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Investigation performed at the University of Utah, Salt Lake City, Utah

Background: Thigh muscle atrophy is a major impairment that occurs early after reconstruction of the anterior cruciate ligament and persists for several years. Eccentric resistance training has the potential to induce considerable gains in muscle size and strength that could prove beneficial during postoperative rehabilitation. The purpose of this study was to evaluate the effects of progressive eccentric exercise on thigh muscle structure following reconstruction of the anterior cruciate ligament.

Methods: Beginning three weeks after reconstruction of the anterior cruciate ligament, forty patients were randomly assigned to a program involving either twelve weeks of eccentric exercises or a standard rehabilitation protocol. Patients were matched by surgical procedure, sex, and age. The final series consisted of two cohorts of twenty patients each who had been treated with one of two types of graft (semitendinosus-gracilis or bone-patellar tendon-bone), with ten patients treated with each of the two rehabilitation protocols in each graft cohort. To evaluate changes in muscle structure, magnetic resonance images of the involved and uninvolved thighs were acquired before and after training. The volume and peak cross-sectional area of the quadriceps, hamstrings, and gracilis and the distal portion of the gluteus maximus were calculated from these images.

Results: The volume and peak cross-sectional area of the quadriceps and gluteus maximus, in both the involved and the uninvolved thighs and in the patients treated with each type of graft, improved significantly more in the eccentric-exercise group ($p < 0.001$). The magnitude of the volume change was more than twofold greater in that group. No significant differences in any hamstring or gracilis structural measurements were observed between the rehabilitation groups. However, the volume and peak cross-sectional area of the gracilis were markedly reduced, compared with the pretraining values, in the patients who had undergone reconstruction with the semitendinosus-gracilis graft.

Conclusions: Eccentric resistance training implemented three weeks after reconstruction of the anterior cruciate ligament can induce structural changes in the quadriceps and gluteus maximus that greatly exceed those achieved with a standard rehabilitation protocol. The success of this intervention can be attributed to the gradual and progressive exposure to negative work through eccentric exercise, ultimately leading to production of high muscle force.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.

Quadriceps atrophy and strength deficits are predominant impairments following reconstruction of the anterior cruciate ligament. The magnitude of atrophy and strength loss often exceeds 20% and 30%, respectively, during the first three months[1-6]. Despite concentrated rehabilitation efforts, a 10% to 20% deficit in quadriceps size and strength still persists for years after surgery[1,2,7-17]. The most important muscle group for lower-extremity function, the quadriceps, is preferentially affected, although other lower-extremity muscles undergo substantial atrophy as well. Deficits in hamstring and gracilis muscle volume of 10% and 30% have been reported after surgical reconstruction with an autologous semitendinosus-gracilis graft[17,18]. Like muscle wasting, muscle weakness is ubiquitous, with strength unlikely to return to preinjury levels. Novel interventions that can safely, feasibly, and effectively overload muscles early after surgery are needed to minimize atrophy

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and weakness that become long-standing.

A muscle's force production ability, and hence its structural and functional response, is greatest when an external force exceeds that of the muscle and the muscle lengthens eccentrically[19]. The resulting work performed by the muscle is termed "negative work" because the change in muscle length is opposite that of the muscle force vector; hence, work (force × distance) is negative. The application of a progressively increasing, high-force eccentric resistance has been shown to safely increase muscle size and strength in healthy and clinical populations and therefore may be suited for use after reconstruction of the anterior cruciate ligament[20-25]. In a recent case report, we reported observing impressive gains in quadriceps size and strength as a result of eccentric training following reconstruction of the anterior cruciate ligament[20]. We have also shown that the gradual and progressive application of eccentrically induced negative work can be tolerated without harmful side effects following this surgery[26].

The purpose of the present study was to evaluate the effects of progressive eccentric exercise on thigh muscle structure in individuals who had undergone reconstruction of the anterior cruciate ligament. Our primary hypothesis was that, compared with standard rehabilitation, eccentrically biased rehabilitation would result in significantly greater improvements in quadriceps volume and peak cross-sectional area in the involved thigh. Furthermore, these structural improvements would lead to superior short-term results in terms of quadriceps strength and performance while preserving knee stability. Secondarily, we hypothesized that there would be no difference in the improvement in hamstring or gracilis muscle volume or peak cross-sectional area between the rehabilitation groups. We further hypothesized that there would be significantly greater improvements in quadriceps volume and peak cross-sectional area in the uninvolved thigh, as it too was incorporated in the training, but there would be no difference between rehabilitation groups with regard to the hamstring or gracilis structure in the uninvolved thigh.

The term *standard rehabilitation* in this paper does not mean that the therapy program met some sort of institutional standard. Instead, it refers to a rehabilitation protocol that we commonly used at our institution.

Materials and Methods

Subjects

Patients diagnosed with a rupture of the anterior cruciate ligament at our University Sports Medicine Center between January 2004 and June 2005 were considered to be potential subjects. They were included in the study if they were between eighteen and fifty years of age, moderately active prior to the injury (a score on the Tegner activity scale[27] of ≥4 points), and willing to comply with the twelve-week training program (starting three weeks after surgery). Patients were excluded if they had had a previous fracture or reconstructive procedure in either lower extremity; abnormal findings on a radiograph of the knee; or a concurrent injury of the posterior cruciate ligament or the lateral collateral ligament, a grade-III tear of the medial collateral ligament, or a substantial articular cartilage lesion. Patients with a large vertical longitudinal meniscal tear were also excluded because of concern about allowing aggressive rehabilitation in these cases. Those who had had a partial meniscectomy or a small meniscal repair were allowed to participate. The graft selection was based on the patient's desire and/or request after he or she had been educated about the choice. The surgeons had a bias toward using bone-patellar tendon-bone grafts in younger patients and hamstring grafts in older patients. The study received approval from the institutional review board at the University of Utah, and all patients provided informed consent before participating.

