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Acute neuromuscular and metabolic responses to a novel low-load combined isometric and isotonic resistance training protocol

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Title Page

Acute neuromuscular and metabolic responses to a novel low-load combined isometric and isotonic resistance training protocol

Abstract

Purpose: This study investigated the acute physiological responses to a novel combined resistance training (CB) protocol—integrating isometric pre-exhaustion with low-load, high-velocity, short-arc isotonic contractions—and compared them against traditional low-intensity slow training (LST) and high-load (HL) training. **Methods:** Forty-eight healthy men were randomly assigned to one of three groups: LST (50% one-repetition maximum [1RM], slow tempo), HL (80% 1RM, normal tempo), or CB (40% 1RM; a 20-s isometric contraction immediately followed by eight high-velocity, short-arc repetitions). Surface electromyography (EMG) and near-infrared spectroscopy (NIRS) of the vastus lateralis, alongside serum IGF-1 concentrations, were assessed during and following three leg-press sets. **Results:** Despite utilizing a 40% 1RM load, the CB protocol elicited mean EMG amplitudes significantly greater than LST during the final set ($p = 0.009$, $g = 1.23$). NIRS analysis demonstrated a significantly lower change in tissue oxygen

saturation (ΔStO_2) in the CB group compared to HL from the initial set ($p = 0.001$; $g = 1.19$), highlighting rapid intramuscular hypoxia. Furthermore, third-set integrated EMG was significantly higher in CB than in both HL ($p = 0.002$, $g = 1.13$) and LST ($p < 0.001$, $g = 1.63$). Serum IGF-1 concentrations exhibited a significant post-exercise elevation across all groups (main effect of time: $p < 0.001$, $\eta_p^2 = 0.712$).

Conclusion: By concurrently demanding high neural drive and inducing profound metabolic stress, the time-efficient CB protocol provides a robust physiological stimulus despite minimal mechanical loading. This approach serves as a practical, joint-friendly alternative for populations necessitating reduced mechanical stress.

Trial registration number: UMIN-CTR (UMIN000060486)

Keywords: Electromyography, Muscle oxygenation, Pre-exhaustion, Resistance exercise, Muscle hypertrophy

Abbreviations

CB Combined isometric and isotonic resistance training

LST Low-Intensity Slow Training

HL High-load training

1RM One-repetition maximum

EMG Electromyography

NIRS Near-infrared spectroscopy

MVIC Maximum Voluntary Isometric Contraction

BFR Blood flow restriction

Pre-test Before training

Post-test Immediately after training

Post-15min 15 min after training

MPF Mean power frequency

Deoxy-Hb Deoxygenated hemoglobin

Total-Hb Total hemoglobin

StO_2 Tissue oxygen saturation

iEMG Integrated EMG

Introduction

Resistance training is a key intervention for preventing sarcopenia, reducing fall risk, and preserving physical function (Rodrigues et al. 2022; Currier et al. 2026).

Recent systematic reviews and network meta-analyses, along with the updated ACSM guidelines, report high-load (HL) training (> 80% one-repetition maximum [1RM]) as the most effective strategy for maximizing strength (Currier et al. 2023; Currier et al. 2026). The efficacy of HL training depends on recruiting high-threshold motor units (fast-twitch fibers) according to Henneman's size principle and applying high mechanical stress (Fry 2004; Schoenfeld 2010). However, heavy loading reduced arterial compliance in older adults (Yasuda 2022), and long-term joint and ligament safety remains a concern (Tschopp et al. 2011). Consequently, clinical application requires caution in older adults with sarcopenia, patients in rehab, or athletes aiming to minimize joint stress.

Low-intensity resistance-training methods that promote hypertrophy without high loads have gained attention to mitigate these risks. Blood flow restriction (BFR) and low-intensity slow training (LST) are well-established techniques (Takarada et al. 2000; Tanimoto and Ishii 2006). These methods induce hypertrophy of a comparable magnitude to HL training by increasing "metabolic stress"—metabolite accumulation (e.g., lactate, hydrogen ions) and acute intramuscular hypoxia—even under low mechanical stress (< 50% 1RM) (Schoenfeld 2013;

Pearson and Hussain 2015; Ozaki et al. 2016).

However, BFR requires professional supervision and precise pressure settings, as improper use can cause injury (Scott et al. 2015; Patterson et al. 2019). As efficacy and safety depend heavily on cuff width and individual arterial occlusion pressure, methodological complexity limits field implementation (Loenneke et al. 2025). Conversely, although LST requires no specialized equipment, its slow speed increases time under tension, prolongs sets, and causes significant discomfort (Ozaki et al. 2015). Furthermore, the slow velocity of LST may limit improvements in muscle power due to the principle of training specificity (Behm and Sale 1993; Usui et al. 2016).

To address these limitations, we propose a novel combined isometric and isotonic resistance training (CB) protocol. This method exploits the physiological benefits of isometric and explosive dynamic contractions (also described as ballistic intent; Pearson et al. 2022; Behm et al. 2024). Sustained isometric contractions at specific joint angles raise intramuscular pressure, inducing ischemia and hypoxia, comparable to BFR (Sadamoto et al. 1983; Wigmore et al. 2006; Oranchuk et al.

2019). The protocol shifts directly from isometric to isotonic contractions without relaxation to sustain ischemia. By pre-exhausting muscles and inducing ischemia during the isometric phase, then boosting neural activity with rapid, short-range isotonic contractions, this approach maximizes motor unit recruitment via compensatory acceleration (Behm and Sale 1993; Wilk et al. 2020), delivering a strong stimulus even at low loads.

Therefore, this study aims to examine the acute neuromuscular, metabolic, and hormonal responses to the novel CB protocol (40% 1RM) and compare them to conventional LST (50% 1RM) and HL (80% 1RM). We hypothesized that the CB protocol would elicit significant neuromuscular activity and metabolic stress. By comparing the magnitudes of these responses across the three protocols, we aimed to evaluate the efficacy of the CB method as a time-efficient training strategy with low mechanical loads.

Methods

Participants

Fifty healthy male university students participated in the study. Table 1 shows the

physical characteristics of the participants. Inclusion criteria were: (1) no regular resistance training within the past year and (2) no history of lower-limb musculoskeletal injury. Most participants were recreationally active.

Table 1. Physical characteristics of participants.

Characteristics	LST (n=15)	HL (n=17)	CB (n=16)	*P*-value
Age (years)	21.1 ± 0.7	20.9 ± 0.7	21.0 ± 0.7	0.89
Height (cm)	171.6 ± 5.4	172.1 ± 5.0	174.1 ± 6.0	0.41
Weight (kg)	63.7 ± 5.1	61.8 ± 6.1	65.8 ± 8.7	0.26
BMI (kg/m²)	21.6 ± 1.4	20.9 ± 1.8	21.6 ± 2.1	0.35
Fat thickness (mm)	4.8 ± 0.8	5.0 ± 1.2	4.5 ± 1.2	0.42
1RM (kg)	93.9 ± 24.1	87.7 ± 39.4	98.3 ± 39.1	0.69

Note: Values are presented as mean ± SD. LST, low-intensity slow training; HL, high-load training; CB, combined training; BMI, body mass index. P-values indicate the results of one-way ANOVA. No significant differences were observed among the groups in any physical characteristics.

All participants gave written informed consent after receiving comprehensive verbal and written explanations of the purpose, procedures, and potential risks of the study. This study adhered to the Declaration of Helsinki and was approved by

the Ethics Committee of the Nittazuka Medical Welfare Center (Approval No. 2024-28). The protocol was pre-registered with the University Hospital Medical Information Network (registration no. UMIN000060486).

