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L-Carnitine L-tartrate supplementation favorably affects biochemical markers of recovery from physical exertion in middle-aged men and women

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Abstract

The purpose of this study was to examine the effects of Carnipure tartrate (Lonza, Allendale, NJ) supplementation (total dose of 2 g/d of L-carnitine) on markers of performance and recovery from physical exertion in middle-aged men and women. Normally active and healthy men (n = 9, 45.4 ± 5.3 years old) and women (n = 9, 51.9 ± 5.0 years old) volunteered to participate in the investigation. Double-blind, placebo, balanced treatment presentation and crossover design were used with 3 weeks and 3 days of supplementation followed by a 1-week washout period before the other counterbalanced treatment was initiated. After 3 weeks of each supplementation protocol, each participant then performed an acute resistance exercise challenge of 4 sets of 15 repetitions of squat/leg press at 50% 1-repetition maximum and continued supplementation over the recovery period that was evaluated. Blood samples were obtained at preexercise and at 0, 15, 30, and 120 minutes postexercise during the acute resistance exercise challenge and during 4 recovery days as well. Two grams of L-carnitine supplementation had positive effects and significantly ($P \leq .05$) attenuated biochemical markers of purine metabolism (ie, hypoxanthine, xanthine oxidase), free radical formation (malondialdehyde), muscle tissue disruption (myoglobin, creatine kinase), and muscle soreness after physical exertion. However, markers of physical performance (ie, strength, power, get up and go) were not affected by supplementation. These findings support our previous findings of L-carnitine in younger people that such supplementation can reduce chemical damage to tissues after exercise and optimize the processes of muscle tissue repair and remodeling.

1. Introduction

Even in individuals as young as 40 years, the effects of increasing age can result in a decline of both basic functional ability and quality of life. This is due, in large part, to increased free radical formation, reduction in the concentrations of important hormones, and changes in the circulatory system. After exercise, these events lead to the attenuation of the recovery processes and delays in the recovery of skeletal muscle as a result of reductions in the molecular signals stimulating protein synthesis [1-3]. For older individuals, enhancement of any of these recovery processes would be of a distinct advantage, most notably in allowing more rapid recovery after physical exertion. Apart from the obligatory role of the carnitine system in transporting long-chain fatty acid into mitochondrial matrix for fat oxidation [4], a novel role for L-carnitine has recently been demonstrated: L-carnitine can reduce chemical damage to tissues after exercise and optimize the processes of muscle tissue repair and remodeling [5]. Our area of interest is the potential for L-carnitine to result in quicker recovery

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and therefore allow a more active recreational lifestyle mediating improved fitness.

The recovery process in the neuromuscular system from strenuous exercise is predominantly focused on the repair and remodeling of damaged muscle tissue. These processes are influenced by the ability of the body to deliver blood to target tissues, releasing oxygen, hormones (eg, anabolic hormones such as growth hormones or insulin-like growth factor–I), immune cells, and nutrients to the damaged muscle tissue during and after exercise [6-8]. Ischemia in endothelia cells results in the increased oxidative stress and compromised blood flow regulation [9], which lead to the cascade of biochemical events including purine catabolism, free radical formation, membrane disruption, and muscle soreness. These biochemical events have been shown to be attenuated by L-carnitine administration [10,11]. Our laboratory has proposed that L-carnitine supplementation could protect against L-carnitine deficiency in vascular endothelial cells, thereby reducing signs of damage by improving blood flow regulation and delivery of oxygen to muscle tissues during and after exercise [11].

Previous research from our laboratory provided the first evidence to support the theoretical potential for the use of L-carnitine supplementation in exercise recovery. These studies demonstrated that 2 g of elemental carnitine being supplied by L-carnitine L-tartrate (LCLT) per day attenuated the effect of hypoxia after resistance exercise, resulting in less tissue damage, reduced muscle soreness, and quicker recovery [12,13]. We also reported that 2 g of elemental carnitine being supplied by LCLT increased androgen receptor content at rest and enhanced testosterone levels after resistance exercise [14]. Spiering et al [15] further demonstrated the effectiveness of both 1 and 2 g of elemental carnitine being supplied by LCLT doses in attenuating metabolic stress and the hypoxic chain of events leading to muscle damage and soreness after resistance exercise.

Although recent work has clearly shown that LCLT is effective in assisting recovery from strenuous resistance exercises [13,15], it is not known if LCLT supplementation has a similar effect in older men and women. Therefore, the purpose of this study was to examine the effects of LCLT supplementation on markers of recovery from physical exertion in men and women between 40 and 65 years of age.

2. Methods

2.1. Experimental design and approach to the problem

This study used a balanced, crossover, placebo-controlled research design to examine the effects of LCLT supplementation on muscle damage and on metabolic and physical performance markers of recovery after a resistance exercise protocol. Subjects within each sex were matched for age, body size, activity background, and strength in a squat/leg press exercise and then randomly assigned to start with either an LCLT or placebo supplementation period in a double-blind fashion. Each subject therefore acted as his or her own control.

The study consisted of 2 supplementation periods (one period of LCLT and one of placebo). Each period required supplementation of 3 weeks and 3 days, followed by an acute resistance exercise challenge (ARET) day (or D0), and then 3 subsequent recovery visits (D1, D2, D4) over the next 4 days after the ARET. For each period, subjects supplemented for the 3 weeks with either 2 g of elemental carnitine being supplied by LCLT or placebo per day before their ARET day. Subjects were then evaluated during recovery from the workout for 4 more days. Subjects continued to take their capsules for 3 days during the recovery period after the workout.

