# Effect of Different Frequencies of Creatine Supplementation on Muscle Size and Strength in Young Adults

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## Abstract

Candow, DG, Chilibeck, PD, Burke, DG, Mueller, KD, and Lewis, JD. Effect of different frequencies of creatine supplementation on muscle size and strength in young adults. *J Strength Cond Res* 25(7): 1831–1838, 2011–The purpose was to determine if creatine supplementation, consumed immediately before and immediately after exercise, with different dosing frequency (i.e., 2 or 3 d $wk^{-1}$) could enhance the gains in muscle size and strength from resistance training (RT) in young adults. A group of 38 physically active, nonresistance trained university students (21–28 years) was randomly allocated to 1 of 4 groups: CR2 (0.15 g·$kg^{-1}$ creatine during 2 d $wk^{-1}$ of RT; 3 sets of 10 repetitions; $n = 11$, 6 men, 5 women), CR3 (0.10 g·$kg^{-1}$ creatine during 3 d $wk^{-1}$ of RT; 2 sets of 10 repetitions; $n = 11$, 6 men, 5 women;), PLA2 (placebo during 2 d $wk^{-1}$ of RT; $n = 8$, 5 men, 3 women), and PLA3 (placebo during 3 d $wk^{-1}$ of RT; $n = 8$, 4 men, 4 women) for 6 weeks. Before and after training, measurements were taken for muscle thickness of the elbow and knee flexor and extensor muscle groups (ultrasound), 1-repetition maximumleg press and chest press strength, and kidney function (urinary microalbumin). Repeated-measures analysis of variance showed that strength and muscle thickness increased in all groups with training ($p < 0.05$). The CR2 (0.6 ± 0.9 cm or 20%; $p < 0.05$) and CR3 groups (0.4 ± 0.6 cm or 16.4%; $p < 0.05$) experienced greater change in muscle thickness of the elbow flexors compared to the PLA2 (0.05 ± 0.5 cm or 2.3%) and PLA3 groups (0.13 ± 0.7 cm or 6.3%). Men supplementing with creatine experienced a greater increase in leg press strength (77.3 ± 51.2 kg or 62%) compared to women on creatine (21.3 ± 10 kg or 34%, $p < 0.05$). We conclude that creatine supplementation during RT has a small beneficial effect on regional muscle thickness in young adults but that giving the creatine over 3 d $wk^{-1}$ did not differ from giving the same dose over 2 d $wk^{-1}$.

**Key Words** resistance training, muscle thickness, gender, kidney function

## Introduction

Creatine is a guanidine-derived compound naturally produced in the body (i.e., 1–2 g $d^{-1}$) from reactions involving the amino acids arginine, glycine, and methionine and consumed in the diet primarily from red meat and seafood (i.e., 1–2 g $d^{-1}$) (42). We have previously found a significant increase in muscle mass and strength from creatine supplementation in young adults (7,17), possibly because of an increase in high-energy phosphate metabolism (4,6), satellite cell activity (40), cellular hydration status (3), hormonal proliferation (i.e., insulin-like growth factor 1 [IGF-I]) (4), and muscle protein kinetics (15,30). Emerging evidence now suggests that creatine supplementation, in close proximity to resistance training (RT), is an important strategy for creating an anabolic environment for muscle growth (5,11,12).

For individuals initiating a structured RT program, it is unclear whether the volume (load × sets × repetitions) or frequency of RT is more important for developing muscle mass and strength. We previously found no differences in muscle accretion (2.2%) and strength (i.e., leg press and chest press; 22–30%) in young adults ($n = 29$; 23 women, 6 men) who performed equal-volume RT 2 d $wk^{-1}$ (i.e., 3 sets of 10 repetitions; 9 whole-body exercises) compared to 3 d $wk^{-1}$ (i.e., 2 sets of 10 repetitions; 9 whole-body exercises) (8) for 6 weeks. On the other hand, creatine monohydrate supplementation may be more beneficial if dosing is spread out into lower, more frequent doses. For example, lower and more frequent doses of creatine is more effective for achieving creatine retention and preventing the production of toxic metabolites, compared to higher, less frequency doses (36). However, it is unknown whether lower and more

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frequent doses of creatine would be more beneficial than higher, less frequent doses for increasing muscle mass and strength during an RT program.

