

Moderated Blood Flow Restriction after Anterior Cruciate Ligament Reconstruction

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Moderated Blood Flow Restriction after Anterior Cruciate Ligament Reconstruction

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Hypothesis- Patients in the moderated blood flow (Delfi) restriction group will have significantly increased muscle strength, thigh circumference, HGH and IGF levels, and no significant differences in knee range of motion, Lachman exam, KT2000, IKDC, Tegner, PROMIS surveys, VAS scores, or CK levels compared with standard ACL rehabilitation patients.

Background:

ACL injury is a common and potentially devastating injury. Approximately 80,000 ACL tears occur annually in the United States (1). 50,000 of those will go on to have ACL reconstruction surgery (2). Goals of reconstruction surgery and rehabilitation include: joint stability, restoration of knee function, and return to preinjury activities. The quadriceps is critical to dynamic joint stability, and weakness of this muscle group is related to poor functional outcomes. Because of this, identifying strategies to minimize quadriceps weakness following ACL injury and reconstruction is of great clinical interest (3).

Moderated blood flow training, was developed in 1966 by Dr. Yoshiaki Sato of Japan. This training technique uses specialized pneumatic belts, placed on the upper arms or legs that moderate blood flow to the distal extremity leading to engorgement of blood in the arms and legs. This exercise method has been shown to be safe and effective in producing muscle hypertrophy at lower intensity training (4,5). Typically a training intensity of more than 65% of one repetition maximum (1 RM) is considered the minimum intensity required to achieve muscle hypertrophy and strength gains (6). However, such intensive weight may not be possible or safe in the postoperative patient population. With moderated blood flow training, substantial muscle hypertrophy can occur using a training intensity as low as 20% of 1 RM (6). Moderated blood flow training provides a safe, less intense, but still effective means to promote muscle hypertrophy in the post-operative ACL patient. We hypothesize that patients randomized to standard physical therapy with moderated blood flow training will demonstrate significantly increased muscle strength, muscle mass, HGH, IGF levels, and no significant differences in knee range of motion, Lachman exam, KT2000, VAS scores, and CK levels compared with standard physical therapy without moderated blood flow in post-

operative ACL patients. This in turn could lead to faster, yet safer, return to functional day-to-day activities and sport.

Objectives: To determine if there are significant differences in muscle strength, thigh circumference, knee range of motion, VAS, IKDC, Tegner, PROMIS surveys, HGH, IGF, CK levels, KT2000, and Lachman's exam in those patients that participate in moderated blood flow postoperative ACL physical therapy vs. standard ACL post-operative physical therapy.

Study Procedures

- a. The study will be a prospective, randomized, controlled trial between two treatment cohorts. A total of 50 patients will be enrolled in the study. Informed consent will be obtained in clinic or by phone (Patient IQ e-consent) prior to any surgical intervention, per the IRB protocol. Enrollees will receive a copy of the consent and HIPAA form. All patients that meet inclusion criteria who consent to participate in the study will then be randomly assigned to either the control group or moderated blood flow therapy group. Randomization will occur by autogenerated permuted 1:1 block randomization using electronic assignment from the orthopaedic research team prior to initiation of post-operative therapy. The control group will undergo standard of care, post-operative ACL reconstruction rehabilitation. The treatment group will also receive standard ACL rehabilitation combined with Delfi moderated blood flow restriction therapy. Patients will follow up at standard of care clinic visits and participate in the same standard of care physical therapy protocol for ACL reconstruction. Baseline measurements of thigh circumference, knee ROM, KT 2000, Lachman exam, and labs for HGH, IGF, and CK will be obtained preoperatively. Patients will also complete preoperative IKDC, Tegner, PROMIS, and VAS pain surveys. Measurements of thigh circumference and knee range of motion will occur at 2 week intervals post operatively. Strength testing will start at 6 weeks post-operatively. These measurements will occur during standard therapy sessions. KT 2000 and Lachman exam will be performed at 4, 6, 8, and 12 months post operatively. A standard functional return to sport evaluation will be performed at the 4, 6, 8, and 12 month postoperative visits. Labs for HGH, IGF, and CK will be drawn at 2, 6, 12, and 24 weeks. VAS pain scores will be recorded before and after each therapy session. The PROMIS, IKDC, and Tegner surveys will be given at 4, 6, 8, 12 month intervals. The study will conclude at 12 month follow up. All post-operative visits will be standard of care. No additional clinic visits will be required for this study. Background patient information will be collected including age, sex, BMI, and co-morbidities.
- b. The control group will be necessary to provide a baseline measure on which moderated blood flow therapy will be compared.
- c. Blinding of the subject will not be possible as the patient will be able to recognize if they have or have not had the moderated blood flow (Delfi) device applied during therapy and application of a sham-device is not practical or considered standard of care. Evaluators performing measurements will be blinded to the patient's treatment group during assessment of muscle strength, thigh circumference, knee range of motion, Lachman exam, and KT2000. Surgeons will also be blinded to the respective treatment groups. All other outcome measures are objective and quantitative.

