

## THE EFFECTS OF SUPPLEMENTATION WITH CREATINE AND PROTEIN ON MUSCLE STRENGTH FOLLOWING A TRADITIONAL RESISTANCE TRAINING PROGRAM IN MIDDLE-AGED AND OLDER MEN

M.G. BEMBEN<sup>1</sup>, M.S. WITTEN<sup>2</sup>, J.M. CARTER<sup>3</sup>, K.A. ELIOT<sup>4</sup>, A.W. KNEHANS<sup>4</sup>, D.A. BEMBEN<sup>1</sup>

1. Neuromuscular Lab, Dept. Health & Exercise Science, U. Oklahoma, Norman, OK, 73019; 2. Center on Aging, U. Colorado & Health Science Center, Aurora, CO, 80045; 3. Norman Regional Hospital Health Club, 3700 W. Robinson, Norman, OK, 73072; 4. Dept. Nutritional Sciences, U. Oklahoma Health Sciences Center, Oklahoma City, OK, 73104. Corresponding author: Michael G. Bemben, PhD, University of Oklahoma, Department of Health and Exercise Science, 1401 Asp Ave. Room 115 HHC, Norman, OK 73019, mgbemben@ou.edu, Phone: (405) 325-2717

**Abstract:** *Objectives:* Creatine and protein supplementation can enhance the training outcomes of young subjects, but it is not clear if there are benefits for older individuals. Therefore, the purpose of this study was to determine the effects of creatine and protein supplementation on strength gains following a traditional resistance training program for middle-aged and older men. *Design, Setting, Participants:* This study assessed changes in strength of men aged 48-72 years following 14 weeks of resistance training supplemented with creatine and/or protein. A double-blind, randomized, placebo-controlled design placed 42 males into one of four groups: Resistance Trained Placebo (RTP, n=10); Resistance Trained Creatine (RTC<sub>Cr</sub>, 5g Cr, n=10); Resistance Trained Protein (RTP<sub>Pr</sub>, 35g whey Pr, n=11); or Resistance Trained Creatine and Protein (RTC<sub>CrPr</sub>, 5g Cr and 35g Pr, n=11). *Intervention:* All groups trained 3 days per week for 14 weeks. The resistance training program was based on progressive overload. Training loads corresponded to 80% 1RM (one repetition maximum strength), 3 sets of 8 repetitions for the following exercises: knee extension/knee flexion; bicep curl/tricep extension; military press; lat pull down; seated leg press; and bench press. *Measurements:* 1 RM for each exercise and measures of lean body mass were assessed prior to and following the 14 week program. *Results:* Each group significantly ( $p < 0.05$ ) increased strength and lean body mass, however, there were no significant group effects or group X trial interactions. *Conclusion:* Resistance training in middle-aged and older men significantly increased muscular strength and added muscle mass with no additional benefits from creatine and/or protein supplementation.

**Key words:** Creatine monohydrate, whey protein, weight training, strength, aging.

### Introduction

The aging process brings about a number of physiological changes, such as the loss of muscle protein and a concomitant decline in lean body mass, strength, and power, as well as increases in fat mass, all of which have been implicated in a decline of physical performance and function (1). These changes can ultimately result in an increased dependency on others, reduced abilities to perform acts of daily living, and limit recreational and occupational pursuits (2).

Various interventions have been proposed on how to effectively improve the rate of protein synthesis and slow the rate of protein degradation in order to elicit skeletal muscle hypertrophy and improved strength (3-7). Resistance training for older adults has become increasingly popular as an effective intervention, especially when combined with increased dietary protein intake in order to provide an adequate stimulus to improve strength and promote the anabolic development of muscle (8-11).

It has been reported that aging results in reduced levels of resting phosphocreatine (PCr), perhaps due to a decrease in Type II muscle fiber number and size. These changes may also, in part, be responsible for the age-related reductions in skeletal muscle size, mitochondrial enzyme activity, and high-energy phosphate metabolism, all associated with the decline in muscle mass, strength, and endurance capacity (12, 13).

Studies also suggest that creatine (Cr) supplementation can increase the concentrations of both creatine and phosphocreatine in skeletal muscle (14) which may provide the means necessary for improved strength by an increase in muscle mass when combined with resistance training, however, less is known when training older participants. It would then seem possible that older individuals involved in resistance training might benefit from a combined program of Cr and protein (Pr) supplementation compared to individual supplementation or resistance training without any supplements.

