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Acute effect of citrulline malate supplementation on upper-body resistance exercise performance in recreationally resistance-trained men

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Running Head: Effect of citrulline malate supplementation

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ABSTRACT

To investigate the effect of citrulline malate (CM) supplementation on upper-body resistance exercise performance, twelve recreationally resistance-trained men (21.4±1.6 y; 163.0±46.2 cm; 85.0±12.4 kg) underwent two testing sessions administered in a randomized, double-blind fashion. During each visit, participants were provided either 8 g of CM or a placebo (PL) 40 min prior to beginning a standardized warm-up and initiating a barbell bench press resistance exercise protocol consisting of 5 sets of 15 repetitions at 75% 1RM with 2-minute rest intervals. Participants were instructed to complete as many repetitions as possible until either reaching 15 repetitions or muscular failure. Total number of repetitions performed and power output were recorded for each set. Subjective measures of energy, focus, fatigue, and perceived exertion, along with muscle thickness of the triceps brachii, were assessed before and after exercise. Significant ($p<0.05$) main effects for time were observed for all variables except for subjective feelings of energy ($p=0.085$). A group × time interaction ($F=2.86$, $p=0.034$, $n^2=0.21$) was observed for repetitions performed, where participants performed more ($p=0.015$) repetitions on set 3 during PL (5.7±1.2 repetitions) compared to CM (4.6±1.2 repetitions). However, during set 4, participants tended ($p=0.089$) to perform more repetitions during CM (4.8±1.8 repetitions) compared to PL (4.3±1.3 repetitions). No other differences were observed between trials. Supplementation with 8 grams of CM 40 min prior to the barbell bench press resistance exercise protocol did not increase exercise performance, augment the muscle swelling response to training, or alter subjective measures of focus, energy, and fatigue in recreationally resistance-trained men.

Keywords: L-citrulline; nitric oxide; sports supplementation; ergogenic aid; bench press

INTRODUCTION

Pre-workout nutritional supplementation has become increasingly popular among recreational and competitive athletic populations as a means of boosting exercise performance (8). Recently, citrulline malate (CM) has garnered much attention for its potential to increase nitric oxide (NO) production, which may enhance resistance exercise performance (10, 19, 23, 24). NO is known to increase vasodilation and blood flow, which may increase nutrient delivery and waste-product clearance (e.g., plasma lactate, ammonium) (1, 6). Thus, acute improvements to muscular function via increased blood flow derived from NO synthesis may improve resistance to fatigue during exercise (2).

The potential beneficial effects of CM may be attributed to the synergistic combination of both L-citrulline and malate at the cellular metabolic level. L-citrulline is a nonessential amino acid that functions as a precursor to L-arginine, which synthesizes NO when catalyzed by the enzyme nitric oxide synthase (NOS) (18). In contrast to L-arginine, orally supplemented L-citrulline bypasses hepatic metabolism and is transported to the kidneys where it can be directly converted to L-arginine (2), making it a more efficient means of elevating plasma arginine concentrations. In support, oral L-citrulline supplementation has been shown to raise plasma arginine concentrations and augment NO-dependent signaling in a dose-dependent manner in healthy men and women (17, 21). Supplementation with L-citrulline has been hypothesized to elicit an increase in NO synthesis from NOS via increased L-arginine availability (21). Furthermore, malate is an intermediate of the tricarboxylic acid cycle, and supplementation may augment energy production and increase the rate of adenosine triphosphate (ATP) production (1, 2).

Malate has been proposed to mitigate lactic acid production by allowing continued pyruvate production for energy utilization (23).

Therefore, an increased efficiency of ATP production in combination with an elevation in blood flow to the skeletal muscle may tentatively improve exercise performance.

Although still in its infancy, recent investigations have demonstrated a positive ergogenic effect following acute CM supplementation on submaximal resistance exercise performance to exhaustion (10, 19, 23, 24). Following an acute 8 g dose of CM, resistance-trained men and women improved the number of repetitions performed to exhaustion during upper-body resistance exercise (19), lower-body resistance exercise (10, 24), and body weight exercises (men only) (23). The primary mechanism believed to improve performance is centered around improved blood flow to exercising muscles (i.e., the muscle swelling response). These observed improvements in muscular endurance would also be suggestive of improved maintenance of power during each repetition (i.e., reduced fatigue index). That is, each successful repetition is indicative of sufficient barbell velocity to overcome inertia, produce momentum, and reach a mechanically advantageous position (5). However, little is known regarding the effect of CM supplementation on the muscle swelling response or muscular power output during dynamic resistance exercise. Therefore, the aim of this study was to investigate the effect of CM supplementation on repetitions completed, power output, the muscle swelling response, and subjective measures of focus, energy, and fatigue during upper-body resistance exercise in recreationally resistance-trained men.

