Quadriceps Weakness, Atrophy, and Activation Failure in Predicted Noncopers After Anterior Cruciate Ligament Injury

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Background: Quadriceps weakness is common after anterior cruciate ligament injury, especially in those who do not compensate well for the injury (“noncopers”). Both atrophy and activation failure have been demonstrated in this population but have not been directly related to quadriceps weakness.

Hypotheses: (1) Quadriceps strength, volumes, and cross-sectional areas of the noncopers would be smaller than those of the contralateral muscles, whereas other muscles would not demonstrate atrophy. (2) Quadriceps muscle activation deficits would be observed. (3) Atrophy and activation failure would account for the quadriceps weakness in these patients.

Study Design: Cross-sectional study, Level of evidence, 3.

Methods: Seventeen noncopers with isolated anterior cruciate ligament injury underwent burst-superimposition strength and activation testing of the quadriceps and magnetic resonance imaging of 12 muscles an average of 2 months after injury. Morphological characteristics was described by digitally reconstructing each muscle from the axial images and calculating muscle volume and peak cross-sectional area.

Results: The quadriceps muscles of the anterior cruciate ligament–deficient limb were significantly weaker (average 25%) than those of the uninjured side; activation failure (8%-10%) was observed for the quadriceps muscles of both limbs. The total quadriceps, vastus lateralis, and vastus intermedius volume and cross-sectional area were significantly smaller in the anterior cruciate ligament–deficient limb. There was no significant atrophy of any other muscle or muscle group. Atrophy and activation failure explained more than 60% of the variance in quadriceps weakness ($P = .004$).

Conclusion: The quadriceps femoris weakens soon after acute anterior cruciate ligament injury. Activation deficits and atrophy occur and affect quadriceps strength. Rehabilitation techniques that address activation deficits as well as atrophy may be necessary to restore quadriceps strength.

Keywords: knee; morphology; inhibition; athletes

Quadriceps femoris muscle weakness is common after ACL rupture in people who do not compensate well for the injury (“noncopers”). Evidence suggests that there may be an important neurosensory connection between the ACL and the quadriceps muscles that is disrupted when the ACL is ruptured. Loss of feedback from mechanoreceptors in the ACL may result in chronic suppression of recruitment of high-threshold motor units during voluntary contraction of the quadriceps, presumably via elimination of feedback from the ACL to gamma motor neurons. There is indirect evidence in support of these findings in studies of quadriceps atrophy and failure of voluntary activation after ACL injury. Atrophy alone may not account for the loss of muscle strength (eg, peak torque or force measurements) demonstrated after ACL rupture. Most studies have shown a lack of correlation between quadriceps femoris muscle cross-sectional area (CSA), morphological measures, and muscle strength in ACL-deficient patients, although there have been no recent studies of the morphological characteristics of the quadriceps after...
ACL rupture. Even though muscle force and CSA are strongly and directly related in studies of healthy muscle, muscle volume appears to be better related to muscle torque, the measured strength variable in most studies and in the clinic. Perhaps the calculation of muscle volume would allow for a more accurate prediction of the contribution of atrophy to muscle weakness. Studies of quadriceps activation after ACL rupture have demonstrated significant impairment of voluntary activation (inhibition), suggesting that a major consequence of ACL rupture is altered motor unit utilization, which presumably results in atrophy. Konishi et al have demonstrated abnormal gamma loop function in the involved and uninvolved quadriceps femoris muscle of patients with ACL rupture. Recent reports have demonstrated bilateral quadriceps weakness; and (2) the ability to hop on 1 leg without pain. All of the subjects had been enrolled in a preoperative rehabilitation program designed to control impairments in preparation for surgery. Enrollment exclusion criteria included a previous ACL injury, concomitant ligament abnormality, fractures, knee joint effusion, an abnor-
mal gait pattern, and the presence of hip or ankle abnormality. All predicted noncopers were required to have recent ACL injuries to prevent confounding effects from chronic knee instability (mean ± SD duration = 3.2 ± 2.0 months; range, 0.5-6.0 months). The mean scores on the screening examination (timed hop scores: 89% ± 11%; Knee Outcome Survey–Activities of Daily Living Scale score: 81.5% ± 11%; global rating of knee function: 61% ± 15%; and episodes of giving way: 4 ± 2) demonstrate that the noncopers were indeed suffering from repetitive knee instability and poor function. This study was approved by the University of Delaware Human Subjects Review Committee, and all subjects provided signed informed consent forms for participation.