The purpose of this study was to assess changes in upper body and lower body muscular strength of middle-aged and older men (age 48-72 yrs) following a 14-week resistance training program when combined with Pr and/or Cr supplementation. We hypothesized that all participants would benefit from the resistance training program by increasing muscular strength, but those who were supplemented with Cr, Pr, or both, would be able to augment their training improvements, especially for the combined Cr and Pr group.

### Subjects and Methods

#### Study Sample

Forty-two male subjects aged 48-72 years volunteered. Following a complete explanation of the purpose and

## THE EFFECTS OF SUPPLEMENTATION WITH CREATINE AND PROTEIN ON MUSCLE STRENGTH

procedures of the investigation, written informed consent was obtained from each subject as approved by the university's Institutional Review Committee (IRB). Subjects were healthy and had not resistance trained for at least the previous 12 months and those aged 55 and older were required to obtain medical approval from their own personal physicians. Subjects were then randomly assigned into one of four groups; 1) resistance training placebo (RTP,  $n=10$ , mean age  $56.1\pm1.4$  years, mean height  $177.0\pm1.8$  cm, mean weight  $98.0\pm7.6$  kg); resistance training with creatine (RTC<sub>r</sub>,  $n=10$ , mean age  $56.1\pm1.8$  years, mean height  $177.4\pm2.4$  cm, mean weight  $91.1\pm5.2$  kg); resistance training with protein (RTP<sub>r</sub>,  $n=11$ , mean age  $58.2\pm2.0$  years, mean height  $175.6\pm2.0$  cm, mean weight  $88.3\pm4.4$  kg); or resistance training with creatine and protein (RTC<sub>r</sub>Pr,  $n=11$ , mean age  $57.2\pm2.2$  years, mean height  $179.6\pm2.3$  cm, mean weight  $92.6\pm5.1$  kg). Based on numerous previous studies (7, 11, 15, 16, 17) it was determined that a minimum of 10 subjects for each group would be needed to achieve a statistical power of 0.80, thus reducing the chance of making a Type II error for our study (18).

### ***Dietary Analysis and Supplementation Protocol***

Following individual educational sessions utilizing food models, conducted by a registered dietician, total daily energy intake was estimated by use of a three-day dietary log at baseline and at the end of the training program (19). Food records were analyzed for energy nutrient content using Food Works 2.0 nutrition software (McGraw Hill). Based on many previously published reports, subjects then began a two week constant loading phase for the supplementation portion of this study (20-24). This was only necessary for the individuals in the two Cr groups (RTC<sub>r</sub> and RTC<sub>r</sub>Pr); however, to maintain the double blind condition, the other two groups (RTP and RTP<sub>r</sub>) also went through a loading phase consisting only of the placebo (480 mL of Gatorade™). Gatorade was chosen as the placebo since it is commonly consumed during exercise sessions and it has no, or only minimal, protein sparing effects as a potential ergogenic aid. The RTC<sub>r</sub> and the RTC<sub>r</sub>Pr groups loaded 7 g of creatine monohydrate with 480 ml of the glucose solution (Gatorade™) on each of 3 days per week for the 2 weeks prior to the training intervention. Once training began, the RTP group consumed the placebo (480 ml of Gatorade™), the RTC<sub>r</sub> group consumed (5g Creatine with 480 ml Gatorade™), the RTP<sub>r</sub> group consumed (35g whey protein (Old Fashioned Natural Products, Santa Ana, CA) with 480 ml of Gatorade™), and the RTC<sub>r</sub>Pr group consumed (5g creatine and 35g whey protein with 480 ml Gatorade™) immediately after each supervised training session (25). A research assistant administered supplementation and ensured that each subject completed the ingestion of their drink in a timely fashion following the completion of each training session.