In the morning of D0, fasting and resting blood samples, measures of muscle soreness, and functional tests (ie, strength/power and mobility) were obtained. Subjects reported to the laboratory again 3 hours after lunch. Subjects performed the functional tests again followed by the ARET (4 sets of 15 repetitions) with either a squat for male subjects or a leg press exercise for female subjects. During the ARET, blood samples were obtained at preexercise and at 0, 15, 30, and 120 minutes postexercise. Measures of muscle soreness were collected at preexercise and at 0 and 120 minutes postexercise. The recovery visits took place on the mornings of D1, D2, and D4 (at +24, +48, and +96 hours after D0, respectively). During the recovery visits, fasting and resting blood samples, measures of muscle soreness, and functional tests were obtained.

After a 1-week washout period, subjects consumed the opposite supplement of their first supplementation period (either LCLT or placebo) for another 3 weeks and 3 days and performed the exact same exercise protocol and associated measures of recovery. A 1-week washed period was long enough to ensure that serum total carnitine concentrations had returned to the baseline values before the testing days (verified by resting serum total carnitine concentrations on D0; Fig. 1).

2.2. Subjects

Nine men and 9 women volunteered to participate in this study. All subjects were healthy and recreationally active but, after activity histories were collected, had not participated in any systematic resistance training for years, if at all. Thus, the context for this study was that these subjects were physically active but would not be considered resistance trained. Subject characteristics are presented in Table 1. Subjects had not taken nutritional supplements (such as L-carnitine, creatine, ephedra, or hormonal substances) for at least 6 months before the study. Medical history questionnaires confirmed the absence of any musculoskeletal injuries or medical conditions. All subjects were fully informed of the research design and associated benefits and risks of the investigation before signing an informed

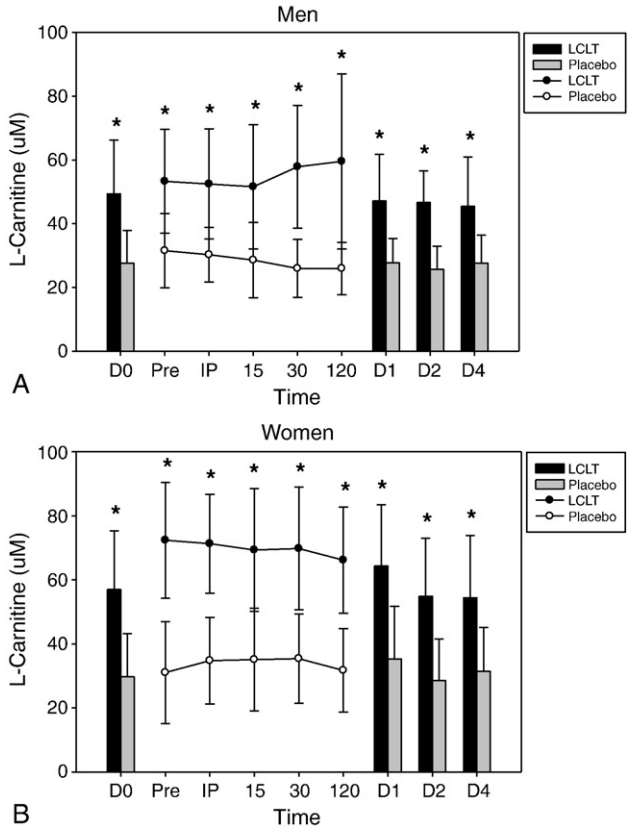

Fig. 1. Serum total carnitine responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values. D0 indicates resting value in the morning of resistance exercise workout day; D1, D2, and D4, resting values in the morning of recovery days 1, 2 and 4 after the exercise workout; pre, IP, +15, +30, and +120, values at preexercise and at 0, 15, 30, and 120 minutes postexercise.

consent approved by the University of Connecticut institutional review board for use of human subjects.

2.3. Procedures

2.3.1. Treatment conditions

Subjects were asked to continue their normal exercise routine (except as specified around and during the testing periods) and maintain their normal diet during the course of intervention. To ensure consistency of their physical activities and diet during the 2 supplementation periods, subjects were asked to record their physical activity and to repeat the same physical activities from the first supplementation period during the second supplementation period. Subjects were also asked to record their diet from 3 days before the first testing day through the end of the recovery days. They then repeated the diet from the first phase of supplementation period during the second supplementation phase. Each subject met with a registered dietician and was instructed on how to keep and record food records that could be reproduced in the subsequent period. Exercise, alcohol consumption, or pain medication was not allowed 60 hours before D0 through the testing on D4.

Table 1
Subject characteristics (mean ± SD)

	Men (n = 9)	Women (n = 9)
Age (y)	45.4 ± 5.3	51.9 ± 5.0
Height (cm)	175.4 ± 5.2	164.7 ± 8.8
Body weight (kg)	82.2 ± 12.0	65.4 ± 5.6
BMI	26.6 ± 3.1	24.2 ± 2.1

Values are means ± SD. BMI indicates body mass index.

2.3.2. Supplementation protocol

During the supplement trials, subjects were provided with capsules of Carnipure tartrate (LCLT, Lonza, Allendale, NJ) with written instructions to consume 2 capsules with breakfast and 2 with lunch for a total dose of 2 g of L-carnitine per day. During their placebo trials, subjects were provided with an identical-looking placebo (powdered cellulose) and identical instructions. Subjects were asked to keep a capsule record to ensure compliance with supplementation. Supplementation commenced 3 weeks before the ARET and continued through 3 days of recovery period for a total of 3 weeks and 3 days of supplementation. The dose of 2 g of L-carnitine per day was chosen to maximize plasma carnitine concentrations without exceeding the renal threshold for carnitine [16,17].