METHODS

Experimental Approach to the Problem

This study was designed as a randomized, double-blind, placebo-controlled, counterbalanced crossover research study. Participants reported to the Human Performance Laboratory on three separate occasions and after having refrained from resistance training for 48 hours prior to each visit. The first visit was used to obtain anthropometric data and to determine the participants' one repetition-maximum (1RM) for the barbell bench press exercise, while the second and third visits were experimental sessions. Each visit was separated by approximately one week. Upon arrival experimental sessions, participants completed baseline (BL) assessments of energy, focus, fatigue, and perceived exertion via subjective questionnaires, along with an assessment of muscle swelling via ultrasonography. Participants were then provided with either a CM supplement or a placebo and asked to remain seated for 40 minutes. At 40 min post-supplement ingestion (PRE), participants initiated a standardized warm-up followed by a barbell bench press resistance exercise protocol. During the resistance exercise protocol, the total number of repetitions performed, as well as the power (mean and peak) produced during each repetition, were recorded for each set. All BL assessments were repeated at PRE and immediately post-exercise (IP). The two experimental trials occurred at the same time of day between 0800 and 1000 hour.

Participants

Twelve recreationally resistance-trained men (21.4 ± 1.6 y; 163.0 ± 46.2 cm; 85.0 ± 12.4 kg; 3.5 ± 1.6 y of resistance training experience) volunteered to participate in this research study.

This sample size was justified by a priori power analysis based on previous work by Glenn et al. (10) to yield a moderate effect size of 0.25, an alpha of 0.05, and power of 0.80. Inclusion criteria required participants to have at least one year of resistance training experience. Additionally, all participants were free of any physical limitations, medications, and supplements that may affect performance, as determined by a health and activity questionnaire. Following an explanation of all procedures, risks, and benefits, each participant provided his written informed consent prior to participation in this study. The research protocol was approved by the Hofstra University Institutional Review Board prior to participant enrollment.

Procedures

Maximal strength testing

The 1RM strength test for the barbell bench press exercise was conducted using methods previously described (12). Briefly, each participant performed a standardized series of dynamic exercises followed by two warm-up sets using a resistance of approximately 40-60% of their estimated 1RM for 6-10 repetitions and 60-80% of estimated 1RM for 3-5 repetitions, respectively. Subsequently, the resistance load was increased conservatively over the course of 3-5 maximal trials (one-repetition sets) to determine the 1RM. Each maximal trial was separated by 3-5 minutes of rest. The 1RM was recorded as the maximum load that the participant could lift for one repetition while maintaining proper technique.

A successful lift required each participant to begin the lift holding the barbell with a conventional shoulder width grip and their elbows fully extended. Participants then lowered the barbell until lightly touching the chest (i.e., participants were not permitted to bounce the bar off their chest) before returning the bar back to the starting position. Throughout the entire lift, participants were required to maintain contact between their feet and the floor, as well as their hips, shoulders, and head with the bench (12). Proper technique was monitored and enforced via the presence of a certified strength and conditioning specialist (CSCS) at each testing session.

Supplementation

During each experimental trial and 40 min prior to beginning a standardized warm-up, participants ingested either 8 g of pure L-citrulline DL-malate powder (CM; Bulk Supplements, Henderson, NV, USA) mixed with 500 ml of water or PL. This dosage is consistent with previous investigations (10, 19, 23, 24). The PL consisted of non-caloric flavored water and was indistinguishable in appearance. An outside researcher mixed all supplements in a sealed shaker bottle combined with a fruit punch flavoring (Mio^{TM}, Northfield, IL, USA). Both CM and PL were served in disposable white plastic bottles with participants wearing a nose clip to further mask any taste or smell. After consuming the supplement, participants underwent a 40 min seated rest period. Oral administration of L-citrulline have shown to result in peak plasma concentrations ~42 min following ingestion (17, 21).

