

# Quadriceps Function and Patient-Reported Outcomes After Anterior Cruciate Ligament Reconstruction in Patients With or Without Knee Osteoarthritis

# Grant E. Norte, PhD, ATC, CSCS\*; Jay Hertel, PhD, ATC, FNATA†; Susan A. Saliba, PhD, PT, ATC, FNATA†; David R. Diduch, MD‡; Joseph M. Hart, PhD, ATC, FNATA, FACSM†

\*School of Exercise and Rehabilitation Sciences, Athletic Training Program, University of Toledo, OH; †Department of Kinesiology, Sports Medicine Program and ‡Department of Orthopaedic Surgery, University of Virginia, Charlottesville

**Context:** Relationships between quadriceps function and patient-reported outcomes after anterior cruciate ligament reconstruction (ACLR) are variable and may be confounded by including patients at widely different time points after surgery. Understanding these relationships during the clinically relevant phases of recovery may improve our knowledge of specific factors that influence clinical outcomes.

**Objective:** To identify the relationships between quadriceps function and patient-reported outcomes in patients <2 years (early) and >2 years (late) after ACLR, including those with posttraumatic knee osteoarthritis.

Design: Cross-sectional study.

Setting: Laboratory.

**Patients or Other Participants:** A total of 72 patients after ACLR: early (n = 34, time from surgery =  $9.0 \pm 4.3$  months), late (n = 30, time from surgery =  $70.5 \pm 41.6$  months), or osteoarthritis (n = 8, time from surgery =  $115.9 \pm 110.0$  months).

Main Outcome Measure(s): The total Knee Injury and Osteoarthritis Outcome Score (KOOS) and Veterans RAND 12-Item Health Survey (VR-12) were used to quantify knee function and global health. Predictors of patient-reported outcomes were involved-limb and symmetry indices of quadriceps function (isokinetic strength [peak torque, total work, average power], maximum voluntary isometric contraction torque, fatigue index, central activation ratio, Hoffmann reflex, active motor threshold) and demographics (age, activity level, pain, kinesiophobia, time since surgery). Multiple linear regression analyses were used to predict KOOS and VR-12 scores in each group.

**Results:** In the early patients, knee-extensor work, active motor threshold symmetry, pain, and activity level explained 67.8% of the variance in the KOOS score (P < .001); knee-extensor work, activity level, and pain explained 53.0% of the variance in the VR-12 score (P < .001). In the late patients, age and isokinetic torque symmetry explained 28.9% of the variance in the KOOS score (P = .004). In the osteoarthritis patients, kinesiophobia and isokinetic torque explained 77.8% of the variance in the KOOS score (P = .010); activity level explained 86.4% of the variance in the VR-12 score (P = .001).

**Conclusions:** Factors of muscle function and demographics that explain patient-reported outcomes were different in patients early and late after ACLR and in those with knee osteoarthritis.

*Key Words:* global health, isokinetic strength, knee function, limb symmetry, neuromuscular function

## **Key Points**

- Factors of quadriceps function that explained patient-reported outcomes were different in patients early and late after anterior cruciate ligament reconstruction and in those with osteoarthritis.
- Patient-reported outcomes were best explained in patients early after reconstruction and in those with osteoarthritis, suggesting the need for early identification of impairments.
- Objective measures of quadriceps function and subjective patient-related factors (pain, activity level, kinesiophobia) should be included when assessing patient-reported outcomes after anterior cruciate ligament reconstruction.

A nterior cruciate ligament injury and reconstruction (ACLR) remains common among active young and middle-aged individuals.<sup>1</sup> Reconstructive surgery not only presents early challenges with regard to functional restoration but can also threaten the return to physical activity,<sup>2</sup> long-term joint health,<sup>3</sup> and quality of life.<sup>4</sup> Persistent quadriceps weakness is modifiable and remains of particular interest to many clinicians and researchers given its association with posttraumatic sequelae, such as self-reported disability<sup>5</sup> and osteoarthritis.<sup>6</sup> Deleterious consequences of muscle weakness are typically thought to develop over a long duration, yet tibiofemoral-joint–space narrowing has been observed in patients with quadriceps weakness within 4 years of reconstruction.<sup>7</sup> Because an alarming proportion of patients may experience degenerative changes within the first and second decades after ACLR,<sup>8</sup> early identification of modifiable impairments is paramount.

Establishing relationships between clinician- and patientbased outcomes is necessary to assign meaning to

Downloaded from https://prime-pdf-watermark.prime-prod.pubfactory.com/ at 2025-06-18 via free access

commonly observed clinical impairments and to develop evidence-based patient-assessment paradigms. The association between quadriceps muscle function and patientreported outcomes has been widely studied in response to ACLR, with a particular focus on clinician-based outcomes. Specifically, measures of quadriceps strength (eg, isometric and isokinetic torque) are most commonly represented. However, a multimodal approach to strength assessment may be appropriate to describe the functional capacity of muscle. For example, the total work performed during a given task can be quantified to reflect the ability of the muscle to produce force over a given range of motion. Total knee-extensor work has been identified<sup>9</sup> as a unique factor able to discriminate between patients after ACLR and healthy individuals better than peak isometric or isokinetic torque. Functional capacity can be further examined by muscle power, which reflects the rate at which muscle can generate force. Interestingly, knee-extensor power was a stronger determinant of walking and stair ambulation in patients with knee osteoarthritis than isometric strength,<sup>10</sup> suggesting its role in functional performance in this population. Large-magnitude deficits in both knee-extensor work and power have been observed in patients after ACLR. These data appear to indicate that each may contribute to patient-reported outcomes, yet this is unknown.

Underlying neurologic factors (eg, central activation failure, spinal-reflex excitability, corticospinal excitability) have also been studied relative to quadriceps strength and subjective knee function,<sup>11–13</sup> suggesting that more sophisticated measures of central nervous system functioning may be meaningful contributors to patient-reported outcomes. More recently, quadriceps fatigue has also been reported to uniquely describe patients after ACLR,<sup>14</sup> although the relationship between fatigue and patient-reported outcomes is unclear. Unfortunately, conflicting findings on the relationships between objective and subjective outcomes make it difficult to apply clinical recommendations. For example, isometric knee-extension torque has been shown to explain 7.8% to 61.0% of the variance in subjective knee function at an average of  $3.7^{15}$  and  $4.5^{12}$  years after ACLR, respectively. These large discrepancies may be due in part to the inclusion of patients at widely disparate time points after surgery. To elucidate the effect of impaired quadriceps neuromuscular function, it may be necessary to examine such relationships at distinct clinical time points.