Surgical Procedures

Two surgeons performed all of the ligament reconstructions in the patients in this study, and each used an arthroscopically assisted technique with a semitendinosus-gracilis or bone-patellar tendon-bone autograft. For the semitendinosus-gracilis procedure, a 3.5-cm incision was made over the medial aspect of the tibia, directly over the semitendinosus and gracilis tendons. Sutures were placed in a whip-stitch fashion in the distal 2.5 cm of each of the tendons. With use of a tendon stripper, the tendons were harvested and fashioned into two grafts, each 22 cm in length. With the aid of arthroscopy, the stump of the torn anterior cruciate ligament was débrided and a lateral notchplasty was performed to ensure that the over-the-top position could be identified. With use of an anterior-cruciate-ligament aiming guide, a guidewire was drilled into the anatomic footprint of the anterior cruciate ligament to position the tibial tunnel. The femoral tunnel was placed at the 10 o'clock position (right knee) or 2 o'clock position (left knee). The graft was passed through the knee and an EndoButton continuous loop (Smith and Nephew, Andover, Massachusetts) was used to secure the graft on the femoral side. The ends of the semitendinosus and gracilis graft were tensioned with use of the Linvatec Tensioner System (Largo, Florida). Sixty newtons of tension was placed on the semitendinosus graft, and 40 N was placed on the gracilis graft. An Intrafix device (DePuy Mitek, Raynham, Massachusetts) or an Arthrex resorbable interference screw (Naples, Florida) was used to secure the tibial side of the graft. The suture ends from the graft were then tied over a bicortical post and washer to provide back-up fixation[28].

For the bone-patellar tendon-bone procedure, an incision was made to approach the patella, patellar tendon, and proximal part of the tibia. A 10 by 25-mm-long block was harvested from the patella along with a 10-mm-wide strip of patellar tendon and a 10 by 30-mm tibial bone plug. With use of a tibial aimer, a guide pin was placed into the tibia and then overdrilled with an appropriately sized tibial drill bit. After this, a 6-mm over-the-top aimer was placed at the 10 o'clock position on the femur for a right knee or the 2 o'clock position for a left knee to accurately select the starting point for the femoral tunnel. This over-the-top aimer allowed for a 1-mm cortical rim on the back of the femoral tunnel when a 10-mm graft was used. A Beath pin was drilled up into position and

TABLE I Details of the Postoperative Rehabilitation Programs

	Rehabilitation Regimen
Phase I (duration, 2-3 wk)	Early range-of-motion exercises with emphasis on gaining full knee extension; weight-bearing as tolerated after bone-patellar tendon-bone procedure and touch-down weight-bearing after semitendinosus-gracilis procedure; straight-leg strengthening, functional exercise, and gait training. Goals for progression to phase II: minimal pain and effusion, 0°-100° range of motion of knee, good quadriceps contraction
Phase II* (duration, 2-3 mo)	Endurance training (bicycling, stair-stepper, etc.); progressive resistance training (leg presses, calf presses, mini-squats, hamstring curls, etc.), with emphasis placed initially on low resistance and multiple repetitions and then gradually replaced with sets of increasing resistance and fewer repetitions; battery of balance exercises and beginning-level plyometric exercises. Goals for progression to phase III: full range of motion, hopping on one leg without pain
Phase III (duration, 3-6 mo)	Continued progressive resistance and endurance training; jogging/running progression and advanced plyometric exercises; advanced strengthening and functional exercise training to prepare individual for full return to activity/sports. Goals for returning to full activity: 90% strength and performance ability compared with uninvolved lower extremity

*For those in the eccentric-exercise group, the twelve-week eccentric ergometry training program began three weeks after surgery.

then overdrilled to the exact length of the bone-tendon-bone graft with the appropriately sized drill bit. At this point, the cross-pin aimer (RIGIDfix system; (DePuy Mitek) was placed in the knee up into the femur. The cross-pin sleeves were then drilled percutaneously from lateral to medial into the lateral cortex. The graft was pulled up into position. The cross-pins were drilled, and resorbable pins were placed. After good fixation was obtained, the tibial end was tensioned. An interference screw was then placed next to the bone block in an interference-fit fashion[29].

Eccentric and Standard Rehabilitation Programs

A randomized matched design was used after the surgery to randomly assign patients to either an eccentric or a standard-rehabilitation group. Patients were matched by graft type, sex, and age. For example, after the first patient, a thirty-five-year-old man who had undergone a reconstruction of the anterior cruciate ligament with a semitendinosus-gracilis autograft, was randomized (by coin flip) into one group, the second man who had the same graft type and was between the ages of thirty-two and thirty-eight was assigned to the other group. The standard rehabilitation protocol that all patients followed was a criterion and time-based, three-phase rehabilitation program from this institution that emphasized closed-chain exercises, functional training, and gaining an early range of knee motion (Table I). The exercise prescription was determined by the individual response to exercise. Specifically, if exercises were completed without an increase in knee pain or effusion, the patient was considered ready to progress. Other exercises were then added or current exercises were continued at a higher intensity, frequency, and/or duration.

After ligament reconstruction, all patients completed two to three weeks of phase-I exercises that focused on controlling pain and effusion, gaining a full range of motion of the knee, and attaining basic quadriceps function (Table I). Beginning three weeks following surgery, patients in the eccentric-exercise group continued with standard rehabilitation and also began a twelve-week progressive negative-work exercise program using one of two recumbent eccentric ergometers, described previously in detail[20,23,26,30]. The first ergometer was similar to a recumbent cycle. It was replaced by a second, more durable and comfortable ergometer (Eccentron, Denver, Colorado) similar to a recumbent stepper. The cycle ergometer was used by the first five patients, and the stepper ergometer was used thereafter. Both ergometers induced eccentric contractions of the knee and hip extensors and negative work of similar magnitude (Fig. 1). During each exercise session, the negative work rate was visible on the computer monitor, and the total amount of negative work (measured in kilojoules) was recorded. The pedal speed was self-selected and ranged from 20 to 40 revolutions per minute. Patients were positioned on the ergometer so that the negative work would occur from approximately 20° to 60° of knee flexion, effectively minimizing the possibility of a knee hyperextension injury. The intensity of the exercise was based on the Borg rating of perceived exertion scale[31]. The first session was five minutes in duration at a "very, very light" intensity. If a patient had a favorable response to exercise (such as absence of increased knee pain, effusion, or excessive fatigue), he or she was allowed to gradually progress to a "hard" intensity and a maximum duration of thirty minutes (Table II). Conducting the exercise regimen in this manner has been shown to be safe and feasible after reconstruction of the anterior cruciate ligament[26]. Patients had to complete a minimum of 80% of the training sessions to continue in the study. Beginning three weeks postoperatively, the patients in the standard-rehabilitation group continued with the standard rehabilitation protocol. In an attempt to equalize the total exercise time between the groups, these patients were instructed to follow an exercise regimen that was similar to the one used by the eccentric-exercise group except that the patients in the standard-rehabilitation group used a concentric ergometer (gradually progressing to a "hard" intensity and a duration of thirty minutes).