Experimental Design

A randomized parallel-group design was used in accordance with the CONSORT statement (Fig. 1). Fifty participants were randomly assigned to one of three groups using a computer-generated random number sequence: LST, HL, or CB. To ensure allocation concealment, group assignments were disclosed only after baseline measurements, immediately before training. Two participants withdrew due to vasovagal reactions and extreme fatigue, leaving 48 for the final analysis (LST, n = 15; HL, n = 17; CB, n = 16).

Experimental Procedures

All sessions were conducted between 08:00 and 10:00 to minimize diurnal physiological variations. Participants fasted for 10 h before the experiment (water ad libitum) and abstained from caffeine, alcohol, and vigorous exercise for 24 h before testing.

The 1RM for the right leg press (BK1600; Senoh Corporation, Tokyo, Japan) was estimated using Brzycki's (1993) equation at least 48 h before the experimental session. The participants also performed familiarization trials. This estimation ensured the safety of untrained participants.

Experimental Protocol

Fig. 2 depicts the experimental-day timeline.

1. **Rest and Preparation:** Participants rested in the supine position for 15 min while the probes (electromyography [EMG], near-infrared spectroscopy [NIRS], and accelerometer) were attached.
2. **Baseline Measurements:** After 3 min of baseline NIRS recording, a physician inserted a 22G indwelling cannula into the antecubital vein for pre-sample blood collection.
3. **Maximum Voluntary Contraction:** Isometric knee extension strength was measured at 90° knee flexion for 5 s, with the mean of the middle 3 s used as the normalization reference (100% maximum voluntary contraction [MVIC]).
4. **Warm-up:** Participants performed a 5-min warm-up on a cycle ergometer (50

W, 60–80 rpm).

5. **Training Intervention:** Participants completed three sets of the assigned protocol using a single-leg press with the right leg.
6. **Post-measurements:** Blood samples were collected immediately after training (Post-test) and 15 min after exercise (Post-15min).

Resistance Training Protocols

All groups completed three sets with a 1-min rest (Fig. 3). Participants followed a metronome beat for movement tempo and were instructed to breathe naturally to avoid the Valsalva maneuver.

1. **Low-intensity slow training:** 50% 1RM, with 3-s concentric, 1-s isometric (at the end of the concentric phase), and 3-s eccentric phases. Eight repetitions were performed using the non-locking technique to maintain continuous muscle tension.
2. **High-Load training:** 80% 1RM, with 1-s concentric and 1-s eccentric phases. Eight repetitions were performed using the full range of motion.
3. **Combined isometric and isotonic resistance training:** Participants performed a 20-s sustained isometric contraction at 40% 1RM with a 70° knee

flexion angle. This duration was selected based on pilot testing to induce sufficient pre-exhaustion and ischemia while ensuring subsequent dynamic exercise performance. This was immediately followed by eight short-arc repetitions centered around 70°. The target displacement was maintained within a narrow range (approximately 10°–20°). To optimize the hypertrophic stimuli of eccentric loading and facilitate a stretch-shortening-like cycle, participants were instructed to initiate the first dynamic repetition with an intentional eccentric phase (i.e., a slight increase in knee flexion beyond 70°). This enabled the execution of ballistic, rebound-like movements. To maximize compensatory acceleration and adhere to the 100-bpm tempo (~0.6 s per phase), the range of motion was not restricted by mechanical blocks, thereby preserving the participants' ballistic intent.

Measurements

Electromyography

Surface EMG of the right vastus lateralis muscle was recorded using wireless sensors (Ultium EMG, Noraxon Inc., Scottsdale, AZ). Electrodes were placed distal to the NIRS probe following SENIAM guidelines (Hermens et al. 2000).

Signals were sampled at 2000 Hz and processed with a fourth-order Butterworth bandpass filter (20–450 Hz), followed by full-wave rectification and smoothing (fourth-order low-pass filter, 6 Hz cutoff) to create a linear envelope. Data were then normalized to %MVIC.

Frequency analysis was performed using a Fast Fourier Transform with a Hamming window (2000 points [1.0 s], 50% overlap). Analysis intervals are defined as follows:

- **Mean Electromyography Activity (%MVIC) and Mean Power Frequency:** The entire repetition phase was analyzed for LST and HL, while only the "isotonic phase" (eight repetitions) was analyzed for CB.
- **Integrated Electromyography:** Calculated for the entire repetition phase in LST and HL, and for CB, as the sum of the isometric (20 s) and isotonic phases.
- **Mean Power Frequency Slope:** The rate of change in mean power frequency (MPF) was calculated using linear regression analysis as an index of muscle fatigue, with CB analyzed only during the isotonic phase.

Near-Infrared Spectroscopy

Muscle oxygenation dynamics of the right vastus lateralis were evaluated using a dual-wavelength (770 nm and 830 nm) NIRS device (Hb14-4; Astem Co., Ltd.) with a 30 mm interoptode distance. Subcutaneous fat thickness (measured via ultrasound) was corrected using the methods described by Lin et al. (2000) and Niwayama et al. (2000). Relative changes (Δ) in oxygenated hemoglobin, deoxygenated hemoglobin (Deoxy-Hb), total hemoglobin (Total-Hb), and tissue oxygen saturation (StO_2) were calculated relative to resting values. Mean values were calculated for the entire set in LST and HL and for the isotonic phase in CB.

Biochemical Analysis

Blood samples were collected at three time points (Pre-test, Post-test, Post-15min) to measure serum IGF-1 concentrations. After serum separation, samples were stored at -80 °C and quantified by an external laboratory (BML, Tokyo, Japan) using an enzyme-linked immunosorbent assay.

Statistical Analysis

Data were analyzed using Python (ver. 3.13.1) and pingouin (ver. 0.6.0). All data are presented as mean ± standard deviation in both the text and figures. The normality of the data distribution was assessed using the Shapiro-Wilk test. Although some variables slightly violated this assumption, we proceeded with parametric analyses because the F-test is highly robust to deviations from normality, particularly when sample sizes are nearly equal across groups, in both between-subjects (Blanca et al. 2017) and repeated-measures designs (Blanca et al. 2023). Levene's test was used to confirm the homogeneity of variance. Mauchly's test evaluated the assumption of sphericity, and the Greenhouse-Geisser correction was applied when the assumption was violated. IGF-1 and EMG data were analyzed using a two-way mixed-design ANOVA. The recalculated NIRS data (Δ values) were analyzed using a one-way ANOVA to compare groups at each set. Tukey's honest significant difference post-hoc test was applied when significant interactions or main effects were observed. Hedges' g and partial eta squared (η_p^2) were calculated as the effect sizes. The magnitudes of the effect sizes were interpreted using established thresholds originally proposed for standardized mean differences (Cohen 1988): $<$ 0.20 as trivial, 0.20–0.49 as small, 0.50–0.79 as medium, and $\geq$ 0.80 as large for Hedges' g, and 0.01 as small, 0.06 as medium,

and 0.14 as large for η_p^2. Statistical significance was set at $p < 0.05$.

The sample size was calculated using G*Power 3.1. Based on previous research using a similar protocol (Tanimoto and Ishii 2006), an effect size of $f = 0.50$, $\alpha = 0.05$, and $1-\beta = 0.80$ was used to detect group differences, resulting in a required sample of 42 participants (Cohen 1992).

