The Effect of Creatine Supplementation on Strength Recovery After Anterior Cruciate Ligament (ACL) Reconstruction

A Randomized, Placebo-Controlled, Double-Blind Trial

Timothy F. Tyler,* Stephen J. Nicholas, Elliott B. Hershman, Beth W. Glace, Michael J. Mullaney, and Malachy P. McHugh
From NISMAT at Lenox Hill Hospital, New York, New York

Background: Creatine supplementation has been shown to augment training-induced strength gains. The purpose of this study was to examine the effect of creatine supplementation on recovery of muscle strength after anterior cruciate ligament (ACL) reconstruction.

Hypothesis: Creatine supplementation will facilitate strength gains after ACL reconstruction.

Study Design: Double-blind, prospective, and randomized clinical trial.

Methods: Sixty patients were randomized into creatine or placebo groups. Quadriceps and hamstring strength and power were measured isokinetically. Hip flexor, abductor, and adductor strengths were measured with a handheld dynamometer prior to surgery and at 6 weeks, 12 weeks, or 6 months after surgery.

Results: From 6 weeks to 12 weeks after surgery, there were significant increases in strength on the involved side for knee extension (47%), knee flexion (27%), hip flexion (20%), hip abduction (9%), and hip adduction (17%). These strength improvements were unaffected by creatine supplementation with similar effects in the creatine and placebo groups. From 6 weeks to 12 weeks after surgery, there were significant increases in power on the involved side for knee extension (46%) and knee flexion (26%), but these effects were not affected by creatine supplementation. At 6 months, creatine supplementation did not affect outcome as measured by the single leg hop test for distance or the knee outcome score.

Conclusions: The results demonstrate that patients do not benefit from creatine supplementation during the first 12 weeks of rehabilitation after ACL reconstruction.

Keywords: creatine; ACL; rehabilitation; atrophy; strengthening

INTRODUCTION

Loss of quadriceps muscle strength is a common problem following ACL reconstruction and other knee surgeries.[18,19,22,23] This loss of strength is initially caused by quadriceps inhibition with subsequent muscle atrophy.[6,24] Rehabilitation after ACL reconstruction places an emphasis on regaining normal quadriceps strength.[16,28] In recent years, patients have been allowed to return to sport as early as 4 to 6 months.[20] However, residual quadriceps weakness can often prevent successful return to sport.

Different attempts have been made in an effort to retard the amount of quadriceps atrophy that occurs after surgery.[17-19,22,23,28] Electrical stimulation,[17,22,23] continuous passive range of motion, immediate weightbearing,[28] and varying the surgical timing[20] have had limited success in preventing muscle weakness. Recently, creatine supplementation has been shown to enhance the ability to maintain muscular force and power output during repeated bouts of resistive exercise in healthy men and women.[25,27,30] The best dietary sources are animal products, although creatine can also be synthesized endogenously.

The purpose of creatine supplementation is to increase either total creatine stores or phosphocreatine (PCr) stores, within muscle. Supplementation increases the rate of resynthesis of PCr following exercise. Various studies have

*Address correspondence to Timothy F. Tyler, NISMAT at Lenox Hill Hospital, 130 East 77th Street, New York, NY 10021.

The American Journal of Sports Medicine, Vol. 32, No. 2
DOI: 10.1177/0363546503261731

shown increased muscle PCr levels after supplementing with 20 g to 30 g of creatine daily.[1] The amount stored is variable between individuals and is greatest in those who begin with the lowest PCr levels.[9] The maximal storage capacity of the muscle appears to be 150 to 160 mmol/kg.[7] Accordingly, studies have employed a loading method of 20 to 30 g/day for 5 to 7 days, followed by 5 g/day to maintain elevated muscle PCr levels.[29]

Creatine supplementation has been shown to increase power and work capacity in short-term nontraining studies.[29] Creatine supplementation significantly enhances the ability to maintain muscular force and power during exhaustive strength training in healthy individuals.[25,27,30] In the pathological population, 1 year of creatine supplementation in patients with gyrate atrophy of the choroid and retina resulted in a 43% increase in muscle fiber diameter after supplementation.[21] The purpose of this study was to examine the effect of oral creatine supplementation on recovery of muscle strength after ACL reconstruction in a prospective and randomized double-blind trial.

MATERIALS AND METHOD

Subjects

Sixty patients scheduled for ACL reconstruction gave informed consent to participate in the study. The 33 men and 27 women had a mean height of 1.71 m ± 0.1 m, weight of 70.7 kg ± 1.9 kg, and age of 30.4 ± 1.0 years. Each patient agreed to have a battery of tests prior to surgery, which included a knee outcome score (KOS); height, weight, and body fat analysis; goniometric knee range of motion; isokinetic knee strength testing; and hip strength testing. These tests were repeated at 6, 12, and 24 weeks after surgery. In addition, at 6 months a single leg hop test for distance was performed and a KOS was recorded. The same tester performed all measurements.

