EFFECTS OF RESISTANCE EXERCISE INVOLVING DIFFERENT INTRA-SET REST DISTRIBUTIONS ON MUSCULAR PERFORMANCE, METABOLIC, HORMONAL AND CARDIOVASCULAR RESPONSES IN RESISTANCE-TRAINED MEN: A RANDOMIZED CROSSOVER STUDY

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Abstract:

This study compared the acute effects of traditional (TRD) and two intra-set rest resistance exercise (RE) structures—cluster sets (CLS) and inter-repetition rest sets (IRS)—on muscular performance, cardiovascular responses, metabolic and perceptual fatigue, and endocrine markers in resistance-trained men. Ten participants (age: 31±7.3 years; training experience: 5.1±2.3 years) completed six RE sessions involving three bilateral knee extension sets of 10 repetitions at 70% 1RM. Sessions were randomized and separated by ≥5 days. Each protocol (CLS, IRS, TRD) was performed twice—once for performance outcomes (maximum number of repetitions [MNR], total load lifted [TLL]) and once for physiological measures (blood lactate, rating of fatigue [ROF], growth hormone [GH], insulin-like growth factor 1 [IGF-1], heart rate [HR], blood pressure [BP], and rate-pressure product [RPP]). No significant condition × time interactions were observed for cardiovascular measures (BP, HR, RPP, all $p>.05$), and area under the curve analysis showed no significant differences between the protocols. Both CLS and IRS yielded significantly higher MNR and TLL versus TRD ($p<.05$). Post-exercise lactate and ROF were highest in TRD and lowest in IRS ($p<.05$). GH increased significantly immediately post-exercise in all the protocols ($p<.001$), with no between-group differences. IGF-1 increased non-significantly post-exercise and declined toward baseline after 30 minutes. Intra-set rest strategies (i.e., CLS and IRS) seems to improve acute performance and reduce fatigue without elevating cardiovascular stress beyond traditional configurations. These strategies are effective for maximizing training output while managing GH secretion, blood lactate changes, and perceptual fatigue in resistance-trained men.

Keywords: *weight training, muscular endurance, fatigue, hormones, blood lactate*

Introduction

Resistance exercise (RE) is a cornerstone of athletic performance enhancement and health promotion. However, the configuration of RE protocols can significantly influence acute physiological responses, including cardiovascular stress, neuromuscular fatigue, and hormonal and metabolic changes (Girman, Jones, Matthews, & Wood, 2014; Jukic, Ramos, Helms, McGuigan, & Tufano, 2020; Río-Rodríguez, Iglesias-Soler, & Fernandez del Olmo, 2016; Tufano, Brown, & Haff, 2017). Traditional set structures, which involve performing all repetitions sequentially within a set followed by rest, are commonly used but may impose greater mechanical and metabolic stress (Girman, et al., 2014; Oliver, et al., 2015). Recently, alternative configurations such as intra-set rest, cluster sets, and rest redistribution protocols have garnered attention due to their potential to modulate fatigue and cardiovascular strain while maintaining training volume and intensity (Gifford, et al., 2022; Girman, et al., 2014; Páez-Maldonado, et al., 2024; Río-Rodríguez, et al., 2016).

Emerging evidence suggests that set configurations, which include short recovery intervals between repetitions or subsets of repetitions, may attenuate the acute cardiovascular response to RE. Studies have reported reduced heart rate (HR), systolic blood pressure (SBP), and rate pressure product (RPP) during intra-set rest protocols compared to the traditional set, indicating lower hemodynamic load during exercise (Ribeiro-Torres, et al., 2020; Rúa-Alonso, et al., 2022). Similarly, Río-Rodríguez et al. (2016) demonstrated that intra-set rest mitigated central and peripheral fatigue while reducing cortical excitability alterations and cardiovascular stress during isometric knee extension. These responses appear to stem from improved oxygen delivery and reduced vascular resistance, as supported by Gifford et al. (2022), who found that brief rest between repetitions enhanced blood flow and exercise tolerance.

In addition to mechanical and neuromuscular demands, acute homeostatic hormonal responses to RE are believed to play a significant role in muscular performance and adaptation (Izquierdo, et al., 2006). Among the variables that can influence these endocrine responses, set configuration has emerged as a relevant factor. Growth hormone (GH), a primary anabolic hormone, typically exhibits a transient elevation following high-volume RE, with its magnitude and duration modulated by factors such as intensity, total workload, and rest intervals (Tufano, et al., 2019). In contrast, the acute response of insulin-like growth factor 1 (IGF-1)—another key regulator of muscle growth, tissue repair, and cellular signaling—remains less well-defined. While traditional set protocols often elicit robust GH elevations, set configuration strategies may produce comparable hormonal responses despite reduced metabolic stress (Girman, et al., 2014; Merrigan, Tufano, Fields, Oliver, & Jones, 2020; Oliver, et al., 2015). These findings suggest that acute endocrine responses may be preserved under intra-set rest protocols, offering a potential strategy for optimizing hormonal stimuli without excessive physiological strain. Nevertheless, it remains unclear whether set configuration influences acute changes in IGF-1 concentration.

Moreover, previous research has also shown that incorporating intra-set rest periods—either every two or six repetitions—results in lower blood lactate concentrations and reduced fatigue responses compared to traditional set structures during full-squat exercises in trained men (Páez-Maldonado, et al., 2024). These findings suggest that intra-set rest strategies may be effective in mitigating metabolic and perceived fatigue while maintaining performance.

Despite the growing body of research on alternative set structures, there is currently no research that has simultaneously examined the interplay of cardiovascular responses, perceived fatigue, and metabolic and hormonal changes using matched training volumes in resistance-trained individuals. Therefore, the present study aimed to compare the acute effects of a traditional set structure and two different intra-set rest distributions on muscular performance, cardiovascular stress, blood lactate, perceived fatigue, and endocrine markers (i.e., GH and IGF-1) in resistance-trained men. By equating load, repetitions, and total rest time between conditions, we sought to isolate the impact of rest distribution on functional muscular performances and these key physiological outcomes.

Method

Participants

The required sample size for this study was estimated through an a priori power analysis based on prior investigations in the field (Gifford, et al., 2022; Río-Rodríguez, et al., 2016). The analysis was performed using G*Power software (version 3.1.9.4; Heinrich Heine University, Düsseldorf, Germany) with the following parameters: effect size f=0.40, alpha level=0.05, statistical power=0.80, and an assumed correlation of 0.5 among repeated measures (Beck, 2013). Results indicated that a minimum of ten participants would be sufficient for detecting significant effects in a repeated-measures design. This design type is particularly efficient as it reduces between-subject variability and thereby enhances statistical power, making it suitable for studies with smaller sample sizes (Strale, 2024).