Results

Electromyographic Activity

Mean Electromyographic Activity (%MVIC)

A significant main effect of group was observed for the mean EMG activity of the vastus lateralis across all sets (Set 1: $F(2, 45) = 3.25$, $p = 0.048$, $\eta_p^2 = 0.126$, medium; Set 2: $F(2, 45) = 4.07$, $p = 0.024$, $\eta_p^2 = 0.153$, large; Set 3: $F(2, 45) = 4.99$, $p = 0.011$, $\eta_p^2 = 0.182$, large; Table 2, Fig. 4a). Post-hoc comparisons revealed that in Set 1, HL activity was significantly higher than LST ($p = 0.049$, $g = 0.84$, large). Although the CB group (isotonic phase) had higher values than the LST group, the difference was not statistically significant ($p = 0.142$, $g = 0.75$, medium). HL was not significantly different from CB ($p = 0.881$, $g = 0.16$, trivial).

In Set 2, the CB (p = 0.043, g = 1.00, large) and HL groups (p = 0.043, g = 0.86, large) showed significantly higher %MVIC than the LST group. In Set 3, the CB group remained significantly more active than the LST group (p = 0.009, g = 1.23, large), whereas HL did not differ significantly from the LST group (p = 0.088, g = 0.75, medium).

Table 2. Electromyographic activity variables during leg press exercise.

Variable	Set	LST (n=15)	HL (n=17)	CB (n=16)	*P*-value
%MVIC	1	77.6 ± 40.1	116.7 ± 51.4*	109.1 ± 43.3	0.048
	2	80.7 ± 43.7	126.7 ± 61.0*	127.4 ± 49.1*	0.024
	3	86.4 ± 43.2	124.9 ± 57.7	142.1 ± 47.5*	0.011
iEMG (μV·s)	1	1864.5 ± 1152.8	2168.3 ± 1061.5	2585.0 ± 1137.2	0.206
	2	1833.7 ± 1247.3	2193.3 ± 1253.9	2571.6 ± 957.5	0.220
	3	1676.6 ± 621.2	1905.7 ± 1021.2	3058.4 ± 1014.1*†	< 0.001
MPF (Hz)	1	84.0 ± 9.2	80.0 ± 12.8	77.1 ± 9.7	0.216
	2	81.0 ± 10.0	77.4 ± 11.6	74.9 ± 12.3	0.338
	3	80.3 ± 10.7	77.1 ± 11.8	69.1 ± 15.7	0.054

Note: Values are presented as means ± SD. LST, low-intensity slow training; HL, high-load training; CB, combined training; %MVIC, mean muscle activity normalized to maximum voluntary contraction; iEMG, integrated electromyography; MPF, mean power

276 frequency. In the CB group, %MVIC and MPF were analyzed during the isotonic phase,
277 while iEMG reflected total activity (isometric and isotonic phases).
278 $^{*}P < 0.05$ vs. LST (Set 1: HL, $g = 0.84$; Set 2: HL, $g = 0.86$; CB, $g = 1.00$; Set 3: CB, g
279 $= 1.23$; iEMG Set 3: CB, $g = 1.63$).
280 $^{\dagger}P < 0.05$ vs. HL (iEMG Set 3: CB, $g = 1.13$).
281 Effect sizes (Hedges' g) are reported for significant pairwise comparisons.
282

283 **Integrated EMG**

284 Integrated EMG (iEMG) did not differ significantly between groups in Set 1 ($p =$
285 0.206) or Set 2 ($p = 0.220$; Fig. 4b). However, a significant main effect of group
286 emerged in Set 3 ($F(2, 45) = 10.41$, $p < 0.001$, $\eta_p^2 = 0.316$, large). Post-hoc analysis
287 revealed that total iEMG was significantly higher in the CB group than in the HL
288 ($p = 0.002$, $g = 1.13$, large) and LST groups ($p < 0.001$, $g = 1.63$, large). HL and
289 LST did not differ significantly ($p = 0.760$).
290

291 **Mean Power Frequency**

292 Absolute MPF values and the rate of change (slope) did not differ significantly
293 between groups in any set (all $p > 0.05$). Although there was a trend toward higher
294 absolute MPF in Set 3, it was not statistically significant ($F(2, 45) = 3.13$, $p =$
295 0.054, $\eta_p^2 = 0.122$, medium).

296

297 **Muscle Oxygenation (Near-Infrared Spectroscopy)**

298 A one-way ANOVA revealed a significant difference between groups on ΔStO_2
299 across all sets (Set 1: $F(2, 45) = 7.43$, $p = 0.002$, $\eta_p^2 = 0.248$, large; Set 2: $F(2,$
300 $45) = 8.99$, $p < 0.001$, $\eta_p^2 = 0.285$, large; Set 3: $F(2, 45) = 12.20$, $p < 0.001$, $\eta_p^2 =$
301 0.352, large; Table 3, Fig. 5a). In Set 1, the CB group had significantly lower
302 ΔStO_2 than that in the HL group ($p = 0.001$, $g = 1.19$, large), whereas LST did not
303 differ significantly from HL ($p = 0.140$). In Sets 2 and 3, the CB (Set 2: $p < 0.001$,
304 $g = 1.26$, large; Set 3: $p < 0.001$, g = 1.50, large) and LST groups (Set 2: $p = 0.028$,
305 $g = 0.98$, large; Set 3: $p = 0.003$, $g = 1.37$, large) showed significantly lower ΔStO_2
306 values than those in the HL group.

307

308 Table 3. Muscle oxygenation variables during leg press exercise.

Variable	Set	LST (n=15)	HL (n=17)	CB (n=16)	P-value
Δ StO_2 (%)	1	-31.4 ± 8.4	-22.6 ± 10.6	-37.1 ± 13.1†	0.002
	2	-31.1 ± 6.2†	-21.8 ± 11.3	-36.0 ± 10.9†	< 0.001
	3	-35.0 ± 7.6†	-19.1 ± 8.6	-34.3 ± 11.1†	< 0.001
Δ Deoxy-Hb	1	0.024 ± 0.010	0.017 ± 0.011	0.023 ± 0.011	0.143
	2	0.026 ± 0.012	0.017 ± 0.010	0.026 ± 0.013	0.036
	3	0.026 ± 0.011†	0.016 ± 0.009	0.026 ± 0.013†	0.012

Note: Values are presented as means ± SD. Δ StO2, change in tissue oxygen saturation; Δ Deoxy-Hb, change in deoxygenated hemoglobin; Δ Total-Hb, change in total hemoglobin; LST, low-intensity slow training; HL, high-load training; CB, combined training. For the CB group, values were analyzed during the isotonic phase. No significant differences were observed in Δ Total-Hb levels among groups.

$^{\dagger}P < 0.05$ vs. HL.

Δ StO_2 (Set 1: CB, $g = 1.19$; Set 2: CB, $g = 1.26$; LST, $g = 0.98$; Set 3: CB, $g = 1.50$; LST, $g = 1.37$).

Δ Deoxy-Hb (Set 3: CB, g = 0.91, LST, g = 1.02).

Effect sizes (Hedges' g) are reported for significant pairwise comparisons.

Regarding ΔDeoxy-Hb, a one-way ANOVA indicated significant differences in Set 2 ($F(2, 45) = 3.57$, $p = 0.036$, $\eta_p^2 = 0.137$, medium) and Set 3 ($F(2, 45) = 4.91$, $p = 0.018$, $\eta_p^2 = 0.179$, large). Although a significant main effect was observed in Set 2, post-hoc comparisons revealed no significant differences compared to the HL group (Fig. 5b). In Set 3, however, ΔDeoxy-Hb was significantly higher in both the CB ($p = 0.036$, $g = 0.91$, large) and LST groups ($p = 0.012$, $g = 1.02$, large) compared to the HL group. ΔTotal-Hb levels did not differ significantly among groups at any set (Set 1: $p = 0.134$; Set 2: $p = 0.186$; Set 3: $p = 0.243$).

