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original research

Persistent Neuromuscular and Corticomotor Quadriceps Asymmetry After Anterior Cruciate Ligament Reconstruction

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Context: Return to activity in the presence of quadriceps dysfunction may predispose individuals with anterior cruciate ligament reconstruction (ACLR) to long-term joint degeneration. Asymmetry may manifest during movement and result in altered knee-joint–loading patterns; however, the underlying neurophysiologic mechanisms remain unclear.

Objective: To compare limb symmetry of quadriceps neuromuscular function between participants with ACLR and participants serving as healthy controls.

Design: Descriptive laboratory study.

Setting: Research laboratory.

Patients or Other Participants: A total of 22 individuals with ACLR (12 men, 10 women) and 24 individuals serving as healthy controls (12 men, 12 women).

Main Outcome Measure(s): Normalized knee-extension maximal voluntary isometric contraction (MVIC) torque (Nm/kg), quadriceps central activation ratio (CAR) (%), quadriceps motor-neuron–pool excitability (Hoffmann reflex to motor wave ratio), and quadriceps active motor threshold (AMT) (% 2.0 T) were measured bilaterally and used to calculate limb symmetry indices for comparison between groups. We used analyses of variance to compare quadriceps Hoffmann reflex to motor wave ratio, normalized knee-extension MVIC torque, quadriceps CAR, and quadriceps AMT between groups and limbs.

Results: The ACLR group exhibited greater asymmetry in knee-extension MVIC torque (ACLR group = 0.85 ± 0.21, healthy group = 0.97 ± 0.14; $t_{44} = 2.26$, $P = .03$), quadriceps CAR (ACLR group = 0.94 ± 0.11, healthy group = 1.00 ± 0.08; $t_{44} = 2.22$, $P = .04$), and quadriceps AMT (ACLR group = 1.13 ± 0.18, healthy group = 1.02 ± 0.11; $t_{34} = -2.46$, $P = .04$) than the healthy control group.

Conclusions: Asymmetries in measures of quadriceps function and cortical excitability were present in patients with ACLR. Asymmetry in quadriceps strength, activation, and cortical excitability persisted in individuals with ACLR beyond return to recreational activity. Measuring the magnitude of asymmetry after ACLR represents an important step in understanding long-term reductions in self-reported function and increased rate of subsequent joint injury in otherwise healthy, active individuals after ACLR.

Key Words: quadriceps activation, limb symmetry index, transcranial magnetic stimulation

Key Points

- The anterior cruciate ligament reconstruction (ACLR) group exhibited a weaker, less activated quadriceps and less cortical excitability in the reconstructed limb than in the contralateral limb and in the limbs of the healthy control group.
- Asymmetry in quadriceps strength, activation, and cortical excitability persisted in individuals with ACLR beyond return to recreational activity.
- Chronic asymmetry indicated reduced dynamic force absorption at the knee and may explain the increased rate of knee reinjury and chronic joint degeneration after ACLR.

After injury and subsequent anterior cruciate ligament reconstruction (ACLR), persistent joint effusion and soft tissue damage can lead to altered afferent output from the knee joint that manifests as muscle weakness and reductions in muscle activation.[1,2] Quadriceps weakness, reduced quadriceps activation, and functional quadriceps asymmetry are common clinical problems after ACLR. These alterations in quadriceps function have been related to altered gait patterns and reduced physical performance throughout rehabilitation and well after return to activity.[3,4] This persistent dysfunction may reduce the ability of individuals with ACLR to adapt to the demands of physical activity, resulting in abnormal knee-joint loading.[5–7] Researchers[8,9] have hypothesized that the combination of joint trauma from initial injury and surgery, along with long-term functional adaptation due to persistent lower extremity neuromuscular dysfunction, may predispose individuals with ACLR to higher rates of reinjury and knee-joint osteoarthritis. Understanding the clinical and neurophysiologic manifestations of quadriceps dysfunction

Table 1. Participant Demographics

Variable	Group, Mean ± SD (Minimum, Maximum)		*P* Value
	Healthy Control	Anterior Cruciate Ligament Reconstruction	
Sex	12 men, 12 women	12 men, 10 women	.97
Age, y	21.7 ± 3.6 (18.0, 30.0)	22.5 ± 5.0 (18.0, 35.0)[a]	.58
Height, cm	168.0 ± 8.8 (152.4, 182.9)	172.9 ± 7.1 (162.6, 190.5)	.05[b]
Mass, kg	69.3 ± 13.6 (46.7, 91.2)	74.1 ± 15.5 (55.3, 112.5)	.27
Body mass index	24.3 ± 3.2 (19.1, 30.6)	24.6 ± 4.0 (19.5, 33.6)	.81
Visual analog scale for current pain, cm (range, 0–10)	0.0 ± 0.0 (0.0, 0.0)	0.2 ± 0.1 (0.0, 1.2)	.33
Current Tegner Activity Scale score (range, 0–10)	6.1 ± 1.7 (5.0, 9.0)	6.4 ± 1.2 (5.0, 9.0)	.53
Lower Extremity Functional Scale (range, 0–80)	79.5 ± 2.1 (70.0, 80.0)	74.8 ± 7.2 (53.0, 80.0)	.004[a]
International Knee Documentation Committee score (range, 18–100)	99.3 ± 1.6 (95.4, 100.0)	87.2 ± 12.6 (57.5, 100.0)	<.001[a]

[a] The data were positively skewed.
[b] Indicates difference between groups ($P \leq .05$).

after ACLR is essential to developing targeted treatment and clearer criteria for return to activity.