Therefore, the primary purpose of this study was to determine if equal-dosage creatine supplementation, consumed immediately before and immediately after exercise, with different dosing frequency (i.e., 2 or 3 d $wk^{-1}$), could increase muscle thickness and strength in young adults. Although there is limited research on the potential adverse effects of creatine supplementation, the majority of research suggests that creatine is well tolerated (26). Creatine is a nitrogenous containing amine compound that is readily converted to creatinine and excreted through the kidneys (31). An increase in dietary creatine may cause unwanted stress to kidney function. Therefore, a secondary purpose was to assess the effects of creatine supplementation on urinary microalbumin, an indicator of kidney function.

## Methods

### Experimental Approach to the Problem

The study used a placebo-controlled, repeated-measures design where subjects were randomized, based on body mass and gender, to 1 of 4 groups: CR2 (0.15 $g \cdot kg^{-1}$ or ~12 g creatine during 2 d $wk^{-1}$ of RT), CR3 (0.10 $g \cdot kg^{-1}$ or ~8 g creatine during 3 d $wk^{-1}$ of RT), PLA2 (placebo during 2 d $wk^{-1}$ of RT), and PLA3 (placebo during 3 d $wk^{-1}$ of RT). The allocation of participants to creatine supplementation or placebo was double blind, whereas blinding for the frequency of dosing (i.e., 2 or 3 d $wk^{-1}$) was not blinded. Subjects were required to come into the laboratory on 2 occasions at the beginning of the study; once for familiarization with the RT equipment and again for baseline testing. Subjects were instructed not to engage in additional physical activity that was not part of their normal daily routine or change their diet for the duration of the study. The dependent variables measured were (a) muscle thickness of the elbow and knee flexors and extensors, (b) leg press and chest press 1-repetition maximum (1RM) strength, (c) urinary microalbumin (an indicator of kidney function), and (d) diet. Detailed procedures for assessing muscle thickness (12), strength (15), urinary microalbumin (19), and diet (15) are previously described. Therefore, only a brief summary is presented. A retrospective creatine side-effect assessment was administered at the end of the study to determine if supplementing with creatine only on RT days was well tolerated. The retrospective assessment consisted of yes or no responses concerning severe muscle fatigue and soreness, continuous stiffness or tightness, muscle pulls or strains, joint soreness, and gastrointestinal function abnormalities (18). At the end of the study, subjects were asked whether they perceived they were on the creatine supplement or placebo.

### Subjects

Fifty (26 men, 24 women) physically active, nonresistance trained, university students volunteered for the study, which occurred between February and April. We chose to use nonresistance trained subjects because they would have a greater potential for improving muscle size and strength compared to trained individuals. Forty-eight subjects were needed to achieve 80% power as determined using the nomogram of Day and Graham (21) based on a mean muscle hypertrophy of the elbow and knee flexor and extensor muscle groups from creatine supplementation of 4.1 cm (15) with an *SD* from the means of 0.68, assuming a difference parameter (i.e., *SD* of the means/*SD* of measurements) of 0.9 at an alpha value of 0.05. Baseline physical activity was determined by having each subject fill out a leisure time exercise questionnaire (23) where the number of times on average per week strenuous (i.e., heart beats rapidly; running, jogging), moderate (i.e., not exhausting; fast walking, dancing), and mild exercise (i.e., minimal effort; yoga, house work) was performed. Students were also required to fill out a Physical Activity Readiness Questionnaire, which assesses an individual's readiness for participation in exercise training programs and includes questions related to heart conditions, angina at rest or during physical exercise, balance and bone or joint problems that may affect exercise performance. No contraindications to exercise were indicated. Subjects were excluded if they had

**Table 1.** Mean (*SD*) subject characteristics and physical activity performed at baseline for creatine and placebo groups.*

| Group | Age (y) | Body mass (kg) | Height (cm) | Strenuous activity (times per week) | Moderate activity (time per week) | Mild activity (times per week) |
|---|---|---|---|---|---|---|
| CR2 (6 men 5 women) | 22 (3) | 77 (15.6) | 175 (7.4) | 3.5 (1.4) | 2.5 (1.8) | 5.0 (3.3) |
| CR3 (6 men, 5 women) | 23 (4) | 71 (9.4) | 171 (8.4) | 3.2 (1.7) | 3.7 (2.1) | 6.1 (2.5) |
| PLA2 (5 men, 3 women) | 26 (4) | 76 (16) | 172 (9.3) | 2.9 (1.6) | 3.6 (2.5) | 4.9 (2.5) |
| PLA3 (4 men, 4 women) | 22 (2) | 71 (13.4) | 170 (9.7) | 3.7 (1.4) | 3.3 (2.4) | 6.0 (1.9) |