Serum IGF-1 Concentration

Serum IGF-1 concentrations showed no significant group × time interaction ($F(4, 90) = 0.34$, $p = 0.849$, $\eta_p^2 = 0.015$, small) or main effect of group ($F(2, 45) = 0.12$, $p = 0.889$, $\eta_p^2 = 0.005$, trivial). However, a significant main effect of time was observed ($F(2, 90) = 111.12$, $p < 0.001$, $\eta_p^2 = 0.712$, large). Because sphericity was violated for the time effect ($p = 0.008$), the Greenhouse-Geisser correction was applied ($p_{GG} < 0.001$). IGF-1 levels significantly increased from Pre-test to Post-test and returned to baseline levels at Post-15 min across all groups (Table 4, Fig. 6).

Table 4. Changes in serum IGF-1 concentrations.

Time point	LST (n = 15)	HL (n = 17)	CB (n = 16)
Pre-test	227.5 ± 59.6	220.9 ± 41.4	220.5 ± 47.6
Post-test #	243.5 ± 72.7	236.2 ± 46.4	232.5 ± 48.6
Post-15 min	219.8 ± 65.4	213.8 ± 41.2	211.6 ± 43.8

Note: Values are presented as means ± SD. LST, low-intensity slow training; HL, high-load training; CB, combined training; Pre-test, before exercise; Post-test, immediately after exercise; Post-15 min, 15 min after exercise. No significant group × time interaction or main effect of group was observed. A significant main effect of time was observed ($p < 0.001$), with values at Post-test significantly higher than those at Pre-test in all groups.

# $p < 0.05$ vs. Pre-test (main effect of time).

Discussion

In this study, we compared acute physiological responses to a novel low-intensity resistance training protocol, CB, which integrates isometric contractions with high-velocity short-arc isotonic contractions, with those of traditional LST and HL. The primary findings were that the CB protocol at 40% 1RM (1) produced mean muscle activity (%MVIC) of a comparable magnitude to the HL protocol at 80% 1RM and (2) induced an earlier intramuscular hypoxic environment (ΔStO_2 reduction) than HL, of a comparable magnitude to LST. Furthermore, in the third set—when fatigue accumulation was greatest—CB showed the highest iEMG levels. By sustaining an isometric contraction, this method increases intramuscular pressure and simulates BFR-like ischemia.

Mechanisms of Enhanced Muscle Activity

Notably, despite the low load (40% 1RM), surface EMG amplitudes during the CB protocol were comparable to those observed in HL (80% 1RM) exercise (Fig. 4a). While we acknowledge that surface EMG is a

proxy for neural drive rather than a direct measure of single motor unit behavior, these robust amplitudes strongly suggest a high degree of motor unit recruitment. Although low-intensity BFR training effectively promotes hypertrophy, a 25-year review indicates that low-load training is generally inferior to HL training for increasing maximal strength (Loenneke et al. 2025). By inducing acute neuromuscular activity equivalent to that of HL exercise, the CB protocol presents a physiological profile that addresses this typical limitation of low-load training, although long-term equivalence in strength outcomes remains to be determined.

Three physiological mechanisms may explain this effect. First, the initial isometric contraction induces localized pre-exhaustion. Although findings on traditional pre-exhaustion using single-joint exercises are inconsistent (Gentil et al. 2007), the sustained isometric contraction in the CB protocol likely induces localized fatigue in low-threshold motor units. Consequently, maintaining the required force during the subsequent isotonic phase necessitates greater recruitment of high-threshold Type II fibers and higher motor unit firing rates, consistent

384 with Henneman's size principle (Hill et al. 2023; Lowe et al. 2023;
385 Olmos et al. 2024). Previous reports show that low-intensity exercise
386 with BFR progressively shifts recruitment toward high-threshold motor
387 units and increases muscle excitation with fatigue, a mechanism that
388 likely also operates in the CB protocol.
389 A second neurophysiological mechanism relates to enhanced
390 proprioceptive drive. The sustained tension developed during the initial
391 isometric hold can increase the discharge rate of muscle spindle
392 afferents (Burke et al. 1978; Enoka 2015). This heightened
393 proprioceptive feedback provides continuous excitatory input to the
394 alpha motor neurons. Consequently, when transitioning immediately
395 from the isometric hold to the dynamic isotonic phase, this augmented
396 reflex drive likely facilitates the excitability of the motor neuron pool,
397 thereby enhancing motor unit recruitment during the subsequent
398 movements. Third, the high movement velocity (100 bpm) further
399 increased neural drive. Even with light loads, achieving maximal
400 acceleration requires high force output ($F = ma$), a phenomenon termed
401 compensatory acceleration (Behm and Sale 1993; Wilk et al. 2020). Prior

research demonstrates that ballistic movements can recruit high-threshold motor units at lower force levels than slow contractions (Desmedt and Godaux 1977; Aagaard et al. 2002; Duchateau et al. 2006). Together, isometric pre-exhaustion, augmented proprioceptive drive, and high-velocity movement appear to be an effective strategy for maximizing neuromuscular activity under low-load conditions.

Muscle Oxygen Dynamics and Metabolic Stress

NIRS data show that the CB protocol rapidly and significantly reduced muscle oxygenation (ΔStO_2) to levels comparable to those of LST, and significantly lower than those observed with HL exercise (Fig. 5a). Sustained isometric contractions increase intramuscular pressure, thereby significantly restricting blood flow (Sadamoto et al. 1983; Wigmore et al. 2006). Importantly, the lack of significant differences in ΔTotal-Hb among the groups indicates that the total regional blood volume in the working muscle was comparable during the exercises. Given this comparable blood supply, the significantly higher ΔDeoxy-Hb observed in the CB and LST groups during Set 3 directly reflects

enhanced oxygen extraction by the active muscle fibers (Fig. 5b). These dynamics indicate that the CB protocol effectively induces a severe localized hypoxic environment. The resulting hypoxia in the CB group mirrors the metabolic stress environments reported in BFR training and matches the deoxygenation levels in previous NIRS studies (Tanimoto and Ishii 2006). Loenneke et al. (2025) propose that metabolite accumulation during BFR promotes hypertrophy by altering motor unit recruitment via cell swelling and fatigue. Although we did not directly measure intramuscular metabolite concentrations, this severe hypoxic and ischemic condition likely accelerated metabolite accumulation (e.g., lactate and H^+), activating group III/IV afferent fibers (Amann et al. 2010; Pearson and Hussain 2015). This metaboreflex may further augment central motor drive to the agonist muscles, contributing to the significantly higher iEMG observed during the final CB protocol (Fig. 4b). Overall, the CB protocol effectively reproduces the metabolic environment of BFR or LST without requiring external pressure cuffs or prolonged set durations.

Hormonal Response

Serum IGF-1 concentrations increased significantly across all groups, with no between-protocol differences (Fig. 6). This suggests that the CB protocol at 40% 1RM provides sufficient physiological stimulus to evoke an acute endocrine response comparable to that of HL exercise. We specifically selected IGF-1 to allow for direct comparisons with foundational studies on LST and BFR training, which have classically utilized this hormone to characterize exercise-induced systemic metabolic stress (Takarada et al. 2000; Kraemer and Ratamess 2005; Tanimoto and Ishii 2006). Previous studies identify metabolic stress as a key mediator of exercise-induced hormone secretion (Goto et al. 2005). While contemporary literature suggests that transient systemic hormone elevations are not direct predictors of long-term muscle hypertrophy, the capacity of the CB protocol to induce a significant hormonal response at extremely low loads nevertheless reflects a profound systemic exercise stress.