Force- and electromyography-based techniques are used commonly to assess quadriceps function after ACLR.[10–12] These techniques allow researchers and clinicians to measure the peripheral and central sources of persistent quadriceps dysfunction.[10–13] Reductions in quadriceps strength,[10,14] quadriceps activation,[10,14] and cortical drive to the quadriceps[11] have been shown months to years after ACLR. Despite these reports, clinically assessing and detecting quadriceps dysfunction during the terminal phases of rehabilitation remains difficult due to the often subtle reductions in strength and activation.[10,15] The importance of quadriceps function after ACLR cannot be overstated because reduced quadriceps function consistently has been related to long-term quadriceps weakness[10,14] and physical performance[3,16,17] and has been hypothesized to increase the risk for knee-joint osteoarthritis.[7]

Assessment and comparison of range of motion and strength are common clinical tools used to track progress throughout the rehabilitation process. Between-limbs differences, often referred to as *limb asymmetry*, have been proposed as a more effective manner to assess lower extremity dysfunction after knee-joint injury.[18,19] Reductions in quadriceps strength,[4,20] functional performance,[21,22] and gait symmetry[23] have been reported after anterior cruciate ligament (ACL) injury and ACLR. To date, the magnitude of asymmetry, or between-limbs differences, in quadriceps motor-neuron–pool excitability, quadriceps activation, and quadriceps cortical excitability has not been studied in patients with ACLR. A clearer understanding of the magnitude of persistent asymmetry in quadriceps function after ACLR may help clinicians more effectively evaluate and target treatments. Therefore, the primary purpose of our study was to compare symmetry in quadriceps strength, central activation, spinal reflex excitability, and cortical excitability between patients with primary unilateral ACLR and individuals serving as healthy controls. We hypothesized that participants with ACLR would have greater between-limbs asymmetry in quadriceps strength, central activation, spinal reflex excitability via the Hoffmann reflex (H-reflex), and cortical excitability via transcranial magnetic stimulation than participants serving as healthy controls. The secondary purpose of our study was to compare neurophysiologic measures of lower extremity function between individuals with ACLR and individuals serving as healthy controls. We hypothesized that participants with ACLR would have less isometric knee-extension torque, a smaller quadriceps central activation ratio, less quadriceps motor-neuron–pool excitability, and greater quadriceps active motor threshold (AMT) in the involved limb than in the contralateral limb and in both limbs of healthy control participants.

METHODS

Participants

A total of 22 volunteers with ACLR (12 men, 10 women) and 24 healthy volunteers (12 men, 12 women) participated in this study. Participant demographics can be found in Table 1. Participants were recruited from the university community and were included if they were between the ages of 18 and 40 years; had a body mass index less than 35; and were *recreationally active*, which was defined as exercising at least 3 to 5 times each week at a moderate intensity for no less than 30 minutes.[24] They were excluded if they had a self-reported history of lower extremity joint sprain within the 6 weeks before the study or lower extremity surgery within the 6 months before the study; neurologic disorder; cardiopulmonary disorder; or an inability to complete 30 minutes of aerobic exercise. Participants in the ACLR group had undergone unilateral, primary ACLR using a hamstrings or patellar-tendon autograft at least 6 months before the study and had been released to return to full recreational activity by a health care provider (Table 2). Volunteers were excluded from the ACLR group if they had multiple ligament reconstruction; a *clinically failed meniscal repair*, which

Table 2. Anterior Cruciate Ligament Reconstruction Group: Injury and Surgical Characteristics

Variable	Autograft		Total
	Hamstrings	Bone–Patellar Tendon–Bone	
Sex	7 men, 5 women	5 men, 5 women	12 men, 10 women
Time since surgery, mo, mean ± SD (maximum, minimum)	37.3 ± 26.3 (8.0, 80.0)	24.5 ± 15.6 (7.0, 66.0)	31.5 ± 23.5 (7.0, 80.0)
Partial meniscectomy	3 medial, 4 lateral	2 medial, 2 lateral	5 medial, 6 lateral