*RT = resistance training; CR2 = 0.15 $g \cdot kg^{-1}$ creatine during 2 d $wk^{-1}$ of RT, 3 sets of 10 repetitions; CR3 = 0.10 $g \cdot kg^{-1}$ creatine during 3 d $wk^{-1}$ of RT, 2 sets of 10 repetitions; PLA2 = placebo during 2 d $wk^{-1}$ of RT; PLA3 = placebo during 3 d $wk^{-1}$ of RT.

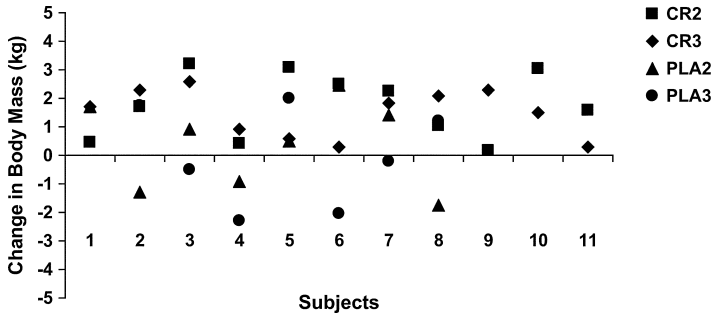


**Figure 1.** Individual change scores (post–pre) in body mass (kg) for the creatine (CR2: $N = 11$, CR3: $N = 11$) and placebo groups (PLA2: $N = 8$, PLA3: $N = 8$).

participated in structured RT or consumed creatine within the past 6 months, if they were vegetarians, if they consumed >150 mg of caffeine daily because this dose of caffeine may impair creatine metabolism (39), if they had pre-existing kidney abnormalities, and if they were smokers. The study was approved by the university ethics review board for research in human subjects at the University of Regina. The subjects were informed of the risks and purposes of the study before their written consents were obtained.

### Supplementation

A research assistant, who was not involved in the study, was responsible for randomizing the subjects and coding the supplements to ensure all subjects and investigators remained blinded throughout the study. Entry and analysis of data were performed by analyzing coded groups (i.e., groups 1–4). The creatine dosage was individualized at 0.15 $g \cdot kg^{-1}$ for subjects randomized to the 2 d $wk^{-1}$ group and 0.10 $g \cdot kg^{-1}$ for subjects randomized to the 3 d $wk^{-1}$ group; thus ensuring an equal dosage of creatine between groups. The creatine dosage was chosen because it is an approximate amount shown to increase muscle mass and strength, without resulting in adverse side effects, in young and older adults (15,17). Creatine and placebo (i.e., rice flour) capsules were identical in taste, texture, color, and appearance. Subjects were instructed to consume half their respective dosage of creatine or placebo immediately before (i.e., 5 minutes) and the other half immediately after (i.e., 5 minutes) each RT session with water because it has been shown that the timing of creatine ingestion is crucial for creating an anabolic environment for muscle growth (11,12). Creatine and placebo capsules were provided to each subject in bundles of 6 bags and placed in a sealed envelope. Each bag contained the subject's supplement for each RT day. Supplementation compliance was monitored by weekly verbal communication and by having subjects return all empty supplement bags before picking up additional bags. We have used this strategy before with success in a number of our other nutritional supplement and RT studies (9,13).

### Procedures

*Muscle Thickness.* Muscle thickness of the elbow and knee flexors and extensors was measured using B-Mode ultrasound (Aloka SSD-500, Tokyo, Japan). Briefly, to measure elbow flexor and extensor muscle thickness, a small mark was drawn on the lateral side of the right arm to indicate 50% of the distance down from the acromion process to the olecranon process. A mark was placed on the bulk of the biceps and triceps where the center of the ultrasound probe was placed. To measure elbow flexor muscle thickness, each subject placed their right arm flat on a table with the belly of the biceps facing upward and the forearm supinated. To measure elbow extensor muscle thickness, subjects stood with their back facing the researcher with arms relaxed and fully extended. For knee flexor and extensor muscle thickness, a small mark was drawn on the lateral side of the right leg to indicate 70% of the distance down from the greater trochanter to the lateral epicondyle of the tibia (2). A mark was placed as a reference point on the bulk of the vastus lateralis and biceps femoris where the center of the