Accordingly, ten resistance-trained men were recruited (age: 31±7.3 years; body mass index [BMI]: 26.5±1.4 kg/m^2; training experience: 5.1±2.3 years). All participants had engaged in regular RE (3-4 sessions per week) for at least two years, including a combination of compound and isolation exercises performed at moderate to high intensities (approximately 70-85% of one repetition maximum [1RM]). They were recreationally trained but not involved in competitive sports and maintained consistent training frequency (3.6±0.7 sessions/week) during the six months leading up to the study. Inclusion criteria required participants to be aged 18-40 years, have normal BP, a minimum of two years of structured RE experience, and no history of musculoskeletal injury, chronic illness, or use of performance-enhancing substances. The study protocol adhered to the Declaration of Helsinki, and informed consent was obtained from all participants prior to data collection.

Procedures

A within-subjects repeated-measures design was used in this study. Participants were instructed to maintain their habitual diet and avoid strenuous physical activity for at least 24 hours prior to each testing session, following established recommendations (Duncan, Lyons, & Hankey, 2009). They were also asked to refrain from consuming caffeinated beverages after 6:00 p.m. on the day before testing to minimize external influences on cardiovascular measurements. Testing sessions, and all cardiovascular and blood measurements were conducted between 3:00 and 5:30 p.m. to minimize circadian variation in endocrine and hemodynamic responses.

Participants were also instructed to obtain at least eight hours of restful sleep on the night prior to each testing session.

To ensure standardization and participant readiness, a familiarization session was conducted one week before the intervention. During this session, anthropometric data—including height, body mass, and BMI—were recorded using standardized procedures (Esparza-Ros, Vaquero-Cristóbal, & Marfell-Jones, 2019). Participants were then thoroughly briefed on the experimental protocol, and written informed consent was obtained in accordance with ethical standards. Following the orientation, participants completed a 1RM test for the knee extension exercise based on validated testing protocols (Arazi, Aboutalebi, Taati, Cholewa, & Candow, 2022).

Five days following the familiarization session, participants commenced the main testing phase. Each individual completed six distinct RE sessions, consisting of cluster sets (CLS), inter-repetition rest sets (IRS), and traditional sets (TRD), administered in a randomized order. To minimize potential carry-over effects, a minimum of five days of rest was provided between sessions. Each RE protocol was performed twice: once to assess muscular performance and once to evaluate additional physiological variables, as illustrated in Figure 1.

Muscle strength testing

Maximal strength was assessed using a 1RM test for the knee extension exercise. Prior to testing, participants completed a standardized warm-up that included 10 minutes of cycling on a stationary ergometer followed by dynamic stretching targeting both the upper and lower limbs. The 1RM testing procedure adhered to the recommendations of the National Strength and Conditioning Association (Baechle & Earle, 2008) and recent literature (Arazi, et al., 2022). Participants began with a warm-up set of approximately five repetitions at 50% of their estimated 1RM, followed by one to two sets of 2-3 repetitions at 60-80% of the estimated 1RM. Thereafter, single-repetition attempts were made with progressively heavier loads until the maximum load that could be lifted with the proper technique was identified. At least three minutes of rest were provided between attempts to minimize fatigue, and most participants achieved their 1RM within 4-5 sets.

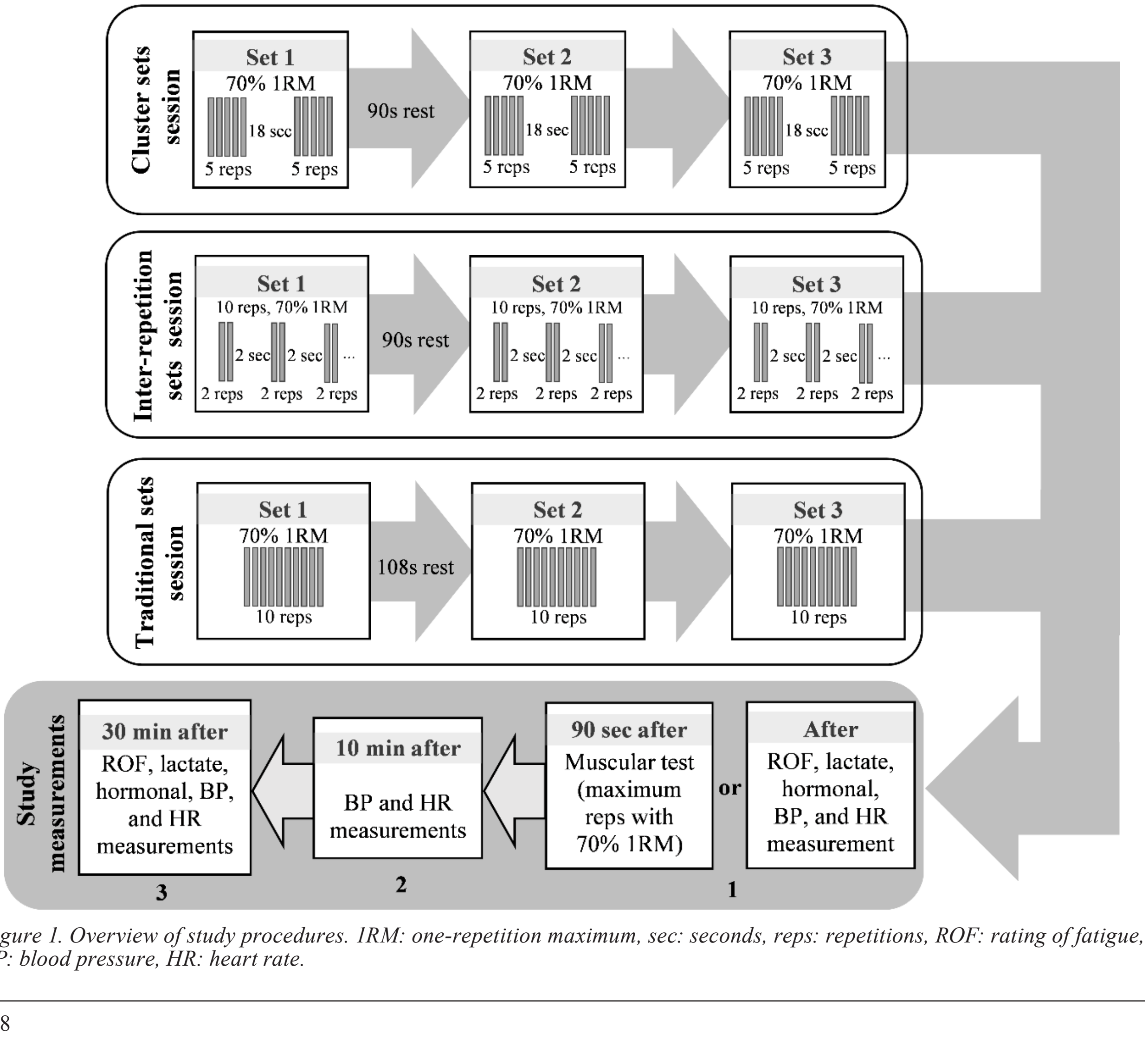

Figure 1. Overview of study procedures. 1RM: one-repetition maximum, sec: seconds, reps: repetitions, ROF: rating of fatigue, BP: blood pressure, HR: heart rate.