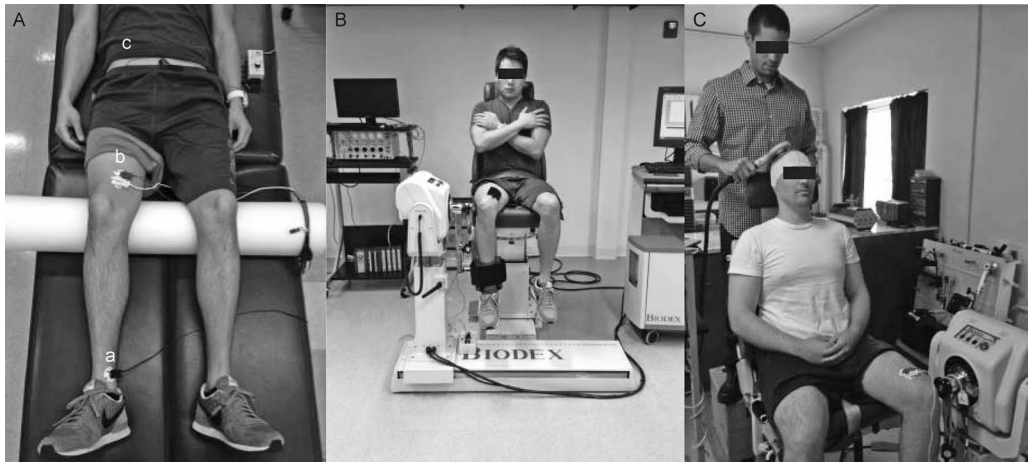

Figure 1. Testing position and setup for A, quadriceps Hoffmann reflex; B, quadriceps superimposed-burst technique; and C, quadriceps active motor threshold testing. [a] Indicates ground electrode. [b] Indicates recording electrodes. [c] Indicates stimulating electrode.

was defined as joint-line pain or chronic effusion that was confirmed through self-report and investigator palpation; a substantial chondral-resurfacing procedure; substantial surgical complication; or history of graft failure. They were considered to have potential graft failure if substantial asymmetrical joint laxity was present as measured by a knee arthrometer (KT1000; MEDmetric Corp, San Diego, CA) or if they reported having received a diagnosis of reinjury from a physician. *Limb dominance* for all participants was established as the limb that each would use to kick a ball for maximal distance. All participants provided written informed consent, and the study was approved by the University of Virginia Institutional Review Board for Human Subjects.

Procedures

Participants were instructed to abstain from consuming caffeine and exercising for at least 12 hours before reporting for a single testing session lasting about 2 hours. All participants completed testing in the same order (quadriceps H-reflex, quadriceps superimposed burst technique, and quadriceps AMT), and the right limb was tested first. They rested at least 5 minutes between components of the testing session.

Patient-Reported Outcomes

All participants completed 4 measures of self-reported symptoms and function. The Tegner Activity Scale was used to assess physical activity level at the time of testing; a higher score indicates a higher activity level. A 10-cm visual analog scale was used to evaluate knee pain at the time of testing. The Lower Extremity Functional Scale was used to measure self-reported lower extremity function, and the International Knee Documentation Committee subjective evaluation form was used to determine knee-specific function at the time of testing.

Quadriceps H-Reflex

The quadriceps H-reflex was collected bilaterally using surface electromyography (model MP 150; BIOPAC Systems, Goleta, CA). Signals were amplified with a gain of 1000 from disposable, 10-mm pregelled silver-silver chloride electrodes that were placed on skin that was shaved, debrided, and cleansed with isopropyl alcohol. We placed the electrodes superficial to the vastus medialis obliquus muscle, parallel to the fiber orientation, and 2 cm apart. The stimulating electrode was positioned over the femoral nerve in the inguinal fold[25] and a dispersive electrode, on the ipsilateral posterior thigh (Figure 1).

Participants were positioned supine on a treatment table with their knees flexed to approximately 15° and were instructed to relax throughout the course of testing. Short-duration (1-millisecond) square-wave stimuli were triggered manually with a minimum rest of 10 seconds between stimuli until maximal peak-to-peak amplitude H-reflex and motor wave (M-wave) were observed (Figure 2). The maximal peak-to-peak amplitude H-reflex represents the number of motor neurons available for use in a given state, whereas the maximal peak-to-peak amplitude M-wave represents activation of the entire motor-neuron pool for a given muscle.[12] Electromyographic data were bandpass filtered at 10 to 500 Hz and notch filtered at 60 Hz. The H-reflex to M-wave (H:M) ratio was calculated using the mean peak-to-peak amplitudes.[25] This ratio is thought to represent the proportion of the total motor-neuron pool that can be recruited.[26]

Knee-Extension Strength and Quadriceps Central Activation Ratio

Knee-extension maximal voluntary isometric contraction (MVIC) torque was measured using a Biodex multimodal dynamometer (System 3; Biodex Medical Systems, Inc, Shirley, NY) with a remote access port. Data were digitized at 125 Hz (MP150; BIOPAC Systems, Inc, Santa Barbara, CA). Participants were secured to the chair and instructed to maintain good seated posture (Figure 1). They completed 1 practice trial each at 50% and 75% and 2 practice trials at 100% of perceived effort before performing an MVIC at 90° of knee flexion using their knee extensors. Participants rested a minimum of 1 minute between all MVIC trials to reduce the effect of fatigue due to multiple high-intensity contractions. The investigator (C.M.K.) provided constant oral encouragement, such as "keep going" and "push harder," until the participant achieved a plateau representing MVIC for at least 2 seconds.[27] The investigator immediately completed a subjective evaluation of each