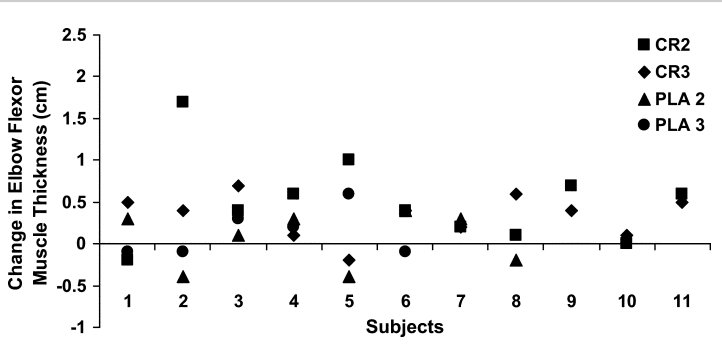


**Figure 2.** Individual change scores (post–pre) in elbow flexor muscle thickness (cm) for the creatine (CR2: $N = 11$, CR3: $N = 11$) and placebo groups (PLA2: $N = 8$, PLA3: $N = 8$).

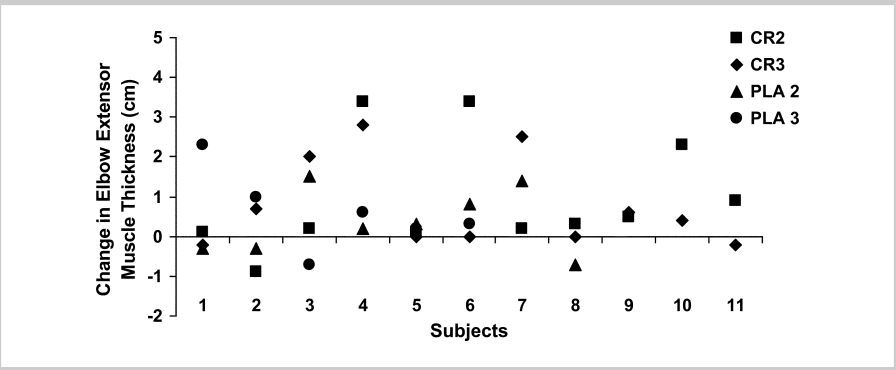


**Figure 3.** Individual change scores (post–pre) in elbow extensor muscle thickness (cm) for the creatine (CR2: $N = 11$, CR3: $N = 11$) and placebo groups (PLA2: $N = 8$, PLA3: $N = 8$).

ultrasound was placed. For each muscle thickness measurement, precise markings on the skin were taken using overhead transparency film to ensure that identical sites were measured on each occasion. The same researcher performed the baseline and posttesting assessments. Reproducibility of muscle thickness measurements was determined by testing 28 subjects 1 week apart. The coefficients of variation for muscle thickness measurements were 2.6% (elbow flexors), 1.7% (elbow extensors), 3.1% (knee flexors), and 0.9% (knee extensors) (10).

*Muscle Strength.* Leg press and chest press strengths were assessed using a 1RM standard testing procedure as previously described (14,15) before and after the study. Briefly, to measure the 1RM leg press, a unilateral, horizontal leg press machine (Lever Pulse Fitness; Winnipeg, MB, Canada) was used. After a demonstration, subjects were positioned in the leg press so that a 90° angle at the knee was achieved and feet placed shoulder width apart. Subjects were instructed to push the weight away from their body to almost full extension, without locking the knees, before returning to the starting position. After 5-minutes of cycling on a stationary cycle ergometer, subjects performed 2 warm-up sets in order: 1 set of 10 repetitions using a weight determined by each subject to be comfortable and 1 set of 5 repetitions using increased weight. Two minutes after the warm-up sets, weight was then progressively increased for each subsequent 1RM attempt with a 2-minute rest interval. The 1RM was usually reached in 4–7 trials, independent of the 2 warm-up sets.