Resistance exercise protocol

After resting 40 minutes, participants completed a general and specific warm-up before the resistance exercise protocol. The general warm-up consisted of 5 minutes of cycling at low intensity on an upright stationary bike followed by a series of dynamic exercises: 10 body weight squats, 10 body weight walking lunges, 10 dynamic walking hamstring stretches, 10 dynamic walking quadriceps stretches, and 10 body weight pushups. For the specific warm-up, participants performed two sets on the bench press using 40% and 60% 1RM resistance for 8 and 4 repetitions, respectively. Two minutes of rest separated each warm-up set. Subsequently, participants completed the resistance exercise protocol, which consisted of 5 sets of up to 15 repetitions at 75% 1RM with 2-min rest between sets. Participants were instructed to complete as many repetitions as possible until either reaching 15 repetitions or muscular failure. Failure was defined as the inability to complete a full repetition without assistance. Researchers recorded the total number of repetitions completed during each set. The upper body resistance training protocol was designed to be typical of an athlete focusing on muscular hypertrophy, and 15 repetitions were deemed as the upper limit of repetitions given the relatively high load selection.

Power measures

Power output during the barbell bench press exercise was measured for each repetition with a linear position transducer (Tendo™ Power Output Unit, Trencin, Slovak Republic). The linear position transducer attaches to the end of the barbell, which measures linear displacement and time to calculate mean and peak barbell velocity. Power was calculated from the barbell load entered into the microcomputer and barbell velocity detected by the unit.

Prior to the investigation, intraclass correlation coefficient ($ICC_{3,1}$), standard error of the measurement ($SEM_{3,1}$), and minimal difference (MD) values for barbell velocity values measured by the linear position transducer during a single repetition of the bench press ($ICC_{3,1}$=0.91, $SEM_{3,1}$=0.04 m sec^{-1}, MD=0.09 m·sec^{-1}) were determined in 10 active, resistance-trained men (26.8±3.5 years; 92.6±6.5 kg; 180.5±6.6 cm) demonstrating high test-retest reliability. Peak and mean power outputs were recorded for each repetition. For subsequent analysis, the average peak (PP) and mean power (MP) output values were calculated for each set. Additionally, a fatigue index for peak and mean power was calculated from the slope of all peak and mean power output values recorded for each repetition within each set, respectively. For this measure, a positive value would indicate an increase in power as repetitions progressed within a set, whereas a negative value would indicate a decrease in power. A value of zero would indicate that power remained consistent across the entire set.

Subjective feelings and ratings of perceived exertion

Questionnaires were provided at BL, PRE, and IP. Participants were instructed to assess their subjective feelings of focus, energy, and fatigue using a 15-cm visual analog scale (VAS). The scale was anchored by the words "low" and "high" to represent extreme ratings where the greater measured value represents the greater feeling. Questions were structured as "My level of focus is." Participants were asked to rate their feelings at each time point by marking on the corresponding line. The validity and reliability of VAS has been previously established (15). Ratings of perceived exertion (RPE) via the OMNI weightlifting scale (20) were also recorded following each set of the barbell bench press exercise, as well as following the entire resistance exercise protocol.

Muscle swelling assessment

Muscle thickness was measured at BL, PRE, and IP to assess the muscle swelling response to resistance exercise (7, 22). Noninvasive skeletal muscle ultrasound images were collected from the triceps brachii of the dominant arm using B-mode ultrasound imaging with a 12-MHz linear probe (VSCAN, General Electric Medical Systems, Milwaukee, WI, USA). Prior to image collection, the anatomical location of interest was identified using standardized landmarks for the triceps brachii muscle (16). A single technician performed landmark measurements and obtained images in duplicate for all participants. Landmark identification of the triceps brachii required the participant to straddle the examination table and internally rotate their dominant shoulder, flex the elbow, and rest their dominant hand upon their thigh. The specific landmark for the triceps brachii was identified at 60% of the distance from the acromion process of the scapula to the lateral epicondyle of the elbow. Following application of a water-soluble gel, the probe was placed perpendicular to the tissue interface without depressing the skin. Muscle thickness was determined as the distance between the subcutaneous adipose tissue and intermuscular interface. Prior to the investigation, $ICC_{3,K}$, $SEM_{3,K}$, and MD values for muscle thickness of the triceps brachii were determined in 10 healthy college-aged males using methodology described above ($ICC_{3,K}$=0.93, $SEM_{3,K}$=0.13, MD=0.34 cm).