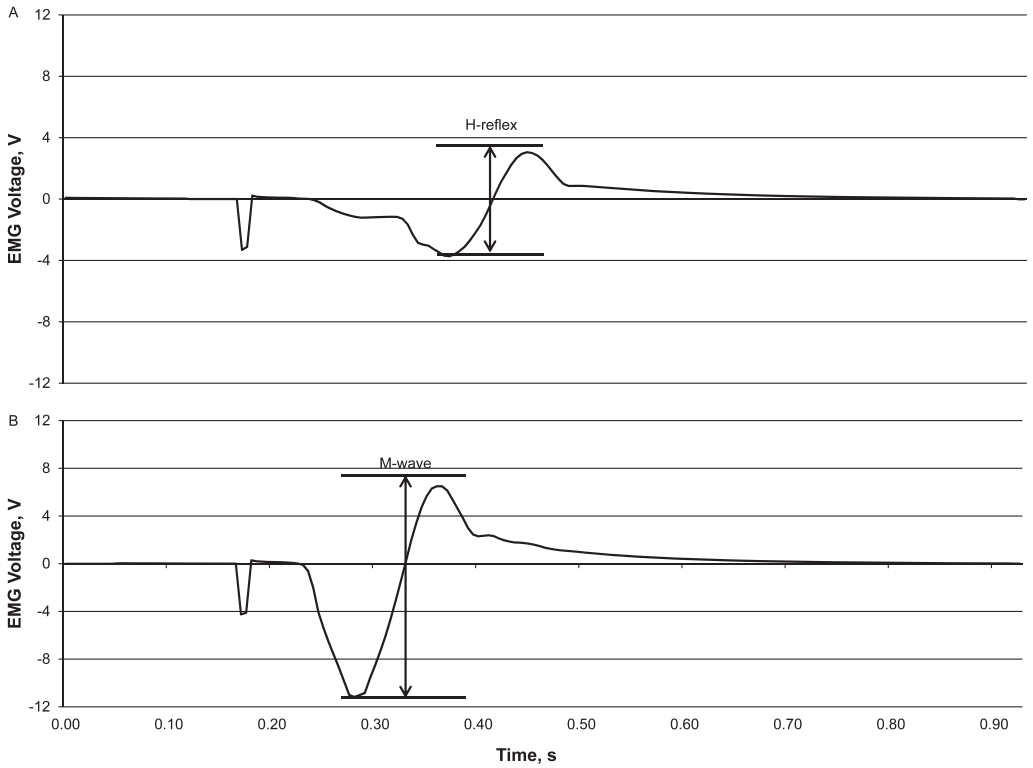

Figure 2. Sample data for maximal A, Hoffmann (H) reflex; and B, motor (M) wave. Abbreviation: EMG, electromyography.

trial, and trials with excessive force fluctuations were repeated after a sufficient rest period. All participants completed 2 trials that were deemed appropriate for analysis. Knee-extension MVIC torque was normalized to body mass (Nm/kg) to allow for comparison among participants.

Quadriceps central activation ratio (CAR) was measured bilaterally at the same time as knee-extension MVIC torque using the superimposed-burst technique.[28,29] After the investigator determined that the knee-extension torque had reached a plateau representing the MVIC, a 100-millisecond train of 10 square-wave pulses of electrical stimulation at an intensity of 125 V, a pulse duration of 600 μ, and a frequency of 100 pulses per second was delivered to the quadriceps using a Grass S88 dual-output, square-pulse stimulator (Grass-Telefactor, West Warwick, RI) with the STMISOC stimulus-isolation unit (BIOPAC Systems, Inc) and two 3×5-in (7.62-×12.7-cm) pregelled stimulating electrodes placed over the proximal vastus lateralis and distal vastus medialis. This stimulus produced a transient increase in torque (T_{SIB}), known as a *superimposed burst*, that was compared with the average torque value for a manually identified 200-millisecond window immediately before the stimulation (T_{MVIC}; Figure 3). These values were used to calculate the quadriceps CAR (Equation 1).[30]

$$\mathrm{CAR} = \frac{T_{MVIC}}{(T_{MVIC} + T_{SIB})} \quad (1)$$

Quadriceps AMT

Participants remained in the same testing position described for the quadriceps superimposed-burst technique. They were fitted with ear plugs and nonlatex swim caps upon which 2 perpendicular lines (1 connecting the external ear tragi and 1 sagittal line separating the hemispheres of the brain) were drawn to aid in locating the appropriate stimulation site over the primary motor cortex (Figure 1).[11] Participants were instructed to perform an isometric knee-extension contraction at an intensity equal to 5% of their MVICs during each stimulation.[31] A MagStim Novametrix 200 transcranial magnetic stimulator (The MagStim Company, Ltd, Wales, UK) with a flat 70-mm figure-8 (double) magnetic coil that provided a maximal magnetic field strength of 2.0 T was used to elicit motor-evoked potentials (MEPs) during quadriceps AMT testing. The coil was placed on the contralateral side of the skull from the testing limb at a 45° angle to the intersection of the 2 reference lines drawn on the swim cap. The coil was moved systematically to find the site that elicited the largest peak-to-peak amplitude MEP in response to a 2.0-T stimulation. Vastus medialis obliquus AMT was established by reducing stimulation intensity by increments of 5% until no MEP could be measured. At this point, the stimulus intensity was increased progressively by 1% until 5 of 10 consecutive stimuli resulted in a measurable MEP. The AMT was reported as a percentage of the maximal stimulus intensity (% 2.0 T), with a greater AMT indicating lesser cortical excitability.[31]

Limb Symmetry Index

A limb symmetry index (LSI) was calculated for normalized knee-extension MVIC torque, quadriceps CAR, quadriceps H:M ratio, and quadriceps AMT in all participants.[21] In the ACLR group, LSI was calculated as shown in Equation 2. Limb symmetry indices greater than 1.00 indicate that the ACLR limb had a greater value for a