Resistance exercise sessions and muscular performance assessment

All experimental sessions were supervised by the same researcher to ensure consistency. Verbal encouragement was provided throughout each trial to standardize motivational factors. As shown in Figure 1, each session involved three sets of bilateral knee extension exercise performed at 70% of 1RM load.

To assess muscular performance, participants completed a single set to volitional failure at 70% of their 1RM, with the maximum number of repetitions (MNR) recorded as an indicator of muscular endurance. Repetitions were only counted if executed with proper form and full range of motion. To standardize repetition tempo, a metronome was employed during the familiarization session, set to a cadence of 2-seconds for the concentric phase and 2-seconds for the eccentric phase, resulting in a total duration of four seconds per repetition (Corrêa, et al., 2022). Participants were instructed to maintain this tempo throughout all RE sessions; however, the metronome was not used beyond the familiarization session (Evangelista, et al., 2019). This approach was adopted to strike a balance between methodological standardization and practical applicability. Limiting metronome use to the familiarization phase was intended to avoid overreliance on external auditory cues and to promote intrinsic pacing control. Encouraging participants to self-regulate tempo fosters internalization of movement patterns and may enhance long-term adherence to proper technique. This strategy is supported by previous research, which suggests that dependence on external aids may hinder the development of autonomous motor control (Wilk, Zajac, & Tufano, 2021). Furthermore, this methodology aligns with recommendations that while intentional tempo control is beneficial, it does not need to be rigidly enforced during every repetition or set (Wilk, et al., 2020). Notably, during the familiarization session, most participants naturally adhered to the prescribed tempo even in the absence of a metronome, although its use during this session ensured initial consistency across all participants.

Moreover, the total load lifted (TLL) per set was calculated as the number of repetitions multiplied by the external load, expressed in kilogram-force (kgf). The present study prioritized ecological validity by focusing on muscular performance that hold greater practical relevance for RE prescription.

Blood lactate and fatigue assessment

Capillary blood samples were collected from the middle finger to assess blood lactate concentrations. Measurements were obtained using a portable lactate analyzer (Lactate Pro 2, Arkray, Kyoto, Japan), following the manufacturer's instructions. This device has been validated for use within the physiological range of 0.5 to 25.0 mmol·L^{-1} and has demonstrated high reliability in exercise settings (Pyne, Boston, Martin, & Logan, 2000). Furthermore, to assess post-exercise fatigue, the rating of fatigue (ROF) scale—a validated 11-point scale designed for use during and after exercise—was administered 30 minutes following the fourth set (Micklewright, St Clair Gibson, Gladwell, & Al Salman, 2017). This delay was chosen to reflect residual fatigue rather than acute discomfort during exertion.

Blood sampling and analysis

Participants remained seated during venous blood collection to minimize variability related to posture. A trained phlebotomist inserted an indwelling catheter into a superficial vein within the antecubital region of the arm, following standard aseptic technique. The catheter (BD Biosciences, San Jose, CA) was used to facilitate repeated sampling and was flushed with 2-3 mL of sterile 0.9% sodium chloride solution (BD Biosciences) to maintain patency. Prior to each blood draw, a waste sample (~3 mL) was discarded using a vacutainer to ensure sample purity. For the analysis of serum GH and IGF-1, blood samples were collected into 5-mL serum separator tubes (BD Biosciences) without additives. Samples were kept on cooling beads for approximately 30 minutes to allow clot formation, followed by centrifugation at 2500 g for 10 minutes using a tabletop centrifuge (KETHINK KT-H120R, Hunan, China). The resulting serum was divided into multiple aliquots and stored at −80 °C for subsequent batch analysis. GH concentrations were determined using a high-sensitivity enzyme-linked immunosorbent assay kit (ELISA) (Enzo Life Sciences, Farmingdale, NY), with an intra-assay coefficient of variation (CV) of 6.2%. IGF-1 was also measured using a commercially available sandwich ELISA (ALPCO, 22-IGFHU-E01, Salem, NH), and the intra-assay CV was 5.8%.

Cardiovascular measurements

Cardiovascular variables were measured using an automated oscillometric BP monitor (Glamor, TMB-1112, China) on the participant's non-dominant arm while seated comfortably, with the cuff positioned at heart level. Participants abstained from food and drink during data collection to control for confounding factors.

To enhance measurement reliability, three readings were taken at each time point at one-minute intervals, and the mean of the three values was used in the analysis. This protocol is consistent with recommended practices for BP assessment in exercise research (Smith & Fernhall, 2011). Mean BP (MBP) was calculated using the standard formula:

$$[(\text{SBP} - \text{diastolic BP}) / 3] + \text{diastolic BP},$$

and rate pressure product (RPP) was computed as:

$$(\text{SBP} \times \text{HR}) / 100,$$

both of which are established markers of cardiovascular load and myocardial oxygen demand (Taati, Arazi, & Kheirkhah, 2021).

Statistical analysis

All statistical analyses were conducted using SPSS software (version 22.0, IBM Corp., Armonk, NY, USA), with the significance level set at p<.05. Data normality was assessed via Shapiro-Wilk tests and Q-Q plots. Due to deviations from normality in some variables, data were transformed using the aligned rank transform (ART) procedure via the ARTool package (v2.2.2) in R (Wobbrock, Findlater, Gergle, & Higgins, 2011), which permits valid factorial analyses of non-parametric data. Normal and transformed data were subjected to repeated-measures ANOVA to assess main effects and condition × time interactions across the three protocols (CLS, IRS, and TRD) and different time points. When significant effects were observed, Tukey's *post-hoc* tests were applied for pairwise comparisons. Effect sizes were also calculated using Cohen's *d*, with thresholds interpreted as small (0.2), moderate (0.6), large (1.2), and very large (2.0), consistent with prior literature in resistance training (Taati, et al., 2021).