Dietary control

Participants were instructed to maintain their normal dietary intake leading up to experiment trials and to abstain from the use of any other dietary supplements. Participants were instructed how to accurately record everything they consumed during the 24 h prior to the first experimental trial. For the following experimental trial, *participants were asked to duplicate the content, quantity, and timing of their daily diet during the 24 h prior. Participants reported to the Human Performance Laboratory for each experimental session following an overnight fast and were instructed not to eat or drink (except water) in the morning.*

Statistical analysis

Prior to statistical procedures, all data were assessed for normal distribution, homogeneity of variance, and sphericity. If the assumption of sphericity was violated, a Greenhouse-Geisser correction was applied. A 2 (condition) × 5 (time) repeated measures analysis of variance (ANOVA) was utilized to determine the effect of the supplement during each set for repetitions performed, all power measures, and RPE. Additionally, a separate 2 (trial) × 3 (time point) repeated measures ANOVA was utilized to determine the effect of the supplement on subjective feelings and muscle thickness. In the event of a significant F ratio, separate one-way repeated measures ANOVA with Bonferroni adjustment were performed to assess the main effect for time during each condition, while separate dependent t-tests were used to assess conditional differences during each set. For effect size, partial eta squared statistics were calculated, and according to Green et al. (11), 0.01, 0.06, and 0.14 were interpreted as small, medium, and large effect sizes, respectively. Significance was accepted at an alpha level of $p \leq 0.05$, and all data are reported as mean ± standard deviation.

RESULTS

Performance measures

A condition × time interaction (F=2.86, p=0.03, n^2=0.21) was observed for the number of repetitions performed during the bench press. During CM, a greater (p<0.001) number of repetitions were performed on set 1 (13.5 ± 2.2 repetitions) compared to all other sets, while the repetitions performed on set 2 (8.1 ± 1.9 repetitions) were greater (p<0.001) than sets 3-5. No differences (p>0.99) were observed between sets 3-5. Similarly, during PL, the repetitions performed on set 1 (12.9 ± 2.7 repetitions) and set 2 (8.3 ± 2.0 repetitions) were greater (p<0.001) than those performed on all subsequent sets. However, repetition differences among sets 3-5 were variable. Between conditions, participants performed more (p=0.02) repetitions on set 3 of PL (5.7 ± 1.2 repetitions) compared to CM (4.6 ± 1.2 repetitions), but then tended (p=0.089) to perform more repetitions during set 4 of CM (4.8 ± 1.8 repetitions) compared to PL (4.3 ± 1.3 repetitions). There were no significant differences (p=0.88) in total repetitions performed between CM and PL conditions (35.3 ± 6.5 and 35.8 ± 6.5 repetitions, respectively). Repetitions performed during each set of the bench press under both conditions are illustrated in Figure 1.

[INSERT FIGURE 1 HERE]

Averaged measures of power for each condition are illustrated in Figure 2. Although significant main effects for time were observed for PP (F=12.16, p<0.001, n^2=0.60) and MP (F=28.52, p<0.001, n^2=0.78), no differences were observed between conditions. Additionally, a trend for a main time effect in MP (F=3.71, p=0.052, n^2=0.32) was noted, where compared to set 1, greater (p<0.001) declines in MP were observed on set 2 (mean difference: -9.89 Watts·repetition^{-1}) and set 3 (mean difference: -

15.24 Watts·repetition^{-1}) before remaining consistent. No differences were observed between conditions in fatigue index for peak ($F=1.827$, $p=0.15$) and mean power ($F=3.560$, $p=0.06$).

[INSERT FIGURE 2 HERE]

Muscle swelling, subjective feelings, and ratings of perceived exertion

A significant main effect for time was observed for muscle thickness ($F=82.48$, $p<0.001$, $n^2=0.88$), where muscle thickness at IP was greater ($p<0.001$) than BL (mean difference=0.55 cm) and PRE (mean difference=0.51 cm). Nine out of 12 participants exceeded the MD values at IP during PL trial, while 10 out of 12 participants exceeded the MD values at IP during CM trial. However, no differences were observed between conditions. Likewise, significant ($p<0.05$) main effects for time were observed for all subjective feelings and ratings of perceived exertion except for feelings of energy ($p=0.085$), but no differences between conditions were noted. Changes in muscle thickness and subjective measures are indicated in Figure 3 and Table 1, respectively.

[INSERT FIGURE 3]

[TABLE 1 HERE]

DISCUSSION

The aim of the present study was to investigate the effect of CM supplementation on repetitions completed, power output, the muscle swelling response, and subjective measures of focus, energy, and fatigue during upper-body resistance exercise in recreationally resistance-trained men. The results of this study indicate that 8 g of CM, administered 40 min prior to the barbell bench press resistance exercise protocol, did not increase exercise performance, alter subjective measures, or augment the muscle swelling response to training in recreationally resistance-trained men.

