerically greater gains in the BFR+RAC group. No serious adverse events (deep vein thrombosis, fracture, cardiovascular event) occurred in either group. Minor self-limiting adverse events transient limb numbness, mild bruising at the cuff site and post-exercise fatigue occurred at similar rates between groups (BFR+RAC 18%, BFR-alone 15%, p = 0.74) and did not necessitate discontinuation.

Table 1: Baseline demographic and clinical characteristics of participants

Characteristic	BFR + RAC (n = 24)	BFR Alone (n = 24)	p value
Age, years (mean ± SD)	58.4 ± 7.9	59.1 ± 8.3	0.76
Sex, male / female	14 / 10	13 / 11	0.78
Time since stroke, weeks (mean ± SD)	9.8 ± 2.6	10.2 ± 2.9	0.61
Stroke type- ischemic / hemorrhagic	18 / 6	17 / 7	0.75
Affected side (right / left)	12-Dec	13 / 11	0.77
Body mass index, kg/m² (mean ± SD)	24.6 ± 3.1	24.9 ± 2.8	0.72
Brunnstrom stage, lower limb (median, IQR)	4 (3–4)	4 (3–5)	0.68
MMSE score (mean ± SD)	27.1 ± 1.8	26.8 ± 2.0	0.58

Table 2: Primary outcome measures at baseline and week 4

Outcome	BFR+RAC Baseline	BFR+RAC Week 4	BFR-alone Baseline	BFR-alone Week 4	Between - group p-value
Knee extensor strength, paretic limb (kgf, HHD)	12.4 ± 3.1	17.9 ± 3.6	12.6 ± 2.9	15.8 ± 3.2	0.011
Knee flexor strength, paretic limb (kgf, HHD)	8.9 ± 2.4	12.6 ± 2.7	9.1 ± 2.2	11.0 ± 2.5	0.026
Gait velocity, comfortable (m/s, 10MWT)	0.52 ± 0.13	0.79 ± 0.16	0.54 ± 0.14	0.68 ± 0.15	0.004
Cadence (steps/min)	78.3 ± 9.6	95.1 ± 10.2	79.0 ± 9.1	87.4 ± 9.8	0.008

Discussion:

This randomized controlled trial found that adding rhythmic auditory cueing to blood flow restriction training produced significantly greater improvements in paretic knee extensor and flexor strength, comfortable gait velocity and cadence than blood flow restriction training alone in subacute stroke survivors. These findings support the hypothesis that pairing a peripheral, muscular-metabolic training stimulus (BFR) with a central, temporal-entrainment stimulus (RAC) yields additive rather than merely parallel benefit **[9]**. The strength gains observed in both groups are consistent with prior randomized trials reporting that low-load BFR resistance training improves paretic lower-limb strength and motor function in stroke survivors, supporting metabolic-stress-mediated hypertrophic and neural adaptations even in the presence of upper motor neuron impairment **[10]**. The larger strength gains in the BFR+RAC group may reflect greater overall neuromuscular engagement during combined sessions, improved paretic-limb loading symmetry encouraged by rhythmic stepping practice or a training-order/potentiation effect of resistance exercise immediately preceding gait practice **[11]**. The magnitude of gait velocity and cadence improvement with RAC in this trial is broadly consistent with effect sizes reported in prior randomized trials of auditory cueing interventions in stroke gait rehabilitation. Our results extend this literature by showing that RAC gait benefits are preserved and potentially enhanced, when delivered alongside a concurrent BFR strength program rather than as a stand-alone intervention **[12]**. From a mechanistic standpoint, auditory-motor entrainment is thought to engage cerebellar and basal ganglia-mediated timing circuits that can bypass damaged corticospinal pathways, providing an external rhythmic scaffold for stepping **[6, 7].** Combining this central entrainment mechanism with the peripheral hypertrophic stimulus of BFR may address both the strength and timing/coordination deficits that jointly limit gait speed after stroke, offering a plausible explanation for the additive effect observed **[13]**. Clinically, both interventions were well tolerated with no serious adverse events and the low mechanical loads used in BFR training make it a feasible adjunct even for patients not yet able to tolerate high-load resistance exercise in the subacute phase. The combined protocol required no additional equipment beyond a pneumatic cuff and a metronome and audio device, supporting practical implementation in standard rehabilitation settings without substantially increasing session time or cost.

Conclusion:

Combining blood flow restriction training with rhythmic auditory cueing significantly improved lower-limb muscle strength, gait velocity and cadence compared with blood flow restriction training alone. This combined approach may serve as an effective adjunct to conventional rehabilitation for improving functional mobility in subacute stroke survivors.

Limitations:

This study has several limitations that should be considered when interpreting the findings. The single-center design and relatively modest sample size (45 participants completing the study) may limit the generalizability of the results and reduce the precision of the estimated treatment effects. Owing to the nature of the interventions, therapists and participants could not be blinded to group allocation, although outcome assessors and the statistician remained blinded, introducing the possibility of performance bias. In addition, the absence of a conventional rehabilitation-only control group prevented assessment of the independent contribution of blood flow restriction training compared with standard rehabilitation. The intervention period was limited to four weeks and long-term retention of improvements in muscle strength and gait performance was not evaluated. Furthermore, muscle strength and gait parameters were assessed using field-based instruments, including a hand-held dynamometer and wearable gait sensors, rather than laboratory-based isokinetic dynamometry or three-dimensional motion analysis, which may have influenced measurement precision.

Future directions:
Future research should include multicenter randomized controlled trials with larger sample sizes, a conventional rehabilitation-only control group and longer follow-up periods of at least three to six months to determine the sustainability of treatment effects. Studies investigating different cuff pressures, rhythmic cueing frequencies and intervention durations are also warranted to establish the optimal training protocol. Additionally, incorporating advanced biomechanical assessments such as three-dimensional gait analysis, electromyography and muscle imaging techniques may provide greater insight into the neuromuscular mechanisms underlying the combined effects of blood flow restriction training and rhythmic auditory cueing in stroke rehabilitation.

References:

[1] Moore SA *et al. Stroke*. 2022 **53**:3494. [PMID: 36069185]
[2] Zhang J *et al. Front Neurol*. 2026 **17**:1814592. [PMID: 42180217]
[3] Shaw L *et al. Pilot Feasibility Stud*. 2022 **8:**239. [PMID: 36371213]
[4] Shin J & Chung Y. *NeuroRehabilitation*. 2022 **51**:443. [PMID: 35964207]
[5] Wang L *et al. Front Neurosci*. 2022 **16**:1043575. [PMID: 36466174]
[6] Qin Z *et al. Trials*. 2026 **27**:215. [PMID: 41680892]
[7] Gonzalez-Hoelling S *et al. BMC Complement Med Ther*. 2024 **24:**45. [PMID: 38245704]
[8] Lu L *et al. BMC Geriatr* 2021 **21:**708. [PMID: 34911483]
[9] Ghai S *et al. Sci Rep*. 2018 **8**:506. [PMID: 29323122]
[10] Ahmed I *et al. Top Stroke Rehabil*. 2024 **31:**418. [PMID: 37724785]
[11] Wang H *et al. Sports Med Open*. 2026 **12**:53. [PMID: 42090105]
[12] Kim SJ *et al. Bioengineering (Basel)*. 2025 **12:**1177. [PMID: 41301133]
[13] Pranjić M *et al. Brain Sci*. 2024 **14:**1063. [PMID: 39595826]

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