2.3.3. Physical exertion protocols (exercise workout)

The squat exercise protocol for male subjects was performed on a Plyometric Power System (Innervations Inc, Lismore, Australia) that was previously described in detail [18]. Briefly, the Plyometric Power System allows only vertical movement of the bar along 2 steel shafts with minimum friction. Because the women in this study lacked any squat experience and were somewhat fearful of performing the exercise, to promote an increased psychologic comfort level and prevent possible acute injury in this study, a supine leg press exercise protocol was performed on a Plyo Press Machine (Frappier Acceleration Sports Training, Minot, ND) for women. One week after familiarization, each subject completed a submaximal squat/leg press exercise to predict their 1-repetition maximum (1-RM). Subjects performed exercises for 8 to 12 RM repetitions. The 1-RM was then predicted using the Epley equation (1-RM = [1 + 0.033 * number of reps] * load) [8]. The Epley equation has been shown to be validated in predicting 1-RM for untrained individuals [19]. This submaximal testing was used to avoid a maximal strength test and therefore reduce the strain placed on the untrained subjects in this stress protocol.

The ARET was performed in the afternoon, 3 hours after consuming a midday meal with the supplement. After a standardized warm-up (5 minutes of cycling followed by light dynamic stretching), subjects performed 10 vertical jumps on force plate followed by mobility tests (described below). Subjects then performed 4 sets of 15 repetitions of

squat/leg press exercises with a load equal to 50% of their previously estimated 1-RM squat/leg press. There was a 2-minute recovery between each set. The loading for the squat/leg press exercise protocol was selected because it causes hypoxic stress to muscle tissue, minor muscle disruption, but not severe damage, thereby allowing the operational mechanisms for LCLT to reduce hypoxia-mediated biochemical responses to the exercise stress [8].

2.4. Vertical jump testing

A counter movement vertical jumping test was performed on a force plate to determine muscle function and power capabilities. Subjects began the exercise with hands at the waist in a standing position. Subjects then initiated 10 consecutive maximal-effort jumps without pausing between jumps. Vertical jump testing was performed in the morning before the ARET (D0) and on recovery days 1, 2, and 4 (D1, D2, and D4) after the exercise workout. In addition, vertical jump testing was also performed before the ARET workout and 5 minutes after the ARET.

2.4.1. Handgrip testing

Subjects performed a maximal isometric handgrip strength test with their dominant hand. Three trials were performed, and the best score was recorded. After a 15-minute rest, subjects performed an isometric handgrip at 40% of their maximal load for as long as possible, with no more than 2 seconds less than the 40% cutoff level. The total time of the 40% handgrip test was used as measure of muscle endurance. The handgrip testing was performed in the morning before the resistance exercise workout (D0) and on recovery days 1, 2, and 4 (D1, D2, and D4) after the exercise workout.

2.4.2. Functional mobility testing

Subjects were assessed for functional performance in the morning before the resistance exercise workout (D0) and on recovery days 1, 2, and 4 (D1, D2, and D4) after the exercise workout. In addition, functional mobility testing was performed before the squat/leg press exercise protocols on D0. The functional performance assessments were performed in the following order: (1) timed up and go, (2) stair climbing, (3) unilateral anterior reach, and (4) the medial step-down test [20]. Subjects participated in 2 familiarization sessions before initial testing. All tests were administered by the same investigator and used standard procedures [20]. Three trials were given per assessment, with the best score recorded for analysis (except as noted).

Briefly, for the timed up and go, on the verbal signal "go," each subject ascended from the standard chair, walked forward 3 m, and then walked back and sat down as fast as possible. For the stair-climbing test, each subject ascended and descended the stairs (10 stairs) as quickly as possible. For the unilateral anterior reach, each subject (with hands positioned on the hips) extended one leg out as far as possible (while balancing on the opposite leg) over a standard tape measure while keeping the anterior foot close to the floor. Subjects then tested the opposite leg. For the medial step-down test, each subject repeatedly stepped down from the side of a step until the heel lightly touched the floor and then returned to starting position. Subject performed as many step-downs as possible for 1 minute (only 1 trial was performed per leg for this test).

2.4.3. Perceived muscle soreness

Perceived general muscle soreness was assessed using a 10-cm–long linear visual analog scale with labels that corresponded to *no pain* and *extreme pain* at either end. Subjects marked their level of subjective pain using a vertical line along the continuum, and the distance was reported as the raw score [11]. Muscle soreness was assessed at rest in the morning before the resistance exercise workout (D0) and on recovery days 1, 2, and 4 (D1, D2, and D4) after the exercise workout. In addition, muscle soreness was also assessed before the squat/leg press exercise workout, immediately postexercise, and 120 minutes postexercise on the D0 afternoon.

2.4.4. Blood collection

Morning blood samples were obtained on the ARET day (D0) and on recovery days 1, 2, and 4. They occurred at the same time each morning after a 12-hour overnight fast and abstinence from alcohol and any strenuous exercise other than the study. Subjects reported to the laboratory between 7:00 and 9:30 AM and rested quietly for 10 minutes in the semirecumbent position. Approximately 20 mL of blood was then obtained from an antecubital vein.

