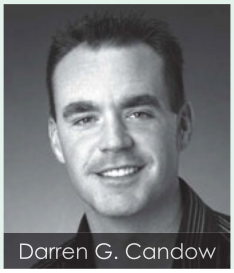
Darren G. Candow

SCOTT C. FORBES[1], XAVIER WALTZ[1], DARREN G. CANDOW[2*]
*Corresponding author
1. University of Calgary, Faculty of Medicine, Department of Physiology and Pharmacology, Alberta, T2N 4N1, Canada
2. University of Regina, Faculty of Kinesiology & Health Studies, Regina, S4S 0A2, Saskatchewan, Canada


# Creatine timing on muscle mass and strength: Appetizer or Dessert?

**KEYWORDS: supplements, creatine, strength, muscle mass, timing**

Abstract Resistance training is a potent stimulus to enhance skeletal muscle hypertrophy and strength. Combining creatine supplementation with resistance training may be an effective strategy to enhance the physiological adaptations from resistance training alone. Emerging evidence suggests that the timing of creatine supplementation may be an important regulator of muscle hypertrophy and strength. Creatine ingested before and after resistance training sessions appear to be an effective strategy to increase muscle mass and strength, with slightly greater benefits if creatine is consumed after exercise compared to before. This brief review will evaluate the literature pertaining to the strategic ingestion of creatine and resistance training resulting in practical creatine supplementation strategies.

## INTRODUCTION

It is well established that the mechanical stimuli from resistance training increases muscle protein synthesis (1). Although the machinery for stimulating muscle protein synthesis is increased after resistance training (2), the anabolic response may be delayed post-exercise (3). The combination of creatine supplementation and resistance training may lead to greater muscle benefits than resistance training alone in young and older adults (4, 5). Furthermore, the timing of creatine ingestion may be an important factor for creating an anabolic environment for muscle growth (5). Emerging evidence suggests that creatine supplementation, in close proximity to resistance training sessions, may provide superior benefits compared to creatine intake at other times of the day (6, 7). While the mechanistic actions explaining the greater benefits from timed creatine ingestion are unknown, it is possible that blood flow kinetics and creatine transport are involved (8, 9). Therefore, the purpose of this review is to 1) briefly outline the potential beneficial effects of creatine supplementation, 2) review the emerging evidence involving the timing of creatine supplementation combined with resistance training, and 3) outline creatine supplementation strategies.

## CREATINE SUPPLEMENTATION

Creatine, methyl-guanidino acetic acid, is a naturally occurring nitrogen-containing compound (5, 10, 11). Creatine excretion occurs at a rate of ~2 $g \cdot d^{-1}$ (12). Creatine can be replaced via endogenous synthesis (1-2 $g \cdot d^{-1}$) in the kidneys, liver, and pancreas or through dietary intake, typically ~1-3 $g \cdot d^{-1}$ (11, 12). Creatine is found in high concentrations in red meat and seafood (12). Ninety-five percent of creatine is stored in skeletal muscle, of which 60-70 percent is phosphorylated (i.e. phosphocreatine) (13). Phosphocreatine rapidly resynthesizes adenosine diphopshate to help maintain adenosine triphosphate (ATP) during high intensity exercise such as resistance training (13). Theoretically, elevated phosphocreatine stores (via creatine supplementation) may increase exercise training intensity and the volume of work performed leading to greater muscle accretion and strength (reviewed in Branch (14); Rawson & Volek (15)). Several purported mechanisms exists which may help explain the typical increase in muscle mass and strength from creatine (4, 5, 10). Creatine supplementation elevates skeletal phosphocreatine and total creatine stores (16) which increases phosphocreatine resynthesis (17) and exercise fatigue resistance (18). Creatine may also influence myocellular water retention due to increased intracellular osmolarity and increase muscle glycogen storage (19). Subsequent muscle cell swelling may stimulate genes regulating various anabolic pathways (20). Furthermore, creatine has been shown to increase satellite cell differentiation (21), activity (22), and content (23); transcription factor activity (24), hormonal secretion (e.g. IGF-1;(25)), muscle protein kinetics (26), and decrease inflammation (27).