Limitations and Future Directions

This study has several limitations. First, it only examined acute responses; therefore, long-term hypertrophic and strength effects remain uncertain. Second, our physiological assessments were limited to a single muscle (vastus lateralis) and relied on surface EMG and NIRS, which serve as indirect proxies rather than direct measures of motor unit recruitment, muscle perfusion, or intramuscular metabolite concentrations. Furthermore, our systemic metabolic analysis was limited to serum IGF-1. Evaluating other circulating metabolites and myokines known to act on the central nervous system, such as blood lactate, brain-derived neurotrophic factor (BDNF), or irisin, would provide a more comprehensive metabolic profile. Third, the sample was limited to healthy young men. Although the low joint loading of the CB method suggests potential applicability for older adults and rehabilitation populations (Hughes et al. 2017; Cruz-Jentoft et al. 2019; Fragala et al. 2019), blood pressure responses were not directly assessed. Accordingly, caution is warranted regarding potential blood pressure elevations during isometric contractions when applying this method in clinical populations.

However, these findings suggest potential applications for athletes. By recruiting high-threshold motor units while minimizing joint stress, the CB method may be useful during early-stage rehabilitation, enabling athletes to maintain muscle function without overloading the injured site. In field settings lacking heavy equipment or feasible bodyweight exercise (e.g., squats), CB may also offer practical and time-efficient means, eliciting a strong physiological stimulus (Lum and Barbosa 2019).

Conclusions

In conclusion, the integration of isometric pre-exhaustion with high-velocity, short-arc isotonic movements provides a robust physiological stimulus despite the use of very low mechanical loads. By simultaneously imposing high neural demands and profound metabolic stress in a time-efficient manner, the CB protocol offers a highly practical, joint-friendly training alternative. These findings hold significant clinical and athletic relevance, presenting a viable strategy for populations requiring minimized joint stress, such as older adults

mitigating sarcopenia or athletes undergoing rehabilitation.

Statements and Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Nittazuka Medical Welfare Center (Approval No. 2024-28).

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

TS contributed to all aspects of this study. TS, KF, KH, and SH conceived and designed the study. TS, TN, and YY prepared the material and collected data. TS performed analysis and wrote the first draft of the manuscript. All authors commented on previous versions of the manuscript and read and approved the final manuscript.

References

Aagaard P, Simonsen EB, Andersen JL, et al, Magnusson P, Dyhre-Poulsen P (2002) Increased rate of force development and neural drive of human skeletal muscle following resistance training. J Appl Physiol (1985) 93:1318-–1326. https://doi.org/10.1152/japplphysiol.00283.2002

Amann M, Blain GM, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA et al (2010) Group III and IV muscle afferents contribute to ventilatory and

cardiovascular response to rhythmic exercise in humans. J Appl Physiol (1985) 109:966-–976. https://doi.org/10.1152/japplphysiol.00462.2010

Behm DG, Sale DG (1993) Velocity specificity of resistance training. Sports Med 15:374-–388. https://doi.org/10.2165/00007256-199315060-00003

Blanca MJ, Alarcón R, Arnau J, et al (2017) Non-normal data: Is ANOVA still a valid option? Psicothema 29:552–557. https://doi.org/10.7334/psicothema2016.383

Blanca MJ, Arnau J, García-Castro FJ, et al (2023) Non-normal Data in Repeated Measures ANOVA: Impact on Type I Error and Power. Psicothema 35:21–29. https://doi.org/10.7334/psicothema2022.292

Brzycki M (1993) Strength testing—predicting a one-rep max from reps-to-fatigue. Journal of Physical Education, Recreation & Dance, 64: 88-90. https://doi.org/10.1080/07303084.1993.10606684

Burke D, Hagbarth KE, Skuse NF (1978) Recruitment order of human spindle endings in isometric voluntary contractions. J Physiol 285:101–112. https://doi.org/10.1113/jphysiol.1978.sp012560

544 Cohen J (1992) A power primer. Psychol Bull 112:155-159.
545 https://doi.org/10.1037//0033-2909.112.1.155

546 Cohen J (1988) Statistical power analysis for the behavioral sciences,
547 2nd ed. L. Erlbaum Associates, Hillsdale, N.J

548 Cruz-Jentoft AJ, Bahat G, Bauer J, et al (2019) Sarcopenia: revised
549 European consensus on definition and diagnosis. Age Ageing
550 48:601. https://doi.org/10.1093/ageing/afz046

551 Currier BS, D'Souza AC, Singh MAF, et al (2026) American College of
552 Sports Medicine Position Stand. Resistance Training Prescription
553 for Muscle Function, Hypertrophy, and Physical Performance in
554 Healthy Adults: An Overview of Reviews. Med Sci Sports Exerc
555 58:851–872. https://doi.org/10.1249/MSS.0000000000003897

556 Currier BS, Mcleod JC, Banfield L, et al (2023) Resistance training
557 prescription for muscle strength and hypertrophy in healthy adults:
558 a systematic review and Bayesian network meta-analysis. Br J
559 Sports Med 57:1211-1220. https://doi.org/10.1136/bjsports-2023-
560 106807

561 Desmedt JE, Godaux E (1977) Ballistic contractions in man:
562 characteristic recruitment pattern of single motor units of the
563 tibialis anterior muscle. J Physiol 264:673-693.
564 https://doi.org/10.1113/jphysiol.1977.sp011689

565 Duchateau J, Semmler JG, Enoka RM (2006) Training adaptations in the
566 behavior of human motor units. J Appl Physiol (1985) 101:1766-
567 1775. https://doi.org/10.1152/japplphysiol.00543.2006

568 Enoka RM (2015) Neuromechanics of human movement, 5. ed. Human
569 Kinetics, Champaign, IL

570 Fragala MS, Cadore EL, Dorgo S, et al (2019) Resistance training for
571 older adults: position statement from the National Strength and
572 Conditioning Association. J Strength Cond Res 33:2019-2052.
573 https://doi.org/10.1519/JSC.0000000000003230

574 Fry AC (2004) The role of resistance exercise intensity on muscle fibre
575 adaptations. Sports Med 34:663-679.
576 https://doi.org/10.2165/00007256-200434100-00004

577 Gentil P, Oliveira E, de Araújo Rocha Júnior V, do Carmo J, Bottaro M

(2007) Effects of exercise order on upper-body muscle activation and exercise performance. J Strength Cond Res 21:1082-1086. https://doi.org/10.1519/R-21216.1

Goto K, Ishii N, Kizuka T, Takamatsu K (2005) The impact of metabolic stress on hormonal responses and muscular adaptations. Med Sci Sports Exerc 37:955-963.

Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G (2000) Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol 10:361-374. https://doi.org/10.1016/s1050-6411(00)00027-4

Hill EC, Rivera PM, Proppe CE, Rojas DHG, Lawson JE (2023) Acute effects of low load blood flow restricted and non restricted exercise on muscle excitation, neuromuscular efficiency, and average torque. J Musculoskelet Neuronal Interact 23:165-174

Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD (2017) Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. Br J Sports Med 51:1003-

1011. https://doi.org/10.1136/bjsports-2016-097071

Kraemer WJ, Ratamess NA (2005) Hormonal responses and adaptations to resistance exercise and training. Sports Med 35:339-361. https://doi.org/10.2165/00007256-200535040-00004

Lin L, Niwayama M, Shiga T, Kudo N, Takahashi M, Yamamoto K (2000) Influence of a fat on muscle oxygenation measurement using near-IR spectroscopy: quantitative analysis based on two-layered phantom experiments and Monte Carlo simulation. Front Med Biol Eng 10:43-58. https://doi.org/10.1163/15685570052061531

Loenneke JP, Hammert WB, Kataoka R, Yamada Y, Abe T (2025) Twenty-five years of blood flow restriction training: what we know, what we don't, and where to next? J Sports Sci 43:2115-2132. https://doi.org/10.1080/02640414.2025.2474329

Lowe TW, Tenan MS, Shah K, Griffin L (2023) Low-load blood flow restriction reduces time-to-minimum single motor unit discharge rate. Exp Brain Res 241:2795-2805. https://doi.org/10.1007/s00221-023-06720-8

612 Lum D, Barbosa TM (2019) Brief review: effects of isometric strength
613 training on strength and dynamic performance. Int J Sports Med
614 40:363-375. https://doi.org/10.1055/a-0863-4539

615 Niwayama M, Lin L, Shao J, Kudo N, Yamamoto K (2000) Quantitative
616 measurement of muscle hemoglobin oxygenation using near-
617 infrared spectroscopy with correction for the influence of a
618 subcutaneous fat layer. Rev Sci Instrum 71:4571-4575.
619 https://doi.org/10.1063/1.1322578

620 Olmos AA, Montgomery TR, Sears KN, et al (2024) Blood flow
621 restriction increases motor unit firing rates and input excitation of
622 the biceps brachii during a moderate-load muscle action. J Sports
623 Sci 42:1891-1903.
624 https://doi.org/10.1080/02640414.2024.2413721

625 Oranchuk DJ, Storey AG, Nelson AR, Cronin JB (2019) Isometric
626 training and long-term adaptations: effects of muscle length,
627 intensity, and intent: a systematic review. Scand J Med Sci Sports
628 29:484-503. https://doi.org/10.1111/sms.13375

Ozaki H, Loenneke JP, Buckner SL, Abe T (2016) Muscle growth across a variety of exercise modalities and intensities: contributions of mechanical and metabolic stimuli. Med Hypotheses 88:22-26. https://doi.org/10.1016/j.mehy.2015.12.026

Ozaki H, Loenneke JP, Thiebaud RS, Abe T (2015) Cycle training induces muscle hypertrophy and strength gain: strategies and mechanisms. Acta Physiol Hung 102:1-22. https://doi.org/10.1556/APhysiol.102.2015.1.1

Patterson SD, Hughes L, Warmington S, et al (2019) Blood flow restriction exercise: considerations of methodology, application, and safety. Front Physiol 10:533. https://doi.org/10.3389/fphys.2019.00533

Pearson LT, Behm DG, Goodall S, et al (2022) Effects of maximal-versus submaximal-intent resistance training on functional capacity and strength in community-dwelling older adults: a systematic review and meta-analysis. BMC Sports Sci Med Rehabil 14:129. https://doi.org/10.1186/s13102-022-00526-x

Pearson SJ, Hussain SR (2015) A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. Sports Med 45:187-200. https://doi.org/10.1007/s40279-014-0264-9

Rodrigues F, Domingos C, Monteiro D, Morouço P (2022) A review on aging, sarcopenia, falls, and resistance training in community-dwelling older adults. Int J Environ Res Public Health 19:874. https://doi.org/10.3390/ijerph19020874

Sadamoto T, Bonde-Petersen F, Suzuki Y (1983) Skeletal muscle tension, flow, pressure, and EMG during sustained isometric contractions in humans. Eur J Appl Physiol Occup Physiol 51:395-408. https://doi.org/10.1007/BF00429076

Schoenfeld BJ (2010) The mechanisms of muscle hypertrophy and their application to resistance training. J Strength Cond Res 24:2857-2872. https://doi.org/10.1519/JSC.0b013e3181e840f3

Schoenfeld BJ (2013) Potential mechanisms for a role of metabolic stress in hypertrophic adaptations to resistance training. Sports Med

663 43:179-194. https://doi.org/10.1007/s40279-013-0017-1

664 Scott BR, Loenneke JP, Slattery KM, Dascombe BJ (2015) Exercise with
665 blood flow restriction: an updated evidence-based approach for
666 enhanced muscular development. Sports Med 45:313-325.
667 https://doi.org/10.1007/s40279-014-0288-1

668 Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N (2000)
669 Rapid increase in plasma growth hormone after low-intensity
670 resistance exercise with vascular occlusion. J Appl Physiol (1985)
671 88:61-65. https://doi.org/10.1152/jappl.2000.88.1.61

672 Tanimoto M, Ishii N (2006) Effects of low-intensity resistance exercise
673 with slow movement and tonic force generation on muscular
674 function in young men. J Appl Physiol (1985) 100:1150-1157.
675 https://doi.org/10.1152/japplphysiol.00741.2005

676 Tschopp M, Sattelmayer MK, Hilfiker R (2011) Is power training or
677 conventional resistance training better for function in elderly
678 persons? A meta-analysis. Age Ageing 40:549-556.
679 https://doi.org/10.1093/ageing/afr005

Usui S, Maeo S, Tayashiki K, Nakatani M, Kanehisa H (2016) Low-load slow movement squat training increases muscle size and strength but not power. Int J Sports Med 37:305-312. https://doi.org/10.1055/s-0035-1564255

Wigmore DM, Propert K, Kent-Braun JA (2006) Blood flow does not limit skeletal muscle force production during incremental isometric contractions. Eur J Appl Physiol 96:370-378. https://doi.org/10.1007/s00421-005-0037-0

Wilk M, Tufano JJ, Zajac A (2020) The influence of movement tempo on acute neuromuscular, hormonal, and mechanical responses to resistance exercise-a mini review. J Strength Cond Res 34:2369-2383. https://doi.org/10.1519/JSC.0000000000003636

Yasuda T (2022) Selected methods of resistance training for prevention and treatment of sarcopenia. Cells 11:1389. https://doi.org/10.3390/cells11091389