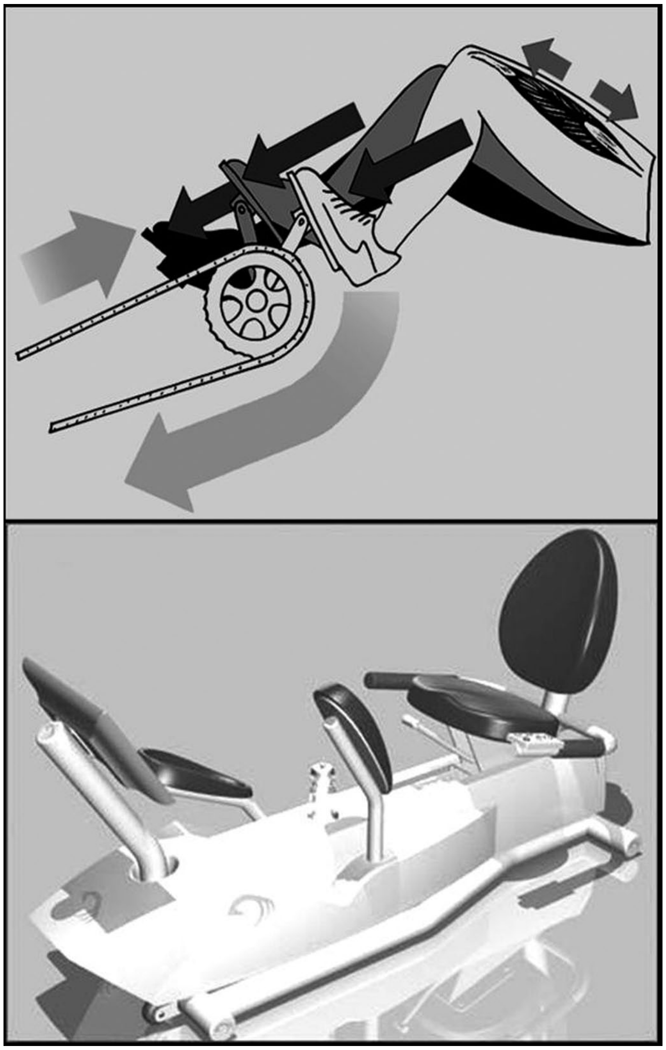

Fig. 1

Two eccentric ergometers. As the motor-propelled pedals move toward the participant (to the right in these figures), he or she resists the pedals from a position of approximately 20° to 60° of knee flexion in a closed-kinetic-chain fashion. Because the magnitude of force produced by the motor exceeds that produced by the participant, the knee and hip extensors act eccentrically, creating negative work.

Determination of Muscle Structure with Magnetic Resonance Imaging

A 1.5-T Signa LX magnetic resonance imaging instrument and body coil (General Electric Medical Systems, Milwaukee, Wisconsin) was used to acquire a coronal scout scan and axial spin-echo T1-weighted images. Both thighs were scanned from the superior border of the femoral head to the tibiofemoral joint line while the subject lay supine in the scanner. The scans were acquired with an image matrix of 256 × 256, a field of view of 40 to 44 cm depending on the size of the subject, a slice thickness of 8 mm, and an interslice distance of 15 mm. After electronic data transfer of magnetic resonance images, cross-sectional areas were measured with use of custom-written image-analysis software (MATLAB; The MathWorks, Natick, Massachusetts) on a desktop personal computer. Muscle volumes could be determined by measuring the muscle cross-sectional area in sequential axial sections across the length of the muscle[32]. On each image, the entire muscle of interest (independent of skin, bone, and fat) was identified and was manually traced with use of a computer mouse. The cross-sectional area of each slice was automatically computed with use of the averaged gray-scale density of the traced muscle. The muscle volume was calculated by multiplying the average of two consecutive measurements of cross-sectional area by the slice thickness plus the interslice distance (23 mm) and then summing those values across the length of the muscle.

A pretraining magnetic resonance imaging scan was acquired for each participant three weeks (mean [and standard deviation], 22.2 ± 3.4 days) after surgery. The follow-up images were acquired fifteen weeks (mean, 107.8 ± 7.5 days) after surgery, following completion of the twelve-week training program. The main objective of this study was to evaluate the effect of the eccentric-exercise intervention on the structure, including the volume (in cubic centimeters) and peak cross-sectional area (in square centimeters), of the thigh muscles. Depending on the size of the subject, the volume was calculated from seventeen to twenty axial slices of the quadriceps,

TABLE II Eccentric Ergometry Exercise Guidelines, Starting Three Weeks After Reconstruction of the Anterior Cruciate Ligament

Training Week	Exercise Session	Intensity (Rate of Perceived Exertion)	Duration *(min)*
1	1	Very, very light	5
	2	Very light	5-10
	3	Fairly light	5-10
2	4	Light	10-15
	5-6	Somewhat hard	10-15
3-4	7-12	Somewhat hard	15-20
5-6	13-18	Somewhat hard	20-25
7-8	19-24	Somewhat hard	26-30
9-12	25-36	Hard	26-30

fourteen to seventeen slices of the hamstrings, and thirteen to sixteen slices of the gracilis. Because the eccentric-exercise intervention was a quadriceps-dominated exercise, the primary outcome measures were changes in the volume and peak cross-sectional area of the quadriceps. However, as a result of the frequency with which patients reported soreness in the gluteal region due to training, we decided to also evaluate the distal portion of the gluteus maximus, from the head of the femur distally. Thus volume was calculated from eight, nine, or ten axial magnetic resonance image slices. The same investigator, who was blinded to whether the imaging was done before of after training, performed all structural measurements in a highly reproducible manner (intraclass correlation coefficients, >0.99).