Evaluation of Muscle Strength and Activation

Injured- and uninjured-side quadriceps strength and activation were assessed by maximal voluntary isometric contraction (MVIC) using the burst-superimposition method. Subjects were seated on a KIN-COM dynamometer (Chattanooga Corporation, Hixson, Tenn) with their hips and knees positioned in 90° of flexion. Velcro® straps were used to secure the distal shank to the dynamometer force arm and the thigh and pelvis to the device’s chair. After the area was cleansed with sterile alcohol, 6 cm × 8 cm self-adhesive electrodes used to deliver the electrical stimulus during testing were placed over the vastus lateralis and vastus medialis muscle bellies. After a 5-minute rest, quadriceps strength testing began. The subjects performed a 5-second maximum effort contraction during which a supramaximal, 10-pulse (600 µs, 130 V), 100 pulses per second train of electrical stimulation was delivered to the muscle to assess muscle activation level (ie, burst-superimposition technique). With a maximal contraction, no increase in force is elicited by the burst. If a subject was unable to activate the quadriceps muscle fully (ie, the burst augmented the force by more than 5%), MVIC testing was repeated up to 2 additional times. The maximal voluntary force recorded during the 3 tests was used in the analysis. Each attempt at achieving an MVIC was separated by at least 5 minutes to minimize the effects of muscle fatigue on test performance. Custom software programmed in LabView (National Instruments, Austin, Tex) was used to identify the maximal force during the volitional effort contraction and the force attributable to the electrical burst.

A quadriceps index was calculated using the following formula: (injured-side force/uninjured-side force) × 100. Volitional activation was estimated using the central activation ratio (CAR) defined by Kent-Braun and Le Blanc. The CAR is calculated by dividing the maximum voluntary force by the total force (including any force augmentation from the burst). A CAR of 1.0 signifies complete activation.

MATERIALS AND METHODS

Subjects

Seventeen subjects with ACL deficiency who were classified as noncopers volunteered to participate in this study. All had been regular participants in activities that challenge the stability of the knee joint, such as basketball, volleyball, and skiing, before sustaining their ACL injuries. The group included 13 male and 4 female participants ranging in age from 15 to 45 years (mean = 24.3 ± 10.8 years). All ACL tears were diagnosed by a sports fellowship–trained orthopaedic surgeon and had been confirmed by MRI, knee arthroscopy, and, subsequently, direct visualization during ACL reconstructive surgery. The noncopers were identified using an established screening examination that differentiates people who may be able to cope with an ACL injury from those who will not be able to cope by using hop testing and self-report questionnaires. This examination differentiates potential copers from noncopers with a high degree of accuracy. Prerequisites for this screening examination included (1) the resolution of physical and functional impairments such as joint effusions, gait abnormalities, and range of motion deficits; and (2) the ability to hop on 1 leg without...
Evaluation of Muscle Morphological Characteristics

Axial spin-echo T1-weighted MRI images were acquired from the level of the ankle mortise to the iliac crest while subjects lay supine in a 1.5-T SignaLX scanner (General Electric Medical Systems, Milwaukee, Wis). The images were acquired in 4 sequences: lower leg, knee, thigh, and pelvis. Both limbs were imaged simultaneously using the scanner’s body coil. The imaging protocol was as follows: repetition time (TR) = 350 milliseconds, echo time (TE) = 9 milliseconds, slice thickness = 10 mm (except in the knee section where it was 5 mm to acquire more detailed tendon data), gap between slices = 1.5 mm (except in the knee section where it was 1.0 mm), with a 256 × 160 matrix and a field of view that varied with subject size.

