Creatine Supplementation Enhances Isometric Strength and Body Composition Improvements Following Strength Exercise Training in Older Adults

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We sought to determine whether creatine monohydrate (CrM) supplementation would enhance the increases in strength and fat-free mass that develop during resistance exercise training in older adults. Twenty-eight healthy men and women over the age of 65 years participated in a whole-body resistance exercise program 3 days per week for 14 weeks. The study participants were randomly allocated, in a double-blind fashion, to receive either CrM (5 g/d + 2 g of dextrose; n = 14) or placebo (7 g of dextrose; n = 14). The primary outcome measurements included the following: total body mass, fat-free mass, one-repetition maximum strength for each body part, isometric knee extension, handgrip, and dorsiflexion strength, chair stand performance, 30-m walk test, 14-stair climb performance, muscle fiber type and area, and intramuscular total creatine. Fourteen weeks of resistance exercise training resulted in significant increases in all measurements of strength and functional tasks and muscle fiber area for both groups (p < .05). CrM supplementation resulted in significantly greater increases in fat-free mass and total body mass, as compared with placebo (p < .05). The CrM group also showed a greater increase in isometric knee extension strength in men and women, as compared with placebo (p < .05), and also greater gains in isometric dorsiflexion strength (p < .05), but in men only. There was a significant increase in intramuscular total creatine in the CrM group (p < .05). Finally, there were no significant side effects of treatment or exercise training. This study confirms that supervised heavy resistance exercise training can safely increase muscle strength and functional capacity in older adults. The addition of CrM supplementation to the exercise stimulus enhanced the increase in total and fat-free mass, and gains in several indices of isometric muscle strength.

Aging is associated with a reduction in total muscle mass and an increase in intramuscular fat and connective tissue. These changes are correlated with reduced strength, type II fiber area (1,2) and number (3), motor unit number (4), and circulating anabolic hormones (5–7). Aging also results in a progressive decline in functional capacity that leads to impaired mobility, increased risk of falls, a loss of independence, disability, and increased consumption of health care resources (8).

Countermeasures designed to maintain or enhance muscle mass and strength in aging may have important functional implications for older adults. The most effective non-pharmacological intervention identified is resistance exercise training, which has been consistently shown to partially reverse age-associated decrements in muscle strength and mass in older men and women (9–13). Importantly, improvements in functional capacity and independence have been documented following resistance training, even in very old men and women (14).

Creatine monohydrate (CrM) supplementation has been shown to accentuate gains in fat-free mass and strength in response to resistance training in young men and women (15–17). Intramuscular creatine concentrations are ~25% lower in older (18) and middle-aged adults (19) than in younger individuals. People with low intramuscular total creatine concentrations show an enhanced ability to increase intracellular creatine content following CrM supplementation (20). For example, increases in phosphocreatine (PCR) were greater in middle-aged than young individuals (19). Consequently, older adults may benefit more from a combination of resistance exercise and CrM supplementation than do young men (15,17) and women (16). Given the relative safety of CrM supplementation (21), it may be an efficacious, safe, and less expensive alternative to pharmacological interventions in the treatment of age-related sarcopenia.

A few studies have examined the effects of CrM on muscle function in older adults (19,22–26). Two have examined the potential for CrM to enhance the gains in strength and fat-free mass following a resistance training program (22,26), and they reported conflicting results. One study found that CrM supplementation did not enhance gains in strength induced by resistance training (22). In contrast, a more recent study found that CrM supplementation and resistance exercise training, as compared with resistance training alone, resulted in significantly greater increases in lean body mass and strength in elderly men (26). A limitation to the interpretation of both of these studies was the lack of any direct measurements of muscle fiber size or creatine content or any functional outcome.

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measurements. A final issue of importance was that in the positive study, only men were studied (26), whereas in the negative study, both men and women were evaluated (25). Gender is an important factor to consider, for we have found that during acute CrM supplementation, men show a greater increase in fat-free mass (27) and only men showed a reduction in amino acid oxidation and protein breakdown following CrM supplementation (28).

We hypothesized that CrM supplementation would enhance the resistance exercise-mediated increases in strength, functional capacity, muscle fiber area, and body composition in elderly men and women. In addition, we hypothesized that both the exercise training and the CrM supplementation would not result in significant side effects.