Assessment of Knee Stability and Functional Status

Routine clinical examinations, which included an assessment of knee stability with use of the KT-1000 device (MEDmetric, San Diego, California), were completed prior to reconstruction of the anterior cruciate ligament and fifteen weeks following the surgery. These examinations also included isokinetic strength testing and the single-leg hop-for-distance test. Quadriceps and hamstring strength (peak torque) were assessed with use of a Kin Com isokinetic dynamometer (Chattecx, Chattanooga, Tennessee). Patients were tested concentrically at $60° \cdot s^{-1}$ in a seated position with the hips and knees in 90° of flexion and the thighs, pelvis, and upper body firmly strapped to the seat of the dynamometer. Prior to testing, a warm-up consisting of three repetitions (at 50%, 75%, and 100% intensity) was completed. After a brief rest period of one minute, patients completed three separate trials at 100% intensity. The peak torques of the three trials were averaged, and the average was recorded. For the hop-for-distance test, patients were instructed to hop as far as possible, always landing on the same leg. Hopping with each leg was tested three times, and the maximal distance was recorded. The average of the two farthest hops was recorded. The strength and performance indices (the value for the involved limb divided by the value for the uninvolved limb) were used for statistical analysis. Patients also completed the Activities of Daily Living Scale of the Knee Outcome Survey and the Lysholm questionnaire. Although the focus of this research was on muscle structure, these measures were included to establish the short-term functional status of the patients prior to surgery and after the twelve-week training program.

Statistical Methods

The sample size was based on preliminary data with use of improvement in quadriceps volume resulting from a twelve-week eccentric resistance training program as the primary outcome measure. This showed that nine patients in each group would be sufficient to achieve significance with 80% power and an α level set at 0.05. In order to analyze the effects of eccentric exercise independent of graft type, because both a semitendinosus-gracilis and a bone-patellar tendon-bone graft were used for the surgical reconstructions, twenty patients treated with each graft type (with ten treated with each exercise regimen in each graft group)—i.e., a total of forty individuals—were recruited to participate. Data were analyzed with SPSS software (version 13.0; SPSS, Chicago, Illinois). Descriptive statistics for categorical variables and measures of central tendency for continuous variables were calculated to summarize the data. Tests for outliers and assumptions of the parametric statistical tests were performed. A two-way mixed repeated-measures analysis of variance with factors of group and time was used to analyze mean differences in muscle volume and peak cross-sectional area between the eccentric and standard-rehabilitation groups. The Pearson product-moment correlation was used to correlate improvements in muscle volume and peak cross-sectional area. An independent t test was used to analyze mean differences in knee laxity, quadriceps and hamstring strength, hopping distance, and self-reported scores fifteen weeks after surgery between the eccentric and standard-rehabilitation groups. Significance levels for all statistical analyses were set at $\alpha < 0.05$.

Results

All forty patients who enrolled completed the study. Preoperative demographic and physical characteristics were similar between the intervention groups; however, those treated with the bone-patellar tendon-bone graft were significantly younger and more active than those treated with the semitendinosus-gracilis graft (see Appendix). Thirty-two of the forty patients had surgery within four months after the injury (at a mean of 45.1 ± 24.5 days in the eccentric-exercise group and at a mean of 41.8 ± 29.3 days in the standard-rehabilitation group). The time between the initial ligament tear and the surgery was longer than one year for five patients (two in the eccentric-exercise group and three in the standard-rehabilitation group). Three individuals in the eccentric-exercise group and four in the standard-rehabilitation group had small meniscal lesions that were repaired, and three individuals in both groups had meniscal lesions that were débrided or resected.

The twenty patients in the eccentric-exercise group completed a mean of 31.1 ergometry sessions (range, twenty-nine to thirty-six sessions), for an overall compliance rate of 86%. No significant differences in results were observed between the cycle and stepper ergometers ($p = 0.86$). Overall, the participants completed an average of 738 minutes of eccentric ergometry. The patients reported that they performed lower-extremity weight-lifting, excluding the eccentric ergometry, on a mean of 15.3 days during the twelve-week training period. In comparison, the twenty patients in the standard-rehabilitation group averaged 709 minutes of concentric ergometry. Those patients reported that they performed lower-extremity weight-lifting on a mean of 25.4 days during the twelve-week training period. The number of reported days on which weight-lifting was performed was significantly greater in the standard-rehabilitation group ($p < 0.01$).

Volume and Peak Cross-Sectional Area

Quadriceps

Compared with the pretraining measurements, the posttraining quadriceps volume and peak cross-sectional area in the involved thigh increased significantly in both the eccentric and the standard-rehabilitation group ($p < 0.001$). However, these increases in the quadriceps volume and peak cross-sectional area were significantly greater ($p < 0.001$), by more than two-fold, in the eccentric-exercise group (mean improvement, 23.1% ± 12.9% and 24.2% ± 12.6%, respectively) than in the standard-rehabilitation group (mean improvement, 8.8% ± 9.3% and 9.3% ± 9.4%). There was a significant correlation between improvement in quadriceps volume and improvement in peak cross-sectional area in the involved thigh ($r = 0.98$, $p = 0.01$). The greater than twofold increase in quadriceps hypertrophy in the eccentric-exercise group was observed in both the semitendinosus-gracilis and the bone-patellar tendon-bone cohort, although the overall magnitude of improvement was smaller (nonsignificantly so) in the bone-patellar tendon-bone cohort (Figs. 2 and 3 and Appendix).

Nine of the ten patients in the eccentric-exercise group who had been treated with a semitendinosus-gracilis graft demonstrated a quadriceps volume increase of >20%, whereas nine of the ten patients in the standard-rehabilitation group who had been treated with a semitendinosus-gracilis graft demonstrated a volume increase of <15%. In contrast, five of the ten patients in the eccentric-exercise group who had been treated with a bone-patellar tendon-bone graft demonstrated a quadriceps volume increase of >20%, whereas eight of the ten patients in the standard-rehabilitation group who had been treated with a bone-patellar tendon-bone graft demonstrated a volume increase of <10% (see Appendix).

The quadriceps volume and peak cross-sectional area in the uninvolved thigh increased significantly in both the eccentric and the standard-rehabilitation group ($p \leq 0.001$), although these structural increases were significantly greater ($p < 0.001$) in the eccentric-exercise group (mean improvement, 11.2% ± 5.1% and 11.0% ± 4.9%, respectively) than in the standard-rehabilitation group (mean improvement, 3.0% ± 3.3% and 3.1% ± 3.7%). The improvement in the uninvolved thigh was significantly greater in the individuals who had been treated with the bone-patellar tendon-bone graft ($p < 0.001$) than it was in those who had been treated with the semitendinosus-gracilis graft (Figs. 2 and 3 and Appendix). There was a significant correlation between improvement in quadriceps volume and improvement in peak cross-sectional area in the uninvolved thigh ($r = 0.92$, $p = 0.01$).