Figures

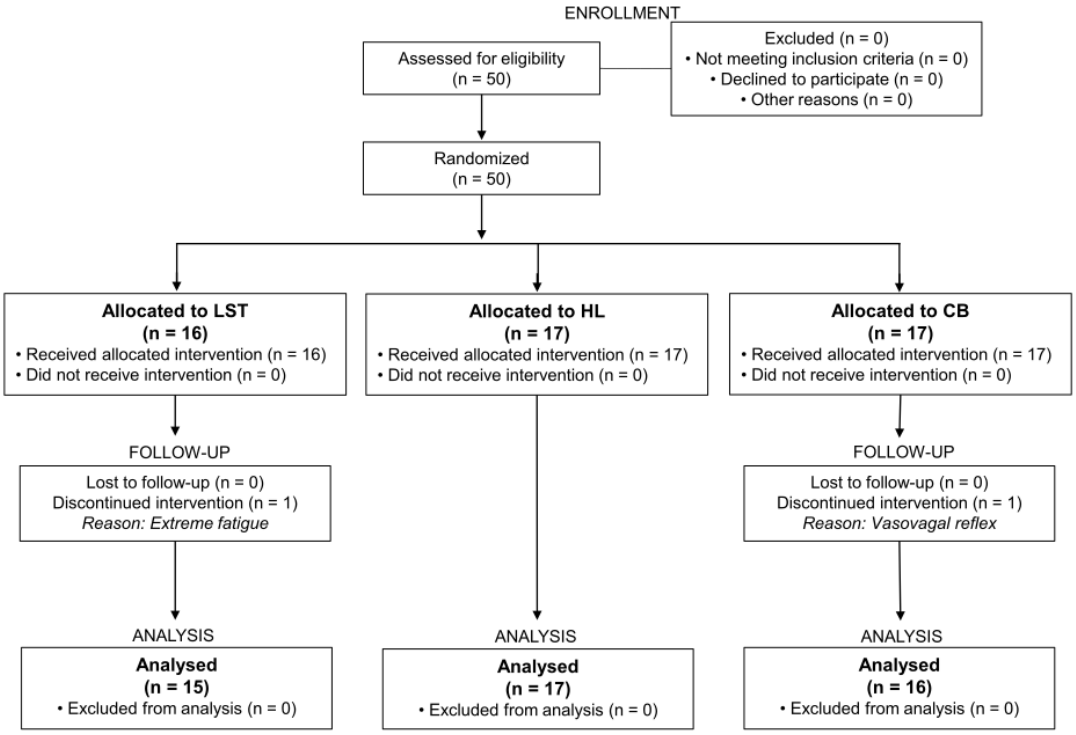


Figure 1

CONSORT flow diagram of the study

Participants were randomly assigned to the LST, HL, or CB groups. Two participants withdrew because of vasovagal reflex or extreme fatigue, resulting in a final sample of 48 participants for analysis.

LST, low-intensity slow training; HL, high-load; CB, combined training



Figure 2

Experimental protocol timeline

The protocol included a 15-min rest period for setup, followed by baseline measurements, MVIC testing, warm-up, and the main resistance training session (three sets). Blood samples were collected at baseline (Pre-test), immediately post-exercise (Post-test), and 15 min into recovery (Post-15 min).

NIRS, near-infrared spectroscopy; MVIC, maximum voluntary isometric contraction.

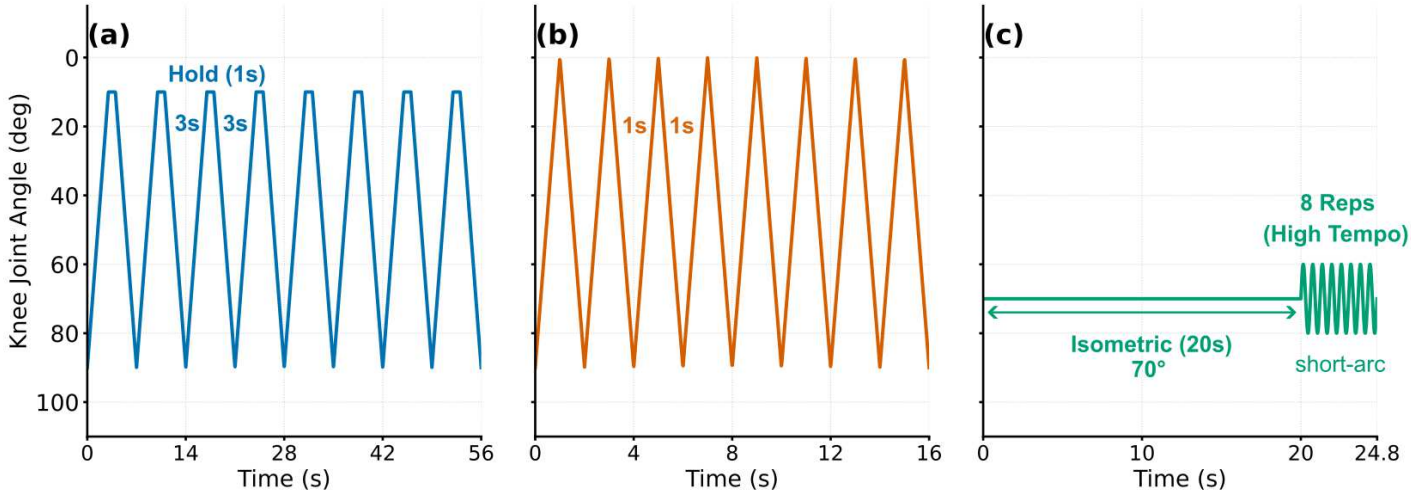


Figure 3

Schematic overview of the three resistance training protocols

(a) LST: 50% 1RM with slow tempo (3 s concentric, 1 s isometric, 3 s eccentric) and no joint lockout. (b) HL: 80% 1RM performed at a normal tempo (1 s concentric, 1 s eccentric). (c) CB: 40% 1RM, comprising a 20-s isometric contraction, followed by eight high-velocity, short-arc isotonic repetitions.

LST, low-intensity slow training; HL, high-load training; CB, combined training

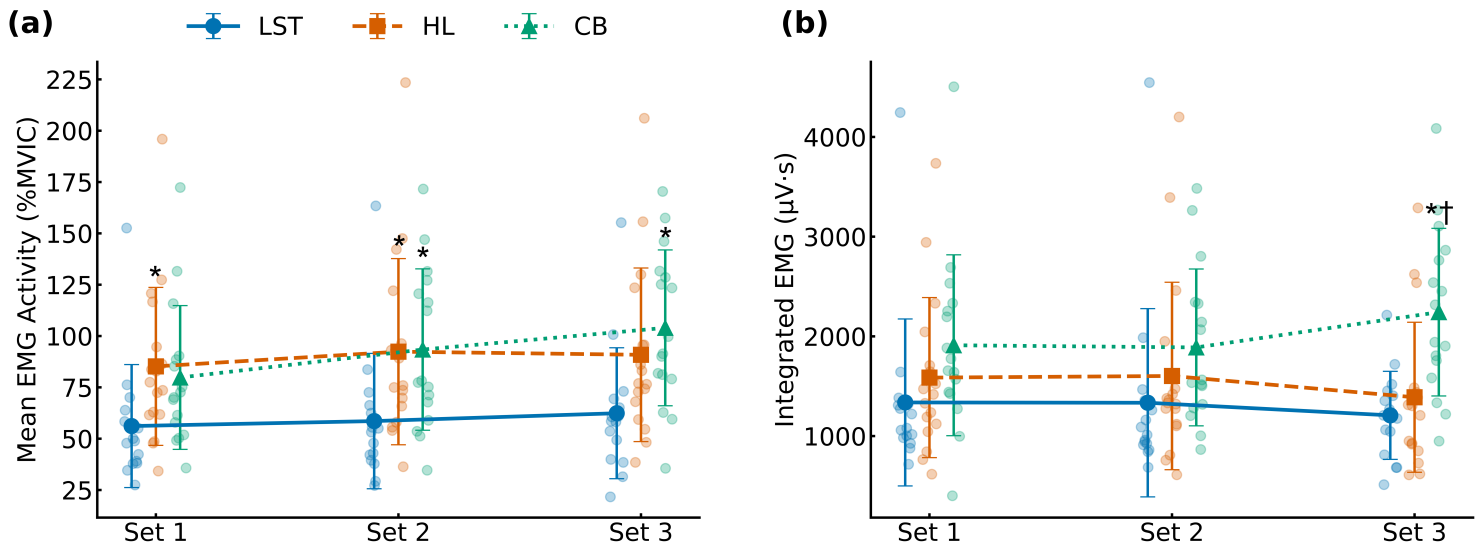


Figure 4

Electromyographic responses across three sets: (a) %MVIC and (b) iEMG

Values are presented as mean ± SD. *p < 0.05 vs. LST, †p < 0.05 vs. HL.