The afternoon of the ARET, subjects again rested quietly for 10 minutes in the supine position. However, a flexible catheter was inserted into a forearm vein for the ARET and kept patent with a 10% heparin-lock/saline solution. Before all blood collections, 3 mL of blood was withdrawn and discarded to avoid dilution of the samples; and approximately 20 mL was subsequently collected. Whole blood from both tubes was then centrifuged (1500*g* for 15 minutes at 4°C), and resultant serum or EDTA plasma was divided into appropriate aliquots and stored at −80°C until subsequent analyses. Blood samples were collected both at preexercise and at 0, 15, 30, and 120 minutes after the squat/leg press exercise protocol. Subjects rested quietly in a seated position during the 2-hour postexercise recovery period.

2.5. Blood analyses

All assays were performed within the shelf life of each analyte when stored at −80°C, and the sample was only thawed once before analyses. Serum L-carnitine was assessed in the presence of acetyl–coenzyme A by measuring the CoASH set free during acetyl transfer to L-carnitine by the enzyme L-carnitine acetyltransferase. The CoASH was trapped with 5,5′-dithiobis-2-nitrobenzoic acid and measured spectrophotometrically at 412 nm. Serum hypoxanthine and xanthine oxidase were analyzed in duplicate using the Amplex Red reagent-based assay

(Molecular Probes, Eugene, OR). Myoglobin was assayed in duplicate using an enzyme-linked immunosorbent assay (Diagnostic Automation, Calabasas, CA). Creatine kinase (CK) levels (Diagnostic Chemicals, Oxford, CT) were determined at 340 nm on a spectrophotometer (Spectronic 601; Milton Roy, Rochester, NY). Plasma lactate and glucose were determined using an YSI Lactate/Glucose Analyzer model 2300 STAT (Yellow Springs Instruments, Yellow Springs, OH). Nonesterified fatty acid levels were analyzed with an ACS-ACOD method from Wako Diagnostics (Richmond, VA). Plasma malondialdehyde (MDA) was measured using the methods described by Wong et al [21] and modified as described by McBride et al [22]. A phosphoric acid solution (0.44 mol/L) and a thiobarbituric acid solution (42 mol/L) were added to plasma samples and placed in a water bath at 100°C for 60 minutes, then placed in an ice-water bath (0°C) until analysis. A methanol-NaOH solution was added to the boiled samples before being centrifuged to precipitate the plasma protein. The protein-free plasma was extracted, and the absorbance was read at 532 nm on a spectrophotometer. In addition, all samples were thawed only one time; and all intraassay and interassay coefficients of variance for each analyte were less than 10%.

2.5.1. Statistical analyses

A 2-way repeated-measures analysis of variance was used to evaluate changes over time in the LCLT and placebo trials. We tested for linear assumptions; and especially if a sphericity correction was needed, we used the Huynh-Feldt correction because we have higher variance in the blood variables and it is less conservative than the Greenhouse-Geisser correction. Any variables that did not meet the assumption were logarithmically corrected and tested again. We made a pairwise comparison with a Bonferroni correction for all of the comparisons. Statistical power in this study ranged from 0.81 to 0.93 for the various variables (nQuery Advisor; Statistical Solutions, Saugus, MA). Test-retest reliability of the measures using an intraclass correlation coefficient was from *R*s greater than or equal to 0.90. Data are presented as mean ± SD. The criterion for significance in this investigation was set at $P < .05$.

3. Results

3.1. Serum L-carnitine

Compared with placebo, serum total L-carnitine concentrations were significantly higher at all time points measured during LCLT in both men and women, with no differences between men and women (Fig. 1).

3.2. Purine catabolism

For both LCLT and placebo conditions, serum hypoxanthine concentrations increased significantly after exercise (IP, +15, and +30) and peaked at the IP time point in men. No significant difference from baseline was seen by 2 hours after exercise, and no further changes were observed during recovery days. Hypoxanthine concentrations were significantly lower in LCLT condition immediately after exercise and 15 minutes after exercise in men. No differences were observed during recovery days between 2 conditions in men. A similar trend of hypoxanthine concentrations were also observed in women after exercise and during recovery days, with little difference in time points. In women with both conditions, hypoxanthine concentrations peaked at the +15 time point. No significant difference from baseline was seen by 2 hours after exercise, and no further changes were observed during recovery days. Hypoxanthine concentrations were significantly lower in LCLT condition 15 and 30 minutes after exercise in women. No differences were observed during recovery days between 2 conditions in women (Fig. 2).

In men, xanthine oxidase concentrations significantly increased over baseline at the IP and +15 time points for both conditions, peaked at +15, and gradually returned to baseline by 120 minutes after exercise. However, the LCLT condition was significantly lower than placebo at the