Gluteus Maximus

The distal portion of the gluteus maximus, beginning from the superior border of the femoral head, was analyzed. Compared with the pretraining values, the posttraining volume and peak cross-sectional area of the gluteus maximus of the involved lower extremity increased significantly in both the eccentric and the standard-rehabilitation group ($p < 0.001$). The magnitude of these structural increases was significantly greater ($p < 0.001$), by more than twofold, in the eccentric-exercise group (mean improvement, 25.3% ± 12.9% and 26.5% ± 10.5%, respectively) than in the standard-rehabilitation group (mean improvement, 9.8% ± 9.3% and 9.6% ± 10.5%) (Fig. 3 and Appendix). There was a significant correlation between improvement in the volume and improvement in the peak cross-sectional area of the gluteus maximus of the involved lower extremity ($r = 0.94$, $p = 0.01$). The greater than twofold increase in gluteus maximus hypertrophy in the eccentric-exercise group was observed in both the semitendinosus-gracilis and the bone-patellar tendon-bone cohort, although the overall magnitude of improvement was smaller (nonsignificantly so) in the semitendinosus-gracilis cohort.

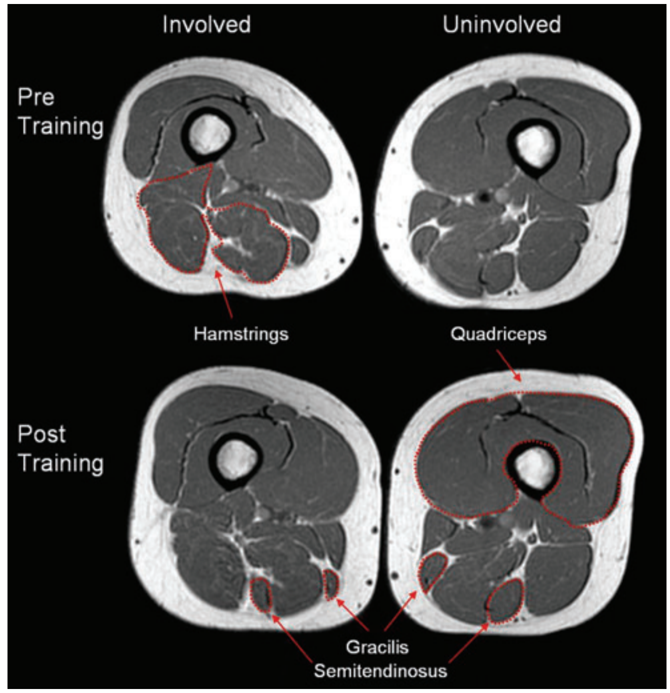

Fig. 2

T1-weighted magnetic resonance images of the involved and uninvolved thighs, acquired approximately 14 cm superior to the tibiofemoral joint line, in a subject treated with a semitendinosus-gracilis graft and assigned to the eccentric-exercise group. Note the relatively positive change in quadriceps size and the relatively negative change in gracilis size between the pretraining and posttraining assessments.

The volume and peak cross-sectional area of the gluteus maximus of the uninvolved thigh increased significantly in the eccentric-exercise group (mean improvement, 11.1% ± 5.1% and 10.2% ± 6.4%, respectively; $p < 0.001$) but not the standard-rehabilitation group (mean improvement, 2.5% ± 6.1% and 3.8% ± 6.8%; $p = 0.19$) (Fig. 3 and Appendix). There was a significant correlation between improvement in the volume and improvement in the peak cross-sectional area of the gluteus maximus of the uninvolved lower extremity ($r = 0.83$, $p = 0.01$).

Hamstrings

Comparison of the pretraining and posttraining values revealed no significant differences in the improvements in hamstring volume or peak cross-sectional area in either the involved or the uninvolved thigh between the eccentric and standard-rehabilitation groups (p range, 0.23 to 0.90). However, there was