**METHODS**

**Subjects**

Fifteen men (67.8 ± 4.0 y) and 15 women (69.3 ± 6.3 y) volunteered to participate in a 14-week resistance training program. Each subject underwent a thorough screening, including a telephone interview, a medical evaluation, and a 12-lead electrocardiogram before and after progressive cycle ergometry to 6 METS (metabolic equivalents) on a mechanically braked cycle ergometer (Monarch, Sweden). Exclusion criteria included evidence of coronary heart disease; congestive heart disease; uncontrolled hypertension; chronic obstructive pulmonary disease; diabetes mellitus; renal failure; major orthopedic disability; and smoking. All the women were postmenopausal and were not taking hormone replacement therapy. The study was approved by the McMaster University Medical Ethics Committee.

Of the original 30 volunteers, 15 men and 13 women completed all aspects of the study. Two women in the creatine group dropped out during the training for personal reasons unrelated to the training or supplementation.

**Nutritional Supplementation**

Prior to training, subjects were randomly assigned in a double-blind manner to either a CrM (Neotine, Avicena, Cambridge, MA; 5 g of CrM + 2 g of dextrose/d for 14 weeks) or placebo (PL; 7 g of dextrose/d for 14 weeks) group. The CrM group consisted of 8 men and 6 women; the PL group consisted of 7 men and 7 women (Table 1). The flavor and appearance of the supplements were indistinguishable by the subjects and the investigators. Subjects were instructed to consume their supplement dissolved in juice and to return their empty sachets on a weekly basis to ensure compliance. A 3-day dietary record was completed prior to and after training (including the minimal contribution from the supplements). The diets were analyzed by using a commercially available program (Nutritionist V, First Data Bank, San Bruno, CA), and the subjects maintained similar dietary patterns during the study.

**Strength Training**

Training was conducted three times weekly on nonconsecutive days for 14 weeks. Each training session was preceded by a 5-minute warm-up and followed by stretching of the muscle groups involved in the resistance exercises. Twelve exercises were used to train the major muscle groups of the upper and lower body in a circuit set system, using weight training machines (Universal Gym Equipment Inc., Cedar Rapids, IA). Subjects performed 10 repetitions of each arm exercise and 12 repetitions of the remaining exercises. Training progressed from one set of each exercise at 50% of the initial one-repetition maximum (1 RM) strength to three sets at 80% of 1 RM over the training period. The 1 RM was reevaluated every 2 weeks, and the training loads were adjusted accordingly.

**Testing**

All testing procedures were conducted before and after 14 weeks of resistance training, with post-testing at 48 hours following the last exercise bout.

**Dynamic strength testing.**—Before initial strength testing, two low-intensity training sessions were completed to habituate the subjects to equipment and proper techniques. Prior to and after training, the 1 RM was used to assess strength in four different exercises (upright chest press, leg press, arm flexion, and knee extension). The preliminary 1 RM values were used to calculate the initial training load of 50% of 1 RM. In addition, at the end of the training program, each subject performed as many repetitions as possible with the pretraining 1 RM to provide a measure of endurance.
Table 2. Body Composition Before and After Training

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Creatine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBM (kg)*</td>
<td>84.1 ± 14.0</td>
<td>85.5 ± 13.5</td>
<td>65.4 ± 16.2</td>
<td>66.5 ± 16.8</td>
</tr>
<tr>
<td>FFM (kg)*</td>
<td>56.0 ± 7.1</td>
<td>57.4 ± 7.4</td>
<td>33.7 ± 3.7</td>
<td>35.7 ± 4.1</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>22.0 ± 5.4</td>
<td>22.3 ± 5.8</td>
<td>21.4 ± 9.7</td>
<td>17.3 ± 12.1</td>
</tr>
<tr>
<td>BF (%)</td>
<td>27.0 ± 3.9</td>
<td>26.8 ± 4.7</td>
<td>36.2 ± 11.8</td>
<td>34.2 ± 9.9</td>
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<tr>
<td><strong>Placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBM (kg)*</td>
<td>76.6 ± 9.8</td>
<td>76.2 ± 9.7</td>
<td>66.2 ± 14.0</td>
<td>66.2 ± 13.7</td>
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<tr>
<td>FFM (kg)*</td>
<td>52.0 ± 5.3</td>
<td>52.0 ± 5.8</td>
<td>37.2 ± 1.8</td>
<td>37.8 ± 2.0</td>
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<tr>
<td>FM (kg)</td>
<td>12.2 ± 2.9</td>
<td>12.1 ± 3.0</td>
<td>24.2 ± 11.2</td>
<td>23.9 ± 11.8</td>
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<tr>
<td>BF (%)</td>
<td>18.3 ± 2.1</td>
<td>18.1 ± 2.0</td>
<td>36.4 ± 11.2</td>
<td>35.5 ± 12.6</td>
</tr>
</tbody>
</table>