Table 1. Participant characteristics (n=10)

Variable	Mean ± SD	Range
Age (years)	31 ± 7.3	18-40
Height (cm)	173 ± 4.3	168-180
Body mass (kg)	79 ± 5.9	69-88
Body mass index (kg·m^{-2})	26.5 ± 1.4	24.4-28.7
RE experience (years)	5.1 ± 2.3	2-10
RE frequency (sessions/week)	3.6 ± 0.7	3-5
Resting SBP (mmHg)	122 ± 5.4	112-128
Resting DBP (mmHg)	75.3 ± 5	68-81
Resting MBP (mmHg)	90.7 ± 4	84.7-95.7
Resting heart rate (bpm)	78.7 ± 4.9	70-86
Resting RPP (mmHg·bpm/100)	95.8 ± 9.3	79.5-109
Knee extension 1RM (kg)	88 ± 8	78-101

Note. RT = resistance exercise; BP = blood pressure; SBP = systolic BP; DBP = diastolic BP; MBP = mean BP; RPP = rate-pressure product; 1RM = one-repetition maximum.

Results

Descriptive statistics for the participants' anthropometric profiles, baseline cardiovascular measures, and knee extension 1RM loads are shown in Table 1. All participants completed the study protocol in full, with no dropouts, injuries, or reported adverse effects during or after the sessions.

Cardiovascular responses to exercise

No significant time × condition interactions were observed for SBP, diastolic BP (DBP), MBP, HR, and RPP (*p*>.05). However, *post-hoc* analyses

Table 2. Hemodynamic responses to resistance exercise with and without inter-set static stretching

Variable	Condition	Baseline	Post-exercise	10 min post	30 min post	Time × Condition
SBP (mmHg)	CLS	123.8 ± 6.6	141.8 ± 13.5^{a}	126 ± 7.1	124.4 ± 4^{b}	F = 0.116 *p* = 0.994
	IRS	123.3 ± 5.9	138.7 ± 8.6^{aaa}	124.8 ± 7.4^{bb}	125 ± 4.1^{bbb}	
	TRD	123.2 ± 5.4	139.1 ± 10.4^{aaa}	124.3 ± 6.8^{bb}	123.6 ± 3.6^{bbb}	
DBP (mmHg)	CLS	76.3 ± 6.5	77 ± 10.2	71.7 ± 10.3	73.9 ± 4.7	F = 0.071 *p* = 0.998
	IRS	74.1 ± 9.2	72.6 ± 3.5	69.4 ± 9	73.3 ± 8.1	
	TRD	74.3 ± 8.2	74.3 ± 7.8	70.7 ± 9.9	72.6 ± 7	
MBP (mmHg)	CLS	92.1 ± 5.3	98.6 ± 9.4	89.8 ± 8.3	90.7 ± 3.7	F = 0.124 *p* = 0.993
	IRS	90.5 ± 7.3	94.6 ± 3.7	87.9 ± 7.5	90.5 ± 6	
	TRD	90.6 ± 5.5	95.9 ± 5	88.6 ± 7.2	89.6 ± 4.1	
Heart rate (bpm)	CLS	78.9 ± 3.9	107.1 ± 11^{aaa}	95.7 ± 9.7^{aaa}	84.4 ± 5$^{a\ bbb\ cc}$	F = 0.12 *p* = 0.994
	IRS	78 ± 2.9	104.8 ± 13.4^{aaa}	94.8 ± 8.7^{aaa}	83.7 ± 3.7$^{a\ bbb\ ccc}$	
	TRD	77.7 ± 3.4	102.7 ± 10.3^{aaa}	94.1 ± 5.4$^{aaa\ b}$	82.9 ± 3.2$^{aa\ bbb\ ccc}$	
RPP (mmHg.bpm/100)	CLS	97.9 ± 9.7	152.7 ± 26.9^{aaa}	121.1 ± 18.3$^{aa\ b}$	105.1 ± 8.9^{bbb}	F = 0.13 *p* = 0.992
	IRS	96.3 ± 7.7	145.6 ± 22.4^{aaa}	118.7 ± 16.5$^{aaa\ b}$	104.7 ± 7.5$^{bbb\ c}$	
	TRD	95.8 ± 7.5	142.5 ± 14.3^{aaa}	117 ± 10.3$^{aaa\ bb}$	102.5 ± 5.5$^{a\ bbb\ ccc}$	

Note. Values are presented as mean ± SD. BP = blood pressure; SBP = systolic BP, DBP = diastolic BP, MBP = mean BP, CLS = cluster sets; IRS = inter-repetition sets; TRD = traditional sets; RPP = rate-pressure product. Tukey's multiple-comparisons test showed significant differences from baseline (^{a}p<0.05, ^{aa}p<0.01, and ^{aaa}p<0.001), immediately post-exercise (^{b}p<0.05, ^{bb}p<0.01, and ^{bbb}p<0.001), and 10 min post-exercise (^{c}p<0.05, ^{cc}p<0.01, and ^{ccc}p<0.001), with no significant difference between the conditions.

using Tukey's test revealed significant increases in SBP (CLS: $p=.015$, $d=-1.01$ [*moderate*]; IRS: $p<.001$, $d=-1.6$ [*large*]; TRD: $p<.001$, $d=-1.7$ [*large*]), HR (CLS: $p<.001$, $d=-3$ [*very large*]; IRS: $p<.001$, $d=-3.1$ [*very large*]; TRD: $p<.001$, $d=-3.9$ [*very large*]), and RPP (CLS: $p<.001$, $d=-2.1$ [*very large*]; IRS: $p<.001$, $d=-2.6$ [*very large*]; TRD: $p<.001$, $d=-3.7$ [*very large*]) immediately post-exercise compared to baseline. SBP and RPP returned to baseline levels within 30 minutes post-exercise in both conditions. In contrast, HR values remained elevated at the 30-minute recovery time point (CLS: $p=.042$, $d=-0.9$ [*moderate*]; IRS: $p=.023$, $d=-1$ [*moderate*]; TRD: $p=.004$, $d=-1.2$ [*large*]). Overall, the patterns of change in BP, HR, and RPP were similar between the sessions; however, SBP appeared to recover more rapidly following the IRS and TRD protocols compared to the CLS (Table 2).

To evaluate the cumulative cardiovascular response over time, AUC values were compared between the two protocols. The analysis revealed no statistically significant differences in AUC for SBP ($F=0.075$, $p=.93$), DBP ($F=0.162$, $p=.851$), MBP ($F=0.192$, $p=.826$), HR ($F=0.13$, $p=.881$), or RPP ($F=0.181$, $p=.835$), as illustrated in Figure 2.