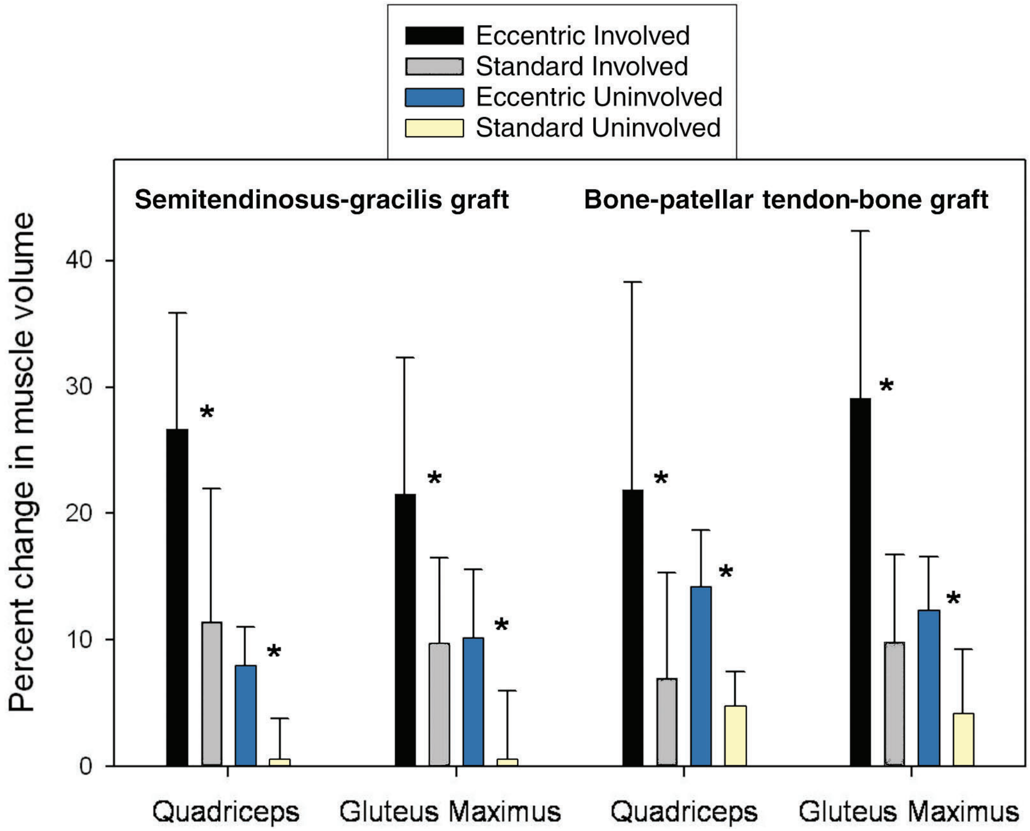

Fig. 3

Changes in the volumes of the quadriceps and gluteus maximus muscle in the involved and uninvolved lower extremities during the twelve-week training period after treatment with a semitendinosus-gracilis or bone-patellar tendon-bone graft. The asterisks indicate a significant difference in muscle-volume improvement between the eccentric and standard-rehabilitation groups ($p \leq 0.005$).

a significant difference between graft types, as the hamstring volume and peak cross-sectional area in the involved thigh increased significantly, compared with the pretraining values, in the bone-patellar tendon-bone cohort ($p \leq 0.006$) but not in the semitendinosus-gracilis cohort (p range, 0.13 to 0.53; Appendix and Fig. 4). There was a significant correlation between improvement in the hamstring volume and improvement in the hamstring peak cross-sectional area in the involved ($r = 0.89$, $p = 0.01$) and uninvolved ($r = 0.62$, $p = 0.01$) thighs.

Gracilis

Comparison of the pretraining and posttraining measurements also showed no significant differences in the improvements in the gracilis volume or peak cross-sectional area in either the involved or the uninvolved thigh between the eccentric and standard-rehabilitation groups (p range, 0.35 to 0.92). However, whereas the gracilis volume and peak cross-sectional area in the involved thigh decreased significantly, compared with the pretraining values, in the semitendinosus-gracilis cohort ($p < 0.001$), no significant changes were observed in the bone-patellar tendon-bone cohort (p range, 0.16 to 0.78). The gracilis volume and peak cross-sectional area in those who had undergone the semitendinosus-gracilis graft procedure decreased 18.6% ± 7.0% and 13.0% ± 10.1% in the eccentric-exercise group and 16.7% ± 12.4% and 10.0% ± 11.9% in the standard-rehabilitation group (Figs. 2 and 4 and Appendix). There was a significant correlation between improvement in the gracilis volume and improvement in the peak cross-sectional area in the involved ($r = 0.91$, $p = 0.01$) and uninvolved ($r = 0.69$, $p = 0.01$) thighs.

Assessment of Knee Stability and Functional Status

The functional status measures are presented in a table in the Appendix. With the numbers studied, there were no significant differences in the knee laxity measured with the KT-1000 device (with manual maximum force) between the eccentric (mean, 1.6 ± 1.8 mm) and standard (mean, 1.7 ± 1.0 mm) rehabilitation groups fifteen weeks after reconstruction of the anterior cruciate ligament ($p = 0.83$). The overall quadriceps strength index was significantly greater in the eccentric-exercise group than in the standard-rehabilitation group ($p = 0.03$). There were no significant differences between groups with regard to the hamstring strength index ($p = 0.49$) or hop index ($p = 0.09$); however, the hop index was significantly greater in

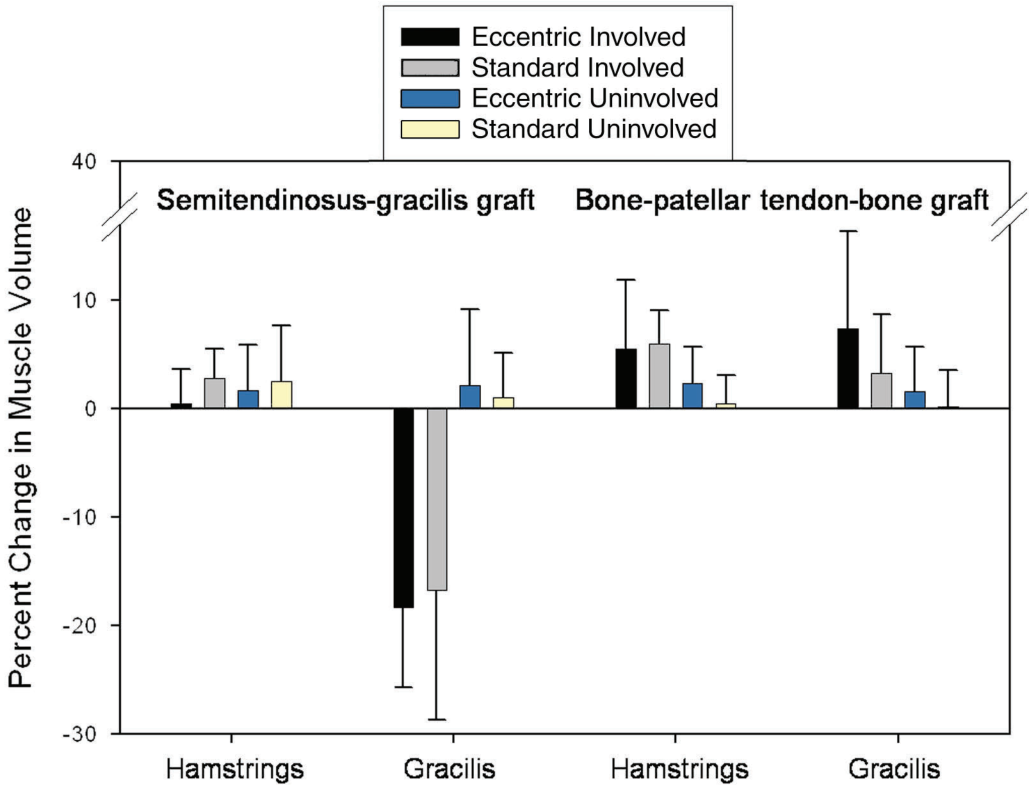

Fig. 4

Changes in the volumes of the hamstring and gracilis muscles in the involved and uninvolved lower extremities during the twelve-week training period after treatment with a semitendinosus-gracilis or bone-patellar tendon-bone graft. There were no significant differences in muscle-volume changes between the eccentric and standard-rehabilitation groups.

the eccentric-exercise group of the bone-patellar tendon-bone cohort ($p = 0.04$). Scores on the Activities of Daily Living Scale of the Knee Outcome Survey and on the Lysholm scale improved significantly fifteen weeks after surgery, compared with preoperative values, in all groups ($p < 0.001$), but with the numbers studied no significant differences between groups were observed ($p = 0.66$ and 0.93, respectively).