### ***Testing Procedures***

In order to determine baseline levels of muscular strength and appropriate training loads for each muscle group used in

the training program, a standardized one repetition maximum (1RM) protocol was utilized one week prior to training, at week 5 and week 10 of training, and post training. Each subject was instructed on proper lifting technique and the basic fundamentals of training. Cybex® isotonic resistance training equipment (Ronkonkoma, New York) was used for all testing and training. Prior to the initial strength testing, subjects warmed up by cycling on a cycle ergometer, or walking on a treadmill for five minutes, and then performed flexibility exercises for another five to ten minutes. At each piece of resistance training equipment, the subject warmed up using a weight of approximately 50% of their estimated 1RM for a total of five to six repetitions. Subjects then attempted to lift a heavier load until they achieved their maximum weight that they were able to lift. Testing was completed within five attempts and each attempt was separated by one minute of rest. The exercises and muscle groups used during the training protocol, as well as 1RM testing included: knee extensions from a seated position (quadriceps); knee flexion from a seated position (hamstrings); bicep curls from a seated position (biceps); tricep extension from a seated position (triceps); military press from a seated position (deltoids); lat pull downs from a seated position (latissimus dorsi); seated leg press (gluteus maximus and quadriceps); and bench press (pectoralis major), using a Smith Press Machine. Day to day reliability for 1RM measures for our laboratory are between  $r=0.95$  and  $r=0.99$  with coefficients of variation between trials less than 1%.

Changes in lean body mass were assessed by Dual Energy X-ray Absorptiometry (DXA Lunar DPX-IQ) and were reported in a separate publication (19). The coefficient of variation for DXA measures of lean body mass is 1.39% for our laboratory.

### ***Intervention***

The resistance training program incorporated the overload principle and was monitored by trained supervisors to ensure compliance and accuracy. The overload principle ensured that as strength improved for these individuals, workloads were increased to ensure continued adaptations occurred. The training groups met three times per week (Monday, Wednesday, Friday) and performed three sets of eight repetitions at 80% of 1RM for each exercise that was initially strength tested (26). The session began with approximately five minutes of warm up on a cycle ergometer or treadmill, followed by five to ten minutes of flexibility training. Following the warm up period, the resistance training protocol began with subjects beginning with the largest muscle groups and alternating between upper and lower body exercises and recording the number of completed repetitions and sets. Training logs were maintained by each participant that indicated the numbers of repetitions, sets, and loads that were completed for any given workout session. These logs were then reviewed at the end of each day by the training staff. The sessions ended with five to ten minutes of cool down and each session lasted

## JNHA: CLINICAL TRIALS AND AGING

approximately one hour in total. The maximal strength (1RM) for each exercise was re-assessed at weeks 5 and 10 of the training program and the weights were adjusted the following week to ensure progressive overload was maintained throughout the entire training period.

### Statistical Analyses

All data are reported as means + SE, as well as percent change  $\{[(\text{post value} - \text{pre value})/\text{pre value}] \times 100\}$ . Statistical analyses were performed using SPSS 10.0 for Windows. Baseline comparisons between the groups were accomplished by a one way ANOVA. Treatment effects on muscular strength were determined using a two-way (Group (4; RTP, RTCr, RTPr, RTCrPr) X Trial (4; pre, 5 wks, 10 wks, post)) ANOVA with repeated measures and a Bonferroni paired samples procedure was used as a post-hoc test when significant group effects were found. Group differences for percent (%) change in the dependent variables following training were determined by a one-way ANOVA. Statistical significance was set at an alpha level of  $p \leq 0.05$ .

## Results

### Baseline Measures

At baseline, there were no significant differences in age, height, or weight between the four training groups. As mentioned earlier, three day food journals were kept by each participant prior to beginning the resistance training and at the end of the study. Previously published data reported that there were no differences ( $p > 0.05$ ) between the four groups at the beginning of the training study or at the end regarding any of the dietary parameters of interest (total calories consumed and percentages of fat, carbohydrate and protein) (19). Additionally, there were no significant differences ( $p > 0.05$ ) between the four groups for any baseline measures of isotonic strength for the eight exercises chosen for the training program or for measures of bone-free lean body mass as measured by Dual Energy X-ray Absorptiometry (19).

