Knee

Quadriceps Oxygenation During Exercise in Patients With Anterior Cruciate Ligament Reconstruction

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Context: The causes of persistent muscle weakness after anterior cruciate ligament reconstruction (ACLR) are not well known. Changes in muscle oxygenation have been proposed as a possible mechanism.

Objective: To investigate changes in quadriceps muscle oxygenation during knee extension in ACLR-involved and ACLR-uninvolved limbs.

Design: Case-control study.

Setting: Laboratory.

Patients or Other Participants: A total of 20 individuals: 10 patients with primary, unilateral ACLR (7 women, 3 men; age 22.90 ± 3.45 years, height 170.81 ± 7.93 cm, mass 73.7 ± 15.1 kg) and 10 matched control individuals (7 women, 3 men; age 21.50 ± 2.99 years, height 170.4 ± 10.7 cm, mass 68.86 ± 9.51 kg).

Intervention(s): Each participant completed a single data-collection session consisting of 5-second isometric contractions at 25%, 50%, and 75% of the volitional maximum followed by a 30-second maximal isometric knee-extension contraction.

Main Outcome Measure(s): Oxygenated hemoglobin (O2Hb) measures in the reconstructed thigh were continuously recorded (versus the uninvolved contralateral limb as well as the nondominant thigh of healthy control individuals) using 3 wearable, wireless near-infrared spectroscopy units placed superficially to the vastus medialis, vastus lateralis, and rectus femoris muscles. Relative changes in oxygenation were ensemble averaged and plotted for each contraction intensity with associated 90% CIs. Statistical significance occurred where portions of the exercise trials with CIs on the O2Hb graph did not overlap. Effect sizes (Cohen d, 90% CI) were determined for statistical significance.

Results: We observed less relative change in O2Hb in patients with ACLR than in healthy control participants in the rectus femoris at 25% (d = 2.1; 90% CI = 1.5, 2.7), 50% (d = 2.8; 90% CI = 2.6, 2.9), and 75% (d = 2.0; 90% CI = 1.9, 2.2) and for the vastus medialis at 75% (d = 1.5; 90% CI = 1.4, 1.5) and 100% (d = 2.6; 90% CI = 2.5, 2.7). Less relative change in O2Hb was also noted for the vastus medialis in ACLR-involved versus ACLR-uninvolved limbs at 100% (d = 2.62; 90% CI = 2.54, 2.70).

Conclusions: Quadriceps muscle oxygenation during exercise differed between patients with ACLR and healthy control individuals. However, not all portions of the quadriceps were affected uniformly across contraction intensities.

Key Words: knee, blood flow, near-infrared spectroscopy, rehabilitation, muscle physiology

Key Points
- During isometric knee extension, less oxygen consumption was observed in the vastus medialis and rectus femoris muscles of anterior cruciate ligament-reconstructed limbs compared with control limbs.
- Similar reductions in vastus medialis oxygen consumption were observed in the vastus medialis of the reconstructed limb versus the contralateral limb.
- During exercise, when blood flow increases, reduced blood oxygenation may have implications for rehabilitation in patients with anterior cruciate ligament reconstructions.

In the United States alone, 200,000 anterior cruciate ligament (ACL) injuries occur each year. After injury, most of these individuals will undergo an ACL reconstruction (ACLR). The risk for reinjury after an ACLR has been shown to be as high as 33% and involves either graft failure or injury to the contralateral healthy knee. Athletes are 15 times more likely to sustain an ACL injury than nonathletes; competitive sport exposure is a risk factor for ACL injury. Female athletes were 4 times more likely to incur an ipsilateral reinjury and 6 times more likely to incur an injury to the contralateral limb than male athletes. The individuals who sustain an ACL injury are typically young and active, with most being under age 30 and the majority under age 20. Other problems these individuals face after surgery include altered gait patterns, decreased quadriceps function, kinesiophobia, and osteoarthritis.

Nearly 50% of patients with ACLR will develop posttraumatic osteoarthritis within 10 to 15 years after the initial reconstruction. Altered gait patterns and persistent quadriceps muscle weakness have been linked to the hastened development of posttraumatic osteoarthritis. Impaired quadriceps function has often been observed after ACLR, with the average quadriceps strength being only 75% of the contralateral limb. Quadriceps atrophy has been documented even 1 year after ACLR despite the
Table 1. Group Demographics, Injury History, and Patient-Reported Outcome Measures in Individuals With Anterior Cruciate Ligament Reconstruction and the Healthy Group