Time from injury is a historically reported criterion used in return-to-activity decision making after ACLR. Prospective data<sup>16,17</sup> have highlighted the role of time in recovery from ACL injury, demonstrating a continual increase in preoperative quadriceps strength from 6 to 24 months after surgery. However, quadriceps weakness has been recently identified at 20-year follow-up,<sup>18</sup> indicating that time alone may be insufficient to resolve neuromuscular impairments. Quadriceps weakness is well documented at the time of return to activity and is often evaluated by metrics of single-limb and side-to-side limb symmetry indices. Previous authors<sup>5,13,19,20</sup> have examined the utility of both involved-limb and symmetric quadriceps function as markers of good subjective knee function after ACLR, which provide unique insight into time as a mediator of such relationships. Both metrics have been reported<sup>20</sup> to explain a significant amount of the variance in knee

function at an average of 8.2 months, slightly in favor of quadriceps strength symmetry (13% versus 8%). Interestingly, involved-limb quadriceps strength and not symmetry has been related to knee function at an average of 2 years.<sup>19</sup> In contrast, both involved-limb and symmetric quadriceps strength and central activation have been associated with knee function at 2.613 and 3.15 years after surgery, yet involved-limb function has been consistently described as a better indicator of subjective knee function during this time. Although the clinical utility of time from surgery remains in question, these data appear to show that the relationships between specific metrics of objective performance and subjective function are in part mediated by time, with 2 years postsurgery being a possible inflection point. Due to the demonstrably greater risk for secondary or contralateral ACL injury in the first 2 years after surgery,<sup>21</sup> clinicians and researchers must gain a better understanding of the specific factors that are most related to patient-based outcomes during this clinically relevant postoperative period. Currently, the relationships between involved-limb function, limb symmetry indices, and patient-reported outcomes are not fully understood with respect to time from ACLR.

Variable relationships between objective measures of quadriceps function and subjective knee function have been reported, but far less is known about the perception of global health status. The Veterans RAND 12-Item Health Survey (VR-12) is a global health-related quality-of-life measure that has evolved from the 36-item short form (SF-36). Compared with traditional measures of disease-specific function, the VR-12 is unique in that it addresses both physical and mental health status, asking questions regarding general health, emotions, physical activity, pain, and personal feelings after injury.<sup>22</sup> Previous authors<sup>23</sup> have identified relationships between the Lysholm Knee Scoring scale and subscales of the SF-36 at 6 (physical functioning, bodily pain, role emotional) and 12 (role physical, bodily pain, vitality) months after ACLR. However, it is unclear how quadriceps function is related to subjective ratings of global health status. Furthermore, it is unknown how these relationships may continue to change over the life span. Understanding the relationships between objective muscle function and global health-related quality of life may better elucidate the psychological effect of clinical impairments after ACLR. By addressing this knowledge gap, clinicians will be informed on the specific factors affecting quality of life at distinct clinical time points. From a clinical perspective, knowing which factors of objective function are most predictive of patient-reported outcomes may provide a targeted treatment approach to improve patientreported outcomes and mitigate the risk for posttraumatic osteoarthritis.

Therefore, the purpose of our study was to identify the relationships between objective measures of quadriceps function and patient-reported outcomes less than 2 years (early) and greater than 2 years (late) after ACLR, including in patients who developed posttraumatic osteoarthritis. We hypothesized that (1) greater involved-limb and more symmetric quadriceps function would be associated with improved patient-reported knee function and global health early after ACLR, (2) limb symmetry would be most meaningful in patients late after ACLR, and (3) involved-limb function would be most meaningful in patients with osteoarthritis due to bilateral impairments.

#### Table 1. Patient Demographics

	Group					
	Early (n = 34)	Late (n = 30)	Osteoarthritis (n = 8)			
Sex <sup>a</sup>						
Male	20	10	2			
Female	14	20	6			
Graft, % <sup>a</sup>						
Bone-patellar tendon-bone	51.5	27.6	37.5			
Quadruple strand semitendinosus	42.4	48.3	62.5			
Allograft	6.1	24.1	0			
Meniscectomy, % <sup>a</sup>	35.5	37.0	75.0			
Meniscal repair, % <sup>a</sup>	19.4	14.8	12.5			
		Mean $\pm$ SD				
Age, y	$22.5\pm6.3^{d}$	$24.9\pm5.9^{\rm d}$	$45.4 \pm 7.4^{b,c}$			
Height, cm	174.1 ± 11.0	171.7 ± 11.8	170.0 ± 9.7			
Mass, kg	$73.9\pm16.9$	74.9 ± 16.2	$85.2 \pm 24.8$			
Time since surgery, mo	$9.0 \pm 4.3^{c,d}$	$70.5 \pm 41.6^{b,d}$	$115.9 \pm 110.0^{ m b,c}$			
Knee Injury and Osteoarthritis Outcome Score (total)	$87.5\pm9.3^{\rm c,d}$	92.1 $\pm$ 6.0 <sup>b,d</sup>	$76.4 \pm 10.8^{\rm b,c}$			
Veterans RAND 12-Item Health Survey	$80.4 \pm 10.0^{d}$	$82.4 \pm 6.7^{d}$	$68.9 \pm 14.2^{\rm b,c}$			
Tegner Activity Scale	$6.1 \pm 1.9^{d}$	$6.9~\pm~1.6^{d}$	$4.3 \pm 1.7^{\rm b,c}$			
Visual analog scale for pain, cm	$0.7\pm0.9^{\circ}$	$0.2\pm0.5^{b,d}$	$1.2\pm0.8^{b,c}$			
Tampa Scale of Kinesiophobia	$34.4~\pm~5.7$	32.1 ± 6.5	$36.0\pm6.0$			

<sup>a</sup> Fisher exact test.

 $^{\rm b}$  Different than early anterior cruciate ligament reconstruction (ACLR; P  $\leq$  .05).

° Different than late ACLR ( $P \le .05$ ).

<sup>d</sup> Different than ACLR with osteoarthritis ( $P \leq .05$ ).

Secondly, we aimed to identify which measures of quadriceps function best explained patient-reported outcomes in each group and hypothesized that measures of isokinetic strength (work and power) would have the greatest influence on perceived outcomes given their closer association to functional movement. Understanding the relationships between commonly used metrics of objective muscle function and unique constructs of subjective, patient-reported function may aid clinicians in providing targeted treatment approaches to improve patient outcomes.

## METHODS

This was a cross-sectional study of the influence of time since ACLR on the relationship between quadriceps function and patient-reported outcomes. Patients were compared by time since ACLR (*early* = < 2 years, *late* = > 2 years) and the presence of posttraumatic knee osteoarthritis. Explanatory variables were isokinetic kneeextension strength (peak torque, total work, average power) at 90°/s, knee-extension maximum voluntary isometric contraction (MVIC) torque, fatigue index (FI), central activation ratio (CAR), Hoffmann reflex (H-reflex), and active motor threshold (AMT). Dependent variables were regional knee function, measured by the Knee Injury and Osteoarthritis Outcomes Score (KOOS), and global health, measured by the VR-12.

## **Participants**

Seventy-two patients with a history of primary, unilateral ACLR participated in this study (Table 1). Patients with a history of failed reconstruction, multiple-ligament knee injury, a treatable cartilage lesion, lower extremity joint surgery before ACLR, lower extremity injury other than to the ACL within 6 months, concussion within 6 months, or

neurologic impairment were excluded. Graft type and concomitant meniscal procedure (meniscectomy or repair) were not used as exclusionary criteria. Patients assigned to the osteoarthritis group had to have received a physician diagnosis at a minimum of 12 months after ACLR based on radiographic evidence (Kellgren-Lawrence grade  $\geq 2$ ) in 1 or more compartments of the knee. All patients were screened for the use of transcranial magnetic stimulation (TMS) according to published safety and ethical guidelines.<sup>24</sup> Volunteers were recruited from our university, orthopaedic clinic, and local community, and all testing was performed during a single laboratory visit. This study was approved by the Institutional Review Board for Health Sciences Research. Written informed consent was obtained before enrollment, and the rights of all participants were protected.