Notes: Values are means ± SD. TBM = total body mass; FFM = fat/bone-free mass; FM = fat mass; BF = body fat.

*Compared with women, men had high TBM and FFM and lower BF (p < .05).

Creatine monohydrate increases were greater than placebo (p < .05), because of a technical problem with the dual-energy x-ray absorptiometry. Men, creatine (n = 5); women, creatine (n = 5); men, placebo (n = 2); women, placebo (n = 4) for FFM, FM, and % BF. Men, creatine (n = 8); women, creatine (n = 6); men, placebo (n = 7); women, placebo (n = 7) for TBM.

**Isometric strength.**—Handgrip, ankle dorsiflexion, and knee extensor strength were measured by using custom-made isometric devices as previously described (29,30). For each measurement, subjects performed three maximal 5-second voluntary contractions with 1 minute of rest between each of three attempts. The highest peak torque value of each of the attempts was recorded as the maximal isometric strength value.

**Functional testing.**—Three functional ability tests were performed before and after training. The 30-second chair stand test required subjects to rise up and sit down for 30 seconds with arms folded in front of their chests as quickly as possible on a firm, armless chair placed against a wall (31). The timed stair climb required subjects to walk as fast as possible up 14 stairs without the use of railings. The timed walk required subjects to walk a distance of 30 m as fast as possible without the use of external aids. Participants completed each of the functional tests as part of an initial familiarization trial during the recruitment phase. The functional tests were all measured by the same evaluator and were timed to the nearest 0.1 second by using an electronic stopwatch.

**Body composition assessment.**—Body mass and height were measured to the nearest 0.1 kg and 0.5 cm, respectively, using a calibrated electronic scale (Healthometer Pro Series Electronic Scale, Bridgeview, IL). A total body dual-energy x-ray absorptiometry (DEXA) scan (Hologic QDR 4500A, Waltham, MA) was used to determine body fat percentage (%BF), fat mass (FM), fat/bone-free mass (FFM), and bone mineral content (BMC), using the Hologic software program (V.8.26a).

**Muscle, blood, and urine collection.**—Muscle biopsies (~100 mg) were obtained from the vastus lateralis muscle of the dominant leg under local anesthesia (1% lidocaine) with a modified Bergström biopsy needle. One section was mounted in embedding medium (OCT, Tissue-Tek, Torrance, CA), cut, and stained with myosin adenosine triphosphatase (ATPase) at pH 4.3 and 10.1 for fiber type discrimination, as previously described (32). An average of 425 ± 102 (range 252–683) fibers were counted per biopsy for determination of muscle fiber type and mean fiber area.

A second piece of muscle (~10–30 mg) was frozen in liquid nitrogen and stored at −80°C for subsequent determination of creatine (Cr), PCr, and adenosine triphosphate (ATP) concentrations as previously described (33). Intra-assay coefficient of variation (CV) for ATP, PCr, and Cr were 7.3%, 8.5%, and 8.4%, respectively.

Blood was drawn from an antecubital vein into 10-ml nontreated tubes and allowed to clot (serum), and into 5-ml ethylenediamine tetra-acetic acid (EDTA)-treated tubes (plasma). After centrifugation, serum and plasma were stored at −70°C for subsequent analysis of total testosterone (TT), insulin-like growth factor-1 (IGF-1), dehydroepiandrosterone sulfate (DHEAS), and osteocalcin (OC), using radioimmunoassays (Coat-A Count, Diagnostics Products, Los Angeles, CA; OC, Biomedical Technologies, Stoughton, MA; IGF-1, Alpc Diagnostics, Windham, NH). Creatine kinase activity (CK), gamma-glutamyl transferase activity (γGT), and creatinine (Crm) were measured in serum (Kodak, Ektachem, Rochester, NY). Thereafter, a urine sample was collected for subsequent analysis of Crm and Cr by using a standard picric acid method.