| Characteristic                                      | Groupa                             | P Valueb |
|-----------------------------------------------------|------------------------------------|----------|
|                                                     | Anterior Cruciate Ligament         |          |
|                                                     | Reconstruction                     |          |
|                                                     | Healthy                            |          |
| Sex, females/males                                  | 7/3                                |          |
|                                                    | 7/3                                |          |
| Age, y                                              | 22.90 ± 3.45                       | .346     |
|                                                    | 21.50 ± 2.99                       |          |
| Height, cm                                          | 170.81 ± 7.93                      | .930     |
|                                                    | 170.4 ± 7.17                       |          |
| Mass, kg                                            | 73.7 ± 15.1                        | .402     |
|                                                    | 68.86 ± 9.51                       |          |
| Maximal voluntary isometric contraction, involved/uninvolved limb | 1.8 ± 1.0/2.1 ± 0.9 | .0212    |
|                                                    | 2.5 ± 1.1/2.7 ± 1.2                |          |
| Limb symmetry                                       | 0.83 ± 0.21                        | .40      |
|                                                    | 0.90 ± 0.15                        |          |
| Time since surgery, y                               | 3.3 ± 2.47                         | NA       |
|                                                    | NA                                 |          |
| Graft type, hamstrings/bone-patellar tendon-bone    | 4/6                                | NA       |
|                                                    | NA                                 |          |
| International Knee Documentation Committee form score| 83.7 ± 10.6 | .002     |
|                                                    | 98.75 ± 2.07                       |          |

Abbreviation: NA, not applicable.

* Values are mean ± standard deviation except where otherwise indicated.

b P values indicate side-to-side differences within participants. Values < .05 were considered significant.

c Between-groups P value (involved limb) = .198. Cohen d effect size = .64.

completion of rehabilitation.\(^{12}\) After ACLR, nearly 50% of individuals do not return to their preinjury level of activity, which may be related to persistent weakness or other dysfunction.\(^{10,11}\)

In patients with ACLR, an inability to effectively recruit motor units leads to deficits in quadriceps muscle activation.\(^{13–17}\) One reason for persistent muscular weakness is impaired oxygenation of the tissue during exercise or physical activity.\(^{18,19}\) This may reflect changes in oxygenation of the muscle tissue due to injury.\(^{18,19}\) We speculated that because of the Hilton law, the femoral nerve supplying the joint also supplies the quadriceps muscles, and an injury to the articular structures during surgery may cause changes in the somatic nerve supply to the joint and muscle, which consequently affect the sympathetic nerve supply, resulting in tissue oxygenation changes. Interaction between the somatic and sympathetic nerve supplies is controlled by skeletal-muscle blood flow during exercise, and skeletal-muscle contraction causes relaxation of the smooth muscles, which leads to increased oxygenation of the muscles.\(^{19}\) Thus, we theorized that damage to the somatic nervous supply may ultimately induce changes in the sympathetic nerve supply and subsequent changes in tissue oxygenation. However, changes in oxygenation of the quadriceps muscle have not been studied in patients with ACLR. Understanding changes in oxygenation during exercise may be a way of understanding altered motor-unit recruitment, which leads to reduced muscle activation and persistent weakness in patients with ACLR. This information is essential for developing targeted therapies to most effectively treat or prevent chronic muscle weakness in patients with ACLR.

Therefore, the purpose of our study was to compare quadriceps oxygenation between patients with ACLR and healthy control individuals. We hypothesized that individuals with ACLR, unlike healthy control participants, would exhibit decreased quadriceps oxygenation.

METHODS

In this case-control design, the independent variables were group (ACLR and healthy control) and limb (ACLR and contralateral). The dependent variables were oxygenated hemoglobin (O$_2$Hb), International Knee Documentation Committee (IKDC) form score, and isometric quadriceps strength. The study was approved by our institutional review board for health science research.

Participants

Participants were between the ages of 18 and 30 years, were recreationally active, and had no history of vascular or neurologic disorder (Table 1). Individuals were assigned to either the ACLR or healthy group based on their medical history. Those in the ACLR group had undergone a primary, unilateral ACLR an average of 3.3 ± 2.47 years earlier and had been released to unrestricted activity. The healthy individuals had no lower extremity injuries in the past 6 months.

Instruments

We used near-infrared spectroscopy (NIRS) for all oxygenation measures. The NIRS measures were obtained using the PortaMon MK III and Oxysoft software (Artinis Medical Systems, Arnhem, the Netherlands). Measures were recorded at 10 Hz. To measure subjective knee function, all participants completed the IKDC form. A dynamometer (model System 4 Pro; Biodex Medical Systems, Inc, Shirley, NY) was used to measure torque, and AcqKnowledge software (version 4.2; BIOPAC Systems, Inc, Goleta, CA) was used to interpret and process the torque data.