Discussion

In support of our primary hypothesis, this investigation demonstrated that the addition of progressive eccentric exercise, implemented three weeks after reconstruction of the anterior cruciate ligament, safely induced gains in size and strength in key muscle groups that exceeded the gains following a standard rehabilitation program while preserving knee stability. The increases in the sizes of the quadriceps and gluteus maximus muscles were twofold greater than those observed following the standard rehabilitation program. Because muscle atrophy is ubiquitous and profound in the early period following surgery, these structural increases (observed in both the involved and the uninvolved lower extremities and in both the semitendinosus-gracilis and the bone-patellar tendon-bone cohort) are unprecedented, to our knowledge.

Since the potential to overload muscle is greater with eccentric training (compared with the potential with concentric training), as a result of its high force-producing abilities, greater increases in muscle size and strength should not be surprising. High eccentric muscle forces, however, are closely associated with a muscle damage response in individuals not adapted to these forces. In fact, the patients in this study reached negative work levels consistent with those used to induce muscle damage. Another concern with high eccentric muscle forces is the amount of force that such an intervention would place through the healing graft, particularly after a bone-patellar tendon-bone procedure. Yet, as a result of the repeated, gradual, and progressive exposure to negative work, the patients in this study had great improvement in the quadriceps (and gluteal) muscle size without experiencing any deleterious effects. These results suggest that this mode of resistance training may be ideal for safely mitigating the persistent muscle impairments commonly observed following reconstruction of the anterior cruciate ligament, and they support the findings of other investigators who have reported the safe achievement of substantial gains in muscle size and strength by means of progressive eccentric exercise in healthy and clinical populations[20-25].

Exercising a muscle eccentrically is certainly not unusual following reconstruction of the anterior cruciate ligament. There is an intrinsic eccentric muscular component in almost all standard rehabilitation exercises. However, a key point to consider in this study was that the resultant muscular response of hypertrophy most likely corresponds to the magnitude of overload experienced by the muscle. Standard exercises proved beneficial, as evidenced by improvements in quadriceps volume of approximately 10% after twelve weeks of rehabilitation. While this muscular response was favorable, overloading the quadriceps progressively through focused eccentric training safely induced hypertrophic changes that were more than two-fold greater than those following the standard rehabilitation.

Although originally we had no intention of evaluating gluteus maximus structure, it is interesting to compare and contrast the responses of the quadriceps and gluteus maximus to eccentric training between surgical graft types. Subject characteristics differed between the grafts, with the semitendinosus-gracilis cohort consisting of patients who were slightly less active (average Tegner score, 6.2 points compared with 7.3 points in the other graft cohort) and older (35.3 compared with 23.2 years of age). However, despite these differences, progressive eccentric exercise produced substantially greater increases in the sizes of the quadriceps and gluteal muscles of both lower extremities when compared with the increases found after standard rehabilitation. The amount of improvement, however, appeared somewhat graft-specific. In the eccentric-exercise group, the quadriceps and gluteus maximus volumes improved 26.7% and 21.6%, respectively, in the semitendinosus-gracilis cohort compared with 19.8% and 29.1%, respectively, in the bone-patellar tendon-bone cohort.

Whichever graft was used, the gluteus maximus appeared to have recovered more completely than the quadriceps by fifteen weeks after surgery when the uninjured extremity was used for comparison. The size increase in the gluteus maximus may coincide with the increase in hip extensor strength reported after hamstring reconstruction of the anterior cruciate ligament[33]. These structural results also lend anatomic support to the findings of kinetic studies, which have often demonstrated greater hip extension moments and reduced knee extension moments following reconstruction of the anterior cruciate ligament[34,35]. While the eccentric-exercise paradigm used in this study appears excellent for inducing hypertrophy of the quadriceps and gluteus maximus muscles, it does not appear to prevent imbalances from developing between the knee and hip extensor muscles following reconstruction of the anterior cruciate ligament.

Our secondary hypothesis was that there would be no difference in the improvement in the hamstring or gracilis volume in the involved thigh between rehabilitation groups. Our results supported this hypothesis. Because the eccentric intervention was largely a quadriceps-dominated exercise, it was not surprising that the two rehabilitation groups would be similar with regard to hamstring or gracilis structural changes. There were differences, however, in hamstring and gracilis changes between graft types, most likely as a result of graft site morbidity. In a detailed morphological study, Williams et al.[17] found an overall reduction in hamstring volume of 11% approximately six months following reconstruction of the anterior cruciate ligament with an autologous semitendinosus-gracilis graft but reported a >30% reduction in semitendinosus volume. We did not analyze each hamstring muscle separately; however, on the basis of visual inspection (Fig. 2) we believe that our results would have been similar.

Structural changes in the gracilis also appeared to be graft-dependent. Gracilis volume improved marginally in the bone-patellar tendon-bone cohort, but it decreased substantially in the semitendinosus-gracilis cohort. A reduction in muscle volume of nearly 20% was already evident three weeks after surgery and it increased to a deficit of 35% just twelve weeks later. Intriguingly, only a 4% reduction in the peak cross-sectional area was observed three weeks after surgery; this increased to 15% by the time of the posttraining follow-up assessment. These structural findings were consistent with those reported by Williams et al.[17]. Also, this large deficit in gracilis muscle structure seems to coincide with deficits in hip adductor strength reported after this surgical procedure[33]. Short-term studies have consistently demonstrated substantial reductions in the hamstring and gracilis muscles following reconstruction of the anterior cruciate ligament with an autologous semitendinosus-gracilis graft[11,17,18,36], but long-term studies have not been conducted to determine the extent of recovery of hamstring or gracilis structure, to our knowledge. Because several investigators have observed persistent hamstring strength deficits after this type of surgery[12,36,37], one might anticipate discovering parallel hamstring structural deficits as well. It would also be interesting to determine whether targeted eccentric training for the hamstrings (and possibly the gracilis) would result in positive structural adaptations similar to those observed in the quadriceps and the gluteus maximus in our study.