### Training Effects

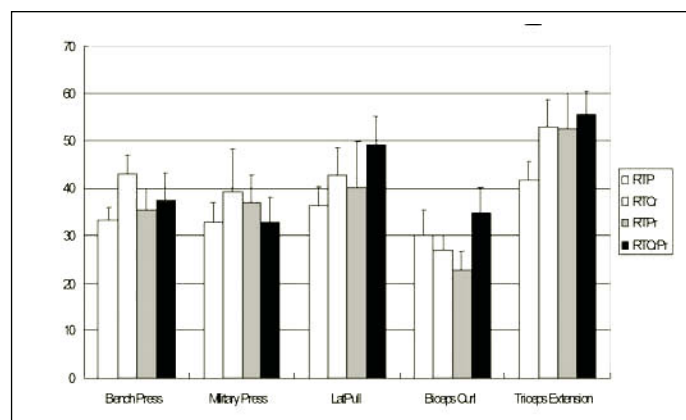
Significant trial effects ( $p < 0.01$ ), but no significant group effects were noted for each muscular strength variable. Only one group X trial interaction (knee extension,  $p < 0.05$ ) was determined for the eight muscle groups that were trained. The two Pr supplemented groups (RTPr and RTCrPr) had significantly larger increases than the other two groups.

Figures 1a and 1b provide the percent improvements in 1RM strength from baseline to post training for each of the eight exercises performed during the training program and for each of the four groups. There were no differences detected between the four groups in their improvements for each of the exercises performed following the resistance training program with the exception of the knee extensors, as mentioned above. The 2 Pr supplemented groups had a significantly greater increase in strength (~75%) compared to the RTP and RTCr groups

(~50%) for knee extension. Percent improvements ranged from about 30% for the bicep curl (averaged across the four training groups) to about 63% for knee extension.

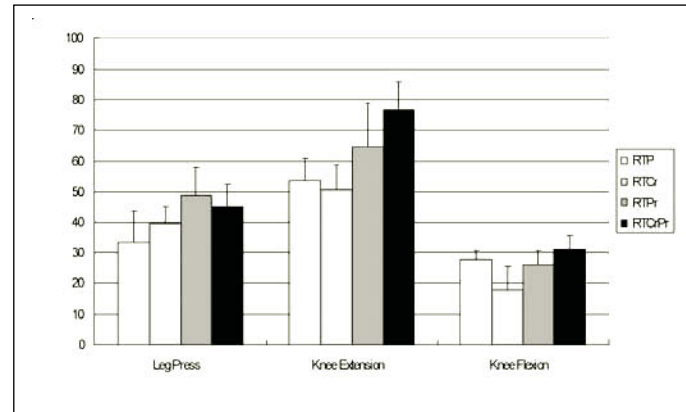
**Figure 1a**

Percent Changes in Upper Body Muscular Strength from Baseline for each Training Group



**Figure 1b**

Percent Changes in Lower Body Muscular Strength from Baseline for each Training Group



## Discussion

This study investigated changes in upper body and lower body muscular strength of older men (age 48-72 yrs) following a 14-week resistance training program combined with whey protein (Pr) and/or creatine monohydrate (Cr) supplementation. The significant increases in muscular strength for the four groups following training was expected, which indicates a successful overload stress stimulus during the training period.

Resistance training in the young and old has been proven to be effective in achieving muscular strength gains, primarily due to adaptations of the neuromuscular system, in as little as a few weeks of training. In fact, Short and Nair (10) reported one week of resistance training alone was sufficient enough to stimulate protein synthesis and result in improved muscular

## THE EFFECTS OF SUPPLEMENTATION WITH CREATINE AND PROTEIN ON MUSCLE STRENGTH

strength in older subjects. Schulte and Yarasheski (9) also reported in only two weeks of vigorous training in older subjects that a doubling in the synthesis rate of myosin heavy chain protein synthesis can occur and result in increased muscular strength. Skeletal muscle hypertrophy, on the other hand, is generally achieved through prolonged training, and was expected with the current protocol. In fact, previously published data reported the changes in muscular strength in the current study were accompanied by significant ( $p < 0.01$ ) increases in the bone-free lean body mass of the arms (mean percent increase = 6.6%) and legs (mean percent increase = 1.8%) for each of the four exercise groups (19). However, the lack of an augmented muscle strength or muscle hypertrophy for the Cr and Pr supplemented groups was somewhat surprising, considering the evidence that the training stimulus, the duration of the training protocol, and the dietary supplements could be considered sufficient enough to result in greater improvements (27). A possible limitation of our research design which may have affected the group changes in strength was that the work performed during any given training session was predetermined for each participant. In other words, since each subject followed a specific workout protocol, even if supplementation with Cr, Pr, or both, allowed for a quicker recovery time between sets or exercises, subjects were not allowed to do additional exercise.