Muscle performance

As shown in Figure 3, both the CLS and IRS protocols resulted in significantly higher MNR compared to the TRD condition (CLS: 8.7±1.2 repetitions, $p=.032$, $d=-0.9$ [*moderate*]; IRS: 8.6±1 repetitions, $p<.001$, $d=-1.9$ [*large*]; TRD: 7.3±0.9

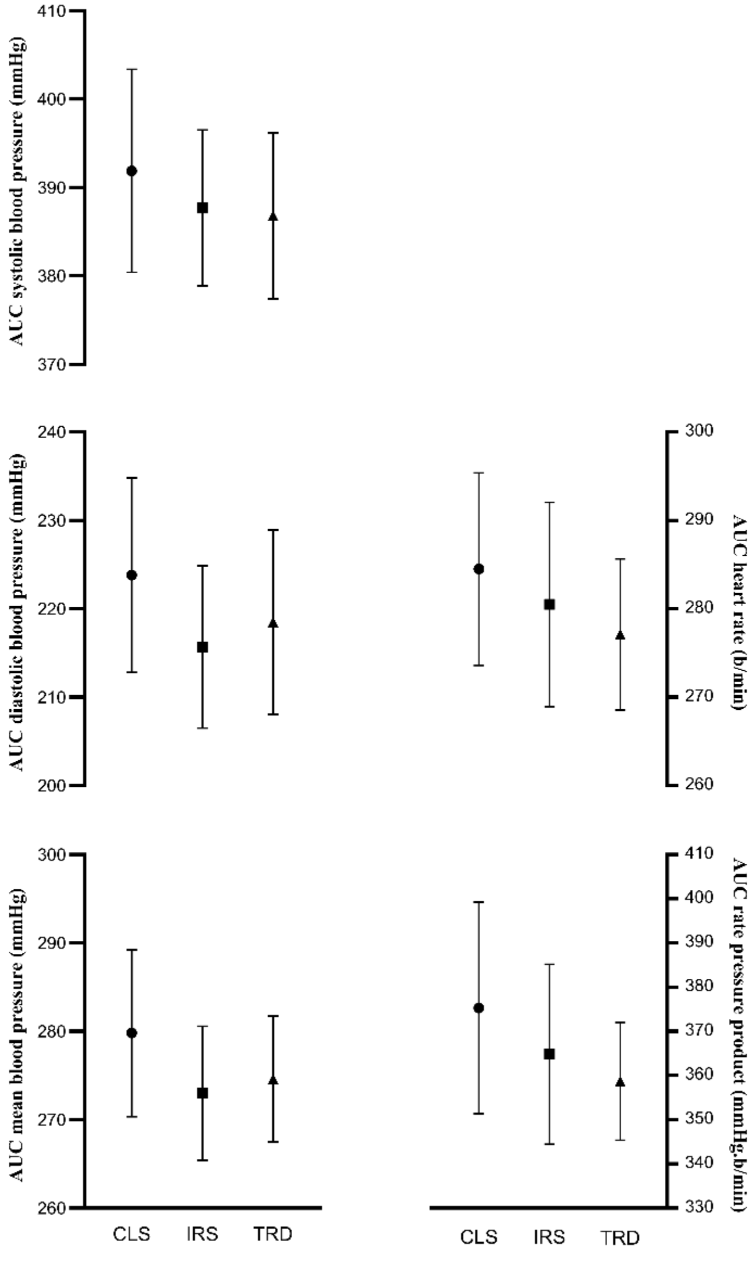

Figure 2. Comparison of area under the curve (AUC) for cardiovascular variables across resistance exercise protocols: cluster sets (CLS), inter-repetition sets (IRS), and traditional sets (TRD). Data are mean ± standard deviation (n=10).

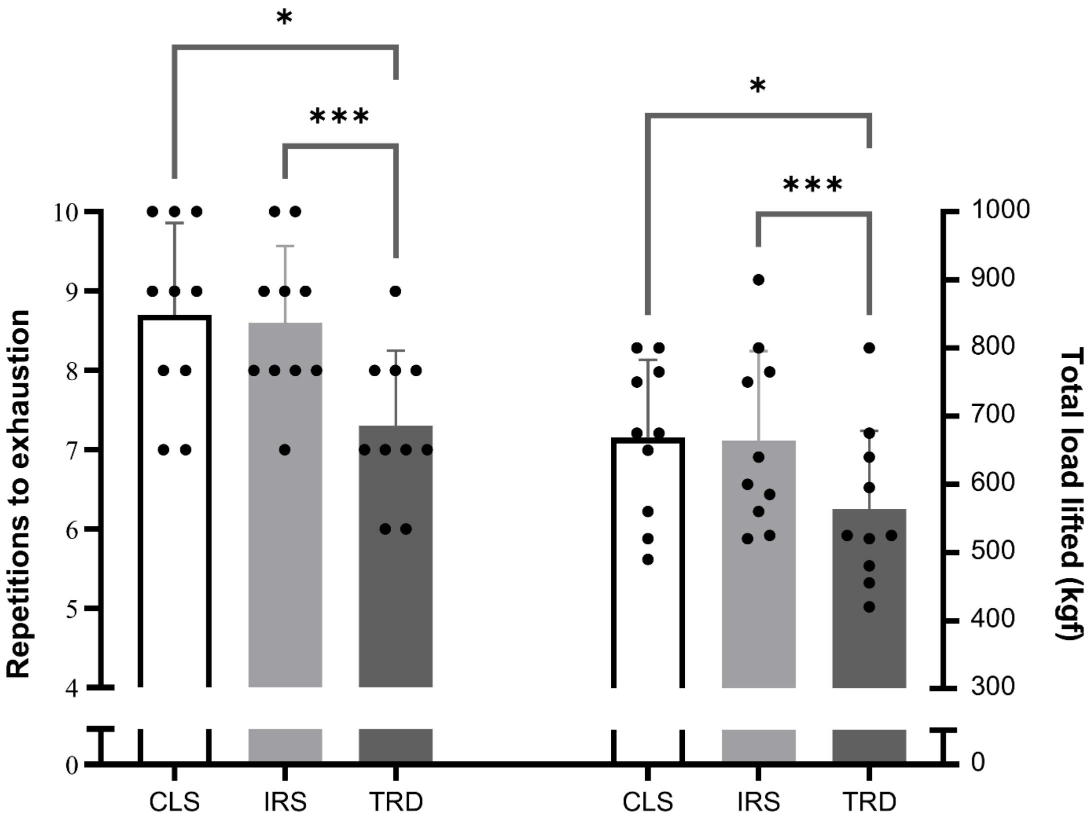

Figure 3. Comparison of muscular performance outcomes across resistance exercise protocols: cluster sets (CLS), inter-repetition sets (IRS), and traditional sets (TRD). Data are mean ± standard deviation (n=10). $^{*}p<.05$, $^{***}p<.001$

repetitions). Similarly, TLL was greater in both CLS (668.5±114 Kgf, *p*=.041, *d*=-0.9 [*moderate*]) and IRS (664.5±131 Kgf, *p*<.001, *d*=-1.8 [*large*]) sessions compared to the TRD (563.5 ± 115.2 Kgf). No significant differences were observed between the CLS and IRS protocols for either MNR or TLL (*p*>.05).