Our final hypothesis was that there would be significantly greater improvement in the quadriceps volume and peak cross-sectional area in the uninvolved thigh in the eccentric-exercise group but there would be no difference between groups with regard to the hamstring or gracilis structure in the uninvolved thigh. Our results support this hypothesis. While eccentric ergometry did not significantly affect the hamstring or gracilis muscle of the uninvolved thigh, the intervention did induce an 11% increase in the quadriceps and gluteus maximus volumes. Williams et al.[17] reported minimal differences between any muscle volumes or peak cross-sectional areas in the uninvolved lower extremity before and after surgery.

It should be considered beneficial to increase muscle size and strength in the uninvolved thigh after surgery. However, when the uninvolved side improves, outcome measures based on a comparison of the involved and uninvolved sides are negatively affected. In this study, for example, without the 11% improvement in the size of the quadriceps in the uninvolved thigh, the volume index would have been 92.4 instead of 83.1. Researchers assessing outcomes often focus on comparing the muscle size, strength, and performance ability of the injured extremity with those of the "normal," uninjured extremity. The assumption seems to be that the uninjured extremity is "normal," thereby providing a valid comparison for the injured extremity. We believe that this assumption is not necessarily true after an injury and reconstruction of the anterior cruciate ligament and that in many cases, including the subject in our recent case report[20], the "normal" limb is also deconditioned and atrophied (albeit to a lesser extent) as a result of a large decrease in the person's typical activity.

In this study, there was considerable variability in the improvement in the quadriceps volume among patients. Several potential confounding factors that ultimately could have influenced a muscle's ability to hypertrophy were also identified (for example, knee pain, lack of range of motion, effusion, compliance, and the amount of pretraining atrophy). In the semitendinosus-gracilis graft cohort, it is difficult to ascertain why the quadriceps mass of the outlier in the eccentric-exercise group did not improve like the others. This individual complied with the exercise program and produced exceptional negative work values during training. However, because he did not have a great amount of atrophy after the surgery (a pretraining volume index of 91.3), he consequently had less potential for improvement. This relationship was reflected by the negative correlation between improvement in quadriceps volume and the pretraining volume index ($r = -0.47$; $r^2 = 0.22$). Essentially, those who began training with a higher quadriceps volume index (less atrophy) had less improvement at the time of follow-up. Another person in the eccentric-exercise group, with demographic characteristics and negative work output values that were nearly identical to those of the outlier, had a pretraining volume index of 91.1. That person demonstrated improvement in the quadriceps volume of nearly 21%. Therefore, we are uncertain why these two individuals in the eccentric-exercise group differed. The outlier in the standard-rehabilitation group was one of the youngest and most active patients (as indicated by the preinjury Tegner score) in the study. She had substantial quadriceps atrophy three weeks after the surgery (a volume index of 71.2) so one might have predicted an above-average increase in quadriceps volume after twelve weeks of rehabilitation. However, the improvement in quadriceps volume (39.3%) was more than twice that of any other patient in the standard-rehabilitation group and the improvement in hamstring volume (22.5%) was more than ten times greater than the average in the semitendinosus-gracilis graft cohort. Standard rehabilitation exercise typically requires the muscle to work both concentrically (pushing and overcoming a resistance) and eccentrically (pushing but yielding to the same resistance)[38]. This subject, however, reported doing the concentric portion (i.e., of the leg press) bilaterally and the eccentric portion unilaterally. She stated that the applied resistance was "more than I could do with one leg alone." It would be compelling to credit her extraordinary results to eccentric training, but we cannot draw such conclusions from this study. Other factors such as pretraining atrophy, age, or preinjury activity level may have contributed considerably.

In the bone-patellar tendon-bone cohort, the worst result in the standard-rehabilitation group and second worst in the eccentric-exercise group occurred in individuals who struggled to gain full passive knee extension (ultimately falling 3° to 5° short) and who experienced mild-to-moderate anterior knee pain throughout training. The person with the second worst result in the standard-rehabilitation group was not highly compliant with the weight-lifting regimen during the training period. The worst result in the eccentric-exercise group was in an individual who sustained two blunt injuries to the knee (from slipping on ice and landing on the knee) three weeks apart during the study period. Thus, rehabilitation following reconstruction of the anterior cruciate ligament is multifaceted, with outcomes being affected by a myriad of factors.

The current study had several limitations. Rehabilitation guidelines were provided for both groups, but postoperative activity levels were not documented even though differences in total activity between individuals can be confounding. A more detailed description of weight-lifting-specific activities would have been useful. While attempts were made to treat both groups equally, there was no way to completely blind patients to their treatment-group assignment. Although the study was appropriately powered, the sample size was small, and there were substantial differences between the graft types that limit generalizability. Finally, perhaps the greatest limitation of the study is that the outcomes that we reported were short-term. It is unknown whether the positive structural changes observed in this study will result in long-term benefits in terms of muscle size, strength, or performance. However, the considerable clinical attention and effort toward mitigating quadriceps atrophy and weakness during the first three months following reconstruction of the anterior cruciate ligament suggest that this is an essential time period for restoring muscle structure and function. At the time of writing, we were collecting data on this cohort one year after surgery to further understand the effects of eccentric training after reconstruction of the anterior cruciate ligament.

In conclusion, this study demonstrated that progressive eccentric resistance exercise implemented three weeks after reconstruction of the anterior cruciate ligament can induce changes in the structure of the quadriceps and gluteus maximus that greatly exceed (by more than twofold) those changes following an institutional standard rehabilitation program. These structural increases were observed in both the involved and the uninvolved thighs and with both the semitendinosus-gracilis and the bone-patellar tendon-bone grafts. The gradual and progressive exposure to negative work allowed the patients in this study to safely increase the intensity of eccentric training and greatly enhance structural changes of the quadriceps and gluteus maximus. Because the forces produced across a muscle during negative work are of the greatest magnitude of any muscle action, an eccentric intervention may be ideal for mitigating the persistent muscle impairments commonly observed after reconstruction of the anterior cruciate ligament.

Appendix

eA Tables showing preoperative patient characteristics, muscle volume data, and patient functional status measures are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

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