Previous research has investigated the effect of 8 g of CM administered 1 hour prior to a resistance exercise protocol on repetitions performed to exhaustion (10, 19, 23, 24). In resistance-trained adults, CM supplementation prior to exhaustive bench press protocols using 60-80% 1RM with 1-min rest intervals has shown to increase the number of repetitions performed during sets 3 and 4 by up to 17.5% (~1 repetition) (19) and to increase total repetitions performed over 6 sets (34.1 ± 5.7 vs. 32.9 ± 6.0 repetitions) (10). Likewise, following CM supplementation, Wax et al. (23) observed improvements in repetitions performed during an upper-body, body weight protocol consisting of chin-ups (32.2 ± 5.6 vs. 28.4 ± 7.1 repetitions), reverse chin-ups (32.1 ± 7.1 vs. 26.6 ± 5.6 repetitions), and push ups (97.7 ± 36.1 vs. 89.1 ± 37.4 repetitions) (23). Studies have also demonstrated improved repetitions to failure during lower-body resistance exercise following CM supplementation. In resistance-trained adults, CM supplementation has shown to increase total repetitions performed during 6 sets of a leg press protocol using 80% 1RM with 1-min rest intervals (66.7 ± 30.5 vs. 55.1 ± 20.6 repetitions) (10). Similarly, Wax et al. (24) observed increases in repetitions performed during 5 sets of the leg press, hack squat, and leg extension exercises to muscular failure using 60% 1RM with 3 min rest intervals in advanced weight lifters. Interestingly, Cutrufello et al. (4) found that a 6-g dose of L-citrulline did not improve the total number of repetitions to fatigue during 5 sets of bench press at 80% 1RM with 30-second rest intervals in recreationally-trained men and women (4). Our data appear to support the latter investigation.

Though it is unclear why CM supplementation did not improve performance in our study, it is possible that the timing of supplementation and the recreational training status of the participants may have played a part. However, following oral administration of L-citrulline of doses up to 10 g, peak plasma concentrations have shown to occur ~42 min following ingestion (17, 21).

One of the primary mechanisms by which CM may improve exercise performance is via enhanced vasodilation and blood flow to exercising muscles. NO-induced vasodilation may help supply more oxygen and nutrients to the muscle cells while improving the clearance of metabolic waste-products generated during exercise (1, 6). Additionally, superior blood flow and muscle swelling has been hypothesized to influence cellular functions such as anabolic signaling (13, 14) and protein synthesis (9). To the best of our knowledge, this is the first study to assess muscle thickness of a secondary muscle group (as an indirect measure of blood flow) and to assess participants' ability to maintain power during resistance exercise. However, the results indicated that 8 g of CM did not augment the muscle swelling response to training or alter peak and mean power outputs in recreationally resistance-trained men.

Supplementation with CM does not appear to act as a stimulant or alter resting heart rate during resistance exercise (10, 24). Nevertheless, Glenn et al. (2015) reported a significant decrease in RPE following CM supplementation during upper-body resistance exercise (i.e., bench press) compared to a placebo; however, overall RPE was not altered by CM supplementation during lower-body resistance exercise (i.e., leg press) (10). CM supplementation also failed to alter RPE scores during an intermittent sprint cycling protocol followed by a cycle time-to-exhaustion test in well-trained males (3).

In the current study, CM supplementation did not alter subjective measures of focus, energy, and fatigue. Additionally, CM supplementation did not modify the participants' RPE during or following the resistance exercise protocol.

In conclusion, supplementation with 8 g of CM 40 min prior to beginning a standardized warm-up and initiating a barbell bench press resistance exercise protocol did not increase exercise performance, alter subjective measures, or augment the muscle swelling response to training in recreationally resistance-trained men. Future research is warranted to further examine the acute effect of CM supplementation on resistance exercise performance, along with the impact on hypertrophy, strength, and performance outcomes following chronic supplementation.

PRACTICAL APPLICATIONS

Supplements containing CM are often marketed to improve resistance exercise performance via enhanced blood flow derived from NO synthesis. Although preliminary studies have reported increases in repetitions performed to exhaustion following administration of 8 g of CM, the results of the current study do not support this notion. Furthermore, CM supplementation did not augment subjective measures or the muscle swelling response to training in recreationally resistance-trained men. More studies are needed to determine the overall efficacy of CM supplementation as an ergogenic aid. Future research is necessary to further evaluate the acute and chronic effects of CM supplementation on resistance training outcomes, along with investigations into the potential mechanisms by which these improvements may manifest.

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CONFLICT OF INTEREST

All authors report no conflicts of interest.