The muscle volume and peak CSA of 12 muscles were evaluated by digitally reconstructing each muscle from the MRI images. The muscles studied included the hamstring muscle group (semitendinosus, semimembranosus, biceps femoris–long head, and biceps femoris–short head), quadriceps muscle group (vastus lateralis, vastus medialis, rectus femoris, and vastus intermedius), sartorius, gracilis, and the medial and lateral gastrocnemius muscles. In addition to evaluating the 12 individual muscles, we assessed the characteristics of the total quadriceps and total hamstring muscles groups. Muscle shape was digitally reconstructed by tracing the outer margin of each muscle in each axial image in which it was present using a digitization tablet (Intuos2, Wacom Technology Corp, Vancouver, Wash) and IMOD software (University of Colorado, Boulder, Colo). The contours of each muscle were then grouped and used to build patient-specific triangle-based mesh surface models using Nuages software (INRIA, Sophia-Antipolis, France). All digitization was performed by a single rater who demonstrated a high level of reproducibility in a preliminary test-retest reliability study including ACL-deficient and uninjured subjects (n = 8; intraclass correlation coefficients ranged from 0.951 to 0.998 for the 12 muscles studied). Muscle volumes were calculated using subroutines from the Visualization Toolkit (Kitware Inc, Clifton Park, NY). The proximal and distal tendons of the muscles were excluded from the analyses of muscle volume to obtain measurements that more precisely described the volume of contractile tissue present. The peak CSA of each muscle was calculated by first transforming the contours of each muscle from pixel coordinates to physical coordinates (millimeters) using parameters from the MRI header and then running a trapezoidal integration algorithm that calculated the area encompassed within each contour (plane). The contour of each muscle with the greatest plane area defined its peak CSA.

Data Management and Analysis

Uninvolved quadriceps MVIC was adjusted for activation level to create a valid quadriceps index. The values of the uninvolved limb were compared to ACL-deficient limb muscle strength, activation, CSAs, and volumes using paired t tests with Bonferroni correction; the adjusted significance level (α) was .0084. Multiple linear regression was used to assess the effect atrophy (volume and CSA) and activation of the quadriceps on quadriceps weakness.

A priori statistical power to detect a difference of 5% in volume and CSA given the variances of our pilot subjects using paired samples tests gives a power of >0.9 for our sample size (17) and the adjusted P value of .0084. The suggested sample size from the a priori tests for a power of 0.8 was between 9 and 15 subjects depending on the muscle.

RESULTS

There was no significant difference (P = .039) between the CARs of the ACL-deficient limb (.92 ± .06) and uninjured-limb (.92 ± .06) quadriceps muscles. The quadriceps muscles of the ACL-deficient limbs (mean = 1096.85 ± 279.76 N) were significantly weaker (P < .001) than those of the uninjured limbs (mean = 1482.06 ± 346.65 N). The average quadriceps index was 75% ± 12%. The vastus lateralis, vastus intermedius, and total quadriceps volumes (P < .001, P = .007, P < .001, respectively) and CSAs (P = .001, P = .001, P < .001, respectively) from the ACL-deficient limbs were significantly smaller than the respective values from the quadriceps muscles of the uninjured limbs (Table 1, Figures 1 and 2). There was no difference in the CSAs or volumes of any other muscle (Table 1).

The variance in quadriceps weakness was significantly accounted for by activation deficit and atrophy measured by total quadriceps CSA (R² = 0.623, P = .005). The variance in quadriceps weakness was also significantly accounted for by activation deficit and atrophy measured by total quadriceps volume (adjusted R² = 0.650, P = .004) (Figure 3).

DISCUSSION

Our hypotheses that the involved-side quadriceps volume and CSA would be smaller than in the uninvolved knee were partially supported by the results. Total quadriceps volume and CSA were indeed smaller, but the atrophy was not uniform across the heads of the quadriceps. The vastus lateralis and vastus intermedius were disproportionately affected. The vastus medialis and rectus femoris were not significantly atrophied compared to the uninvolved side. Both the involved and uninvolved quadriceps demonstrated lower activation levels than reported in the literature for young, active subjects without knee injury. There was no difference in activation between the 2 sides. Atrophy (as measured by CSA or volume) and activation accounted for more than 60% of the variance in quadriceps weakness. This relationship was significant.