| First Author, Year | Study Population | Intervention | Duration | Outcome Measure |
|---|---|---|---|---|
| Antonio and Ciccone 2013 | N=19 Recreational Male Bodybuilders; Age 23.1 ± 2.9 yrs; height: 166.0 ± 23.2 cm; Weight: 80.18 ± 10.43 kg | Randomly assigned: CR (5g) PRE or CR (5g) POST RT sessions and anytime on days off; 5 RT sessions/wk | 4 wks | ↔FFM, FM, BM, Bench Press 1RM between groups; Magnitude based inference CR POST possibly more beneficial for FFM, FM, 1RM BP |
| Candow et al. 2014 | N=22 (9 male; 13 females) non-RT healthy older adults; Age 50-64 yrs | Randomly assigned: CR before (n=11) (CR 0.1g/kg before + 0.1g/kg placebo after) or CR after (n=11) (0.1g/kg placebo before + CR 0.1g/kg after); RT 3d/wk | 12 wks | ↔ FFM, limb muscle thickness, BP and LP 1RM and no difference in protein catabolism (but all these parameters were improved by RT). No changes in Kidney function over time. |
| Candow et al. Unpublished | N= 39 (22 women, 17 men); non-RT healthy older adults, Age 50-71 yrs | Randomly assigned: CR before (CR 0.1g/kg before + 0.1g/kg placebo after) or CR after (0.1g/kg placebo before + CR 0.1g/kg after) or a Placebo control; RT 3d/wk | 8 months | Only CR after ↑ LBM and ↑ leg press 1RM compared to placebo ↔ Between CR groups for muscle mass and strength but ↑ greater in CR groups than placebo group. |
| Cribb and Hayes 2006 | N=17 Recreational Male Bodybuilders; PRE-POST group (n=8): Age 21 ± 3; MOR-EVE (n=9): Age 24 ± 4 | Randomly assigned - strength matched: PRE-POST = immediately before and after RT OR MOR-EVE = consumed same supplement > 5 hours before or after RT (Before breakfast and late evening before sleep). Supplementation only on training days (1 g/kg/bw supplement: supplement per 100 g = 40 g protein, 43 g glucose, 7 g CR and < 0.5 g of fat). The participants were instructed to maintain their habitual daily diet during the trial. RT 4 times per wk 10 wks (training time = between 3-6p.m). To minimize the impact of a new program on strength and hypertrophy adaptations, subjects underwent a structured training program (similar to the study 8-12 wk before commencing the study) | 10 wks | PRE-POST (compared to MOR-EVE) ↑ LBM (no change in FM, and reduction of %fat), 1RM Squat, 1RM bench press (no significant effect on dead-lift), Type II fiber CSA, contractile protein content, CR and glycogen muscle content |

Abbreviations: CR = creatine; RT = resistance training; MOR-EVE = morning and evening; FFM = fat free mass; FM = Fat mass; BM = body mass; RM = repetition maximum; BP = bench press; LP = leg press; LBM = lean body mass; CSA = cross sectional area

**Table 1.** Studies Investigation the effects of creatine timing combined with resistance training.

## CREATINE TIMING

The timing of creatine supplementation is proving to be an important regulator of muscle growth (Table 1). The strategic ingestion of creatine immediately before and after resistance training sessions appears more important than ingesting creatine at other times of the day. For example, in the most recent study, we showed that creatine (0.1 g·kg$^{-1}$) immediately before and immediately after resistance training sessions for 8 months produced similar gains in muscle mass and strength. However, compared to placebo, only post-exercise creatine resulted in greater improvements in whole body lean tissue mass (creatine after = 6.2 percent vs. placebo = 1.4 percent) and leg press strength (creatine after = 28.3 percent *vs*. 3.4 percent; unpublished findings). The slightly greater benefit from post-exercise creatine supplementation indirectly supports the findings of Antonio and Ciccone (28) who found a greater muscle benefit from post-exercise creatine supplementation (5 g) in young adults compared to pre-exercise creatine supplementation. We previously found no differences between creatine supplementation (0.1 g·kg$^{-1}$) immediately before vs. after resistance training sessions for 12 weeks in older adults (29). However, a major limitation of the studies by Antonio and Ciccone (28) and Candow et al. (29) was that a placebo (control) was not used for comparison to creatine. Consuming creatine immediately before (0.05 g·kg$^{-1}$) and immediately after (0.05 g·kg$^{-1}$) resistance training sessions (3 days/week, 10 weeks) resulted in greater muscle accretion (2.0 ± 0.3 cm) compared to placebo (0.8 ± 0.3 cm) and resistance training in healthy older males (59-77 years) (30). These results support previous findings of a significant increase in lean tissue mass (6 percent), type II muscle fibre area (29 percent), and insulin growth-factor I (78 percent) in adults (19-55 years) who ingested creatine before (0.03 g·kg$^{-1}$) and after (0.03 g·kg$^{-1}$) resistance training (6 days/ week, 8 weeks) (25, 31). Interestingly, in comparing the effects of creatine ingestion before (0.5 g·kg$^{-1}$) and after (0.5 g·kg$^{-1}$) resistance training (10 weeks) to creatine ingestion in the morning and evening on training days, Cribb et al. (6) showed that creatine ingestion before and after exercise resulted in significantly greater intramuscular creatine content, lean tissue mass, and muscle cross sectional-area of type II fibres.

Although it is difficult to compare results across studies, it has been theorized that these positive results from creatine ingestion before and after exercise may be due to an increase in blood flow and delivery of creatine to exercising muscles (8), an upregulation of the kinetics involved in creatine transport (9), and by an increase in Na+-K+ pump function during exercise (9). Based on the limited studies performed thus far, it appears that creatine supplementation before and after resistance training sessions is important for muscle and strength. Post-exercise creatine ingestion may provide slightly greater benefits than pre-exercise creatine supplementation.

## SUMMARY

Resistance training is an effective strategy to increase muscle mass and strength. Emerging evidence indicates that the timing of creatine supplementation is an important intervention for augmenting the physiological adaptations from resistance training alone. Creatine ingested before and after resistance training sessions appears to be an effective strategy to increase muscle mass and strength, with slightly greater benefits if creatine is consumed post-exercise compared to pre-exercise.

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