For 1RM chest press, subjects were positioned in a bilateral, chest press machine (Lever Pulse Fitness) with both feet on the floor. Subjects were instructed to grasp the bars (overhand grip) approximately shoulder width apart and push the weight away from the body until approximate full extension and then lower the weight back to the starting position. Subjects performed 2 warm-up sets in the order: 1 set of 10 repetitions using a weight determined by each subject to be comfortable and 1 set of 5 repetitions using increased weight. Two minutes after the warm-up sets, weight was then progressively increased for each subsequent 1RM attempt with a 2-minute rest interval. The 1RM was usually reached in 3–6 trials, independent of the 2 warm-up sets. These 2 exercises were chosen as an index of muscular strength because they involve the major muscle groups in the lower and upper body. The testing was supervised by an exercise physiologist from the Canadian Society for Exercise Physiology, the highest designation in Canada. Reproducibility of the strength measures was assessed on 10 subjects, 1 week apart. The leg press and chest press strength measures had coefficients of variation of 3.8 and 3.1%, respectively (14).

*Kidney Function.* To measure microalbumin, an indicator of kidney function, 24-hour urine samples were obtained before and immediately after the 6-week program. Microalbumin was measured using immunochromatographic lateral flow membrane test strips containing specific monoclonal antibody against human albumin (Genzyme Diagnostics, Charlottetown, PEI, Canada). The test gives 1 of 3 results: microalbumin $<18$ mg·L$^{-1}$, $=18$ mg·L$^{-1}$, or $>18$ mg·L$^{-1}$. A test result $>18$ mg·L$^{-1}$ indicates compromised kidney function. Duplicate tests resulted in a coefficient of variation of 0%.

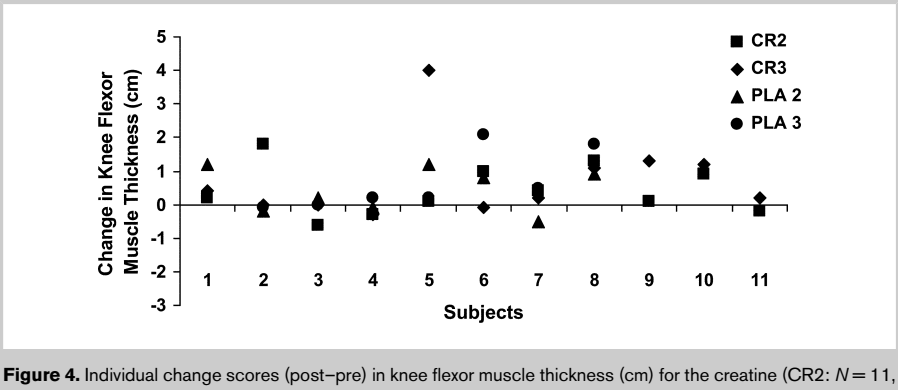


**Figure 4.** Individual change scores (post–pre) in knee flexor muscle thickness (cm) for the creatine (CR2: $N = 11$, CR3: $N = 11$) and placebo groups (PLA2: $N = 8$, PLA3: $N = 8$).

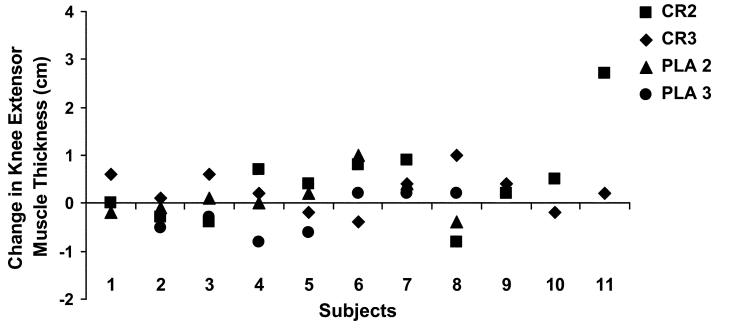


**Figure 5.** Individual change scores (post–pre) in knee extensor muscle thickness (cm) for the creatine (CR2: $N = 11$, CR3: $N = 11$) and placebo groups (PLA2: $N = 8$, PLA3: $N = 8$).

*Dietary Intake.* Dietary intake was recorded before and after the study to assess whether there were differences in total energy and macronutrient composition between the creatine and placebo groups. Subjects used a 3-day food booklet to record what they ate for 2 weekdays and 1 weekend day. Subjects were instructed to record all food items, including portion sizes consumed for the 3 designated days. The Interactive Healthy Eating Index (Center for Nutrition Policy and Promotion, United States Department of Agriculture; http://www.usda.gov/cnpp/) was used to analyze 3-day food records. Each food item was entered and the program provided total energy consumption on average over the 3 days and energy from carbohydrates, fats, and proteins individually.