Blood lactate and perceived fatigue

As depicted in Figure 4, all RE protocols resulted in significant increases in blood lactate concentrations immediately post-exercise compared to baseline (*p*<.001). However, the magnitude of increase varied across the protocols. The TRD condition elicited significantly greater post-exercise lactate levels compared to both the CLS (*p*=0.012, *d*=1) and IRS (*p*<.001, *d*=3.5) conditions. Furthermore, post-exercise lactate was significantly higher in CLS compared to IRS (*p*< .001, *d*=2.6). Consistent with these physiological responses, participants reported higher ROF following the TRD protocol (8.2±1, *p*=.001) and CLS protocol (7.5± 0.8, *p*=.016) compared to the IRS condition (5.9±1), although the difference between TRD and CLS was not statistically significant (*p*>.05). No significant differences in blood lactate or ROF were observed between the protocols at baseline or at the 30-minute post-exercise recovery time point (*p*>.05).

Hormonal changes

All RE protocols elicited a significant acute increase in GH levels immediately post-exercise (CLS: *d*=3.5, IRS: *d*=2.8, TRD: *d*=4, all *p*<.001). No statistically significant differences were observed between the protocols at this time point (*p*>.05). GH levels declined significantly 30 minutes post-exercise compared to immediate post-exercise levels across all the protocols (CLS: *d*=2.7, IRS: *d*=2.3, TRD: *d*=2.8, all *p*<.001). However, both the CLS (*p*= 0.032, *d*=0.8) and TRD (*p*= 0.032, *d*=1.1) conditions maintained GH levels significantly above baseline (Figure 5).

Regarding IGF-1, all the three protocols induced a non-significant increase immediately post-exercise (*p*>.05). However, IGF-1 concentrations at 30 minutes post-exercise were significantly reduced compared to immediate post-exercise levels across all the conditions (*d*=1, *p*<.05), returning toward baseline values.

Discussion and conclusion

This study investigated the acute effects of different intra-set rest structures during RE on muscular performance, blood lactate and perceived fatigue, GH and IGF-1, as well as hemodynamic responses in resistance-trained men. Specifically, we compared the CLS and IRS protocols—both

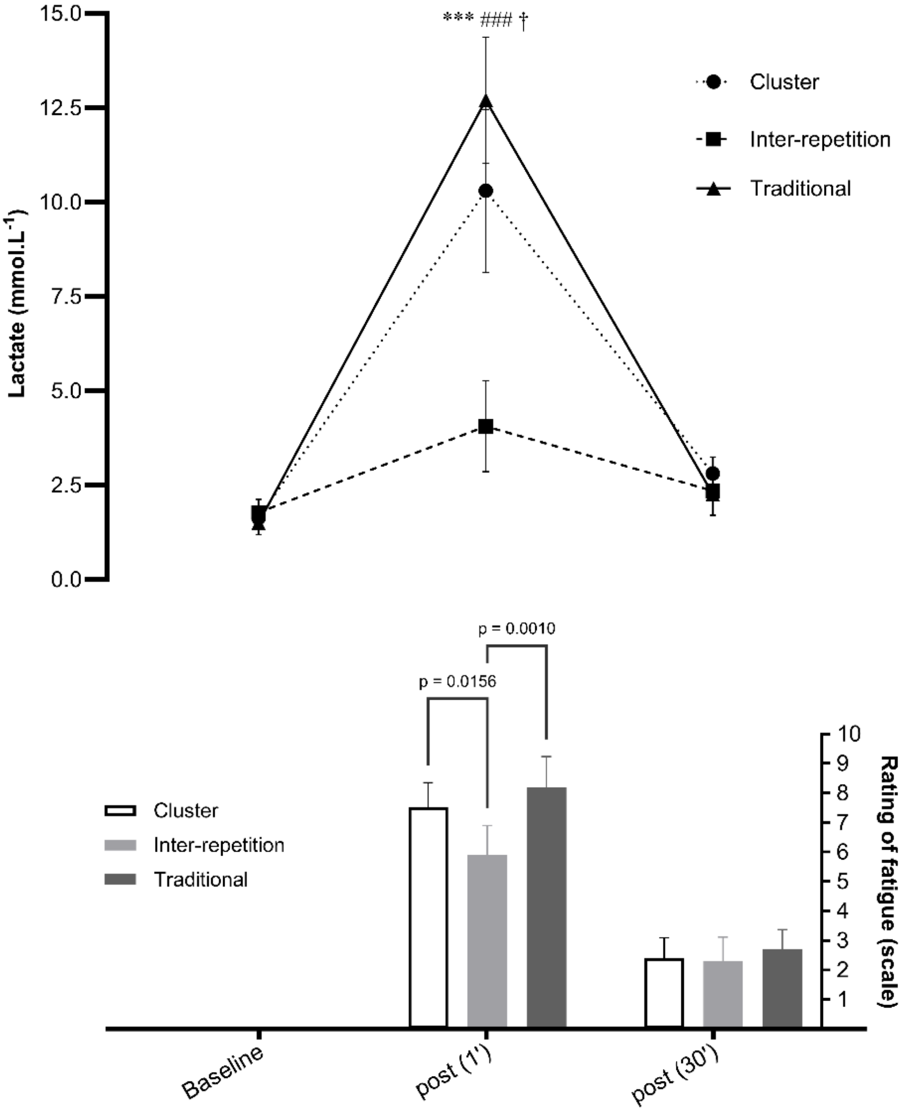

Figure 4. Changes in blood lactate (lines) and rating of fatigue scale (columns) at baseline and post-exercise across protocols. Data are mean ± standard deviation (n=10). ****p<0.001 for cluster vs. inter-repetition sets,* $^{\#\#\#}$ *p<.001 for traditional vs. inter-repetition sets,* †*p<.05 for traditional vs. cluster sets.*

matched for total rest duration—with the TRD set structure. The main findings demonstrated that both intra-set rest configurations led to significantly greater muscular performance, as evidenced by higher MNR and TLL, compared to the TRD structure. These results align with prior research indicating that redistributing rest within a set can enhance performance by attenuating acute fatigue and enhance repetition performance (Jukic, et al., 2020; Oliver, et al., 2015; Tufano, et al., 2017).