Many investigators who have examined the influence of Cr supplementation during resistance training in young subjects, generally reported significant increases in strength, lean tissue mass and body weight (23-31), however, there is the possibility that a given subject pool may contain non-responders (32). The findings of the current study do agree with Bermon et al. (33) and Eijnde et al. (34) who concluded that oral Cr supplementation did not provide additional benefits for fitness, maximal dynamic strength, or isometric endurance in healthy, elderly, male or female subjects, when accompanied by an effective strength training program. The short, two month program in that study could be a primary reason for the lack of significant benefit from the Cr supplemented groups; however, our program which was twice as long, also found no additional benefits of Cr supplementation for this population. Additionally, Stevenson and Dudley (24) also indicated that Cr loading did not augment unilateral strength or multi-set resistance exercise performance when compared to training done in older adults. Subjects in the current study were only required to supplement on training days, therefore, when sessions were missed, supplementation was also missed. No beneficial effects of Cr have also been reported in different athletic groups. Ahmun et al. (35) reported no improvement in rugby players following Cr supplementation (5 g, 4Xdaily, for 5 days) and Hoffman et al. (36) used 6g/day for 6 days and also found no effect on power outputs but they did report a decreased rate of fatigue. Generally, the literature is not clear on whether or not daily Cr supplementation during a training program is necessary in order to achieve maximal benefits from the training, or if supplementing only on the training days is

just as effective.

Our results are also somewhat similar to Deldicque et al. (37) who reported that Cr supplementation did not enhance protein synthesis more than exercise alone. They reported that Cr supplementation did increase the expression of IGF-1 at rest but was not increased following exercise and that any increase in muscle growth was probably due to the enhancement of the anabolic status of the cell and involved IGF. On the other hand, Dorofeyeva and Dorofeyev (38) found that amino acid supplementation increased the adaptation of athletes undergoing extensive exercise training. However, these subjects were much younger, highly trained, and exercised at a much higher intensity than the subjects in the current study. In a study that augmented Cr supplementation with carbohydrates, Theodrou et al. (39) reported there was no added advantage to the carbohydrate plus Cr supplemented group when compared to the Cr only group concerning maximal swim times.

In another study that utilized both Cr and protein supplementation, Burke et al. (3) reported that young males who received a whey protein supplement (similar to the current study) in combination with resistance training had slightly greater increases in lean tissue mass compared to males who trained and received placebo, while those who supplemented with both Cr and Pr had greater increases in lean tissue mass and strength than those that supplemented with only Pr or a placebo. A possible explanation for the current study not showing similar results could be that older people have been reported to have a lower resting muscle phosphocreatine concentration compared to younger people (13). An increase in the percentage of Type I fibers within skeletal muscle occurs with increased age and may explain reduced resting phosphocreatine concentrations found in older subjects. However, the creatine loading protocol in the current study should have been sufficient to ensure that cellular PCr levels were increased prior to beginning the exercise intervention (40). There were however, some significant design differences between the current study and the Burke et al. study (3) that might explain the differences in finding between the two studies. Participants in the Burke et al. study (3) were significantly younger males, were resistance trained, and the supplement dose differed (8 g Cr per day, and 96 g Pr; Burke et al. (3) versus 5 g Cr per day, and 35 g Pr; current study).

## Conclusion

In general, strength and hypertrophy designed resistance training programs can be successful for older men (aged 48-72 years) when based on the concept of progressive overload, however, when the training program is tightly controlled regarding loads, sets, and repetitions, there is no indication that this particular age group can augment their exercise benefits by supplementing with creatine or protein.

*Acknowledgments:* We would like to thank the Gatorade Sports Sciences Institute for partially funding this project.



*Financial disclosure:* None of the authors had any financial interest or support for this paper.