Testing Procedures

Participants provided informed consent before screening and data collection. They were encouraged to limit their physical activity and avoid caffeine for 12 hours before coming to the laboratory. Once in the laboratory, participants were positioned in the dynamometer chair. Three NIRS PortaMon devices were placed over the muscle belly parallel to the muscle fibers of the rectus femoris (RF), vastus medialis (VM), and vastus lateralis (VL; Figure 1). We monitored the signal on the Oxysoft software to ensure that each device was placed over the muscle belly. Once a good signal was present, the devices were covered.
with black cloth to block out any ambient light and then secured with tape.

To ensure a uniform baseline, participants rested in the dynamometer chair for 20 minutes before the start of contractions. After they flexed the knee to 90°, we recorded a 5-second maximal voluntary isometric contraction (MVIC). A custom-written program was used to provide visual feedback to participants during the sustained isometric contractions. We asked them to actively match torque equal to 25%, 50%, and 75% of MVIC for 5 seconds each, with 10 seconds of rest given between contractions. The final contraction was a fatigue trial of 30 seconds at 100% of the MVIC. All measures were then repeated on the contralateral limb. The raw data were exported to Excel (version 16; Microsoft Corp, Redmond, WA) for processing (Figure 2).

**Data Processing**

We normalized the NIRS data to the first point of each trial by subtracting the value from each trial from the starting value, thereby determining the relative difference. Data points with associated 90% CIs for each limb (ACLR-involved limb, ACLR-uninvolved limb, and healthy control limbs) were ensemble averaged and plotted over the course of the trial.

**RESULTS**

**Between-Groups Comparisons: ACLR Versus Healthy Limbs**

We found no differences between the groups with respect to age ($P = .346$), height ($P = .930$), or mass ($P = .402$; Table 1). Differences were present between groups for subjective knee function on the IKDC form ($P = .02$; Table 1). The $O_2$Hb in ACLR-involved limbs demonstrated less relative change than the healthy matched limbs in the RF at 25%, 50%, and 75% of the MVIC (Figure 3). The significant times for 25%, 50%, and 75% of the MVIC in the RF were 1 to 2.5 seconds ($d = 2.08$), 1 to 4.9 seconds ($d = 2.75$), and 1 to 4.9 seconds ($d = 2.03$), respectively (Table 2). We noted less relative change in $O_2$Hb between the ACLR and healthy matched limbs in the VM at 75% and 100% of the MVIC (Figure 3). The significant times for the 75% and 100% intensities in the VM were 1 to 4.9 seconds ($d = 1.46$) and 4 to 29.9 seconds ($d = 1.02$), respectively (Table 2). The $O_2$Hb was not different between the ACLR and healthy matched limbs for 100% MVIC in the RF and 25% and 50% MVIC in the VM (see Figures 2 and 3 and supplemental digital content, showing no difference in RF and VM between the ACLR and healthy limbs). We found no difference in $O_2$Hb between the ACLR-involved and healthy matched limbs for any of the VL contraction intensities (see Figure 4 and supplemental digital content, Figures 1 and 3).
showing no difference in VL between the ACLR and healthy limbs).

**Within-Group Comparisons: ACLR Versus Contralateral Limbs**

We noted less relative change in the O$_2$Hb of the ACLR-involved limb than in the ACLR-uninvolved limb in the same participants for the VM muscles at 100% of MVIC (Figure 4). The significant time for this measure was 3 to 13 seconds (Table 2). However, no differences were evident in the relative change in O$_2$Hb between the ACLR-involved and ACLR-uninvolved limbs at any of the contraction intensities for the RF, VM, and VL muscles.
DISCUSSION

Researchers have attempted to identify neurophysiological factors that have led to poor quadriceps function after ACLR to determine appropriate treatments for improving outcomes. Muscle oxygenation after ACLR has not been studied and was hypothesized to be affected in this population. By measuring relative changes in O$_2$Hb, we were able to examine the oxygenation characteristics of the quadriceps during exercise. During all isometric exercise trials, we observed a smaller magnitude of change in O$_2$Hb in the ACLR limb than in the contralateral or a healthy matched limb (Figures 3 and 4). The O$_2$Hb decreased during contraction for all groups. This decrease signifies that oxygen was not being used as the muscle contracted. Oxygen is an important component in creating adenosine triphosphate for muscle contraction.\(^{21}\) During exercise, skeletal muscle blood flow must increase as the metabolic demands of contracting muscles increase.\(^{21,22}\) The increased oxygen supply is needed to maintain the contraction.\(^{22}\) Our methods allowed us to examine the oxygenation of each quadriceps muscle (RF, VM, and VL) individually during the exercise protocol.