## Procedures

Participants were asked to refrain from caffeine use and intense exercise within 12 hours of testing. The order of testing was maintained throughout the study as we will describe and counterbalanced by the ACLR limb or dominant limb (healthy controls) in each group. To allow each participant ample time to recover from the strengthrelated tests before TMS, tests were performed in alternating fashion. For example, all strength tests (isokinetic, MVIC, FI, and CAR) were recorded in the first limb, followed by the contralateral limb, before the TMS protocol was initiated in the first limb. The duration between strength testing and TMS was not quantified. However, approximately 10 minutes elapsed before the contralateral limb strength assessment and 20 minutes between the first limb strength assessment and TMS. Because it was necessary to obtain an accurate estimate of the MVIC before initiating the TMS protocol, we chose this order to provide ample time for recovery.

Patient-Reported Outcomes. The KOOS<sup>25</sup> has been established as a valid, reliable self-administered questionnaire that is responsive to both short- and long-term changes in functional status and quality of life after ACL injury and reconstruction, meniscectomy, and osteoarthritis.<sup>26</sup> The total KOOS was used to quantify "knee function" as previously reported.<sup>13</sup> Although the International Knee Documentation Committee Subjective Knee Evaluation is widely used for a variety of knee injuries, the KOOS was specifically designed to evaluate patients with osteoarthritis. The KOOS was developed as an extension of the WOMAC Osteoarthritis Index<sup>27</sup> and improves on it by increasing responsiveness<sup>25,28,29</sup> and evaluating both the short- and long-term consequences of knee injury,<sup>26</sup> which may be uniquely suited for cohorts of patients with or without posttraumatic osteoarthritis after ACLR. Previous recommendations<sup>30</sup> supported the use of the KOOS, rather than the International Knee Documentation Committee Subjective Knee Evaluation, for both ACL injuries and osteoarthritis. To assess "global health" quality of life, we used the VR-12, which is similar to the SF-36 and has been demonstrated to be responsive to ACLR.<sup>31</sup> Current activity level, pain, and fear of movement were quantified using the Tegner Activity Scale, visual analog scale (VAS) for pain at rest, and Tampa Scale of Kinesiophobia (TSK), respectively.

Spinal-Reflex Excitability. The H-reflex was used to quantify spinal-reflex excitability as previously described.32 The skin overlying the vastus medialis muscle was shaved, cleaned, and debrided, and 2 recording surface electromyography (EMG) electrodes were placed over the area of greatest bulk. The EMG signal was digitally converted at 2000 Hz via 16-bit data-acquisition system (model MP150; BIOPAC Systems Inc, Goleta, CA), band-pass filtered from 10 to 500 Hz, and processed using AcqKnowledge software (version 4.2; BIOPAC Systems Inc). A stimulator module (model STM100A; BIOPAC Systems Inc) and current isolation unit (model STMISOC; BIOPAC Systems Inc) were used to deliver an electrical stimulus to the femoral nerve. A series of 1-millisecond square-wave stimuli were sequentially administered until the maximum H-reflex and muscle response (M-wave) were identified. Three maximal H-reflexes were averaged and normalized to the average of 3 maximal M-waves (H: M ratio) for analysis.

Isokinetic Strength. Isokinetic knee-extension peak torque, total work, and average power were assessed from 8 repetitions at 90°/s using a multimodal dynamometer (model System 3; Biodex Medical Systems Inc, Shirley, NY). Participants were seated in 85° of hip flexion and 90° of knee flexion (anatomical reference) for the start of each test. A correction for limb weight was used. Participants were ensured a range-of-motion arc of 110°. The testing was explained and included an instruction to "kick out and pull back as hard and fast as possible." A lap belt was used, and participants were asked to keep their head and shoulders against the seat rest with arms crossed over their chest to minimize aberrant movement. Several repetitions were practiced so they could visualize proper technique. Participants were provided real-time visual feedback via a 43-in (109-cm) LCD monitor. Oral encouragement was given to ensure maximal effort. Isokinetic peak torque (Nm/kg), total work (J/kg), and average power (W/kg) values over the 8 repetitions were normalized to body mass as previously described.<sup>33</sup> *Total work* described the total force produced relative to the angular displacement, whereas *average power* reflected the average work produced over the total duration of testing. These measures of work and power are interrelated but were included to provide additional measures of functional capacity rather than maximum capacity alone.

Isometric Strength and Quadriceps Central Activation. Participants remained seated in the dynamometer and completed a standardized acclimatization protocol, consisting of submaximal trials (25%-75% perceived effort), before 3 maximal-effort trials separated by 60 seconds of rest. A supramaximal percutaneous electrical stimulus was delivered to the quadriceps using the superimposed-burst technique during the third MVIC trial. Once the MVIC torque had reached a plateau consistent with the previous trials ( $\pm 10$  Nm), a square-wave stimulator (model S88; GRASS-TeleFactor, West Warwick, RI) with isolation unit (model SIU8T; GRASS-TeleFactor) was used to manually deliver a 100-millisecond train of 10 square-wave pulses to the thigh via 2 self-adhesive electrodes  $(3 \times 5 \text{ in } [7.6 \times 12.7 \text{ m}))$ cm]). Electrodes were positioned over the proximal vastus lateralis and distal vastus medialis. Real-time visual feedback and oral encouragement were given to ensure maximal effort during testing. Previous authors<sup>34</sup> have reported strong within-session (intraclass correlation coefficient; ICC [2,1] = 0.94) and between-sessions (ICC [2,k]= 0.86) reliability with low measurement error (2%) using this technique. Force data were digitally converted at 125 Hz, low-pass filtered at 10 Hz, and processed using AcqKnowledge software. Mean torque was calculated from a 100-millisecond epoch during the maximal contraction plateau or immediately before the superimposed-burst torque. The MVIC torque recorded from 3 maximal trials was averaged and normalized to body mass (Nm/kg) to quantify quadriceps strength. Quadriceps CAR was calculated as previously reported.<sup>34</sup>

Quadriceps Fatigue Index. Quadriceps FI was quantified during a 30-second knee-extension MVIC task as described earlier.<sup>35</sup> Although markedly different from traditional protocols intended to replicate the fatigue experienced during athletic tasks, a recent factor analysis<sup>14</sup> of lower extremity functional tests highlighted the ability of the FI to provide minimal, but appreciable, unique information about patients after ACLR. As proof of concept, previous authors<sup>9</sup> showed that this measure actually caused muscle fatigue in patients after ACLR (mean = 18.2%) and healthy individuals (mean = 21.8%). During this test, participants were instructed to "kick out as hard as possible and to maintain the contraction" while seated in the dynamometer. They were prompted to start kicking, and the 30-second trial began once the participant had achieved his or her perceived maximal effort. Visual feedback and oral encouragement were omitted to minimize the occurrence of transient aberrations in torque. Force data were digitally converted at 125 Hz, low-pass filtered at 15 Hz, and processed using AcqKnowledge software. Mean torque was recorded during a series of 100-millisecond epochs, and the greatest torque epoch from the first 5 seconds of the trial was recorded as the maximal torque  $(T_{Max})$ . The area under the force-time curve (AUFC) for the

entire contraction period from 0 to 30 seconds began at the time point of maximum muscle torque (TPM) and was used to quantify fatigue (Equation 1).