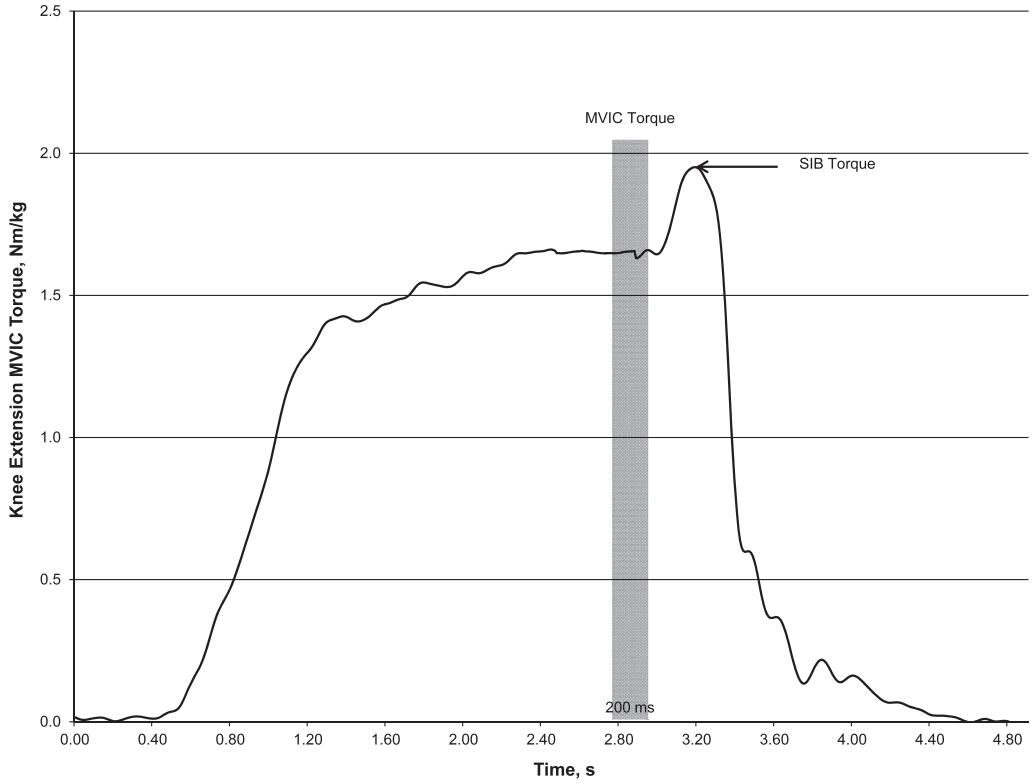

Figure 3. Sample data for normalized knee-extension maximal voluntary isometric contraction (MVIC) torque and calculation of the quadriceps central activation ratio via the superimposed-burst (SIB) technique.

specific measure than the contralateral limb.

$$\text{LSI} = \frac{\text{ACLR Limb}}{\text{Uninvolved Limb}} \quad (2)$$

In the healthy control group, LSIs greater than 1.00 indicate that the nondominant limb had a greater value for a specific measure than the dominant limb (Equation 3).

$$\text{LSI} = \frac{\text{Nondominant Limb}}{\text{Dominant Limb}} \quad (3)$$

Statistical Analysis

A sample-size estimate was completed based on recently published data.[32] For the effect of ACLR on quadriceps CAR, the Cohen d effect size was 1.2; therefore, a minimum of 20 participants per group was needed[32] to find differences while maintaining a statistical power of 80% and an α level of .05.

Between-groups comparisons of demographics and patient-reported outcomes were conducted using separate independent-samples t tests except for sex, which was compared using a Fisher exact test. Group and limb comparisons of normalized knee-extension MVIC torque, quadriceps CAR, quadriceps H:M ratio, and quadriceps AMT were performed using separate 2 (group: ACLR versus healthy) $\times$ 2 (limb: dominant or uninvolved versus nondominant or ACLR side) analyses of variance. Group $\times$ limb interactions that were different were further investigated using Fisher least significant difference post hoc analysis. Between-groups differences in LSIs for knee-extension MVIC torque, quadriceps CAR, quadriceps H:M ratio, and quadriceps AMT were compared using separate independent-samples t tests. We then calculated Cohen d effect sizes with associated 95% confidence intervals (CIs) to determine the magnitude of differences in symmetry between groups. We evaluated the effect of age and time from surgery as a covariate for all between-groups analyses. However, we found no effect for either variable; therefore, they were not included in the final analysis. Statistical analyses were carried out using SPSS statistical software (version 21.0; IBM Corp, Armonk, NY). Effect sizes and 95% CIs were calculated using Excel (version 2010; Microsoft Corp, Redmond, WA).

RESULTS

Demographics

The ACLR group was taller than the healthy control group ($t_{44} = -2.05$, $P = .05$); however, mass and body mass index were not different between groups (Table 1). The ACLR group also reported worse function on the Lower Extremity Functional Scale ($t_{44} = 3.07$, $P = .004$) and worse knee-related function as measured by the International Knee Documentation Committee form ($t_{44} = 4.688$, $P < .001$; Table 1) but no difference on the Tegner Activity Scale of the visual analog scale for pain.