LST, low-intensity slow training; HL, high-load training; CB, combined training; %MVIC, maximum voluntary isometric contraction; iEMG, integrated electromyography.

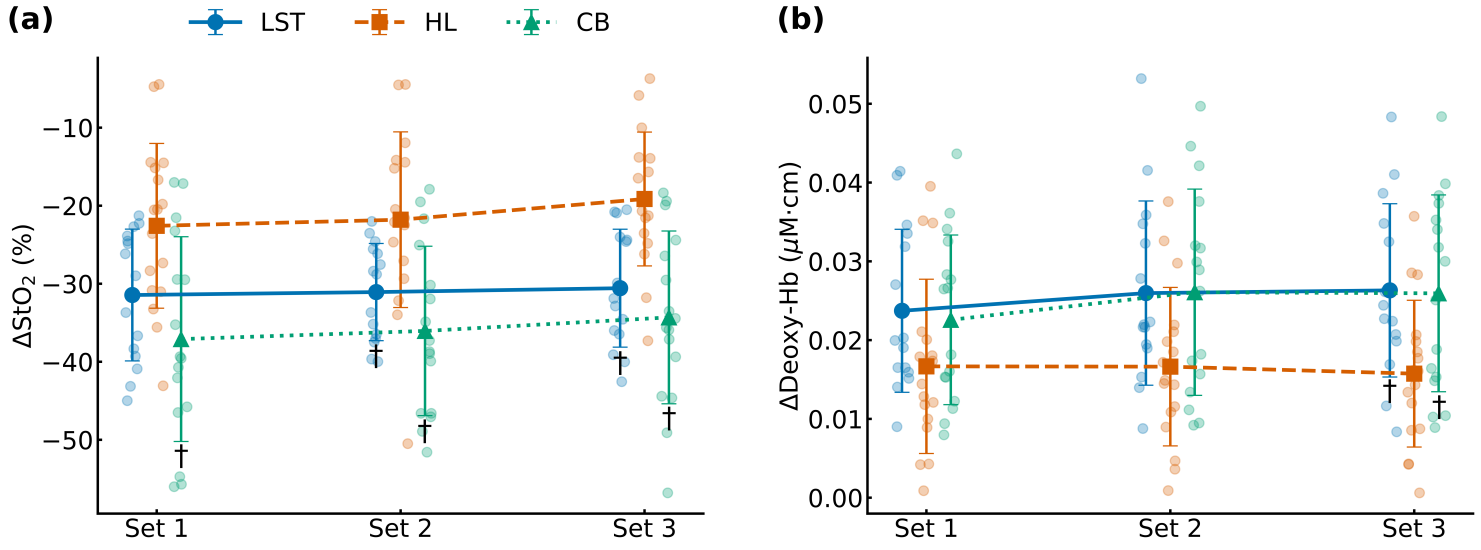


Figure 5

Changes in muscle oxygenation: (a) ΔStO_2 and (b) ΔDeoxy-Hb across three sets

Values are presented as mean ± SD. (a) In the CB group, ΔStO_2 decreases rapidly from the first set, reaching levels comparable to or lower than those in the HL and LST groups. (b) In Set 3, ΔDeoxy-Hb was

significantly higher in the CB and LST groups compared to the HL group, reflecting enhanced oxygen extraction. † $p < 0.05$ vs. HL.

LST, low-intensity slow training; HL, high-load training; CB, combined training.

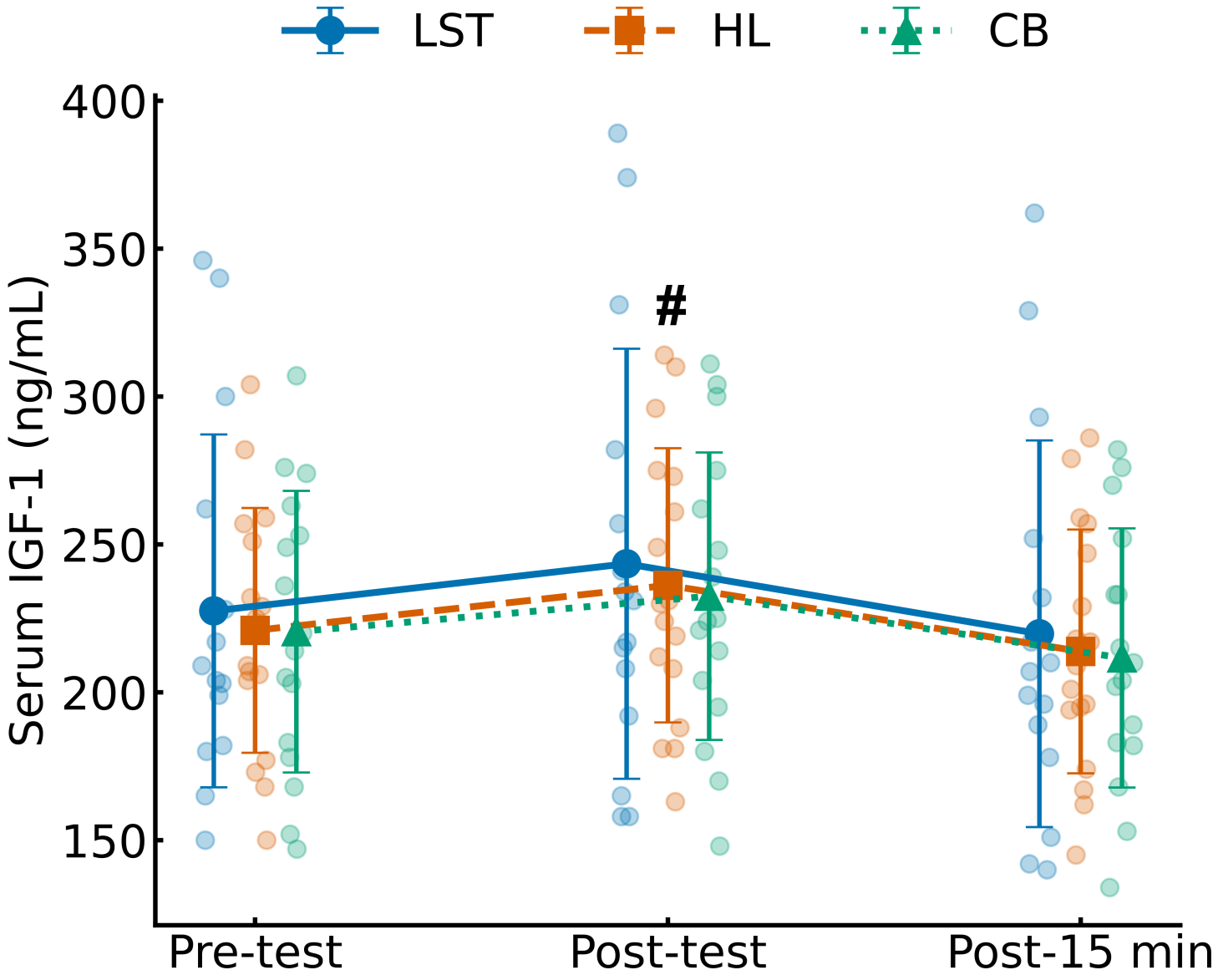


Figure 6

Changes in serum IGF-1 concentrations

Values are presented as mean ± SD. # $p < 0.05$ vs. Pre-test (main effect of time).

LST, low-intensity slow training; HL, high-load training; CB, combined training; Pre-test, before exercise; Post-test, immediately after exercise; Post-15 min, 15 min after exercise.