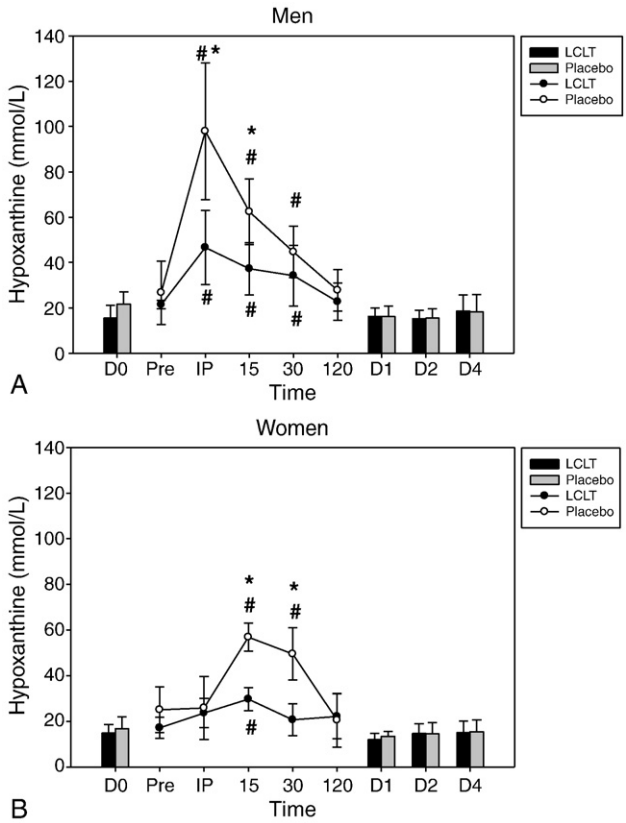

Fig. 2. Serum hypoxanthine responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

IP, +15, and +30 minutes postexercise. No further changes and no differences were observed during recovery days in both conditions in men. Women showed a similar trend to men with minor exceptions in time points. As with men, women peaked at +15 and gradually returned to baseline by 30 minutes. Serum xanthine oxidase concentrations in the placebo condition were significantly higher at the IP and +15 time points for women. The absolute concentrations of xanthine oxidase were significantly higher in men compared with women for the recovery time points after exercise. No further changes and no differences were observed during recovery days in both conditions in women (Fig. 3).

3.3. Free radical generation

For placebo condition, MDA concentrations peaked significantly higher than baseline immediately after exercise and then gradually returned to baseline by 2 hours after exercise in both men and women. For LCLT condition, MDA concentrations did not significantly change after exercise in both men and women. Furthermore, MDA concentrations were significantly lower in LCLT condition than placebo condition after exercise (with the exception of the +120 time point) and during all recovery days in men. However, MDA concentrations were significantly lower in LCLT condition than placebo condition from before exercise until +30 after exercise in women. However, MDA concentrations were similar during recovery days between 2 conditions in women. In addition, MDA concentrations were significantly lower in women than in men at all corresponding time points (Fig. 4).

3.4. Cytosolic proteins

For the placebo condition, serum myoglobin concentrations increased significantly over baseline immediately after exercise and maintained elevated even at 120 minutes after exercise in both men and women. For LCLT condition, myoglobin concentrations increased significantly over baseline only at 120 minutes after exercise in both men and women. Furthermore, myoglobin concentrations in the LCLT condition were significantly lower than those in the placebo condition at IP, +15, and +30 minutes after exercise in both men and women. No significant changes and no differences were observed during recovery days between 2 conditions in both men and women (Fig. 5).

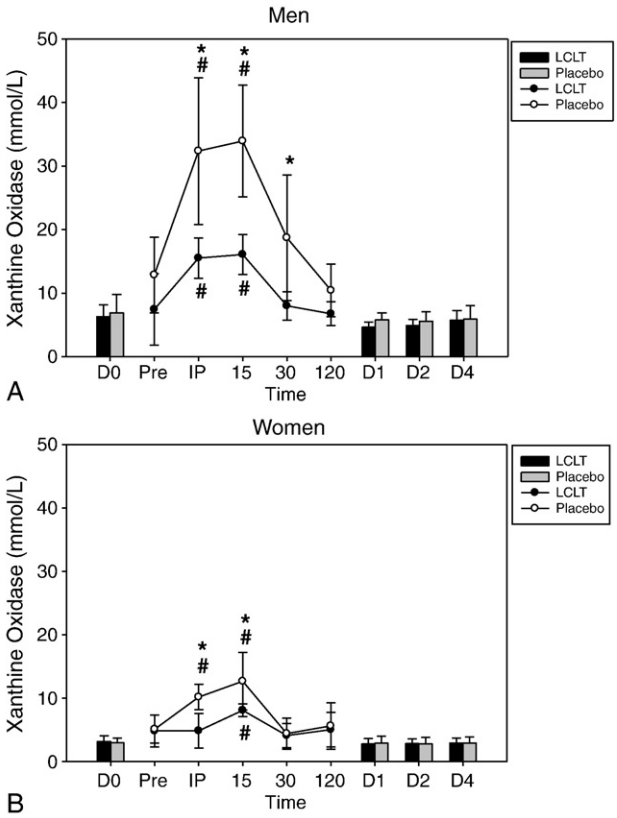

Fig. 3. Serum xanthine oxidase responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P <$ .05 from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