Supplementation

Randomized creatine supplementation took place in a double-blind fashion by administering the creatine or the placebo in tablet form (Highland Laboratories, Eugene, Oregon). Test and placebo products were manufactured to appear similar. Supplementation was assigned randomly during the subject's preoperative testing visit in the physical therapy department 1 week prior to ACL reconstruction. Those volunteers receiving creatine were given 20 g/day for the first 7 days, after which the dosage was reduced to 5 g/day.[30] Subjects began supplement intake the day following surgery and continued supplementation for a 12-week period. The placebo group followed the exact same protocol but ingested calcium as the placebo substance. To monitor compliance, the subject was given exactly enough tablets so that when the subject returned for the next testing session, there would be 5 tablets left in the container. If any subject had more than 13 tablets left (missed more than 2 days of supplementation), he or she was dropped from the study.

Anthropometrics

Height, weight, and percentage of body fat were measured at each testing session. Percentage of body fat was determined using skinfold thickness measurements (Skydex Fayetteville, Arkansas). The formula used to calculate the percentage of body fat was supplied by the manufacturer. This method has been shown to be valid and reliable by other investigators.[13,14]

Knee Range of Motion

Knee extension range of motion was measured goniometrically in supine with the feet elevated and resting on a bolster. In this position, accurate determination of hyperextension is possible. The greater trochanter, lateral joint line, and lateral malleolus were used as landmarks. Knee flexion was measured in the prone position. Knee range of motion is reported as the difference between the involved and noninvolved knees.

Dietary Intake

Due to the potential effect of diet on skeletal muscle creatine, dietary intake of creatine-rich foods was assessed. Subjects were provided with food frequency questionnaires on admission to the study and at completion. In addition, history of creatine supplementation was determined.

Outcome Measures

Outcome measures at 6 months included a single leg hop test for distance and a subjective evaluation consisting of a KOS.[12] For the single leg hop test for distance, each subject was asked to hop from a starting point as far as he or she could using only one leg. The distance in centimeters for the best of 3 jumps was measured for each leg. The percentage difference between the involved and noninvolved sides was recorded.

Knee Strength Testing

Knee extension and flexion torques were measured isokinetically (Biodex, Shirley, New York) at 60°/s and 180°/s in the seated position. Following a submaximal warm-up of 5 maximal contractions at 60°/s, 20 maximal contractions at 180°/s were performed. *Muscle strength* was defined as peak torque at 60°/s, and *muscle power* was defined as the average power during the 20 contractions at 180°/s. If the patient experienced pain during testing, the test was deemed invalid and not included in data collection. Knee extension and flexion strength are reported as percentage deficit: [(noninvolved – involved)/noninvolved] × 100.

Hip Strength Testing

Hip flexion, abduction, and adduction strengths were measured with an instrumented manual muscle-testing device (Lafayette Instruments, Lafayette, Indiana). A force was manually applied with the manual muscle-testing

device in hand to break the muscle contraction. The force to break the muscle contraction was then recorded in newtons. The average of 2 maximum effort tests for each action was taken on both legs for each patient. A break test technique was used for each test using the positions delineated by Kendall and McCreary.[15] Hip flexion was tested in the seated position. The patients were asked to flex their hips so that their thighs elevated 4 in to 6 in off the table. At this point, a breaking force was applied at the distal femur. Abduction strength was tested in the side-lying position. The patient was asked to abduct the leg above horizontal, and a breaking force was applied distally, 1 in above the lateral malleolus. The side-lying position was also used for testing adduction strength. The patient was asked to straighten the leg and then lift the straight leg 12 in off the table, and a breaking force was applied 1 in above the medial malleolus. Muscle strength assessment using a handheld dynamometer has been shown to be a valid and reliable method of measuring strength. Bohannon[4] demonstrated test-retest correlation coefficients of 0.84 to 0.99 for hip strength measurements, indicating good to high reproducibility.

Surgical Technique

Patients were administered general or epidural anesthesia (depending on their own preference), and a pneumatic tourniquet and leg holder were used in every case. Patients underwent a single incision central third endoscopic ACL reconstruction. A superior lateral inflow portal was made so as not to interfere with the vastus medialis oblique. Interference screw fixation was used on the femoral and tibial side. The size of the interference screw was determined by the amount of space created by the boneplug within the tunnel. Once the screw was fixated, the fixation strength was manually tested by the surgeon. The patella defect was grafted with autogenous tibial bone, and the patella tendon defect was closed. The reconstructed knees were braced in a splint locked in extension.