Interestingly, both the CLS and IRS conditions employed equivalent total rest (18 seconds), yet allowing for intermittent recovery within each set. This likely contributed to reduced peripheral fatigue, maintained motor unit recruitment, and improved force output across repetitions (Tufano, et al., 2017). The absence of a significant performance difference between the CLS and IRS conditions suggests that the distribution pattern of intra-set rest (i.e., between reps vs. mid-set) may be less critical than the presence of ISR itself, when total rest is held constant. This reinforces the practical utility of ISR structures across varying RE settings, offering coaches flexibility based on exercise modality, equipment, or logistical preferences.

Regardless of the load used or the number of repetitions performed, completing multiple repetitions consecutively without rest leads to progressive fatigue accumulation. This is typically manifested by reductions in movement velocity, increases in perceived exertion, and elevated levels of metabolic byproducts such as blood lactate (Jukic, et al., 2020; Jukic & Tufano, 2022). In the present study, all RE protocols led to significant increases in blood lactate concentration immediately post-exercise, indicating a substantial contribution of anaerobic glycolysis. However, the magnitude of this increase was significantly lower in the IRS and

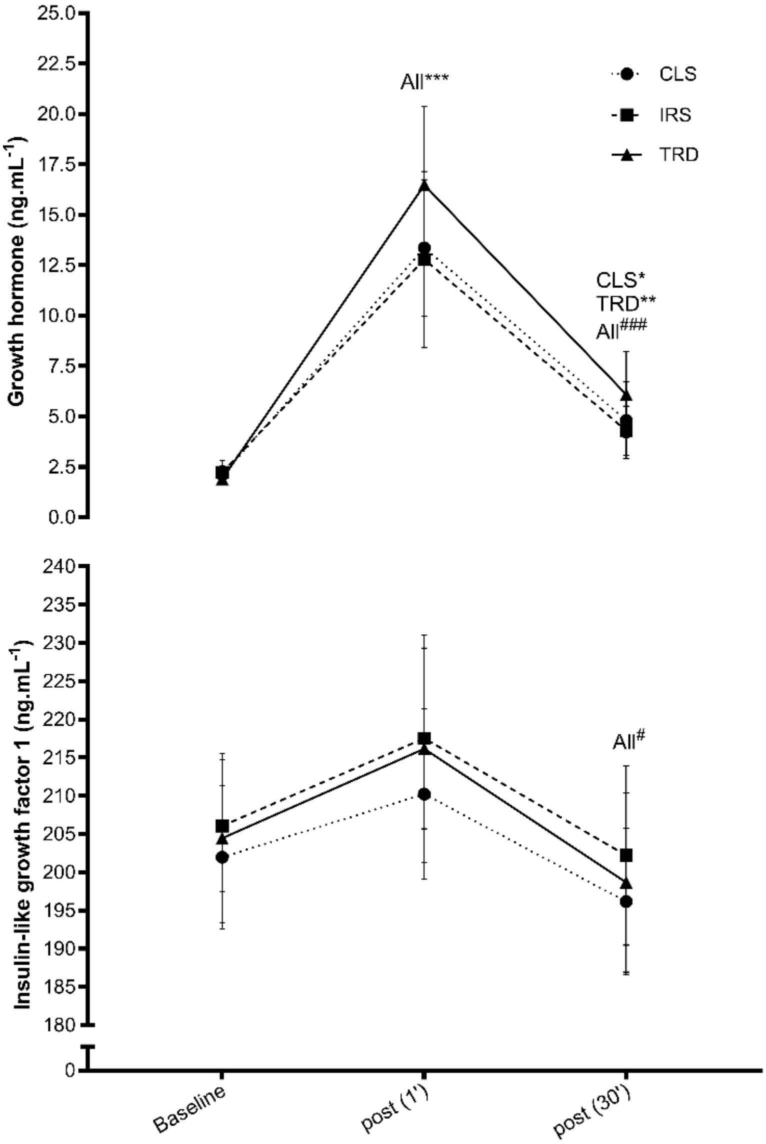

Figure 5. Hormonal responses to resistance exercise protocols: cluster sets (CLS), inter-repetition sets (IRS), and traditional sets (TRD). Data are mean ± standard deviation (n=10). Significant vs. baseline: $^{***}p<.001$, $^{**}p<.01$, and $^{*}p<.05$. Significant vs. post-exercise (1 min): $^{\#\#\#}p<.001$, and $^{\#}p<.05$.

CLS conditions compared to the TRD structure, with the IRS protocol producing the lowest blood lactate response. These findings suggest these two conditions more effectively attenuate metabolic stress, likely by allowing brief recovery periods that partially restore phosphocreatine and reduce reliance on glycolytic energy systems (Schoenfeld, 2010; Tufano, et al., 2017).

Notably, our results are consistent with those of Páez-Maldonado et al. (2024), who reported that cluster set configurations led to significantly lower post-exercise lactate concentrations compared to the traditional set protocols among young trained men. This consistency strengthens the growing evidence base suggesting that redistributing rest within sets mitigates metabolic fatigue without compromising mechanical workload. The current study extends these observations by demonstrating that inter-repetition rest may be even more effective than mid-set clustering in reducing lactate accumulation.

These differences in lactate response likely reflect the ability of brief intra-set rests to limit continuous time-under-tension (Oliver, et al., 2015), allowing intermittent clearance of hydrogen ions and resynthesis of high-energy phosphates, thereby improving buffering capacity and preserving contractile function (Tufano, et al., 2017). From a practical standpoint, minimizing excessive lactate buildup is particularly valuable when repeated bouts of high-intensity exercise are required within a session or during multi-session training days.

Additionally, the metabolic benefits of intra-rest strategies were mirrored by perceptual responses, as participants reported significantly lower ROF following IRS and CLS compared to TRD, with the lowest fatigue values observed after IRS. These findings support previous studies showing that inter-repetition or cluster set formats reduce perceived exertion and enhance repetition quality (Iglesias-Soler, et al., 2012; Merrigan, et al., 2020; Río-Rodríguez, et al., 2016; Tufano, et al., 2017). This aligns with the physiological understanding that intra-set rest mitigates fatigue by restoring phosphocreatine levels and reducing the rate of anaerobic glycolysis, thus supporting force production during muscular efforts (Schoenfeld, 2010). Therefore, the superior muscular performance observed during the IRS and CLS protocols compared to TRD in the current study may be partially explained by lower blood lactate accumulation and consequently reduced perceived fatigue.