**Statistical Analysis**

Values are reported as mean ± SD. All statistics were performed by using a commercially available software program (V5.0, Statistica, Statsoft, Tulsa, OK). All variables were analyzed by using a three-way, repeated-measures analysis of variance: a 2 (condition: Cr vs PL) × 2 (time: before vs after training) design, with repeated measures on the last factor. A level of p < .05 was used to determine significance, and significant differences were further analyzed by using Tukey’s post hoc test.

**RESULTS**

**Subject Characteristics and Body Composition**

The treatment groups were comparable in baseline age, height, weight, %BF, and FFM. Compared with women, men were taller, had greater FFM, total body mass (TBM), and lower %BF, and they had higher daily energy (kilocalories per day) intake (p < .05), with no between-group differences in energy intake or in the proportions of...
protein, fat, and carbohydrate. Nutritional intake was unchanged during the training period (Tables 1 and 2).

There was a greater increase in TBM (1.2 ± 1.7 kg) and FFM (1.7 ± 1.2 kg) for CrM supplementation, as compared with PL (TBM, −0.2 ± 1.3 kg; FFM, 0.4 ± 0.5 kg) following exercise training (Table 2; p < .05). The %BF and fat mass did not change after the training for either group.

**Muscle High-Energy Phosphates**

At baseline, muscle-free Cr, PCr, and total creatine (TCr) were not different between groups; nor were there any gender differences. CrM supplementation increased muscle TCr by 27.0% (men: before, 116.8 ± 14.5 mmol kg⁻¹ vs after, 159.3 ± 23.9 mmol kg⁻¹; women: before, 129.7 ± 25.4 mmol kg⁻¹ vs after, 151.7 ± 18.7 mmol kg⁻¹) with no increases in the PL group (Group × Time interaction, p < .01). In addition, the increase in TCr was greater for men than for women (Group × Gender × Time interaction, p < .05). CrM supplementation also increased muscle PCr in men only (p < .05), and it had no effect on free Cr or ATP concentrations (Table 3).

**Isometric Strength**

At baseline, there were no between-group differences for any of the isometric strength measures. The men were stronger than the women in all three exercises (p < .001). The increase in knee extensor strength was greater for the CrM group (46.2 ± 22.5%) than for the PL group (22.5 ± 14.4%) for both genders (Group × Time interaction, p < .05). There was an increase in dorsiflexion in the CrM group only for the men (17.8 ± 11.6% vs PL 2.2 ± 5.6%; Group × Time × Gender interaction, p < .05). There was no effect of training or supplementation on handgrip strength (Table 4).

**Dynamic Strength**

Following training, 1 RM increased in all four exercises, with no differential increases between treatments (p < .001; Table 4). Compared with the men in the PL group, the men in the CrM group had a significantly higher arm flexion 1 RM (p < .05). There were no other between-group differences in baseline 1 RM for the remaining strength measures. The men had greater maximum voluntary muscle strength (1 RM) than the women on all four exercises tested (p < .001; Table 4). The male subjects improved their absolute 1 RM more than the female subjects in both the arm flexion and seated chest press (Gender × Time, p < .05). The absolute endurance increased after training, such that subjects were able to lift their pretraining 1 RM an average of 31, 13, 13, and 12 times, in the leg press, knee extension, arm flexion, and chest press, respectively (p < .001).

**Muscle Histology**

Fiber type distribution was not altered by training for any group. Type I, type IIa, and type IIx mean fiber areas were greater in men than in women (p < .05). There was an increase in the mean fiber area for type I (p < .05) and type IIx (p < .001) fibers, but not type IIa fibers, following training. The mean fiber area increased more in the type IIx fibers than in type I fibers with training; consequently, there was an increase in the type IIx:type I area ratio (p < .05). In addition, the men had a greater percentage area of type IIx fibers (p < .05) and smaller percentage area of type I fibers (p < .05) than the women (Table 5).