*Resistance Training Program.* All subjects followed the same RT program combined with creatine or placebo for 6 weeks. Six weeks of RT was chosen because this is sufficient duration to produce significant increases in muscle thickness of the elbow flexors and extensors and knee flexors in untrained individuals (1). After familiarization, training sessions were indirectly supervised by Certified Personal Trainers through the Canadian Society for Exercise Physiology. Subjects in the 2 d $wk^{-1}$ groups exercised on Tuesday and Thursday for ~60 minutes, whereas subjects in the 3 d $wk^{-1}$ groups exercised on Monday, Wednesday, and Friday for ~40 minutes. Subjects in the 2 d $wk^{-1}$ groups performed 3 sets of 10 repetitions to muscular fatigue with 1–2 minutes rest between sets for each exercise at an intensity corresponding to a load ≥80% 1RM. Subjects in the 3 d $wk^{-1}$ groups performed 2 sets of 10 repetitions to muscular fatigue with 1- to 2-minute rest between sets for each exercise at an intensity corresponding to a load ≥80% 1RM, thus ensuring equal-training volume between groups. Subjects were instructed to adjust the weight for each set of 10 repetitions so that muscular fatigue occurred near the end of each set (i.e., between the eighth and tenth repetitions). We have previously used a similar RT program successfully to increase muscle mass and strength (8). Resistance exercises performed included leg press, chest press, lat pull-down, shoulder press, leg (knee) extension, leg curl (knee flexion), triceps extension, biceps curl, and standing calf raise. Subjects maintained daily training logs where average training volume per session (weight × sets × repetitions) was determined for each subject. Resistance was increased by 2–10 kg once a subject completed 3 sets of 10 repetitions to muscular fatigue for an exercise.

### Statistical Analyses

A 2 (Treatment: creatine vs. placebo) × 2 (Frequency: 2 vs. 3 days) × 2 (Time: before vs. after training) analysis of variance (ANOVA) with repeated measures on the last factor was used to determine whether there were any differences between groups over time for the dependent variables of muscle thickness, strength, and diet. When interactions or main effects were found, a least significant difference post hoc test was used to determine differences between means. A 2 (Treatment: creatine vs. placebo) × 2 (Gender: male vs. female) × 2 (time) repeated-measures ANOVA was used to determine whether there were differences over time between men and women. A 1-factor ANOVA was used to determine if there were differences in baseline measurements between groups. All results are expressed as means ± *SD*. Effect sizes (ESs) were determined for these changes and classified as small (<0.5), moderate (0.5–0.8), or large (>0.8). Statistical analyses were carried out using SPSS version 11.0 for Windows XP (SPSS, Chicago, IL, USA). Significance was set at $p \leq 0.05$.

## Results

Of the 50 subjects who volunteered, 38 completed the study. Two subjects from each of the creatine groups (3 women, 1 man) and 4 subjects from each of the placebo groups (6 women, 2 men) withdrew because of time constraints. Subject characteristics and physical activity performed at baseline are found in Table 1. There were no significant differences between groups for any of the baseline measurements. There were no differences in dietary intake (i.e., total calories, carbohydrates, fats, and protein) between groups over time. There were no reports of adverse effects from creatine ingestion and all measures for urinary microalbumin before and after training and supplementation were <18 $mg \cdot L^{-1}$. Thirty subjects did not know whether they were ingesting creatine or placebo, 4 subjects correctly guessed they were ingesting creatine, and 4 subjects incorrectly guessed they were on creatine or placebo. The frequency of

RT (i.e., 2 or 3 d $wk^{-1}$) had no significant effect on body mass, muscle thickness, or strength over time.

There was a treatment × frequency × time interaction for body mass ($p < 0.05$). Post hoc analysis indicated that the increase in body mass in the CR2 (1.8 ± 0.2 kg or 2.3%; ES = 0.1) and CR3 (1.5 ± 0.4 kg or 2.2%; ES = 0.1) groups was greater than the PLA3 group (0.2 ± 0.3 kg or 0.2%; $p < 0.05$), with no other differences (Figure 1).