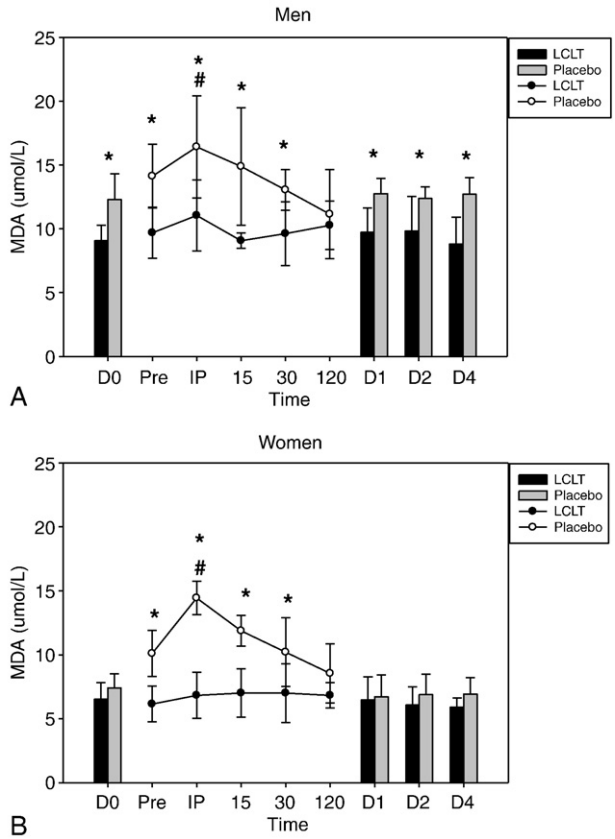

Fig. 4. Plasma MDA responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

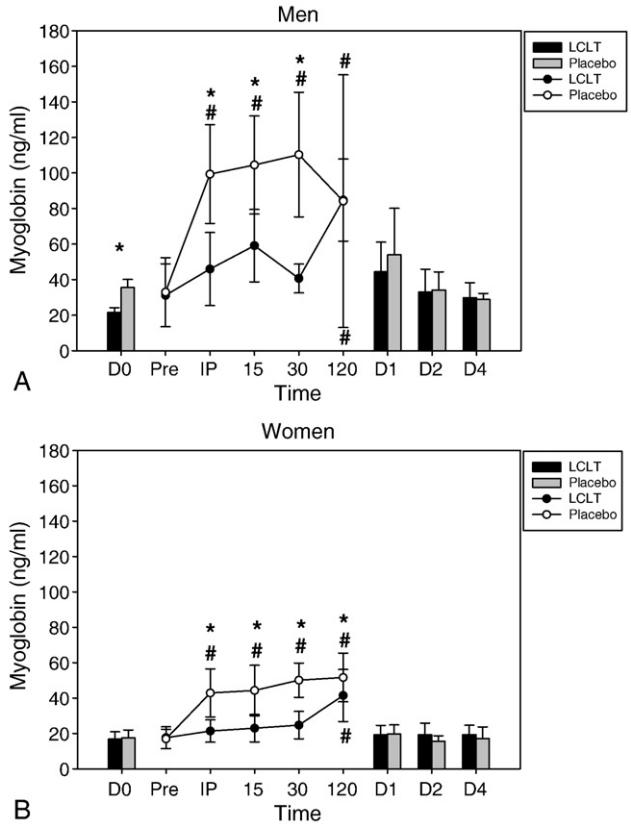

Fig. 5. Serum myoglobin responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

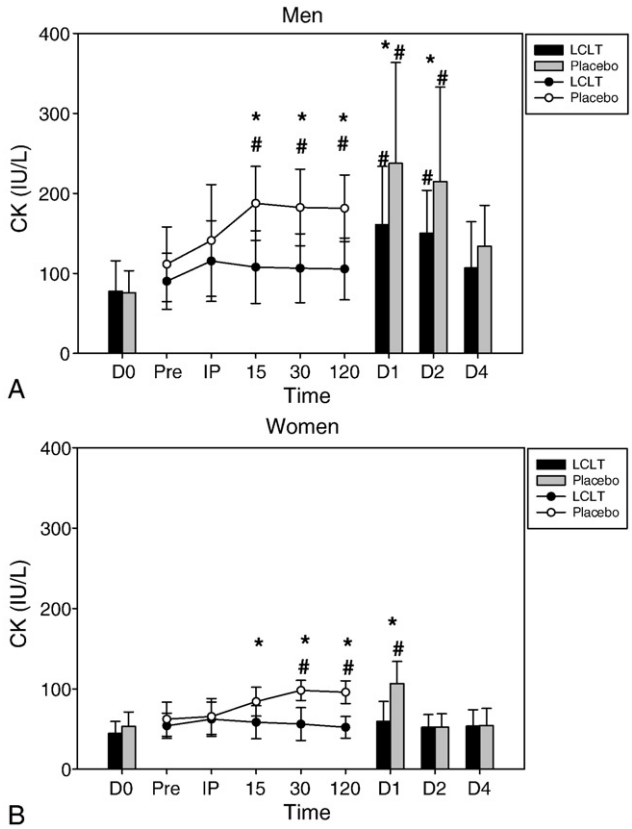

Fig. 6. Serum CK responses (mean ± SD) after 3 weeks and 3 days of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

For placebo condition, CK concentrations increased significantly over baseline at +15, +30, and +120 after exercise in men. Creatine kinase concentrations remained unchanged after exercise in the LCLT condition. Creatine kinase concentration levels were significantly greater in the placebo condition after exercise than in the LCLT condition. For both conditions, CK concentrations peaked on D1 and remained elevated during recovery day 2. Again, CK concentrations were significantly higher in the placebo condition during recovery days than in LCLT condition. In women, CK concentrations increased significantly over baseline at +30 and +120 after exercise and remained elevated during recovery day 1 in placebo condition, whereas CK concentrations did not change after exercise and during recovery days in LCLT condition. Creatine kinase concentrations were significantly higher in the placebo condition than the in LCLT condition after exercise and during recovery day 1 in women (Fig. 6).

3.5. Muscle perceived soreness

For both placebo and LCLT conditions, soreness levels increased significantly over baseline after exercise and remained elevated over baseline during all of the recovery days. In men, soreness levels were significantly lower in the LCLT condition than in placebo conditions both after exercise and during the recovery days 1 and 4. In women, soreness levels were significantly lower in the LCLT condition than in placebo conditions only during the recovery days 1 and 2 (Fig. 7).