**Functional Measures**

The number of chair stands that could be performed in 30 seconds after training increased by 3.5 repetitions for CrM (25%) and 2.9 repetitions for PL (21%; p < .001 main effect for training). Training decreased the 30-m walk time by 1.7 seconds for the CrM group (10%) and 1.5 seconds for the PL group (9%; p < .001 main effect for training). The time to climb 14 stairs was improved by an average of 1.0 seconds for the CrM group (15%) and 1.5 seconds for PL (22%; p < .001 main effect for training). There were no significant main effects or interactions involving the treatment interventions in any of the functional measurements. Male subjects were overall faster than female subjects at the stair climb (p < .05).

**Blood and Urine Analyses**

Plasma Crn concentration increased for the CrM group following training (men, 13% increase; women, 22% increase; p < .05). Plasma CK activity was also higher in the CrM group after training as compared with the PL group (p < .05). The urine Cr:Crn ratio was greater after training in the CrM supplemented group (p < .05). Neither CrM supplementation nor resistance training altered any of the measured hormone concentrations (Table 6).
The current study showed improvements following the method for strength development in older adults. High-intensity resistance training is a safe and effective approach, as demonstrated in the present study (10,34–36). Furthermore, the observations are consistent with data reported in the literature. Improvements were observed in all exercises, which ranged from 26% to 60%, indicating the benefits of CrM supplementation in strength development.

The current results suggest that further research is needed to determine whether CrM supplementation has sustained effects in dwelling older adults. CrM supplementation increased intramuscular total Cr, and it enhanced the exercise-induced gains in TBM, FFM, isometric knee extension in both men and women, and isometric dorsiflexion strength in men. This study demonstrated that 14 weeks of resistance training increased muscle strength, muscle fiber area, and performance on functional tasks in healthy, community-dwelling older adults. CrM supplementation increased intramuscular total Cr, and it enhanced the exercise-induced gains in TBM, FFM, isometric knee extension in both men and women, and isometric dorsiflexion strength in men.

Together, these results confirm that (a) resistance training is an effective countermeasure to sarcopenia and strength loss, and (b) CrM supplementation combined with strength training increased TBM and FFM and improved some of the isometric strength measures as compared with placebo. The ability of older adults to reverse these losses in strength and function through strength exercise training, and the ability of CrM supplementation to enhance these improvements, may ultimately be reflected by an improved quality of life in older adults. The current results suggest that further investigation with a longer intervention duration and a larger sample size is justified to determine whether or not there are beneficial effects of CrM supplementation in strength-trained older adults and whether these are maintained for a longer period of time.

In the present study there were increases in strength for all exercises, which ranged from 26% to 60%. These observations are consistent with data reported in the literature in which older adults trained under similar conditions as in the present study (10,34–36). Furthermore, no injuries were reported during training, confirming that high-intensity resistance training is a safe and effective method for strength development in older adults.

The measurements of functional capacity used in the current study all showed improvements following the strength training program. The 11% improvement in walking speed was consistent with the findings reported by other investigators (35,37). We also reported a significant improvement in the 30-second chair stand, a test that is thought to reflect lower body strength. Other studies evaluating the effect of resistance training on sit-to-stand performance have reported equivocal results (12,37,38), likely attributable to methodological differences and the inherent variability in functional assessments (compared with objective strength measurements). We also found reductions in the time to climb 14 stairs (24%), which confirmed a previous report showing an improvement in stair-climbing performance in community-dwelling older adults following 10 months of resistance training (39). Together, these results suggest that resistance exercise training improves muscular strength, which ultimately can enhance functional tasks that have relevance to activities of daily living.

For example, lower body muscle weakness results in a deterioration of walking speed, and the ability to stairs climb and rise from a chair (40,41), and nursing home residents with a history of falls demonstrated significantly lower dynamic strength measurements of the knees and ankles when compared with nonfallers (42). Ultimately, the practicality of these observations comes from studies that demonstrated a correlation between declining strength and an increased prevalence of falls and fractures (43,44).