Side-to-Side Comparisons

We found group $\times$ limb interactions for quadriceps CAR ($F_{1,44} = 5.31$, $P = .03$) and quadriceps AMT ($F_{1,34} = 4.40$, $P = .04$) but did not find group $\times$ limb interactions for quadriceps H:M ratio ($F_{1,44} = 0.01$, $P = .95$) or normalized

Table 3. Quadriceps Neuromuscular Function and Limb Symmetry in Healthy Participants and Participants With Anterior Cruciate Ligament Reconstruction (Mean ± SD)

	Group					
	Healthy			Anterior Cruciate Ligament Reconstruction		
Measure	Dominant Limb	Nondominant Limb	Limb Symmetry Index	Uninvolved Limb	Involved Limb	Limb Symmetry Index
Quadriceps Hoffmann reflex to motor wave ratio, %	0.26 ± 0.18	0.23 ± 0.16	1.17 ± 0.88	0.31 ± 0.22	0.29 ± 0.20	1.08 ± 0.65
Knee-extension maximal voluntary isometric contraction torque, Nm/kg	3.56 ± 0.73	3.40 ± 0.61	0.97 ± 0.14[b]	3.59 ± 0.80	3.07 ± 1.03	0.85 ± 0.21
Quadriceps central activation ratio, %	91.05 ± 6.71	91.28 ± 7.35[a]	1.00 ± 0.08[b]	89.91 ± 9.22	84.55 ± 10.25	0.94 ± 0.11
Quadriceps active motor threshold, % 2.0 T	63.05 ± 10.33	63.91 ± 10.20	1.02 ± 0.11[b]	56.00 ± 14.47	61.81 ± 11.98	1.13 ± 0.18

[a] Indicates difference between the nondominant limb of the healthy group and the involved limb of the anterior cruciate ligament reconstruction group ($P \leq .05$).
[b] Indicates difference between groups ($P \leq .05$).

knee-extension MVIC torque ($F_{1,44} = 3.80$, $P = .06$). The ACLR limb was less activated than the contralateral limb ($P < .05$) and both healthy limbs ($P < .05$; Table 3). Quadriceps AMT was greater in the ACLR limb than the contralateral limb ($P < .05$) but was not different from either control limb ($P > .05$; Table 3). Quadriceps AMT was also less in the uninvolved limb of the ACLR group than in both limbs of the healthy control group ($P < .05$; Table 3).

Limb Symmetry Indices

The ACLR group exhibited greater asymmetry in knee-extension MVIC torque ($t_{44} = 2.26$, $P = .03$, effect size = –0.67; 95% CI = –1.26, –0.07), quadriceps CAR ($t_{44} = 2.22$, $P = .04$, effect size = –0.63; 95% CI = –1.22, –0.04), and quadriceps AMT ($t_{34} = –2.46$, $P = .04$, effect size = 0.84; 95% CI = 0.14, 1.54) than the healthy control group (Table 3).

DISCUSSION

Participants with ACLR had greater limb asymmetry in force-based measures of quadriceps function and cortical excitability (Figure 4). No difference in quadriceps motor-neuron–pool excitability as measured via the H:M ratio was observed when compared with healthy control participants (Figure 4). The asymmetry in force-based measures that we noted is consistent with previous reports[10,19,22]; however, we are the first to investigate the underlying spinal and cortical sources of quadriceps asymmetry after ACLR.

The quadriceps muscles were weaker and less activated in participants with ACLR than in their healthy counterparts. Reductions in quadriceps strength and greater limb asymmetry after ACLR have been associated with altered landing mechanics,[19,33] reductions in functional performance,[19,22] and decreased patient-reported knee-related function.[34] Without optimal and symmetrical quadriceps function, individuals may have difficulty adapting to the demands of daily function and recreational activity after ACLR due to a decreased ability to absorb knee-joint loads during weight bearing. In this study, participants with ACLR had returned to a level of physical activity similar to that of their healthy counterparts; however, they continued to report reduced knee-related function as measured by the International Knee Documentation Committee form. Additionally, participants with ACLR reported a reduction in general lower extremity function; yet this finding should be interpreted with caution because, whereas statistically different, the between-groups difference did not exceed the minimal clinically important difference for the Lower Extremity Functional Scale (Table 1).[35] The presence of asymmetry in quadriceps function despite a full return to activity after ACLR indicates that individuals who have been able to participate in recreational activity may still be at risk for reinjury and chronic knee-joint degeneration due to an inability to cope with and absorb forces exerted on the knee joint (Figure 4).

Restoration of symmetrical knee-extension strength and quadriceps activation has been commonly reported as an important clinical goal before return to activity after ACLR; however, symmetry alone should be interpreted with caution. Seven participants in the ACLR group displayed symmetrical quadriceps activation (LSI > 95.0%) even though both limbs were well below the previously reported threshold for normal quadriceps activation (CAR > 95.0%).[36] Similar bilateral weakness and activation failure after ACL injury and ACLR has been reported and may indicate neurologically driven "cross-over" effects that limit bilateral strength and function in the presence of unilateral injury.[37,38] During the rehabilitation phase after ACLR, this reduction in contralateral strength and activation to maintain neuromuscular symmetry may represent a desirable, centrally driven reorganization to enable function. However, persistent neuromuscular symmetry after completion of rehabilitation and return to activity despite bilateral quadriceps weakness and activation failure may result in increased knee-joint loading during functional tasks and the adaptation of compensatory strategies, which may have negative consequences for knee-joint health.[3]