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FIGURE LEGEND

Figure 1. Number of repetitions completed during barbell bench press resistance exercise protocol.

Figure 2. Changes in peak (A) and mean (B) bench press power across sets during each experimental condition.

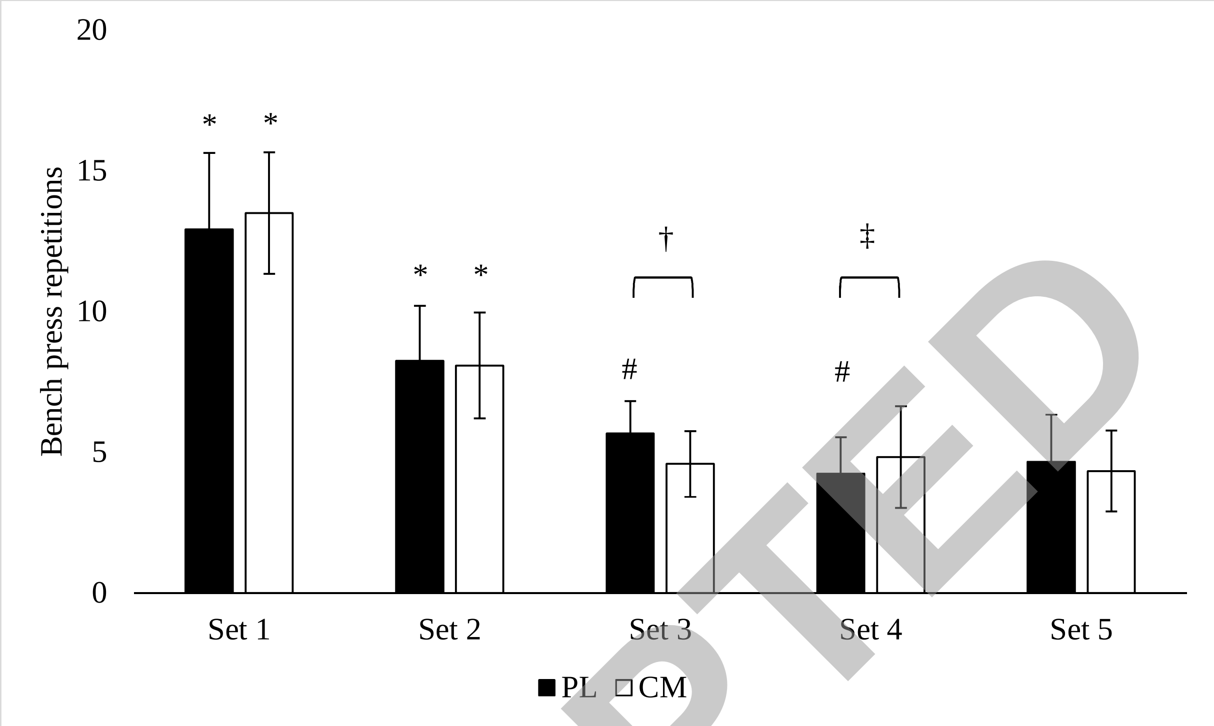
Figure 3. Changes in muscle thickness during each experimental condition.

Table 1. Subjective feelings of focus, energy, fatigue, muscle pump, and perceived exertion.

		BL	PRE	IP
Focus (cm)				
	PL	8.3 ± 4.0	9.8 ± 3.0	11.2 ± 2.6
	CM	9.5 ± 4.2	10.5 ± 4.2	11.4 ± 2.4
Energy (cm)				
	PL	8.5 ± 3.2	9.7 ± 2.9	7.6 ± 3.6
	CM	9.0 ± 4.1	10.3 ± 3.7	7.1 ± 3.8
Fatigue (cm)				
	PL	4.4 ± 3.2	3.4 ± 2.7	9.8 ± 2.6
	CM	2.9 ± 2.7	3.1 ± 2.5	8.3 ± 4.0
Muscle Pump (cm)				
	PL	3.0 ± 3.2	5.5 ± 3.9	12.5 ± 2.4
	CM	3.2 ± 3.0	3.8 ± 3.0	12.0 ± 2.2
Rating of perceived exertion (AU)				
	PL	-	-	8.3 ± 0.8
	CM	-	-	8.3 ± 0.8

Subjective feelings of focus, energy, fatigue, and muscle pump were assessed using a 15-cm visual analog scale and expressed as centimeters (cm). Rating of perceived exertion was assessed using the OMNI weightlifting scale and expressed as arbitrary units (AU).