CrM supplementation during 4 months of resistance training enhanced the improvements in several measures of isometric strength. CrM supplementation further augmented knee extensor strength by 24% in both men and women and dorsiflexion strength by 18% in the men following resistance training but did not affect maximal isometric handgrip strength. The disparity between our results for 1 RM strength and isometric strength may be explained by the increased sensitivity associated with our custom-built isometric devices. These devices allow us to isolate a muscle group and control for all extraneous movements, reducing the variability in strength measurement. The test–retest reliability for our custom-made strength devices is 0.5–2.0%, which is less than that for conventional weight

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**Table 4. Isometric and 1 RM Measurements Before and After Training**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Creatine Men*</th>
<th>Creatine Women</th>
<th>Placebo Men*</th>
<th>Placebo Women</th>
</tr>
</thead>
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<tr>
<td>Knee extension (N m)</td>
<td>153 ± 28</td>
<td>217 ± 36(^{\text{i}})</td>
<td>94 ± 38</td>
<td>126 ± 30(^{\text{j}})</td>
</tr>
<tr>
<td>Dorsiflexion (N m)</td>
<td>54 ± 14</td>
<td>62 ± 15(^{\text{i}})</td>
<td>37 ± 4</td>
<td>40 ± 6</td>
</tr>
<tr>
<td>Grip (kg)</td>
<td>438 ± 63</td>
<td>469 ± 98</td>
<td>259 ± 67</td>
<td>259 ± 76</td>
</tr>
<tr>
<td>1 RM (lb)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seated chest press</td>
<td>116 ± 26</td>
<td>146 ± 33(^{\text{k}})</td>
<td>48 ± 11</td>
<td>63 ± 21(^{\text{l}})</td>
</tr>
<tr>
<td>Arm flexion</td>
<td>81 ± 22(^{\text{j}})</td>
<td>112 ± 18(^{\text{k}})</td>
<td>25 ± 7</td>
<td>40 ± 11(^{\text{l}})</td>
</tr>
<tr>
<td>Leg press</td>
<td>194 ± 47</td>
<td>244 ± 55(^{\text{j}})</td>
<td>111 ± 28</td>
<td>153 ± 54(^{\text{l}})</td>
</tr>
<tr>
<td>Knee extension</td>
<td>119 ± 18</td>
<td>162 ± 24(^{\text{i}})</td>
<td>71 ± 10</td>
<td>113 ± 22(^{\text{j}})</td>
</tr>
</tbody>
</table>

*Notes: Values are means ± SD. 1 RM = one repetition maximum.

*Men were stronger than women on all strength measures (p < .001); \(^{\text{i}}\) indicates a training-induced increase in strength (p < .01); \(^{\text{j}}\) indicates a greater increase in strength for the creatine monohydrate supplemented groups (p < .05); \(^{\text{k}}\) indicates a Group × Gender × Time interaction, with the men in the creatine group showing a significant increase after training (p < .05); \(^{\text{l}}\) the men increased strength by a larger amount compared with the women (p < .05).
The effect of resistance exercise training on FFM in older adults has produced conflicting results. Whereas some studies have reported significant increases in FFM following resistance training (12,13,45), others have reported no increase in FFM (9,22). These equivocal results may be explained by exercise intensity and duration, as well as the precision of measurement. Studies reporting no change in FFM following resistance training have used skinfolds (22) and hydrodensitometry (9) to estimate muscle mass. It is possible that these techniques are not sensitive enough to detect subtle changes in body composition following resistance training (46). In contrast, studies using more sensitive measures to determine body composition such as DEXA (12,13,47) and computerized tomography (11,34,43) have reported increases in FFM following resistance exercise training. In the present study, we did not detect any changes in FFM following resistance exercise training in the PL group; however, the CrM group did show an increase in TBM and FFM as determined by DEXA.

A limited number of studies have investigated the potential benefits of CrM supplementation on body composition in older adults (22,24–26). Most of these studies have been carried out in men and have generated equivocal findings. Rawson and colleagues reported that 30 days of CrM supplementation, without exercise training, did not affect body composition as determined by hydrostatic weighing (25). In addition, 8 weeks of CrM supplementation, with or without resistance exercise training, did not alter anthropometrically determined body composition (22). Our findings are in agreement with a recent study that reported that strength training in conjunction with CrM supplementation induced greater increases in TBM and FFM as compared with strength training without supplementation (26). The increase in TBM and FFM following chronic CrM supplementation combined with resistance training is comparable with findings of other studies in young men (15,17) and women (16).