Rehabilitation

After surgery, patients were weightbearing as tolerated with formal rehabilitation beginning at 1 week. Patients ambulated in a drop-lock knee brace for 4 weeks (first 2 weeks locked). The protocol involved hip progressive resistive exercises at week 0; quadriceps isometrics at week 1; isotonic leg press at week 2; Stairmaster at week 4; isokinetic knee extension at week 6; jogging at 3 months; high-speed, low-friction lateral movement at 4 months (slideboard); cutting and jumping at 4 to 5 months; and, ideally, return to sport at 6 months.

Data Analysis

Mixed-model analysis of variance was used to assess changes in body mass, percentage body fat, muscle strength, and muscle power between the creatine and placebo groups during the study. Changes in body mass, percentage body fat strength, and power were analyzed separately for the supplementation phase (prior to surgery to 12 weeks after surgery) and postsupplementation phase (12 weeks after surgery to 6 months after surgery). Changes in muscle strength and power on the involved side during the supplementation phase were further separated into the catabolic phase (prior to surgery to 6 weeks after surgery) and anabolic phase (6 weeks after surgery to 12 weeks after surgery). The purpose of these analyses was to assess whether creatine supplementation (1) limited early postoperative strength loss, (2) facilitated subsequent strength gains, and (3) had any carryover effects beyond the supplementation period.

The sample size was based on an estimated clinically relevant effect size of 20% (eg, placebo subjects improving strength by 10% versus creatine subjects improving by 30%). A standard deviation of 25% for between-subject changes in strength on the involved was estimated using previous data.[19] Using these estimates, it was calculated that a sample of 25 subjects per group was required to have 80% power to detect a 20% difference in strength changes between the groups at a P value of less than .05.

RESULTS

Compliance

During the initial 6 weeks, 9 subjects dropped out for various reasons (3 creatine, 6 placebo). Two were lost due to complications following surgery (possible deep venous thrombosis, both placebo), 3 were noncompliant with taking the supplement (1 creatine, 2 placebo), and the remaining 4 had gastrointestinal distress (2 creatine, 2 placebo). This left 51 patients at 6 weeks (23 creatine, 28 placebo). At 12 weeks, 44 patients were available for testing (19 creatine, 25 placebo), and at 6 months, 38 patients were available for testing (17 creatine, 21 placebo).

Dietary Analysis

No significant differences were observed between groups in mean estimated intake of animal or dairy products. There was 1 ovo-lacto-vegetarian in the placebo group, and no vegetarians in the creatine-supplemented group. Other than this individual, all subjects ate a minimum of 4 servings of meat per week. The mean weekly intake of meat was 9.6 ± 5.3 servings (85 gm/serving) and 12.4 ± 4.7 servings for the placebo and creatine groups, respectively (P = .1). Three subjects had used creatine in the past, but none had used the supplement within 3 months of study initiation.

Anthropometrics

At the start of the study, the groups were evenly matched for age (creatine 36 ± 1.2 years, placebo 37 ± 1.5 years), height (creatine 1.73 m ± 0.23 m, placebo 1.72 m ± 0.2 m), weight (creatine 74 kg ± 3.5 kg, placebo 74 kg ± 2.6 kg), and percentage body fat (creatine 20.0% ± 1.5%, placebo 23.4% ± 1.3%). There were 16 males and 9 females in the creatine group and 17 males and 18 females in the placebo group.

There was a slight increase in body weight by week 12 (P = .03), but this effect was not different (time by group, P = .52) between the placebo and creatine groups (75.1 kg ± 3.0 kg vs. 75.3 kg ± 3.4 kg, respectively). Similarly, creatine supplementation did not affect body fat percentage (time by group, P = .43).

Muscle Strength

By 6 weeks after surgery, there was a significant loss of strength on the involved side for knee extension (47%, P < .0001) and knee flexion (16%, P < .0001), with no change in hip flexion (P = .06), hip abduction (P = .69), or hip adduction (P = .66). Creatine supplementation did not affect strength losses in knee extension (time × group, P = .7) (Fig. 1) or knee flexion (time × group, P = .43) (Fig. 2). From 6 weeks to 12 weeks, there were significant increases in strength on the involved side for knee extension (47%), knee flexion (27%), hip flexion (20%), hip abduction (9%), and hip adduction (17%) (all P < .001). These strength improvements were unaffected by creatine supplementation (time × group: knee extension P = .67, Fig. 1; knee flexion P = .53, Fig. 2; hip flexion P = .42; hip abduction P = .75; hip adduction P = .35). Following supplementation, strength continued to improve on the involved side (12 weeks after surgery to 6 months) for knee extension (22%, P < .0001) and knee flexion (12%, P < .0001), with no change for hip flexion (P = .15), hip abduction (P = .54), and hip adduction (P = .35). These improvements in knee extension and flexion strength were similar between the creatine and placebo groups (time × group: knee extension P = .34, Fig. 1; knee flexion P = .06; Fig. 2).