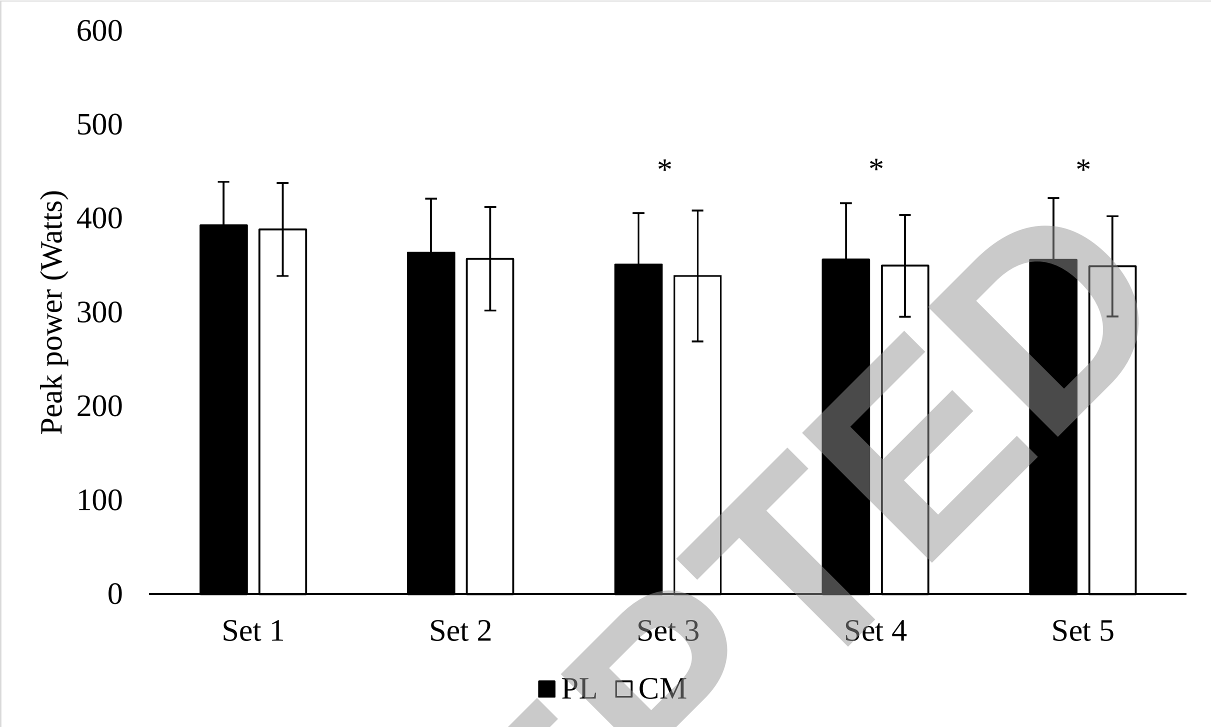
Fig1



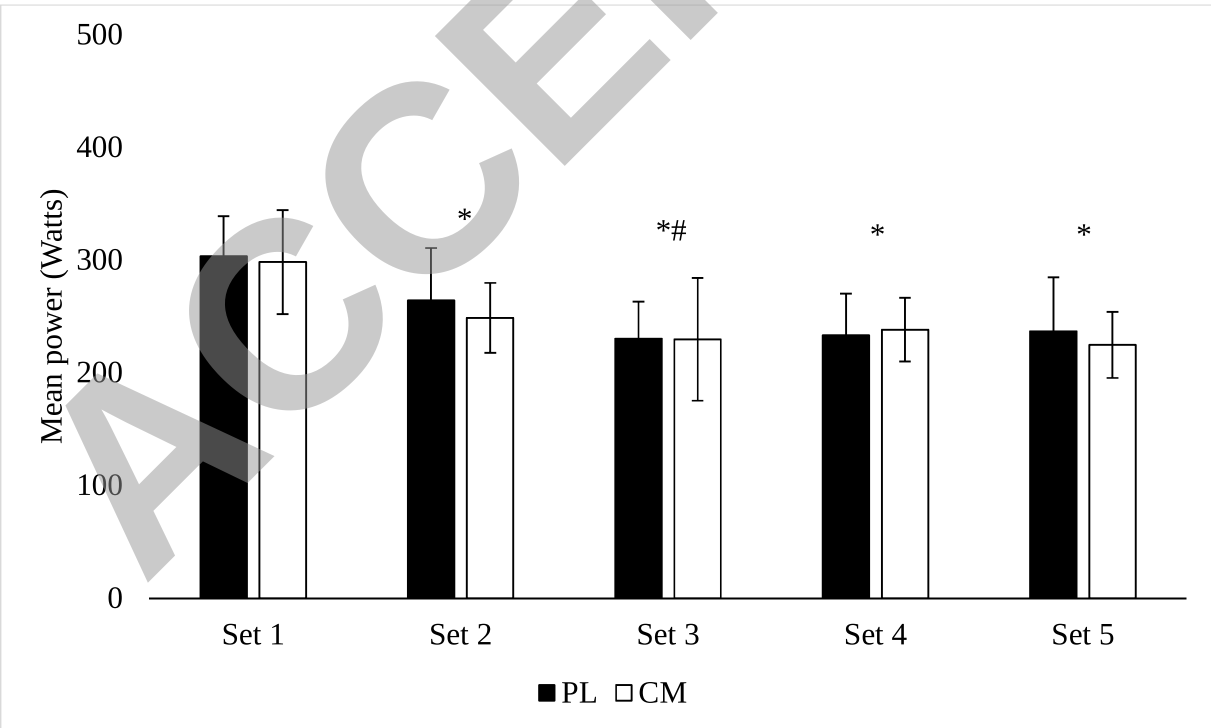
* Significantly (p<0.05) different from all other sets within condition.
# Significantly (p<0.05) different from set 5.
† Significantly (p<0.05) different between conditions.
‡ Trend (p<0.10) for difference between conditions.