Despite conventional clinical wisdom that the vastus medialis is the quickest of the heads of the quadriceps to atrophy, the medialis was not significantly affected. Rather, the vastus lateralis and intermedius were profoundly atrophied. The vastus lateralis and intermedius are the largest of the quadriceps muscles, which may make them more vulnerable to the results of neural disruption that occurs when the ACL is ruptured. There is recent evi-
Lateral gastrocnemius 132.77
Medial gastrocnemius 207.55
Sartorius 87.81
Biceps femoris–short 65.46
Biceps femoris–long 177.29
Semitendinosus 160.04
Semimembranosus 203.48
Total hamstring group 606.26
Vastus medialis 386.68
Vastus intermedius 465.40
Vastus lateralis 592.81

at the Bonferroni adjusted significance level, which was set at .0084.

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tary activation in the quadriceps of the involved and unin-

Injury on the various quadriceps muscles.1,18 Okuyama et al have demonstrated increased oxidative stress and disrupted antioxidant capacity by depression of heat shock proteins—stress proteins that have protective antioxidant properties—in the vastus lateralis and vastus medialis but not the rectus femoris of rats after ACL resection.18 The implications for rehabilitation are large because the focus on the vastus medialis may be misplaced.

There were small but significant alterations in voluntary activation in the quadriceps of the involved and uninvolved knees; this is consistent with recent reports in the literature and necessitates consideration when calculating quadriceps indices.

The implications for rehabilitation are large because the cross-sectional areas of the vastus lateralis and vastus intermedius were significantly smaller in the ACL-deficient legs (11.6% and 8.5%, respectively). RF, rectus femoris; VM, vastus medialis; VL, vastus lateralis; VI, vastus intermedius.

There were small but significant alterations in voluntary activation in the quadriceps of the involved and uninvolved knees; this is consistent with recent reports in the literature and necessitates consideration when calculating quadriceps indices.1,25 To use the uninvolved side as a surrogate for the subject’s normal quadriceps strength, activation level must be used to adjust the strength measures. The unadjusted mean quadriceps index was 82%. When calculated compared to the MVIC of the uninjured quadriceps corrected for activation, the quadriceps index was 75%. Past research has failed to demonstrate a relationship between atrophy and weakness of the quadriceps after ACL rupture. Perhaps this has been both a direct and indirect effect of failing to account for the effect of activation failure. Neither the direct effect of activation failure on the involved quadriceps strength nor the indirect effect of activation failure on the validity of the quadriceps index has been estimated. Consequently, the present study was able to demonstrate that atrophy as measured by either peak CSA or volume combined with activation failure accounted for more than 60% of the variance in the loss of strength. Muscle volume and peak CSA appear to provide similar, accurate information about atrophy.

Quadriceps weakness was profound in this population of ACL-deficient noncopers. An average of 3 months after incident injury, the average quadriceps strength was 75% of that of the uninjured quadriceps. All of the subjects had been enrolled in a preoperative rehabilitation program designed to control impairments in preparation for surgery.6 Despite strengthening exercises, the subjects were quite weak. Quadriceps weakness is a hallmark of noncopers.3,19,20 Noncopers demonstrate aberrant gait patterns that are strongly related to their quadriceps weakness, which can persist after reconstruction.2,16

The results of this study have important implications for rehabilitation and surgical planning. Because both atrophy and activation affect quadriceps strength, rehabilitation specialists should employ techniques that address activation deficits as well as atrophy in their efforts to restore quadriceps strength. The extent of the quadriceps