From prior to surgery to 12 weeks after surgery, there was a small increase in strength on the noninvolved side for knee extension (P < .05) (Fig. 1), with no change for knee flexion (P = .14) (Fig. 2), hip flexion (P = .35), hip abduction (P = .35), or hip adduction (P = .81). Creatine supplementation did not affect strength in the noninvolved side for any of the muscle groups tested (time × group, P = .17-.99).

At 6 months after surgery, there was still a significant strength deficit in knee extension (29%, P < .0001), but there was no deficit in knee flexion strength (5%, P = .16). By 12 weeks after surgery, there were no significant strength deficits in hip flexion (–2%), hip abduction (–3%), or hip adduction (2%).

Muscle Power

By 6 weeks after surgery, there was a significant loss of power on the involved side for knee extension (42%, P < .0001) and knee flexion (18%, P < .0001), but these effects were not affected by creatine supplementation (knee extension: creatine 35%, placebo 47%, P = .14; knee flexion: creatine 16%, placebo 20%, P = .59). From 6 weeks to 12 weeks after surgery, there were significant increases in power on the involved side for knee extension (46%, P < .0001) and knee flexion (26%, P < .0001), but these effects were not affected by creatine supplementation (knee extension: creatine 37%, placebo 55%, P = .43; knee flexion: creatine 23%, placebo 28%, P = .82).

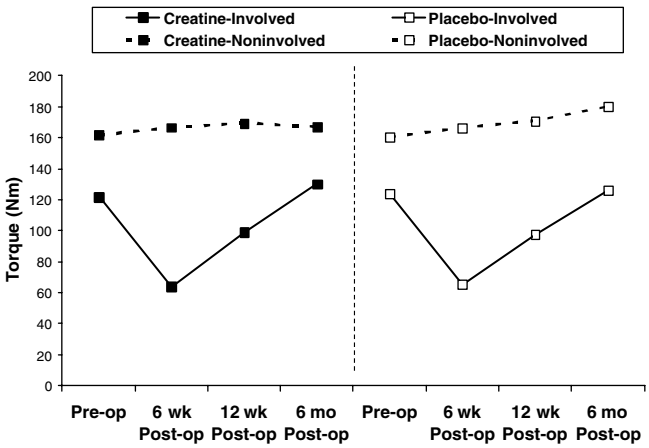

Figure 1. Knee extension strength (peak torque at 60°/s) on the involved side (solid line) and noninvolved side (dashed line) for the creatine group (closed symbols, left side of graph) and placebo group (open symbols, right side of graph). No effect of creatine supplementation at any time point (see Results section for further details). Pre-op, preoperative; Post-op, postoperative.

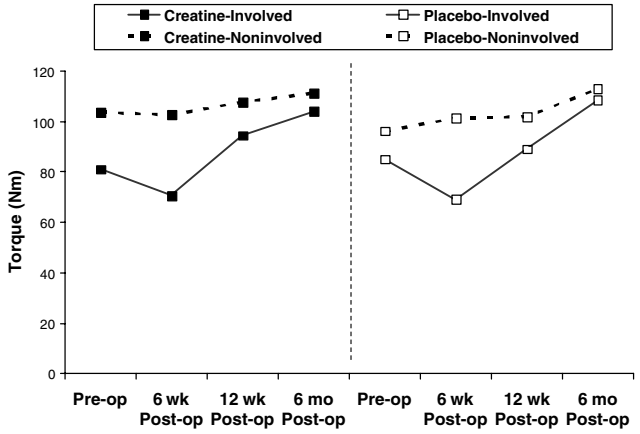

Figure 2. Knee flexion strength (peak torque at 60°/s) on the involved side (solid line) and noninvolved side (dashed line) for the creatine group (closed symbols, left side of graph) and placebo group (open symbols, right side of graph). No effect of creatine supplementation at any time point (see Results section for further details). Pre-op, preoperative; Post-op, postoperative.