## References

1. Roubenoff R, Hughes V. Sarcopenia: Current Concepts. *J Gerontol Medical Series A* 2000; 55A: M716-M724.
2. Hunter G, McCarthy J, Bamman M. Effects of resistance training on older adults. *Sports. Med* 2004; 34(5): 329-348.
3. Burke D, Chilibeck P, Davison K, Candow D, Farthing J, Smith-Palmer T. The effect of whey protein supplementation with and without creatine monohydrate combined with resistance training on lean tissue mass and muscle strength. *Int J Sport Nutr Exerc Metab* 2001; 11: 349-364.
4. Campbell W, Crim M, Dallal G, Young V, Evans W. Increased protein requirements in the elderly; New data and retrospective reassessments. *Am J Clin Nutr* 1994; 60:501-509.
5. Campbell W, Crim M, Young V, Joseph J, Evans W. Effects of resistance training and dietary protein intake on protein metabolism in older adults. *Am J Physiol* 1995; 268: E1143-E1153.
6. Hartman J, Tang J, Wilkinson S, Tarnopolsky M, Lawrence R, Fullerton A, Phillips S. Consumption of fat-free fluid milk after resistance exercise promotes greater lean mass accretion than does consumption of soy or carbohydrate in young, novice, male weightlifters. *Am J Clin Nutr* 2007; 86(2): 373-381.
7. Kerkick C, Rasmussen C, Lancaster S, Magu B, Smith P, Melton C, Greenwood M, Almada A, Earnest C, Kreider R. The effects of protein and amino acid supplementation on performance and training adaptations during ten weeks of resistance training. *J Strength Cond Res* 2006; 20(3): 643-653.
8. Lemon P, Tarnopolsky M, Macdougall J, Atkinson S. Protein requirements and muscle mass/strength changes during intensive training in novice bodybuilders. *J Appl Physiol* 1992; 73:767-775.
9. Schulte J, Yarasheski K. Effects of resistance training on the rate of muscle protein synthesis in frail elderly people. *Int J Sport Nutr Exerc Metab* 2001; 11: S111-S118.
10. Short K, Nair K. Muscle protein metabolism and the sarcopenia of aging. *Int J Sport Nutr Exerc Metab* 2001; 11: S119-S127.
11. Tarnopolsky M, Parise G, Yardley N, Ballantyne C, Olatunji S, Phillips S. Creatine-dextrose and protein-dextrose induce similar strength gains during training. *Med Sci Sports Exerc* 2001; 33(12): 2044-2052.
12. Rawson, E, Wehnert M, Clarkson P. Effects of 30 days of creatine ingestion in older men. *Eur J Appl Physiol* 1999; 80: 139-144.
13. Smith S, Montain S, Matott R, Zientara G, Jolesz F, Fielding, R. Creatine supplementation and age influence muscle metabolism during exercise. *J Appl Physiol* 1998; 85: 1349-1356.
14. Greenhaff P. The nutritional biochemistry of creatine. *J Nutr Biochem*, 11: 1997: 610-618.
15. Brose A, Parise G, Tarnopolsky M. Creatine supplementation enhances isometric strength and body composition improvements following strength exercise training in older adults. *J Gerontol, Series A* 2003; 58: B11-B19.
16. Cribb P, Williams A, Stathis C, Carey M, Hayes A. Effects of whey isolate, creatine, and resistance training on muscle hypertrophy. *Med Sci Sports Exerc* 2007;39(2): 298-307.
17. Olsen S, Aagaard P, Kadi F, Tufekovic G, Verney J, Olesen J, Suetta C, Kjaer M. Creatine supplementation augments the increase in satellite cell myonuclei number in human skeletal muscle induced by strength training. *J Physiol* 2006; 573(2): 525-534.
18. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edition. 1988 Lawrence Erlbaum Associates, Hillsdale NJ.
19. Eliot K, Knehans A, Bemben D, Witten M, Carter J, Bemben M. The effects of creatine and whey protein supplementation on body composition in men aged 48 to 72 years during resistance training. *J Nutr Health Aging* 2008; 12(3): 208-212.
20. Wilder N, Deiuert R, Hagerman F. The effects of low dose creatine supplementation versus creatine loading in collegiate football players. *J Athl Train* 2001; 36(2):124-129.