There was a significant treatment × frequency × time interaction for muscle thickness ($p < 0.05$). Post hoc analysis indicated that muscle thickness significantly increased in all muscle groups with training. The CR2 (0.6 ± 0.9 cm or 20%; ES = 0.6; $p < 0.05$) and CR3 groups (0.4 ± 0.6 cm or 16.4%; ES = 0.5; $p = 0.05$) experienced greater elbow flexor muscle thickness compared to the PLA2 (0.05 ± 0.5 cm or 2.3%) and PLA3 groups (0.13 ± 0.7 cm or 6.3%).

Leg press and chest press strength increased over time ($p < 0.05$), with no significant differences between groups. The increases in leg press strength for the CR2, CR3, PLA2, and PLA3 groups were 63.1 ± 57 kg or 53%, 35 ± 25 kg or 46%, 40 ± 35 kg or 41%, and 40 ± 18 kg or 50%, respectively. The increases for chest press strength for the CR2, CR3, PLA2, and PLA3 groups were 8.6 ± 3.5 kg or 17.5%, 6.6 ± 1.4 kg or 26%, 5.5 ± 0.5 kg or 16%, and 3.6 ± 1.1 kg or 13%, respectively. Men who supplemented with creatine experienced a greater gain in leg press strength (77.3 ± 51.2 kg or 62%) compared to women on creatine (21.3 ± 10 kg or 34%, $p < 0.05$).

## Discussion

To our knowledge, this is the first study to compare the effects of the frequency of equal-weekly dosage creatine supplementation on muscle thickness and strength in non–resistance trained young adults. Unique and important results from this study were as follows: (a) equal-dosage creatine supplementation 2 or 3 d $wk^{-1}$ leads to similar gains in muscle thickness and strength, (b) creatine ingestion before and after RT sessions leads to small improvements in muscle size, and (c) men supplementing with creatine experience greater gains in lower body strength compared to women on creatine.

Using muscle ultrasound, we observed a significant increase in muscle thickness of the elbow flexors (16–20%) after only 6 weeks of creatine supplementation, which supports our previous findings. For example, young adults who ingested creatine (0.2 g·$kg^{-1}$) immediately after performing RT (2 d $wk^{-1}$, 6 weeks) experienced a greater gain in elbow flexor muscle thickness (0.36 ± 0.06 cm or 10.3%) compared to consuming placebo immediately after training (0.24 ± 0.07 cm or 6.3%) (17). In this previous study, the greater increase in elbow flexor muscle thickness from creatine was confirmed by a significant increase in lean tissue mass as assessed by dual-energy x-ray absorptiometry (DXA). In a more recent study also using DXA, creatine supplementation during 4 weeks of RT significantly increased lean tissue mass in young adults (27). Although muscle ultrasound cannot determine whether the increase in muscle size after 6 weeks of creatine supplementation was because of significant muscle protein accretion, we have previously taken muscle biopsies of the vastus lateralis and observed a greater increase in type II muscle fiber cross-sectional area (6) and IGF-I content after only 8 weeks of creatine supplementation (4). These results across studies suggest that short-term (i.e., 4–8 weeks) creatine supplementation influences muscle protein and hormonal kinetics, which may help explain the increase in muscle size.

Although muscle ultrasound cannot differentiate between hydration status, muscle or connective tissue, and intramuscular fat, this technology is still considered a reliable method to accurately measure muscle thickness and cross-sectional area (32,37). For example, muscle thickness measurements of the knee extensors is a significant predictor of knee extensor volume as measured by magnetic resonance imaging (MRI; $r = 0.91$) (29), and muscle thickness of the elbow flexors and extensors are significant predictors of elbow flexors and extensors volume as measured by MRI ($r = 0.96$) (28). However, as shown in Figures 2–5, there was significant variability in muscle thickness measurements between subjects on creatine and placebo. These inconsistencies may be attributed to creatine possibly resulting in net body water retention because subjects on creatine also experienced a significant increase in body mass (1.5–1.8 kg). However, we have previously shown that the percentage of intracellular water to body weight did not differ in subjects supplementing with creatine during RT for 8 weeks, indicating that the increase in intracellular water retention paralleled an increase in dry muscle mass (6).