$$FI = \left[1 - \frac{AUFC_{TPM-30}}{(T_{Max,0-5}) \times (TPM-30)}\right] \times 100$$
 (Equation 1)

Corticospinal Excitability. The AMT was used to quantify corticospinal excitability via TMS. Specifically, a higher AMT was interpreted as lesser excitability. Participants remained seated in the dynamometer, and surface EMG electrodes were placed over the vastus medialis and distal anteromedial tibia for each limb. Participants wore a Lycra (Invista, Wichita, KS) swim cap with bisecting lines and a 1-cm  $\times$  1-cm grid to aid in determination of the optimal stimulus location. Motorevoked potentials (MEPs) were elicited in the vastus medialis using a magnetic stimulator (model MagStim Rapid; MagStim Ltd, Whitland, Carmarthenshire, Wales, UK) with 110-mm double-cone coil. The location that elicited the largest peak-to-peak MEP was considered the "hotspot" and used for the remainder of testing. The AMT was determined by systematically reducing the stimulus intensity from 60% of the maximum stimulator output by 5% until a measurable MEP (>100  $\mu$ V) could no longer be elicited and then increasing by 1% until its return for a minimum of 5/10 trials.<sup>24</sup> Real-time visual feedback was used to aid participants during a force-matching task at 5% of the MVIC. Because the intensity of voluntary motor contraction influences corticospinal excitability, AMT was measured after maximal strength testing to allow us to accurately determine 5% of the MVIC. Additionally, single-pulse TMS has been reported<sup>36</sup> to increase quadriceps activation. The number of stimuli administered to each patient differed, so we decided to measure AMT after strength and activation testing. The EMG signals were digitally converted at 2000 Hz, band-pass filtered from 1 to 5000 Hz, and processed using AcqKnowledge software.

# **Limb Symmetry**

Unilateral data from the ACLR limb and limb symmetry indices (LSIs) were calculated for each measure (Equation 2).

$$LSI = \left(\frac{ACLR \ Limb}{Contralateral \ Limb}\right) \times 100 \qquad (Equation \ 2)$$

# **Statistical Analysis**

Group differences in demographics were assessed using separate 1-way analyses of variance or the Fisher exact test, and all data were examined for normality using the Shapiro-Wilk test. Independent *t* tests were used to evaluate the influence of graft type and meniscal procedure (meniscectomy or meniscus repair) on each outcome measure among the entire cohort to determine the need to control these factors when performing correlations. The Pearson product moment correlation (*r*) was used to identify the relationships between individual measures of quadriceps function and patient-reported function when normally distributed. The Spearman rank-order correlation ( $\rho$ ) was used for nonnormally distributed data. Correlations were performed within each patient group (early ACLR, late ACLR, ACLR with osteoarthritis) for the KOOS and VR-12 separately. The absolute value of correlation coefficients was classified as *very weak* (0.0–0.19), *weak* (0.20–0.39), *moderate* (0.40–0.59), *strong* (0.60–0.79), or *very strong* (0.80–1.0).

Separate multiple linear (stepwise) regression analyses were used to explain the variance in patient-reported outcomes using objective measures of quadriceps function in each group. Only significantly correlated variables ( $P \leq$ .05) were considered for inclusion as explanatory variables in each regression model. Before model entry, we first assessed variables for multicollinearity, and those that were very strongly correlated with one another ( $\geq 0.80$ ) were reduced to include only the variable with the highest correlation. Probability thresholds for variable entry and removal were set at 0.05 and 0.10, respectively. Missing values were replaced with the mean for each respective group. The total  $R^2$ , adjusted  $R^2$ , and change in  $R^2$  were calculated for each step of the respective analysis. The level of statistical significance was set a priori at  $P \leq .05$ . All statistical analyses were performed using SPSS (version 20.0; IBM Corp, Armonk, NY).

# RESULTS

All patients screened for eligibility completed the study (Table 1). The groups did not differ in sex, height, or mass. Patients with osteoarthritis were older than those without it (P < .05). We were unable to elicit a measurable MEP in 3 patients in the early (n = 2) and late (n = 1) ACLR groups. Graft type and meniscal procedure did not influence any outcome measure except for quadriceps FI. Quadriceps FI was lower in patients who received a bone-patellar tendon-bone autograft compared with a hamstrings tendon autograft (14.3% ± 8.0% versus 21.1% ± 9.4%,  $t_{59} = -3.0$ , P = .004). However, this did not result in any statistically significant changes to the reported analyses when controlled (partial correlation) and did not change the interpretation of the data.

# Correlations

Correlation coefficients are presented for each group in Table 2. Among patients early after ACLR, the KOOS score was strongly correlated with isokinetic work (r = 0.627), moderately correlated with isokinetic power (r = 0.627) and torque (r = 0.522), isokinetic power (r = 0.465) and work (r = 0.413) symmetry, AMT symmetry (r = -0.448), MVIC torque (r = 0.405), and pain (r = -0.538) and weakly correlated with isokinetic torque symmetry (r = 0.398), activity level (r = 0.384), and kinesiophobia (r = -0.381). The VR-12 score was moderately correlated with all measures of involved-limb isokinetic strength and symmetry (r = 0.460-0.585), MVIC torque (r = 0.414), and activity level (r = 0.515) and weakly correlated with pain (r = -0.395) and time since surgery (r = 0.351).

Among patients late after ACLR, the KOOS score was moderately correlated with isokinetic torque symmetry (r =0.445) and weakly correlated with isokinetic work ( $\rho =$ 0.388) and power (r = 0.380) symmetry and age (r =-0.461). The VR-12 score was weakly correlated with FI symmetry (r = -0.371).

Among patients with osteoarthritis after ACLR, the KOOS score was strongly correlated with all measures of isokinetic strength (r = 0.649-0.730), MVIC torque (r =

Table 2.	Associations Among	Quadriceps	Function,	Patient Demographics,	, and Patient-Reported	Outcomes
----------	--------------------	------------	-----------	-----------------------	------------------------	----------

	Post-Anterior Cruciate Ligament Reconstruction Group, Correlation Coefficient <sup>a</sup>									
	Early (I	n = 34)	Late (r	ı = 30)	Osteoarthritis (n = 8)					
Variable	KOOS	VR-12	KOOS	VR-12	KOOS	VR-12				
Quadriceps function, Nm/kg										
Peak torque at 90°/s	.522	.539	.261	.000	.723	.809				
Total work at 90°/s	.627	.585	.049	.035	.659	.876				
Average power at 90°/s	.570	.529	.156	013	.730	.866				
Maximum voluntary isometric contraction torque	.405	.414	.117	.245	.649	.843				
Fatigue index, %	227	128	124	.156	.009	367				
Central activation ratio, %	.165 <sup>b</sup>	.109 <sup>b</sup>	063	.118 <sup>b</sup>	.310 <sup>b</sup>	.405 <sup>b</sup>				
Hoffmann reflex, H:M	−.138 <sup>b</sup>	.046 <sup>b</sup>	049	360	.451	200				
AMT, %	003	201	.102	152	.465	281				
Limb symmetry index										
Peak torque at 90°/s	.398	.460	.445	.105	.424	.136				
Total work at 90°/s	.413	.493	.388 <sup>b</sup>	.105 <sup>b</sup>	.396	.394				
Average power at 90°/s	.465	.498	.380	065	.318	135				
Maximal voluntary isometric contraction torque	.138	.268	.276	.097	214	.386				
Fatigue index	.054	.021	013	371	732	126				
Central activation ratio	.133 <sup>b</sup>	.108	.069	.147	.154	.198				
Hoffmann reflex	292 <sup>b</sup>	−.138 <sup>b</sup>	263	.143	.429 <sup>b</sup>	.143 <sup>b</sup>				
AMT, %	448	.007	.101	.163	515 <sup>b</sup>	443 <sup>b</sup>				
Patient demographics										
Age, y	263	119	461	.015	.061	045				
Time since surgery, mo	.178	.351	130 <sup>b</sup>	278 <sup>b</sup>	.111	041				
Activity level (Tegner Activity Scale)	.384	.515	.059	.340	.260	.929				
Pain (visual analogue scale)	538	395	−.214 <sup>b</sup>	.159 <sup>b</sup>	169	076				
Kinesiophobia (Tampa Scale of Kinesiophobia)	381	260		064	771	050				