Fig2

A.

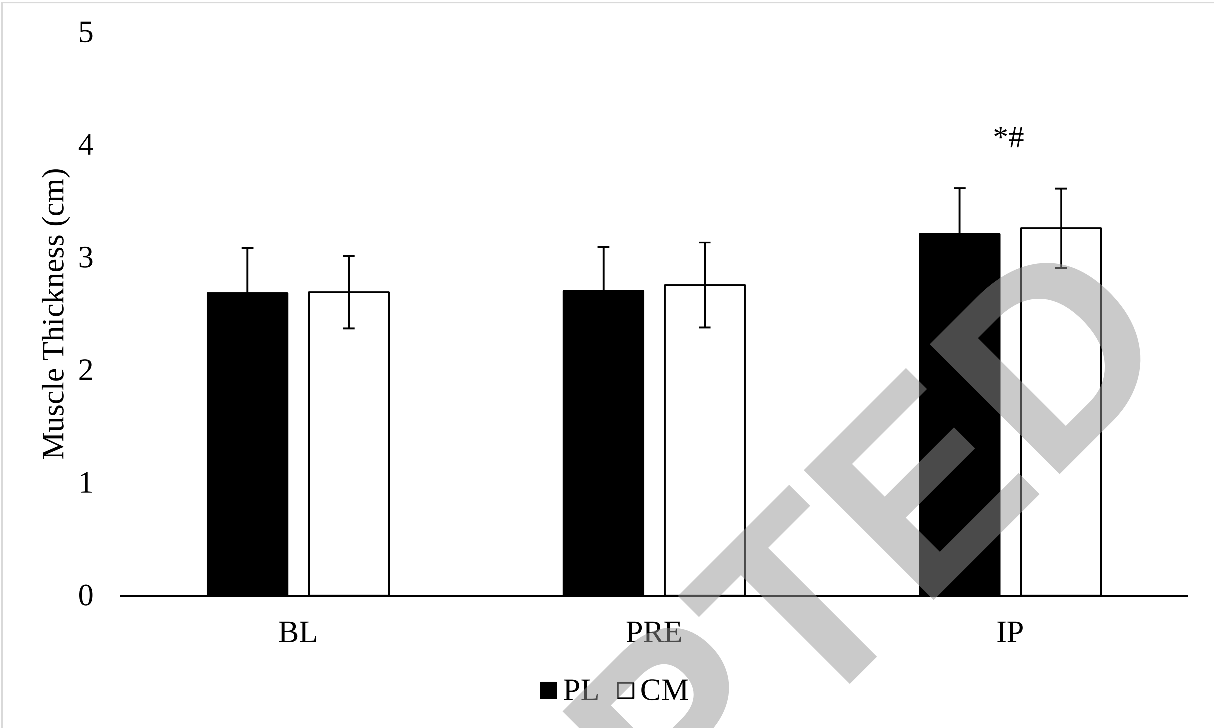


B.



* Significantly (p<0.05) different from Set 1.
# Significantly (p<0.05) different from Set 2.

Fig3



* Significantly (p<0.05) different from BL.
# Significantly (p<0.05) different from PRE.