Muscle hypertrophy after RT requires net synthesis of myofibrillar proteins (33). Although the machinery for stimulating the synthetic rate of muscle proteins is increased after exercise (41), it appears that this response is delayed without creatine or amino acids (12). Results from this study showed that the strategic ingestion of creatine (i.e., 0.05–0.075 g·$kg^{-1}$ immediately before and 0.05–0.075 g·$kg^{-1}$ immediately after each RT session) for 6 weeks was important for increasing muscle size of the elbow flexors (ES = 0.5–0.6), which support our previous findings (15,17). For example, consuming creatine immediately before (0.05 g·$kg^{-1}$) and immediately after (0.05 g·$kg^{-1}$) RT sessions (3 d $wk^{-1}$, 10 weeks, 9 whole-body exercises) resulted in greater whole-body muscle hypertrophy (2.0 ± 0.3 cm) compared to placebo (0.8 ± 0.3 cm) and RT in healthy older men (15). Potentially, these positive results from creatine supplementation before and after RT may be because of an increase in blood flow and delivery of creatine to exercising muscles (24), an upregulation of the kinetics involved in creatine transport (34), and by an increase in $Na^+$–$K^+$ pump function during exercise (34). These findings may have application for coaches, athletes, and exercising individuals for designing optimal creatine supplementation strategies,

which lead to muscle accretion. For example, consuming 0.05–0.075 g·kg$^{-1}$ or 4–6 g of creatine immediately before and 0.05–0.075 g·kg$^{-1}$ or 4–6 g of creatine immediately after each RT session may be beneficial if consumed for a longer period of time (i.e., ≥6 weeks).

It is somewhat puzzling as to why creatine supplementation only increased elbow flexor muscle thickness compared to placebo. One possible explanation may involve the variability in fiber-type composition between individual muscle groups. For example, Johnson et al. (25) found a greater proportion of type II fibers in the elbow flexors (58%) at autopsy in 6 adults. Research studies have shown that creatine supplementation leads to a significant increase in muscle cross-sectional area of type II fibers (6,20) without a subsequent increase in type I fibers; indirectly suggesting that creatine may have increased type II fiber size in the elbow flexors. However, muscle biopsies were not performed in this study, so consensus cannot be made. In addition, we feel that the 9 exercises prescribed in the whole-body RT program targeted all major muscle groups equally. Furthermore, there were no differences in dietary intake between groups over time or differences in training volume between individual muscle groups for creatine or placebo; suggesting that a longer (i.e., >6 weeks) creatine supplementation protocol may have been needed to observe an increase in whole-body muscle thickness.

There was no greater increase in leg press or chest press strength from creatine supplementation, independent of frequency of ingestion. One possible explanation may involve the complexity of the exercises involved. Complex multijoint exercises (i.e., leg press, chest press) involve greater learning and coordination compared to the single-joint exercises (i.e., biceps curl) (35). Therefore, the increase in leg press and chest press strength may have been due to learning, as all 4 groups increased strength equally over time; suggesting that a longer (>6 weeks) creatine intervention may have been required. Another possible explanation may involve the potentially large interindividual differences in initial endogenous creatine stores between subjects (38). Individuals with low resting intramuscular creatine stores (i.e., ~100 mmol kg$^{-1}$ dry mass) experience the greatest benefit from creatine supplementation (6,38). For example, we showed that healthy vegetarian adults who had low initial resting intramuscular creatine concentrations (117 mmol kg mmol kg$^{-1}$ dry mass) experienced a significant increase in total creatine content (PCr and free creatine) from creatine supplementation, which was correlated with an increase in lean tissue mass (6). Furthermore, Casey et al. (16) found a significant correlation between increased intramuscular creatine content in type II muscle fibers and cycling performance in young men. Again, muscle biopsies were not performed in this study, so we are unable to determine resting intramuscular creatine content between students, which may have influenced our results. However, we did observe a significant increase in leg press strength in men who supplemented with creatine compared to women on creatine. Men appear to respond more favorably to creatine supplementation (17), possibly because of reduced intramuscular creatine content allowing for accelerated creatine uptake with supplementation (22). Furthermore, creatine supplementation in men appears to reduce muscle protein catabolism compared to women (30); potentially allowing for accelerated muscle recovery from RT sessions.

## Practical Applications

In conclusion, the results of this study suggest that the frequency of short-term creatine supplementation has a small effect on regional muscle thickness. Consuming approximately 4–6 g of creatine immediately before and 4–6 g of creatine immediately after each RT session may be beneficial if consumed for a longer period of time (i.e., ≥6 weeks). However, the generalizability of these results are limited to short-term training only. Future research should directly compare the effects of longer-term (i.e., ≥6 weeks) creatine supplementation immediately before vs. after RT in untrained and trained adults to further enhance the development of optimal RT and creatine application strategies.

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