We noted a smaller relative change in O$_2$Hb of the ACLR-involved limb during the 30-second VM 100% fatigue trial than in both the contralateral side and the healthy control matched limb. In addition to statistically significant differences at certain intensities, a similar overall trend was seen throughout muscle comparisons between ACLR limbs (ACLR-involved versus ACLR uninvolved) as well as between groups (ACLR versus healthy). A smaller change in O$_2$Hb was observed in ACLR limbs than in contralateral or healthy matched limbs, which indicates that less oxygen was used by the involved quadriceps muscles of the ACLR group and, therefore, that less energy was used for muscle contraction. Decreased oxygen consumption may indicate a decreased level of O$_2$Hb and, as a result, less availability of oxygen as a fuel source for contraction, which suggests tissue oxygenation changes after the ACLR in the ACLR group compared with healthy control individuals.

Similar results were found by Kirby et al.,\(^{23}\) who compared blood flow in response to exercise in younger and older adults. Older adults (aged 64 ± 1 year) had less forearm blood flow at 15% and 25% of MVIC as well as less forearm vasodilation during various exercise intensities.\(^{23}\) Given that older adults commonly experience exercise intolerance, these results suggest that decreased skeletal muscle blood flow may be a contributing factor.\(^{23}\) Alterations in skeletal muscle oxygenation may be a natural consequence of aging. As with other degenerative conditions such as osteoarthritis, patients with ACLR may experience accelerated progression of naturally occurring processes across the lifespan due to their injury. This was demonstrated by the fact that patients in our study were of similar age as the healthy control group and yet displayed altered skeletal muscle oxygenation. The role of these changes across the lifespan in patients with ACLR is an area for future research.

After ACLR, quadriceps muscle performance decreases. The average quadriceps strength of the ACLR limb in our patients was 83% of the uninjured limb, similar to reports in the literature.\(^{9}\) This strength deficit persisted even after patients completed a full rehabilitation program and were released to unrestricted activity. A possible cause of decreased quadriceps strength in patients with chronic knee injuries is arthrogenic muscle inhibition (AMI), which is a decrease in the ability to contract a muscle although neither the muscle nor the nerve that supplies it were damaged.\(^{21}\) The cause of AMI is not well understood. Our findings may add to the understanding of AMI: decreased use of oxygen in the quadriceps. The neural factors that may contribute to reduced muscle activity secondary to blunted oxygen consumption in the quadriceps of patients with ACLR is an important area for future investigation.

Reduced ability to use oxygen during contraction is perhaps another factor that explains persistent muscle weakness but has long been missed by clinicians and researchers.
We observed lower oxygen consumption in the ACLR group, but we are not currently able to identify the underlying mechanism. Our results serve as a starting point to enhance our understanding of the physiological conundrums underlying the oxygenation changes in the quadriceps muscles, which might be among the factors contributing to persistent weakness and poor functional outcomes after surgery. Future authors should also classify individuals with ACLR according to the time since surgery in order to identify when these vascular changes occur. This will allow clinicians to know when to intervene and target impairments after surgery. Perhaps interventions that are designed to increase skeletal muscle blood flow should be implemented early after surgery to limit the effects of inhibition caused by decreased skeletal muscle blood flow.

A limitation of our work was the effect of adipose tissue on the NIRS measurements. The participants were primarily women, which aligned with the increased proportion of ACL injuries in women versus men.24,25 Women may have more adipose tissue, which may limit the measurement capabilities of the NIRS devices; they have a fixed depth of measurement associated with the distance between the infrared lights on the unit. In addition, the depth of penetration meant that we could not measure the vastus intermedius, which restricted the number of quadriceps muscles that could be analyzed. However, even with limitations in depth of penetration of the NIRS device, we still found differences between patients with ACLR and healthy individuals, as well as between limbs of the former. Another limitation was the variety of graft types and times since surgery, which made it difficult to attribute the findings to a particular time point after surgery or patient population. One of the 4 patients with a hamstring graft had the autograft augmented using allograft and also had manipulation under anesthesia, but the patient was an athlete who met the criteria for release to full activity.

CONCLUSIONS

We observed a decrease in \(O_2Hb\) consumption of the quadriceps in the ACLR group when compared with healthy individuals during isometric knee-extension exercise. Those who had undergone ACLR had less oxygen consumption in the VM and RF than healthy control participants and their own contralateral limb. During exercise, the patients with ACLR exhibited muscle weakness and reduced oxygen consumption on the reconstructed side versus the contralateral side, demonstrating a connection between blood flow and muscle weakness in patients with ACLR.

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