Abbreviations: AMT, active motor threshold; KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veterans RAND 12-Item Health Survey.

<sup>a</sup> Bold indicates significant at  $P \leq .05$ .

<sup>b</sup> Spearman  $\rho$ . Missing data: early anterior cruciate ligament reconstruction (AMT: n = 1, limb symmetry index AMT: n = 2), late anterior cruciate ligament reconstruction (AMT: n = 1).

0.649), and kinesiophobia (r = -0.771). The VR-12 score was very strongly correlated with all measures of isokinetic strength (r = 0.809-0.876), MVIC torque (r = 0.843), and activity level (r = 0.929).

#### **Multiple Regression**

Regression results are presented for each group in Tables 3 through 5. Among patients early after ACLR, isokinetic work, AMT symmetry, pain, and activity level predicted 67.8% of the variance in the KOOS score ( $F_{4,29} = 18.4, P < .001$ ). Isokinetic work, activity level, and pain predicted 53.0% of the variance in the VR-12 score ( $F_{3,30} = 13.4, P < .001$ ).

Among patients late after ACLR, current age and peak isokinetic torque symmetry predicted 28.9% of the variance in the KOOS score ( $F_{2,27} = 6.9$ , P = .004). There were no significant predictors for the VR-12 score.

Among patients with osteoarthritis after ACL-R, peak isokinetic torque and kinesiophobia predicted 77.8% of the variance in the KOOS score ( $F_{2,5} = 13.2$ , P = .010). Activity level predicted 86.4% of the variance in the VR-12 score ( $F_{1,6} = 37.9$ , P = .001; Figure).

## DISCUSSION

In support of our hypotheses, both the involved-limb (moderate to strong) quadriceps muscle function and LSIs (moderate) were correlated with patient-reported outcomes

Table 3. Final Regression Model in Patients Early After Anterior Cruciate Ligament Reconstruction

	Knee Injury and Osteoarthritis Outcome Score					Veterans RAND 12-Item Health Survey				
Step/Variable	βÞ	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>c</sup>	βь	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>c</sup>
Total work	1.071	.393	.374	.393 <sup>d</sup>	.001	.383	.342	.322	.342 <sup>d</sup>	.006
Pain	427	.578	.551	.185 <sup>d</sup>	<.001	351	.573	.530	.116 <sup>d</sup>	.008
Active motor threshold symmetry <sup>a</sup>	255	.646	.610	.068 <sup>d</sup>	.008					
Activity level	.234	.717	.678	.071 <sup>d</sup>	.011	.408	.456	.421	.114 <sup>d</sup>	.003

Abbreviation:  $\Delta$ , change in  $\mathbb{R}^2$ .

<sup>a</sup> Missing values (n = 2).

<sup>b</sup> Standardized  $\beta$  coefficients.

<sup>c</sup> *P* value for individual variable in final model.

<sup>d</sup>  $P \leq .05$ .



Figure. A, Relationship between subjective knee function (Knee Injury and Osteoarthritis Outcome Score [KOOS]) and kinesiophobia (Tampa Scale of Kinesiophobia). B, Relationship between subjective global health (Veterans RAND 12-item Health Survey [VR-12]) and current activity level (Tegner Activity Scale) in patients with osteoarthritis after anterior cruciate ligament reconstruction.

early after ACLR. Among patients late after ACLR, weak to moderate correlations were observed only for LSIs and patient-reported outcomes. In contrast, involved-limb measures of quadriceps function were strongly correlated with patient-reported outcomes in patients who had osteoarthritis. With respect to the specific objective factors that explained subjective outcomes, knee-extension isokinetic strength measures (peak torque, total work, average power) exhibited the strongest correlations with subjective knee function (KOOS score) and global health (VR-12 score) in each patient group. Interestingly, patient-reported outcomes were best explained by the objective measures of quadriceps function in patients without osteoarthritis, whereas physical activity level and fear of movement best described outcomes in those with osteoarthritis. Our results suggested that different factors contribute to patientreported outcomes at different time points after surgery and that emphasizing a single outcome measure may not be the best strategy for evaluating all patients after ACLR.

Our findings indicated that both involved-limb quadriceps function and symmetry had meaningful associations with patient-reported outcomes early after reconstruction. Improvements in involved-limb quadriceps function and symmetry have been associated with improved knee function and lower extremity movement patterns at return to sport.<sup>37</sup> Ouadriceps strength and performance symmetry >90% are suggested indicators of a safe return to activity.<sup>38</sup> Within 2 years after ACLR, satisfactory patient-reported outcomes may be best predicted by the combination of greater isokinetic knee-extensor work in the involved limb, less pain at rest, symmetric AMT, and higher current activity level; therefore, a single measure of muscle function may be insufficient to detect meaningful impairments related to subjective knee function and global health. Patients often experience a rapid decline in quadriceps strength and functional performance early after ACLR, resulting in large asymmetries.<sup>37</sup> This may be explained in part by early changes in the muscle volume of the injured limb,<sup>39</sup> as well as decreased central drive to the muscle,<sup>16</sup> which may result in a functional decline of the contralateral limb. Bilateral responses to unilateral injury may confound estimates of limb symmetry and appear to support the additional use of unilateral assessments to identify impairments early after ACLR. This may explain why the combination of a unilateral measure of peripheral muscle function and bilateral measure of central nervous system function was able to predict knee function in patients early after ACLR.

We observed a moderate negative correlation between subjective knee function and AMT symmetry in patients early after ACLR. Our results indicated that patients with more symmetric cortical motor thresholds reported improved knee function. This finding is somewhat surprising, given that symmetry does not necessarily equate to appropriate function (eg, low AMT or high corticospinal excitability) in either limb. Interestingly, no relationship was observed between the involved-limb AMT and patientreported outcomes. However, involved-limb AMT has been identified9 as a strong predictor of patient status (ACLR or healthy). Previous authors<sup>40</sup> have used functional magnetic resonance imaging to identify a reorganization of the cerebral cortex after ACLR, suggesting that an increase in cortical effort is needed to complete a motor task. It is unclear if these changes were linked with altered corticospinal function, yet decreased corticospinal excitability has been recognized in patients as early as 6 months after ACLR<sup>16</sup> and is theorized to have a negative effect on peripheral muscle function.<sup>16</sup> Although brain-related signaling to peripheral muscle may help to explain variances in knee function, the importance of traditional strength measures cannot be overemphasized. Involved-limb quadriceps isometric strength and corticospinal excitability have

Table 4. Final Regression Model in Patients Late After Anterior Cruciate Ligament Reconstruction

	Knee Injury and Osteoarthritis Outcome Score						Veterans RAND 12-Item Health Survey				
Step/Variable	βª	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>b</sup>	β <sup>a</sup>	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>b</sup>	
Age	386	.213	.185	.213°	.024						
Peak torque symmetry	.360	.338	.289	.125°	.032						
No significant predictors							NA	NA	NA	NA	

Abbreviations:  $\Delta$ , change in  $R^2$ ; NA, not available.