21. Wilder N, Gilders R, Hagerman F. The effects of a 10 week, periodized, off-season resistance-training program and creatine supplementation among college football players. *J Health res* 2002;16(3): 343-352.
22. Bemben M, Bemben D, Loftiss D. Creatine supplementation during resistance training in college football athletes. *Med Sci Sports Exerc* 2001; 33(10): 1667-1673.
23. Becque M, Lochmann J, Melrose D. Effects of oral creatine supplementation on muscular strength and body composition. *Med Sci Sports Exerc* 2000;32: 654-658.
24. Stevenson S, Dudley G. Creatine loading, resistance exercise performance, and muscle mechanics. *J Strength Cond Res* 2002; 15(4): 413-419.
25. Esmarck B, Anderson J, Olsen S, Richter E, Mizuno M, Kiaer M. Timing of post exercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. *Am J Physiol* 2001; 282(1): 301-311.
26. American College of Sports Medicine Position Stand – Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009; 41(3): 687-708.
27. Candow D, Little J, Chilibeck P, Abeysekara S, Zello G, Kazachkov M, Cornish S, Yu P. Low-dose creatine combined with protein during resistance training in older men. *Med Sci Sports Exerc* 2008; 40(9): 1645-1652.
28. Earnest C, Snell P, Mitchell T, Rodriguez R, Almada A. Effect of creatine monohydrate ingestion on peak anaerobic power, capacity, and fatigue index. *Med Sci Sports Exerc*, 1994; 26: S39.
29. Kreider R, Ferreira M, Wilson M, Grindstaff P, Plisk S, Reinardy J, Cantler E, Almada A. Effects of creatine supplementation on body composition, strength, and sprint performance. *Med Sci. Sports Exerc* 1998; 30: 73-82.
30. Volek J, Kraemer W, Bush J, Boetes M, Incledon T, Clark K, Lynch J. Creatine supplementation enhances muscular performance during high-intensity resistance exercise. *J Am Diet Assoc* 1997; 97: 765-770.
31. Volek J, Duncan N, Mazzetti S, Staron R, Putukian M, Gomez A, Pearson D, Fink W, Kraemer W. Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training. *Med Sci Sports Exerc* 1999; 31: 1147-1156.
32. Syrotuik D, Bell G. Acute creatine monohydrate supplementation: A descriptive physiological profile of responders vs. nonresponders. *J Strength Cond Res* 2004; 18(3): 610-617.
33. Bermon S, Venembre P, Sachet C, Valour S, Dolisi C. Effects of creatine monohydrate ingestion in sedentary and weight-trained older adults. *Acta Physiol Scand* 1998; 164: 147-155.
34. Eijnde B, Leemputte M, Goris M, Labarque V, Taes Y, Verbessem P, Vanhees L, Ramaekers M, Eynde B, Van Schuylenbergh R, Dom R, Richter E, Hespel P. Effects of creatine supplementation and exercise training on fitness in men 55-75 yr old. *J Appl Physiol* 2003; 95: 818-828.
35. Ahmun R, Tong R, Grimshaw P. The effects of acute creatine supplementation on multiple sprint cycling and running performance in rugby players. *J Strength Cond Res* 2005; 19(1): 92-97.
36. Hoffman J, Stout J, Falco M, Kang J, Ratamess N. Effect of low-dose, short-duration creatine supplementation on anaerobic exercise performance. *J Strength Cond Res* 2005; 19(2): 260-264.
37. Deldicque L, Louis M, Theisen D, Nielens H, Dehoux M, Thissen J-P, Rennie M, Francaux M. Increased IGF mRNA in human skeletal muscle after creatine supplementation. *Med Sci Sports Exerc* 2005; 37(5): 731-736.
38. Dorofeyeva E, Dorofeyev A. Biochemical and heart adaptations to physical training and supplementation with amino acids. *J Strength Cond Res* 2004; 18(4): 738-740.
39. Theodrou A, Havenetidis K, Zanker C, O'Hara J, King R, Hood C, Paradisis G, Cooke C. Effects of acute creatine loading with or without carbohydrate on repeated bouts of maximal swimming in high-performance swimmers. *J Strength Cond Res* 2005; 19(2): 265-269.
40. Bemben M, Lamont H. Creatine supplementation and exercise performance: Recent findings. *Sports Med* 2005; 35(2): 107-125.