The underlying mechanism(s) explaining the increase in TBM and FFM following CrM supplementation remain to be elucidated. Several potential mechanisms have been identified, including increased water retention (48–50), a Cr-stimulated increase in myofibrillar mRNA and protein content (51), or a reduction in whole-body amino acid content (51), or a reduction in whole-body amino acid content (51)
CREATINE INCREASES STRENGTH GAINS FOLLOWING TRAINING IN OLDER ADULTS

Table 6. Blood and Urine Analyses Before and After Training

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Men</th>
<th>Women</th>
<th>Placebo</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine</td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>Blood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT (nmol/l)*</td>
<td>15.4 ± 5.4</td>
<td>16.6 ± 4.9</td>
<td>0.7 ± 0.4</td>
<td>0.6 ± 0.4</td>
<td>19.3 ± 12.6</td>
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<tr>
<td>DHEAS (µmol/l)*</td>
<td>3.7 ± 2.0</td>
<td>3.0 ± 1.8</td>
<td>2.3 ± 1.3</td>
<td>1.8 ± 1.3</td>
<td>2.8 ± 1.5</td>
</tr>
<tr>
<td>IGF-1 (nmol/l)</td>
<td>10.5 ± 3.0</td>
<td>10.9 ± 3.3</td>
<td>10.2 ± 3.1</td>
<td>8.3 ± 4.0</td>
<td>9.0 ± 4.0</td>
</tr>
<tr>
<td>OC (ng/ml)</td>
<td>16.0 ± 4.5</td>
<td>16.1 ± 2.7</td>
<td>17.1 ± 5.1</td>
<td>18.0 ± 5.0</td>
<td>14.1 ± 2.1</td>
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<tr>
<td>CK activity (U/l)</td>
<td>53.3 ± 31.5</td>
<td>107.4 ± 76.44</td>
<td>83.3 ± 85.0</td>
<td>112.3 ± 98.24</td>
<td>83.7 ± 50.0</td>
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<tr>
<td>Cr (mg/mL)</td>
<td>114.1 ± 24.4</td>
<td>126.2 ± 33.44</td>
<td>95.4 ± 16.6</td>
<td>116.3 ± 16.34</td>
<td>107.9 ± 30.3</td>
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<tr>
<td>GGT (U/l)</td>
<td>31.4 ± 23.6</td>
<td>28.4 ± 17.7</td>
<td>17.7 ± 2.4</td>
<td>17.8 ± 3.5</td>
<td>24.7 ± 8.5</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cr (mg/mL)</td>
<td>0.8 ± 0.6</td>
<td>2.2 ± 2.1</td>
<td>0.6 ± 0.4</td>
<td>3.9 ± 4.2</td>
<td>0.4 ± 0.2</td>
</tr>
<tr>
<td>Cm (mg/mL)</td>
<td>0.9 ± 0.4</td>
<td>1.0 ± 0.4</td>
<td>0.7 ± 0.4</td>
<td>0.9 ± 0.6</td>
<td>0.7 ± 0.6</td>
</tr>
<tr>
<td>Cr:Cm ratio</td>
<td>0.89 ± 0.73</td>
<td>2.13 ± 1.97</td>
<td>0.88 ± 0.38</td>
<td>3.46 ± 2.25</td>
<td>0.82 ± 0.75</td>
</tr>
</tbody>
</table>

Notes: Results are means ± SD. TT = total testosterone; DHEAS = dehydroepiandrosterone sulfate; IGF-1 = insulin-like growth factor-1; OC = osteocalcin; CK = creatine kinase; Cm = creatinine; GGT = gamma glutamyl transferase; Cr = creatine.

*Men showed higher values than women (TT, p < .000001; DHEAS, p < .05); 1CrM group increased more than the placebo group (p < .05).

oxidation and protein breakdown (28). Given that the increases in muscle fiber area following resistance exercise training were not differentially affected by CrM supplementation, we cannot conclude that the increase in FFM was due to increases in myofibrillar protein content per se. The same rationale applies to the possibility of an increase in intracellular water (50), for that should also be reflected in an increase in myofiber area. It is important to note that a very small change in muscle fiber area in every muscle in the body could easily account for a 1- or 2-kg increase in FFM and the change in fiber area may be below the limit of detection using routine histochemistry. Future studies will have to address the issues of the potential for CrM to increase intracellular cell volume and induce gene expression (28,51), whether CrM alters nonmuscle protein turnover/cell volume, and, what is most important, whether there are functional correlates to the increase in FFM (whatever that mechanism may be).