<sup>a</sup> *P* value for individual variable in final model.

<sup>b</sup> Standardized  $\beta$  coefficients.

°  $P \leq .05$ .

Table 5.	Final Regression Model ir	Patients With Osteoarthritis	After Anterior Cruciate Ligament Reconstruction
----------	---------------------------	------------------------------	---

	k	Knee Injury and Osteoarthritis Outcome Score						Veterans RAND 12-Item Health Survey					
Step/Variable	β <sup>a</sup>	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>b</sup>	β <sup>a</sup>	$R^2$	Adjusted R <sup>2</sup>	$\Delta R^2$	P Value <sup>b</sup>			
Kinesiophobia	598	.595	.527	.595°	.025								
Peak torque	.526	.841	.778	.246°	.039			0.44	00.40	004			
Activity level						.929	.864	.841	.864°	.001			

Abbreviation:  $\Delta$ , change in  $\mathbb{R}^2$ .

<sup>a</sup> Standardized  $\beta$  coefficients.

<sup>b</sup> P value for individual variable in final model.

°  $P \leq .05$ .

been reported<sup>12</sup> to explain 66% of the variance in knee function. Our results partially agree with these data in that the measures of quadriceps function and patient demographics explained 67.8% of knee function. In contrast to previous results, isokinetic knee-extensor work and AMT symmetry alone accounted for 46.1% of the variance in knee function, which appears to highlight the importance of additional patient-related factors that may influence patientreported outcomes early after ACLR. Earlier authors9 demonstrated the ability of total knee-extensor work to accurately classify group membership (ACLR or healthy) in a broad cohort of patients after ACLR. Work is a biomechanical derivative important in the production (positive work) and absorption (negative work) of energy. To optimize the efficiency of athletic performance and decrease the likelihood of injury, it is likely necessary to maximize the capacity to perform work in either direction (eg, total work, or the ability to exert force over the longest available distance). It is possible that patients who can produce greater total work of the quadriceps are better suited for a return to preinjury activity levels and thus report better knee function. The relationship between quadriceps strength and subjective function is commonly investigated, but quadriceps function alone clearly does not dictate clinical outcomes. Based on our findings, additional patient-related factors such as a higher activity level, less pain, less fear of movement or reinjury, and longer time since surgery may have a positive influence on patientreported outcomes and should be considered when evaluating patients early after ACLR.

Weak to moderately positive correlations were observed between subjective knee function and isokinetic kneeextensor strength (peak torque, total work, and average power) symmetry in patients late after ACLR. Notably, no other measures of objective quadriceps function or patient demographics explained the variance in global health. Anterior cruciate ligament injury and reconstruction are theorized to alter the natural history of muscle function.<sup>41</sup> However, the trajectory of bilateral quadriceps function after unilateral injury is not clear. Previous researchers<sup>42</sup> reported large bilateral deficits in quadriceps central activation in ACL-deficient patients. Yet interlimb asymmetries were reported to be greatest early after ACLR,<sup>43</sup> which may explain why measures of limb symmetry correlated with patient-reported outcomes early after ACLR. Despite the observed relationships between more symmetric isokinetic strength and improved knee function in patients late after ACLR, peak-torque symmetry was the only predictor of knee function, accounting for 12.5% of its variance. Compared with total work, which contributed 39.3% to the predictive ability in patients early after ACLR,

the relationship between involved-limb quadriceps function and symmetry with patient-reported outcomes appeared to diminish beyond 2 years after ACLR. Improved symmetry due to both improved ipsilateral quadriceps function and deterioration of the contralateral limb may mask persistent impairments. This may provide a false sense of good clinical outcomes and underestimate the presence of subclinical impairments, making assessment difficult during this time frame. Beyond the measures of objective quadriceps function, age was negatively correlated with knee function and accounted for 21.3% of its variance, indicating that younger patients reported improved knee function. Increased age at the time of surgery was a predictor of persistent quadriceps weakness up to 9 months after ACLR.<sup>44</sup> Although age explained nearly a quarter of the variance in knee function in our study, the included measures of quadriceps function did not appear to offer good predictive ability for perceived knee function or global health beyond 2 years in patients without osteoarthritis.

Among patients with knee osteoarthritis after ACLR, strong to very strong positive correlations between involved-limb isokinetic and isometric quadriceps strength with knee function and global health were observed. The increased prevalence of osteoarthritis development in the contralateral limb has been observed at 20 years after unilateral ACLR.<sup>3</sup> This, in conjunction with the functional decline that may naturally occur over time in the contralateral limb, may help some patients achieve symmetry despite having poor long-term outcomes. In support of this, our results suggest that greater involvedlimb quadriceps function was highly associated with improved knee function and global health in patients with knee osteoarthritis. Earlier investigators<sup>45</sup> observed strong correlations between involved-limb quadriceps strength and self-reported physical activity in patients with knee osteoarthritis, highlighting the clinical significance of persistent weakness in this population. In further support of the importance of involved-limb quadriceps function in patients with knee osteoarthritis, we found that symmetry in quadriceps function was not correlated with patientreported outcomes. Persistent quadriceps weakness and activation failure have been widely reported<sup>46</sup> in patients with knee osteoarthritis and are often observed bilaterally, which may begin to explain why symmetry indices were not correlated with patient-reported outcomes in our study. Our data suggest that symmetry indices of quadriceps function may be misleading in patients with osteoarthritis because of bilateral weakness. Therefore, measures of involved-limb quadriceps function, specifically related to strength, appear to be most predictive of knee function in this population.

Beyond the objective measures of quadriceps function, kinesiophobia was strongly correlated with knee function, and the current activity level was very strongly correlated with global health in patients with osteoarthritis. Patients with less fear of movement were more likely to report better perceived knee function, and those who were more physically active perceived better health status. The roles of physical activity and quadriceps function in preserving joint health are well established. Decreased physical activity, or inactivity, commonly occurs with aging and is reported to negatively influence quadriceps function.45 In our study, patients with osteoarthritis were older than those without osteoarthritis and had self-reported lower activity levels. Although decreased physical activity in an older patient population is expected, our patients' activity levels were lower than those in previously described normative data,<sup>47</sup> which may have influenced the relationships between the objective physical impairments and patient-reported outcomes. Previous authors<sup>45</sup> have reported an association between quadriceps strength and physical activity in osteoarthritic patients who were highly active but not in those who were less active. Despite this evidence, the role of physical activity as a mediating factor between objective and subjective outcomes remains unclear. Interestingly, the current activity level was the only predictor of global health in these patients, indicating that this may be an adequate surrogate for objective quadriceps function relative to perceived health status in patients with knee osteoarthritis. Both the current activity level and kinesiophobia contributed to more than half of the variance in patient-reported outcomes, reflecting the need to look beyond traditional clinic- or laboratory-based measures of quadriceps strength in this patient population. Age may have had an influence on these relationships; however, by including a subset of patients with diagnosed osteoarthritis, we were able to better understand the potential long-term relationships between subjective and objective outcomes after ACLR. Despite these findings, further investigation of these relationships in patients with osteoarthritis and agematched controls (ACLR without osteoarthritis) is warranted.