Muscle power on the involved side continued to increase from 12 weeks after surgery to 6 months after surgery for knee extension (19%, P < .0001) and knee flexion (11%, P < .01), with no differences between the creatine and placebo groups (knee extension: creatine 17%, placebo 20%, P = .75; knee flexion: creatine 4%, placebo 17%, P = .11).

For the noninvolved side, muscle power increased from prior to surgery to 12 weeks after surgery for knee extension (P < .0001) and knee flexion (P < .01). However, creatine supplementation did not affect these changes in power (P = .58 and .57, respectively).

Outcome Measures

The KOS 6 months after ACL reconstruction was significantly higher than values prior to surgery for both the creatine and placebo groups ($P < .001$). The improvement in the KOS was not different ($P = .16$) between the creatine group (70 ± 11 to 89 ± 8) and the placebo group (76 ± 12 to 89 ± 7). Hop test deficits 6 months after surgery were not different between the creatine and placebo groups (15 ± 18% and 11 ± 14%, respectively; $P = .41$).

DISCUSSION

Recently, creatine supplementation has received considerable attention as a potential ergogenic aid in strength and power activities.[2,3] Several studies and reviews have indicated that creatine supplementation can enhance lean body mass and indices of strength, power, and high-intensity exercise endurance.[5,8] Creatine supplementation can increase muscular stores of creatine phosphate, which can enhance anaerobic endurance capabilities.[30] In addition, creatine supplementation may enhance mitochondrial creatine kinase activity, which would, in turn, increase the rate of aerobic resynthesis of adenosine triphosphate and recovery.[10]

Beneficial effects of short- and long-term creatine supplementation have been demonstrated in nonorthopaedic patient populations. Eleven days of supplementation increased strength in several muscle groups in a group of 81 patients with various neuromuscular diseases compared to a group of 21 patients taking a placebo.[26] One year of creatine supplementation in patients with gyrate atrophy of the choroid and retina resulted in a 43% increase in muscle fiber diameter after supplementation.[21] Both of these studies[21,26] indicate a positive effect of creatine in the absence of specific strength training. Beneficial effects of creatine supplementation have been demonstrated in healthy uninjured subjects following limb immobilization. Hespel et al[11] studied the effect of oral creatine supplementation on disuse atrophy and the expression of muscle myogenic factors. One limb of 21 healthy volunteers was immobilized in a cast for 2 weeks. This was followed by 10 weeks of strengthening while subjects were supplemented with creatine or placebo with similar dosing to the present study (20 g/day for 7 days and 5 g/day for 9 weeks). All subjects demonstrated a decrease in quadriceps strength following the immobilization. The subsequent increase in strength by 12 weeks was greater in the creatine group compared with the placebo group. The creatine group had increased muscle fiber hypertrophy and increased expression of the protein MRF4. Unlike the present study, these were noninjured subjects with normal strength prior to immobilization. Two weeks of immobilization followed by an unrestricted training stimulus are not analogous to the situation after ACL reconstruction.

We hypothesized that creatine supplementation would limit early postoperative strength loss and facilitate subsequent strength gains after ACL reconstruction. However, the results demonstrate that patients do not benefit from oral creatine supplementation during the first 12 weeks of rehabilitation after ACL reconstruction. We were unable to show a significant effect in hip or knee strength at 6 weeks, 12 weeks, or 6 months after surgery. In addition, outcome measures 6 months after surgery (KOS and hop test) were unaffected by creatine supplementation. One possible explanation for creatine supplementation having no effect on limb strength after ACL reconstruction is the lack of a sufficient overload to the muscles being trained. It may be possible that implementing a creatine supplementation protocol at 12 weeks after ACL reconstruction, at the beginning of the more dynamic strengthening program, may prove beneficial.

Statistical power to detect a clinically significant effect is always a concern in clinical trials such as this. In designing the study, we estimated that 25 patients per group would be sufficient. Because there was some loss to follow-up, we reexamined statistical power. Any potential effect of creatine supplementation on knee extension strength would have been most apparent 12 weeks after surgery (end of supplementation period). Based on the observed changes in knee extension strength on the involved side from 6 weeks to 12 weeks, a 20% difference in knee extension strength between the creatine and placebo groups at 12 weeks would have been significant ($P < .05$) at 80% power. Because the observed difference was minimal (2%), it is unlikely that these negative effects were subject to a type II error.

Summary

The results demonstrate that patients do not benefit from creatine supplementation during the first 12 weeks of rehabilitation after ACL reconstruction. Specifically, muscle strength and power changes were unaffected by creatine supplementation. Outcome measures were similarly unaffected.

ACKNOWLEDGMENT

We would like to express our gratitude to Highland Laboratories in Eugene, Oregon for providing the supplement and placebo to make this study possible.

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