<table>
<thead>
<tr>
<th>Muscle(s)</th>
<th>Uninjured Volume</th>
<th>Uninjured Peak CSA</th>
<th>ACL Deficient Volume</th>
<th>ACL Deficient Peak CSA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total quadriceps group</td>
<td>1673.64 ± 345.60</td>
<td>87.34 ± 12.95</td>
<td>1526.94 ± 354.63</td>
<td>79.57 ± 12.90</td>
<td>&lt;.001 &lt;.001</td>
</tr>
<tr>
<td>Vastus lateralis</td>
<td>592.81 ± 137.03</td>
<td>29.66 ± 5.68</td>
<td>516.06 ± 146.32</td>
<td>26.23 ± 5.98</td>
<td>.007 .001</td>
</tr>
<tr>
<td>Vastus intermedius</td>
<td>465.40 ± 93.26</td>
<td>23.41 ± 3.50</td>
<td>431.73 ± 99.74</td>
<td>21.42 ± 3.79</td>
<td>&lt;.001 .001</td>
</tr>
<tr>
<td>Vastus medialis</td>
<td>386.68 ± 94.90</td>
<td>22.08 ± 3.65</td>
<td>358.98 ± 83.58</td>
<td>20.02 ± 3.51</td>
<td>NS NS</td>
</tr>
<tr>
<td>Rectus femoris</td>
<td>226.75 ± 56.05</td>
<td>12.19 ± 2.37</td>
<td>220.17 ± 56.99</td>
<td>11.90 ± 2.42</td>
<td>NS NS</td>
</tr>
<tr>
<td>Total hamstring group</td>
<td>606.26 ± 133.89</td>
<td>40.51 ± 6.38</td>
<td>608.43 ± 125.87</td>
<td>40.21 ± 5.91</td>
<td>NS NS</td>
</tr>
<tr>
<td>Semimembranosus</td>
<td>203.48 ± 55.89</td>
<td>12.26 ± 2.86</td>
<td>203.99 ± 56.45</td>
<td>11.97 ± 2.56</td>
<td>NS NS</td>
</tr>
<tr>
<td>Semitendinosus</td>
<td>160.04 ± 51.89</td>
<td>9.59 ± 2.92</td>
<td>159.37 ± 43.27</td>
<td>9.60 ± 2.59</td>
<td>NS NS</td>
</tr>
<tr>
<td>Biceps femoris–long</td>
<td>177.29 ± 36.85</td>
<td>12.96 ± 2.29</td>
<td>174.04 ± 31.12</td>
<td>12.71 ± 2.04</td>
<td>NS NS</td>
</tr>
<tr>
<td>Biceps femoris–short</td>
<td>65.46 ± 22.62</td>
<td>5.69 ± 1.50</td>
<td>71.03 ± 26.82</td>
<td>5.94 ± 1.37</td>
<td>NS NS</td>
</tr>
<tr>
<td>Gracilis</td>
<td>63.41 ± 13.62</td>
<td>3.51 ± 0.66</td>
<td>67.34 ± 20.89</td>
<td>3.71 ± 1.01</td>
<td>NS NS</td>
</tr>
<tr>
<td>Sartorius</td>
<td>87.81 ± 26.57</td>
<td>2.84 ± 0.69</td>
<td>91.03 ± 25.34</td>
<td>2.95 ± 0.68</td>
<td>NS NS</td>
</tr>
<tr>
<td>Medial gastrocnemius</td>
<td>207.55 ± 40.30</td>
<td>13.82 ± 2.64</td>
<td>209.41 ± 46.59</td>
<td>13.96 ± 3.00</td>
<td>NS NS</td>
</tr>
<tr>
<td>Lateral gastrocnemius</td>
<td>132.77 ± 27.75</td>
<td>12.15 ± 2.51</td>
<td>121.35 ± 25.59</td>
<td>10.45 ± 2.71</td>
<td>NS NS</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. Units = muscle volume, cm³; peak CSA, cm². CSA, cross-sectional area; NS, no significant difference at the Bonferroni adjusted significance level, which was set at .0084.

**Figure 1.** MRI cross sections of the thigh showing quadriceps atrophy. The cross-sectional areas of the vastus lateralis and vastus intermedius were significantly smaller in the ACL-deficient legs (11.6% and 8.5%, respectively). RF, rectus femoris; VM, vastus medialis; VL, vastus lateralis; VI, vastus intermedius.
The weakness and the rapidity with which it occurs should be considered in planning surgical reconstruction in noncopers after range of motion is restored and effusion is resolved.

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