# **CLINICAL IMPLICATIONS**

Our results suggest factors that are important during patient evaluations at different time points after ACLR. The factors that were associated with patient-reported outcomes were different for patients before and after 2 years from surgery and in patients with diagnosed knee osteoarthritis after ACLR. Early after reconstruction, involved-limb quadriceps strength and symmetry indices of strength and corticospinal excitability were important factors. Beyond 2 years, symmetry indices did not appear to be as useful to identify patients with poor subjective outcomes, which may suggest that a portion of these individuals experienced subclinical impairments not related to perceived function and health status. Although very strong associations between involved-limb measures of isokinetic and isometric quadriceps strength and patient-reported outcomes were seen in patients with knee osteoarthritis, physical activity and fear of movement explained more of the variance than any measure of quadriceps function. Overall, relative to other objective measures of quadriceps function, the measures of isokinetic knee-extensor strength appeared to best explain patient-reported outcomes after ACLR, whereas the associations between patient demographics and outcomes varied by time. According to time from surgery, patient-reported outcomes were best explained in patients early and in those with osteoarthritis, indicating the need for clinicians to identify impairments early. The results of this study support the importance of developing optimal evidence-based assessment strategies to identify impairments early after ACLR and effectively guide patient care.

# LIMITATIONS

The cross-sectional design of this study did not allow us to draw conclusions based on the natural history of the relationship among quadriceps function, demographics, and patient-reported function. Although our data suggest associations between the measured variables, they cannot confirm causality. Efforts were made to recruit a homogeneous sample of patients after ACLR. However, the purpose of the study was to investigate the relationships between subjective and objective outcomes during earlyand late-term durations after surgery, making it difficult to match groups on all demographics. Given the distribution of sex, graft type, and meniscal involvement, we believe that the sample in this study represents patients after ACLR. Based on our eligibility criteria, it was possible for a patient to sustain a subsequent knee injury that did not result in a second surgery between the time of ACLR and study enrollment. If this did occur, it would be more likely to affect patients late after ACLR with or without osteoarthritis, which could have negatively influenced neuromuscular function. The primary neuromuscular adaptations observed were early central activation failure and a persistent downregulation of corticospinal excitability. The AMT provides a gross estimate of net excitability, but it does not offer a clear understanding of the underlying alterations in cortical inhibition and excitation. Previous authors<sup>48</sup> have reported an association between cortical inhibition and central activation of the quadriceps, making this an important area of further study.

Patients with osteoarthritis received a physician diagnosis based on radiographic evidence, yet new radiographs were not obtained at the time of study enrollment. As a result, the times between the taking of the initial radiographs to confirm the presence of osteoarthritis and study enrollment varied widely, which may have resulted in changes in severity from the initial diagnosis. Additionally, we were not able to confirm the absence of osteoarthritis in patients early or late after ACLR. Lastly, the sample of patients with osteoarthritis yielded a smaller subject-to-predictor ratio than is conventionally recommended. Although recommendations vary, a ratio of at least 10:1 has been advocated. Despite achieving a 4:1 ratio in this group, correlation coefficients were strong to very strong, with no outliers observed (Table 1, Figure).

# CONCLUSIONS

Factors of quadriceps function that explain patientreported outcomes were different for patients early and late after ACLR and in those with osteoarthritis. These data support the inclusion of both objective measures of quadriceps function and subjective patient-reported factors (pain, activity level, kinesiophobia) when assessing patient-reported outcomes. Collectively, these findings suggest factors that are important during patient evaluations at different time points after ACLR. Clinicians can use the information from this study to formulate assessments that are specific to patients at different time points after surgery.

#### ACKNOWLEDGMENTS

We thank Lindsay Slater, PhD; John Goetschius, PhD, ATC Meaghan McMillen, MEd, ATC; and Stephan Bodkin, MEd, ATC, for their assistance in data collection.

#### REFERENCES

- Griffin LY, Albohm MJ, Arendt EA, et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *Am J Sports Med.* 2006;34(9):1512–1532.
- Ardern CL, Taylor NF, Feller JA, Webster KE. Return-to-sport outcomes at 2 to 7 years after anterior cruciate ligament reconstruction surgery. *Am J Sports Med.* 2012;40(1):41–48.
- Risberg MA, Oiestad BE, Gunderson R, et al. Changes in knee osteoarthritis, symptoms, and function after anterior cruciate ligament reconstruction: a 20-year prospective follow-up study. *Am J Sports Med.* 2016;44(5):1215–1224.
- Filbay SR, Crossley KM, Ackerman IN. Activity preferences, lifestyle modifications and re-injury fears influence longer-term quality of life in people with knee symptoms following anterior cruciate ligament reconstruction: a qualitative study. *J Physiother*. 2016;62(2):103–110.
- Pietrosimone B, Lepley AS, Harkey MS, et al. Quadriceps strength predicts self-reported function post-ACL reconstruction. *Med Sci Sports Exerc*. 2016;48(9):1671–1677.
- Oiestad BE, Juhl CB, Eitzen I, Thorlund JB. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(2):171–177.
- Tourville TW, Jarrell KM, Naud S, Slauterbeck JR, Johnson RJ, Beynnon BD. Relationship between isokinetic strength and tibiofemoral joint space width changes after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2014;42(2):302–311.
- Luc B, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. J Athl Train. 2014;49(6):806–819.
- Norte GE, Hertel JN, Saliba SA, Diduch DR, Hart JM. Quadriceps and patient reported function in ACL reconstructed patients: a principal component analysis. *J Sport Rehabil* [epub ahead of print]. doi: 10.1123/jsr.2017-0080.
- Accettura AJ, Brenneman EC, Stratford PW, Maly MR. Knee extensor power relates to mobility performance in people with knee osteoarthritis: cross-sectional analysis. *Phys Ther.* 2015;95(7):989–995.
- 11. Lepley AS, Ericksen HM, Sohn DH, Pietrosimone BG. Contributions of neural excitability and voluntary activation to quadriceps muscle strength following anterior cruciate ligament reconstruction. *Knee.* 2014;21(3):736–742.
- Pietrosimone BG, Lepley AS, Ericksen HM, Gribble PA, Levine J. Quadriceps strength and corticospinal excitability as predictors of disability after anterior cruciate ligament reconstruction. *J Sport Rehabil.* 2013;22(1):1–6.