Following resistance exercise training, significant increases in type I (11,34,36) and type II (10,11,34,36) muscle fiber area have been consistently reported. More recently, type IIa and type IIx muscle fiber areas have been reported to increase following resistance exercise in an elderly population (52,53). Similarly, in the current study we demonstrated a 13% and 31% increase in type I and type IIx muscle fiber area, respectively, following resistance training; however, we did not observe any effect of CrM supplementation on enhancing muscle fiber area increases. An earlier, longer-term study (1 year) found that Cr supplementation (1.5 g/d) resulted in a significant increase in type II muscle fiber diameter in patients with gyrate atrophy (54). Recently, CrM supplementation was shown to potentiate the increase in muscle fiber area for all three fiber types following resistance training in young men in one study (17); however, when CrM was compared with a postresistance exercise protein-carbohydrate supplement (55), there were no differential changes (yet FFM and TBM were greater for CrM). Given the variability in the determination of muscle fiber area, further experiments will be needed to evaluate the potential link between CrM supplementation and muscle fiber area in an elderly population.

Healthy older men and women (58–75 years) have significantly lower muscle PCr and TCr concentrations compared with young healthy men and women (18,19). The magnitude of the increase in muscle TCr and PCr concentration appears to be inversely proportional to the basal concentration. One study examined basal concentrations of muscle PCr and PCr resynthesis rates in middle-aged (58 ± 4.4 years) male and female subjects before and after Cr supplementation using 31P-MRS (19). This study (19) found that resting muscle PCr content was lower in the middle-aged subjects than it was in the younger subjects, and the middle-aged subjects experienced a greater increase (30%) in muscle PCr stores than younger subjects (15%) following CrM supplementation (19). Together these data suggest that older adults may be at a disadvantage in activities requiring rapid rates of energy turnover. The current study is the first to directly examine intramuscular TCr concentration following CrM supplementation by using the muscle biopsy technique. As hypothesized, CrM supplementation increased muscle TCr in men and women by an average of 26%, which is in agreement with previous findings in young men (20,56,57). Traditionally, long-term CrM supplementation at a lower dosage is often preceded by short-term high dose loading (i.e., 20 g/d for 4–5 days). However, a novel finding of the present study was that the older subjects were able to increase and maintain TCr stores with the ingestion of only 5 g/d for 4 months with no initial loading period.

Most studies have not reported any adverse side effects resulting from short-term (21,58,59) or longer-term (60,61) CrM supplementation. We found that the CrM supplement was well tolerated by the subjects. Plasma Crn concentration and CK activity increased to a greater extent for the CrM-supplemented group following training, yet the levels remained within the normal limits for an older population. An increase in plasma Crn would be expected because the elevated total muscle Cr (nonenzymatic degradation to Crn) and the increased FFM would both increase the rate of
appearance of Crm into the plasma. In addition, urine Crm, but not urine Cr, increased following Crm supplementation. We did not complete a full 24-hour urine collection in the current study; however, previous findings have reported no changes in Crm clearance in response to Crm supplementation (27,58,59). Finally, the liver enzyme γGT also did not change in response to Crm supplementation, which is in agreement with studies also showing no change in indices of hepatic dysfunction following Crm supplementation (61).

Conclusions

In summary, 14 weeks of resistance training resulted in improvements in muscle strength and functional task performance. In addition, there was a greater increase in FFM, improvements in muscle strength and functional task performance. In addition, there was a greater increase in FFM, improvements in muscle strength and functional task performance (27,58,59). Finally, the liver enzyme γGT was not increased in the current study; however, previous findings have reported no change in response to Crm supplementation, which is in agreement with studies also showing no change in indices of hepatic dysfunction following Crm supplementation (61).

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CREATINE INCREASES STRENGTH GAINS FOLLOWING TRAINING IN OLDER ADULTS