3.6. Lactate responses

For both LCLT and placebo conditions, lactate concentrations increased significantly after exercise and peaked at the IP time point, and then gradually returned to baseline by 120 minutes after exercise in both men and women. There were no differences between 2 conditions in both men and women. However, women had lower lactate concentrations than men immediately after exercise and at +15 and +30 minutes after exercise (Table 2).

3.7. Functional mobility

No significant changes and no differences in any of the functional mobility tests were observed during recovery days

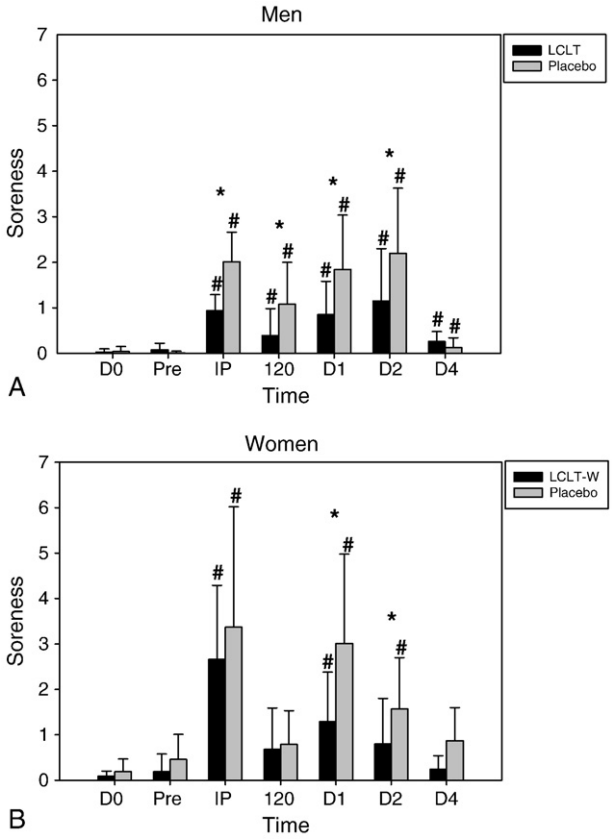

Fig. 7. Perceived muscle soreness (mean ± SD) at D0, before, immediately after, 2 hour, 24 hours, 48 hours, and 96 hours after a resistance exercise challenge, which was measured after 3 weeks of either LCLT supplementation or placebo (A, men; B, women). $^{\#}P < .05$ from corresponding preexercise value. $^{*}P < .05$ between corresponding LCLT and placebo values.

between 2 conditions in both men and women. No sex differences were observed in up and go and stair climbing (Tables 3 and 4).

Table 2
Plasma lactate (in millimoles per liter) in response to a resistance exercise challenge after 3 weeks of either LCLT supplementation or placebo (n = 9 per group) (mean ± SD)

	LCLT	Placebo
Men		
Pre	1.9 ± 0.6	1.9 ± 0.7
IP	11.7 ± 3.0†	11.7 ± 2.7†
+15	10.3 ± 2.8†	9.5 ± 2.1†
+30	6.5 ± 1.8†	6.3 ± 1.7†
+120	1.9 ± 0.51	1.6 ± 0.5
Women		
Pre	1.3 ± 0.5	1.1 ± 0.4
IP	6.1 ± 1.5†	6.3 ± 1.6†
+15	4.2 ± 1.5†	4.1 ± 1.4†
+30	2.8 ± 0.9†	2.7 ± 0.9†
+120	1.1 ± 0.40	1.1 ± 0.2

Values are means ± SD.
† $P < .05$ from corresponding preexercise value.

Table 3
Up and go performance in response to a resistance exercise challenge after 3 weeks of either LCLT supplementation or placebo (n = 9 per group) (mean ± SD)

	LCLT	Placebo
Men		
D0	3.4 ± 0.4	3.5 ± 0.5
D1	3.4 ± 0.3	3.4 ± 0.4
D2	3.3 ± 0.3	3.3 ± 0.3
D4	3.3 ± 0.3	3.2 ± 0.3
Women		
D0	3.5 ± 0.18	3.5 ± 0.3
D1	3.8 ± 0.2	3.6 ± 0.3
D2	3.5 ± 0.2	3.6 ± 0.3
D4	3.4 ± 0.3	3.6 ± 0.3

Values are means ± SD.

4. Discussion

In this study, the primary findings indicate that LCLT supplementation can also beneficially affect postexercise markers of metabolic stress, muscle disruption, and muscle soreness in men and women older than 40 years. The present study and the previous studies [11,17] have supported our working hypothesis that LCLT supplementation attenuates the biochemical and structural stress responses to a high-repetition squat exercise in both younger and older generations.

To verify the effectiveness of the study protocol, serum total L-carnitine and plasma lactate were examined. In both men and women, serum total L-carnitine concentrations were significantly higher at all time points of the study during LCLT supplementation, indicating good compliance with the 3 weeks and 3 days of supplementation protocol. Plasma lactate responses to squat and leg press exercise in both men and women were significantly increased (11.7 vs 6.2 mmol/

Table 4
Stair-climbing performance in response to a resistance exercise challenge after 3 weeks of either LCLT supplementation or placebo (n = 9 per group) (mean ± SD)

	LCLT	Placebo
Men		
D0	4.9 ± 0.8	4.9 ± 0.7
D1	4.9 ± 0.8	4.9 ± 0.7
D2	4.8 ± 0.8	4.8 ± 0.7
D4	4.7 ± 0.7	4.7 ± 0.7
Women		
D0	5.7 ± 0.4	5.8 ± 0.5
D1	5.7 ± 0.4	5.7 ± 0.5
D2	5.6 ± 0.4	5.69 ± 0.4
D4	5.5 ± 0.4	5.7 ± 0.4

Values are means ± SD.