- Kuenze C, Hertel J, Saliba S, Diduch DR, Weltman A, Hart JM. Clinical thresholds for quadriceps assessment after anterior cruciate ligament reconstruction. *J Sport Rehabil.* 2015;24(1):36–46.
- DiFabio M, Slater LV, Norte G, Goetschius J, Hart JM, Hertel J. Relationships of functional tests following ACL reconstruction: exploratory factor analyses of the lower extremity assessment protocol. J Sport Rehabil. 2017;27(2):144–150.
- Goetschius J, Hart JM. Knee-extension torque variability and subjective knee function in patients with a history of anterior cruciate ligament reconstruction. J Athl Train. 2016;51(1):22–27.
- Lepley AS, Gribble PA, Thomas AC, Tevald MA, Sohn DH, Pietrosimone BG. Quadriceps neural alterations in anterior cruciate ligament reconstructed patients: a 6-month longitudinal investigation. *Scand J Med Sci Sports*. 2015;25(6):828–839.
- Roewer BD, Di Stasi SL, Snyder-Mackler L. Quadriceps strength and weight acceptance strategies continue to improve two years after anterior cruciate ligament reconstruction. *J Biomech*. 2011;44(10):1948–1953.
- Risberg MA, Oiestad BE, Gunderson R, et al. Changes in knee osteoarthritis, symptoms, and function after anterior cruciate ligament reconstruction: a 20-year prospective follow-up study. *Am J Sports Med.* 2016;44(5):1215–1224.
- Hohmann E, Bryant A, Tetsworth K. Strength does not influence knee function in the ACL-deficient knee but is a correlate of knee function in the and ACL-reconstructed knee. *Arch Orthop Trauma Surg.* 2016;136(4):477–483.
- Zwolski C, Schmitt LC, Quatman-Yates C, Thomas S, Hewett TE, Paterno MV. The influence of quadriceps strength asymmetry on patient-reported function at time of return to sport after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2015;43(9):2242– 2249.
- Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of second ACL injuries 2 years after primary ACL reconstruction and return to sport. *Am J Sports Med.* 2014;42(7):1567–1573.
- Selim AJ, Rogers W, Qian SX, Brazier J, Kazis LE. A preferencebased measure of health: the VR-6D derived from the veterans RAND 12-item health survey. *Qual Life Res.* 2011;20(8):1337– 1347.
- Ochiai S, Hagino T, Tonotsuka H, Haro H. Prospective analysis of health-related quality of life and clinical evaluations in patients with anterior cruciate ligament injury undergoing reconstruction. *Arch Orthop Trauma Surg.* 2011;131(8):1091–1094.
- Rossi S, Hallett M, Rossini PM, Pascual-Leone A; Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clin Neurophysiol.* 2009;120(12):2008–2039.
- Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)–development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998;28(2):88–96.
- 26. Roos EM, Lohmander LS. The Knee Injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes*. 2003;1:64.
- 27. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol.* 1988;15(12):1833–1840.
- Roos EM, Roos HP, Lohmander LS. WOMAC Osteoarthritis Index-additional dimensions for use in subjects with post-traumatic osteoarthritis of the knee. Western Ontario and MacMaster Universities. *Osteoarthritis Cartilage*. 1999;7(2):216–221.
- Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. *Health Qual Life Outcomes*. 2003;1:17.

- Wang D, Jones MH, Khair MM, Miniaci A. Patient-reported outcome measures for the knee. J Knee Surg. 2010;23(3):137–151.
- Shapiro ET, Richmond JC, Rockett SE, McGrath MM, Donaldson WR. The use of a generic, patient-based health assessment (SF-36) for evaluation of patients with anterior cruciate ligament injuries. *Am J Sports Med.* 1996;24(2):196–200.
- 32. Norte GE, Saliba SA, Hart JM. Immediate effects of therapeutic ultrasound on quadriceps spinal reflex excitability in patients with knee injury. *Arch Phys Med Rehabil*. 2015;96(9):1591–1598.
- Bodkin S, Goetschius J, Hertel J, Hart J. Relationships of muscle function and subjective knee function in patients after ACL reconstruction. Orthop J Sports Med. 2017;5(7):2325967117719041.
- Park J, Hopkins JT. Within- and between-session reliability of the maximal voluntary knee extension torque and activation. *Int J Neurosci.* 2013;123(1):55–59.
- 35. Surakka J, Romberg A, Ruutiainen J, Virtanen A, Aunola S, Maentaka K. Assessment of muscle strength and motor fatigue with a knee dynamometer in subjects with multiple sclerosis: a new fatigue index. *Clin Rehabil.* 2004;18(6):652–659.
- Harkey MS, Gribble PA, Pietrosimone BG. Disinhibitory interventions and voluntary quadriceps activation: a systematic review. J Athl Train. 2014;49(3):411–421.
- Schmitt LC, Paterno MV, Ford KR, Myer GD, Hewett TE. Strength asymmetry and landing mechanics at return to sport after anterior cruciate ligament reconstruction. *Med Sci Sports Exerc*. 2015;47(7):1426–1434.
- Logerstedt D, Arundale A, Lynch A, Snyder-Mackler L. A conceptual framework for a sports knee injury performance profile (SKIPP) and return to activity criteria (RTAC). *Braz J Phys Ther.* 2015;19(5):340–359.
- Norte GE, Knaus KR, Kuenze C, et al. MRI-based assessment of lower extremity muscle volumes in patients before and after ACL reconstruction. J Sport Rehabil. 2018;27(3):201–212.

- Baumeister J, Reinecke K, Schubert M, Weiss M. Altered electrocortical brain activity after ACL reconstruction during force control. J Orthop Res. 2011;29(9):1383–1389.
- Tengman E, Brax Olofsson L, Stensdotter AK, Nilsson KG, Hager CK. Anterior cruciate ligament injury after more than 20 years. II. Concentric and eccentric knee muscle strength. *Scand J Med Sci Sports*. 2014;24(6):e501–e509.
- 42. Urbach D, Nebelung W, Ropke M, Becker R, Awiszus F. Bilateral dysfunction of the quadriceps muscle after unilateral cruciate ligament rupture with concomitant injury central activation deficit [in German]. Unfallchirurg. 2000;103(11):949–955.
- Harput G, Kilinc HE, Ozer H, Baltaci G, Mattacola CG. Quadriceps and hamstring strength recovery during early neuromuscular rehabilitation after ACL hamstring-tendon autograft reconstruction. *J Sport Rehabil.* 2015;24(4):398–404.
- Iriuchishima T, Shirakura K, Horaguchi T, et al. Age as a predictor of residual muscle weakness after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2012;20(1):173–178.
- Pietrosimone B, Thomas AC, Saliba SA, Ingersoll CD. Association between quadriceps strength and self-reported physical activity in people with knee osteoarthritis. *Int J Sports Phys Ther*. 2014;9(3):320–328.
- 46. Pietrosimone BG, Hertel J, Ingersoll CD, Hart JM, Saliba SA. Voluntary quadriceps activation deficits in patients with tibiofemoral osteoarthritis: a meta-analysis. *PM R*. 2011;3(2):153–162.
- Briggs KK, Steadman JR, Hay CJ, Hines SL. Lysholm score and Tegner activity level in individuals with normal knees. *Am J Sports Med.* 2009;37(5):898–901.
- Luc-Harkey BA, Harkey MS, Pamukoff DN, et al. Greater intracortical inhibition associates with lower quadriceps voluntary activation in individuals with ACL reconstruction. *Exp Brain Res.* 2017;235(4):1129–1137.

Address correspondence to Grant E. Norte, PhD, ATC, CSCS, School of Exercise and Rehabilitation Sciences, Athletic Training Program, University of Toledo, 2801 West Bancroft Street, HH 2505H, Mail Stop 119, Toledo, OH 43606. Address e-mail to grant. norte@utoledo.edu.