In the current study, all RE protocols elicited significant acute increases in GH concentration immediately post-exercise, indicating that short-term endocrine activation is a consistent response to RE regardless of rest distribution. However, no significant differences were observed between the TRD, CLS, and IRS structures in terms of peak GH response, suggesting that total exercise volume and intensity may be more critical determinants of GH release than the specific structure of intra-set rest. These results align with the findings of Girman et al. (2014) and Tufano et al. (2019), both of whom reported similar GH elevations following different rest distributions or set structures when load, volume, and rest were matched.

Although immediate post-exercise GH levels did not differ significantly across conditions in our study, differences became evident during the recovery period. Specifically, GH levels remained significantly elevated above baseline at 30 minutes post-exercise in both the CLS and TRD conditions but not in IRS. This sustained elevation in GH may be indicative of prolonged metabolic and neuromuscular stress induced by CLS and TRD, while the earlier return toward baseline in the IRS condition may reflect a faster recovery profile associated with reduced metabolic disruption. These findings are partly consistent with the hormonal kinetics observed by Tufano et al. (2019), who demonstrated that GH levels peaked post-exercise and returned to baseline by 60 minutes across all protocols, despite different rest distributions. Additionally, Oliver et al. (2015) showed that while TRD induced greater GH responses during exercise, both the traditional and cluster protocols led to comparable hormonal profiles over time (Merrigan, et al., 2020), suggesting that metabolic stress and mechanical loading both influenced GH secretion patterns.

As for IGF-1, while all protocols showed a trend toward increased levels immediately post-exercise, these changes did not reach statistical significance. Nevertheless, levels declined significantly 30 minutes post-exercise, indicating a transient post-exercise response. The absence of a robust IGF-1 increase might be attributed to the timing of measurements or the transient nature of IGF-1 elevation in acute settings, which often depends on post-exercise nutrient status, training status, and individual variability (Eliakim & Nemet, 2020; Kraemer & Ratamess, 2005). Although IGF-1 is mechanistically linked to GH, the temporal dissociation between the two hormones is not uncommon, as IGF-1 production is more strongly influenced by chronic training adaptations and hepatic regulation than by acute RE bouts alone (Nindl & Pierce, 2010).

In the present study, no statistically significant differences were observed in acute cardiovascular responses (i.e., BP, HR, and RPP) or in their AUC values between the CLS, IRS, and TRD protocols. These findings suggest that the total cardiovascular load throughout the post-exercise recovery period was comparable across all the set structures, despite significant differences in muscular performance.

These findings are particularly noteworthy given that both the CLS and IRS protocols resulted in greater total work performed (i.e., higher total load lifted), yet did not elicit greater cardiovascular stress compared to the TRD set structure. The comparable hemodynamic responses may be attributed to the matched total intra-set rest time (18 seconds) across the conditions, which likely allowed for partial recovery of cardiovascular and autonomic parameters between repetitions or clusters.

The present findings are also consistent with those of Mayo et al. (Mayo, Iglesias-Soler, Fariñas-Rodríguez, Fernández-del-Olmo, & Kingsley, 2016; Mayo, Iglesias-Soler, Kingsley, & Dopico, 2017), who examined the effects of brief inter-repetition rest versus continuous traditional sets on BP responses during acute RE. In their study, participants performed 40 leg press repetitions in two formats: an intermittent session (18.5 seconds rest between repetitions, totaling 720 seconds) and a continuous session (five sets of eight repetitions with 180 seconds of rest between sets). Both conditions led to significant increases in HR and BP post-exercise compared to baseline, and the peak SBP was slightly higher in the intermittent protocol. Despite structural differences, overall cardiovascular responses remained within tolerable limits and returned toward baseline during recovery—supporting the idea that rest structure has limited long-term impact when volume and intensity are equated.

Mechanistically, continuous repetitions—as in the TRD protocol—may impose greater intramuscular pressure and mechanical compression of blood vessels, potentially elevating afterload and restricting venous return during the set (Lamotte, Fleury, Pirard, Jamon, & Borne, 2010; MacDonald, 2002). In contrast, intermittent rest intervals such as those in CLS and IRS may partially reduce this vascular compression, permitting brief reperfusion phases that help limit acute cardiovascular strain (Rezk, Marrache, Tinucci, Mion, & Forjaz, 2006).

Despite these theoretical advantages, no significant inter-condition differences emerged in AUC values for BP, HR, or RPP, further reinforcing the idea that when total rest and workload are controlled, the distribution of intra-set rest exerts minimal influence on overall cardiovascular burden. From a practical perspective, this finding supports the use of intra-set rest strategies to enhance muscular performance without imposing excessive cardiovascular stress, which may be especially beneficial in populations with cardiovascular considerations.

Despite the valuable insights gained from this study, several limitations should be acknowledged. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, although participants were instructed to maintain their habitual diet, avoid strenuous activity during the 24 hours preceding testing, and obtain sufficient sleep before each visit, these factors were not objectively monitored and may have introduced additional variability. Finally, the study included only resistance-trained men, which restricts the applicability of the findings to other populations such as women, untrained individuals, or clinical groups.

This study demonstrates that incorporating intra-set rest—whether through the CLS or IRS structures—significantly enhances acute muscular performance and attenuates metabolic and perceptual fatigue compared to the TRD configuration in resistance-trained men. Both the CLS and IRS protocols led to greater total lifting volume and repetitions, with reduced blood lactate and perceived fatigue, especially under the IRS condition. Additionally, all protocols induced a significant increase in circulating GH levels post-exercise, with no difference between them, indicating that total training volume may be a primary driver of GH response regardless of set configuration. Conversely, IGF-1 levels exhibited only a modest, non-significant elevation post-exercise, suggesting that acute RE may not be a sufficient stimulus for pronounced IGF-1 changes, likely due to its delayed hepatic regulation and dependence on longer-term training adaptations. These findings highlight the physiological and performance advantages of intra-set rest configurations and provide practical guidance for strength and conditioning professionals seeking to optimize training stimulus while managing fatigue. Future research is warranted to investigate long-term adaptations, broader populations, and additional physiological markers such as muscle activation and recovery kinetics.

From a practical standpoint, CLS and especially IRS can be strategically integrated into training programs when the goal is to increase training volume and maintain movement quality while minimizing excessive fatigue or cardiovascular strain. These configurations may be particularly useful during high-volume phases, technical-strength sessions, or in athletes who require repeated-force production with controlled metabolic load.

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Ethical considerations

This study was approved by the research ethics committee of the East China University of Science and Technology and followed the principles of the Declaration of Helsinki.

Data availability statement

Data are available on reasonable request to the corresponding author.