Spinal[2,10,11] and cortical[11,39–41] sources of muscle inhibition have been implicated in persistent quadriceps weakness after knee-joint injury. Currently, no clearly established methods exist to assess symmetry of the quadriceps AMT or the H:M ratio after knee injury. We used the LSI as an assessment tool due to the ease of calculation and the ability to directly compare the LSI values obtained in this study for normalized knee-

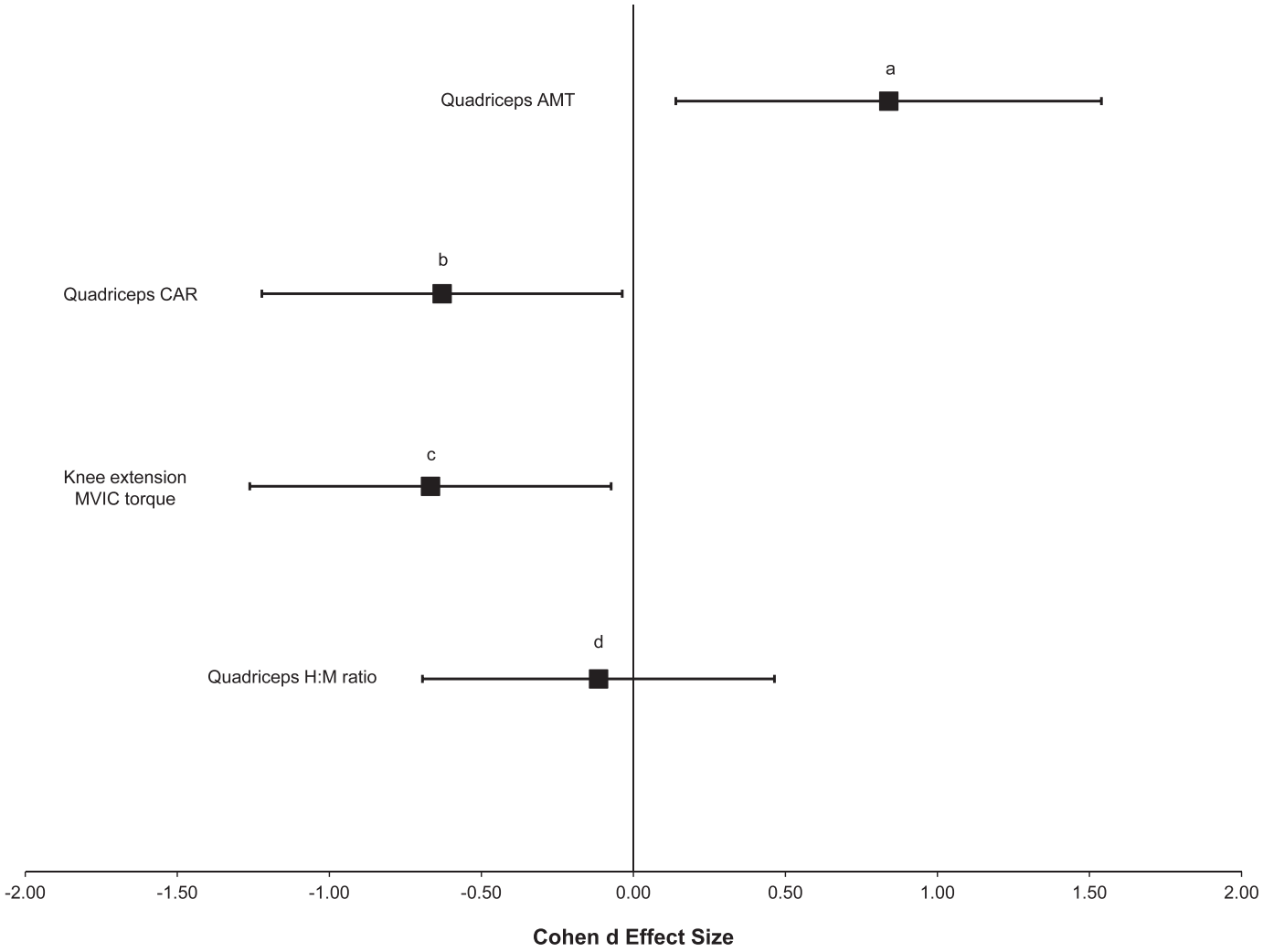

Figure 4. Between-groups Cohen d effect sizes and 95% confidence intervals for limb symmetry indices. Positive values indicate greater limb symmetry index values for the anterior cruciate ligament reconstruction group, and negative values indicate greater limb symmetry index values for the control group. Confidence intervals that do not cross the y-axis indicate an effect of group membership. [a] Effect size = 0.84; 95% CI = 0.14, 1.54. [b] Effect size = –0.63; 95% CI = –1.22, –0.04. [c] Effect size = –0.67; 95% CI = –1.26, –0.07. [d] Effect size = –0.11; 95% CI = –0.69, 0.46. Abbreviations: AMT, active motor threshold; CAR, central activation ratio; MVIC, maximal voluntary isometric contraction; and H:M, Hoffmann reflex to motor wave ratio.