L, respectively) to a similar extent during both LCLT and placebo conditions, indicating a similar glycolytic stress between conditions. In addition, serum total L-carnitine and plasma lactate concentrations demonstrated adherence to the protocol.

High glycolytic rates result in accumulation of adenosine diphosphate and H^+, which activates the adenylate kinase reaction. This results in the formation of adenosine triphosphate (ATP) and adenosine monophosphate from 2 molecules of adenosine diphosphate. This adenosine monophosphate is oxidized to hypoxanthine. As we have previously shown [13,15], serum hypoxanthine was significantly elevated after 5 sets of 15 to 20 RM squats; and this response was attenuated by LCLT supplementation. In the present study, serum hypoxanthine concentrations were significantly elevated after 4 sets of 15 RM squats in men and 4 sets of 15 RM leg press in women. These responses were attenuated by LCLT supplementation. The LCLT supplementation was effective in reducing metabolic stress associated with matching ATP supply and demand in men and women older than 40 years.

Insufficient supply of ATP inhibits calcium ATPase pumps, which increases intracellular calcium. This calcium, in turn, activates the calcium-dependent proteases, which cleave a portion of xanthine dehydrogenase and convert it into xanthine oxidase. Serum xanthine oxidase was significantly elevated after exercise workout in both men and women. However, these responses were attenuated by LCLT supplementation. The present results are in agreement with our previous studies showing that 1 g or 2 g of L-carnitine per day is effective in reducing xanthine oxidase concentrations after acute resistance exercise [15]. The lower xanthine oxidase concentrations after exercise in LCLT group indicate that the calcium pumps were operating more efficiently (perhaps because of better ATP supply) and/or that there was less disruption to the muscle or sarcolemmal membrane. The LCLT supplementation favorably altered postexercise concentrations of xanthine oxidase, a marker of metabolic stress.

Inhibition of xanthine oxidase with allopurinol during exercise has been shown to result in significantly less generation of reactive oxygen species, less accumulation of cytosolic enzymes (CK and lactate dehydrogenase), and less tissue damage after exhaustive exercise [11,23,24]. In a prior work, Volek et al [13] reported that the lower xanthine oxidase concentrations during LCLT was associated with less accumulation of reactive oxygen species (as measured by MDA, the marker used to quantify free radical interaction with cell membrane) and less accumulation of cytosolic proteins (as measured by circulating CK activity and myoglobin).

In the present study, we have observed that plasma MDA concentrations were significantly elevated after squat and leg press exercises only during placebo condition in both men and women. In addition, plasma MDA concentrations were significantly lower at all time points of the study during LCLT supplementation in men, indicating that LCLT resulted in less total exposure of cell membranes to the damaging effects of reactive oxygen species. Volek et al [13] reported that, after the squat exercise protocol, there was a significant increase in plasma MDA that peaked immediately after exercise. Plasma MDA returned to preexercise values by 15 minutes postexercise during LCLT supplementation but remained significantly higher than preexercise values for 180 minutes postexercise during placebo.

Increased generation of reactive oxygen species should be predicted to cause greater disruption/damage to the sarcolemma and greater leakage of cytosolic proteins into the circulation (as measured by circulating CK activity and myoglobin). In a prior work, Volek et al [13] demonstrated that LCLT supplementation reduced muscle damage as measured via magnetic resonance imaging. Previous studies have shown that L-carnitine supplementation reduces postexercise myoglobin [13,15] and CK [13,25] concentrations, indicating that L-carnitine supplementation is capable of mediating muscle damage. In the placebo conditions for the present study, serum myoglobin and CK responses to squat and leg press exercise in both men and women were significantly increased over baseline and over the LCLT condition; in addition, CK concentrations remained greater during recovery days in placebo condition than in LCLT condition. Contrary to placebo condition, the LCLT condition did not show significant elevation except at +120 postexercise for myoglobin and only on D1 for women and both D1 and D2 for men in CK. The LCLT supplementation therefore reduced both myoglobin and CK concentrations, providing additional evidence that LCLT reduces postexercise muscle disruption. Such findings support the additional findings that LCLT significantly reduced muscle soreness immediately after the exercise workout and at 24 and 48 hours postexercise when compared with the placebo condition. These results are in agreement with the previous study [15] showing that both 1 and 2 g of L-carnitine per day reduced muscle soreness during recovery days after resistance exercise workout.

The present study was the first to examine whether LCLT's effects on acute recovery would transfer to functional performance tests. It appears that, on a "short-term" supplement basis, L-carnitine supplementation does not impact functional tests. This could be due to the fact that physical exertion did not cause the dramatic amount of muscle tissue damage or fatigue needed to affect neuromuscular function.

In summary, this study investigated the effects of LCLT supplementation on biochemical markers after a resistance exercise protocol in men and women between 40 and 65 years of age. The major finding and new discovery of the present study were that LCLT supplementation can beneficially affect postexercise markers of metabolic stress, muscle disruption, and muscle soreness in men and women older than 40 years. These findings support our previous working hypothesis that L-carnitine supplementation in younger people can reduce chemical damage to tissues

after exercise and optimize the processes of muscle tissue repair and remodeling. We also examined some classic physical performance measures within the experimental design, but no treatment effect was observed. Overall, these findings support a contribution of LCLT to the overall physiologic health of the individual at the cellular level after physical exertion.

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