extension torque and quadriceps activation. Despite measurable strength asymmetry and reductions in quadriceps activation, no difference in spinal excitability as measured by the H:M ratio was seen between groups or between limbs (Table 3). This result is consistent with the findings of Heroux and Tremblay,[42] who studied participants with ACLR after return to activity. Hopkins and Ingersoll[2] proposed that, in the absence of pathologic muscle conditions or neurologic injury, muscle tissue surrounding the knee joint may be reflexively inhibited to protect the injured joint and limit joint function after acute injury. In some cases, joint effusion and soft tissue damage in the acute phase after reconstruction may lead to altered afferent output from the knee joint, which manifests as persistent quadriceps weakness.[1,2] However, with the resolution of the underlying joint effusion in the acute phase of rehabilitation and the gradual improvement in activity level, these alterations in motor-neuron–pool excitability may become less severe over time. This proposed gradual improvement in motorneuron-pool excitability over the course of rehabilitation and return to physical activity after ACLR may explain the lack of difference in the H:M ratio between limbs within the ACLR group and between groups. This may be explained by the length of time since surgery for the included participants (31.5 ± 23.5 months).

A transition from spinal-level inhibition resulting in reflexive motor shutdown to cortical plasticity has been proposed after knee-joint injury.[11] After ACLR, brain plasticity, as measured through functional magnetic resonance imaging and motor thresholds, has been noted and is thought to substantially affect volitional muscle activation and movement coordination.[42,43] In this study, we observed greater corticomotor asymmetry driven by increased excitability of the primary motor cortex associated with the uninvolved limb, which is thought to indicate less need for volitional drive or cortical effort to facilitate voluntary muscle contraction.[11,31] This finding is somewhat inconsistent with previous reports in the ACLR population; however, the pattern of reduced excitability on

the involved side when compared with the uninvolved side is similar to previously established patterns.[11,42] The source of between-limbs differences remains unclear; however, it may be related to the concept of limb "favoritism," which is commonly observed clinically after knee-joint surgery. Increased reliance on the uninvolved limb during functional tasks may lead to central facilitation of the uninvolved limb while contributing to the persistent reductions in muscle strength and postural control observed in the involved limb after ACLR.[10,44] The cortical excitability asymmetry and lack of differences in motor-neuron–pool excitability observed in our ACLR group may provide insight into the spinal and cortical mechanisms responsible for the chronic quadriceps weakness that persists after ACLR.[1,17,45,46]

Persistent asymmetry in quadriceps strength and activation driven by the involved limb after ACLR may increase the likelihood of poor functional outcomes, reinjury, and long-term joint degeneration.[13,47–49] Investigators[4,14,22,38,50–52] largely have focused on strength-based measures and more functional movement patterns without describing the symmetry of cortical and spinal measures of quadriceps function. Our findings confirm the presence of quadriceps strength and activation asymmetry well past the point of return to activity in a fairly young and active population with uncomplicated ACLR (Table 3). In addition, persistent quadriceps dysfunction and measurable asymmetry may be due to altered cortical excitability, which has been shown to be related to reductions in torque-generating capacity after knee injury.[11] The duration and severity of quadriceps asymmetry after ACLR and return to activity may help to explain the long-term reductions in self-reported function and increased rate of subsequent joint injury commonly seen in otherwise healthy, active individuals.

The purpose of our investigation was to compare neuromuscular and corticomotor limb symmetry between healthy individuals and those with ACLR. Our results indicate clear differences between groups; however, the methods and analysis used in this study have several limitations that may have affected our findings. We used a cross-sectional design because this study was part of a larger investigation with the same design. This design did not allow for as much experimental control as a prospective design may have permitted. We recruited a relatively homogeneous sample of participants through strict inclusion and exclusion criteria; however, the wide range of times since surgery (31.5 $\pm$ 23.5 months) and diverse rehabilitation experiences may have affected the outcome of our study. After finishing this study, we completed all analyses while controlling for participant age and time since surgery; however, the results were not altered, so we presented the uncorrected data in this manuscript. In addition, participants with hamstrings and patellar-tendon autografts were included in this investigation. Currently, the body of evidence related to outcomes after ACLR with varied graft sources is inconclusive, but this may represent a source of variability within the ACLR group that may have affected our results. Additionally, the limb order for testing (right limb first for all testing procedures) may have affected the performance of some participants in the ACLR group. Clinically, most strength-based measures are completed on the uninjured side first to familiarize the participant without provoking potential discomfort or apprehension. Given the design of our data-collection sessions, we had to collect data in a standardized order for all participants. This may represent a limitation in this investigation. To improve on the current design and methods, researchers should attempt to recruit a more homogeneous sample with special consideration for age, activity level, and time since surgery. In addition, prospective longitudinal measurement of neuromuscular and corticomotor function after ACLR may help clinicians better understand the source of persistent lower extremity functional deficits and provide clearer targets for intervention.

CONCLUSIONS

Participants with ACLR exhibited weaker, less activated quadriceps and less cortical excitability in the reconstructed limb than in the contralateral limb and in both limbs of healthy individuals. Asymmetry in quadriceps strength, activation, and cortical excitability persists in individuals with ACLR beyond return to recreational activity. Chronic asymmetry indicates reduced dynamic force absorption at the knee joint and may help to explain the increased rate of knee-joint injury and chronic joint degeneration seen after ACLR.

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