Pre-Trial	Investigator discusses study with the patient in person or by phone and provides the patient with a patient Consent Form (in person or electronic)
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	Patient provides written consent or electronic consent (Patient IE e-consent) to participate in the study (randomization occurs) IKDC, Tegner, PROMIS, VAS surveys completed. Baseline thigh circumference, ROM, Lachman exam, KT2000 performed Baseline HGH, IGF, CK labs obtained
Day 0	Operative procedure: Documentation of the type of ACL graft used.
Post op Day 1-completion of PT	Patients begin standard physical therapy routine +/- moderated blood flow Thigh circumference, and knee ROM performed every 2 weeks. VAS pain survey recorded before and after each therapy session
Post Op Weeks: 2, 6, 12, 24	Labs for HGH, IGF, and CK levels obtained. Strength testing during routine Physical Therapy visits begins at 6 weeks
4 months post-operatively	Functional return to sport evaluation performed by Physical Therapy IKDC, Tegner, PROMIS, VAS surveys completed. Lachman exam and KT2000 performed.
6 months post-operatively	Functional return to sport evaluation performed by Physical Therapy* IKDC, Tegner, PROMIS, VAS surveys completed. Lachman exam and KT2000 performed.
8 months post-operatively*	Functional return to sport evaluation performed by Physical Therapy IKDC, Tegner, PROMIS, VAS surveys completed. Lachman exam and KT2000 performed.
12 months post-operatively	Functional return to sport evaluation performed by Physical Therapy* IKDC, Tegner, PROMIS, VAS surveys completed. Lachman exam and KT2000 performed Patient will be released from all study activities after the 12 month follow-up visit
* If received as standard of care, data will be collected. If not, data will not be collected	

Withdrawal of Subjects: Subjects will be informed that they have the right to withdraw from the study at any time for any reason, without prejudice to their medical care. The Investigator(s) may elect at any time to withdraw a subject from the study for any reason unrelated to the study if such a decision is in the subject's best medical interest. If a subject discontinues the study prematurely, or is withdrawn by the Investigator(s), as much follow-up data as possible will be obtained. The primary reason for termination or discontinuation will be documented in the report of the final results. Subjects who are withdrawn for any reason from the study after treatment will not be replaced. Subjects who withdraw consent and refuse to complete the follow-up assessment will be considered off-study at that time. Attempts will be made to retrieve any follow-up data, in particular, adverse events at the time of study discontinuation. If the Investigator(s) reports a subject as lost to follow-up, an assistant to the Investigator will ensure that documentation is complete regarding the reason(s) this has occurred and will ensure that every attempt is made by the Investigator(s) to contact the subject or significant other persons associated with the subject to determine subject status. Appropriate documentation will consist of at least two documented attempts at contact via telephone by an assistant of the Investigator (s), followed by an attempt to contact via registered US mail or other courier service requiring recipient signature.

1. Inclusion/Exclusion Criteria

Inclusion Criteria:

-Patients between ages 18-40

-Diagnosed with isolated ACL tear and have been indicated to undergo ACL reconstruction

Exclusion Criteria:

- age <18 years old or >40 years old
- Multiligament knee injury
- Revision ACL reconstruction
- History or peripheral vascular disease
- History of deep vein thrombosis or pulmonary embolism
- Any contraindication to moderated blood flow restriction therapy
- Inability to comply with post-operative ACL reconstruction rehabilitation
- If meniscal repair or a cartilage procedure is performed at the time of surgery that would preclude the patient from being able to follow the standard post-operative ACL rehabilitation.

2. Devices

Delfi's PTS Personalized Tourniquet System (Delfi Medical Innovations Inc., Vancouver, Canada), a form of moderated blood flow training, has been used by the Missouri Orthopaedic Institute Department of Physical Therapy for its proven safety and effectiveness in help to promote muscular strength gains, enhance sports performance, and to assist with rehabilitation from injury or surgery.

Moderated blood flow training causes increased blood pooling in the limbs. During exercise lactic acid is then produced. Due to the moderation of blood flow, the lactic acid is retained longer in the muscles. Hypoxia, acidosis, inorganic phosphate, AMP and other local factors have been shown to turn on transcription, and thus, protein synthesis in muscle cells. This local effect results in stimulation of muscle, tendon and vascular growth (5). Muscle receptors also send stronger signals to the brain which in turn causes large quantities of growth hormone to be released. Under the condition of moderated blood flow therapy, it has been shown that even short-term and low-intensity exercise can induce muscle strength, hypertrophy and increasing muscle mass (7-9).

3. Study Statistics

- a. Primary outcome variable will be muscle strength determined by a trained observer blinded to therapy cohort and time point.
- b. Secondary outcome variables will include: thigh circumference, VAS pain scores, IKDC, Tegner, PROMIS surveys, knee range of motion, KT 2000, Lachman exam, lab levels of HGH, IGF, and CK.
- c. Number of patients per group (n=25) was determined from a pre-study power analysis (t-Test) using previously published data on rehabilitation after ACL reconstruction for a desired power of 0.8 and $\alpha = 0.05$. This analysis resulted in recommended sample size of 20 per group. The N of 25 per group was chosen to allow for subjects lost to follow-up.

4. Risks

- a. Patient confidentiality during the course of this study will be protected in compliance with HIPAA requirements as well as the requirements of the University of Missouri Health-Sciences IRB.

After consent is obtained, all subjects will be assigned a study identification number that requires the use of a key in order to decipher a subject's personal identification information. The key will be kept in the Cerner Power Trials database, which is password protected. The study identification number will be used to label all paper data collection instruments.

All subject information in electronic format will be kept in password-protected storage. All subject information in paper format will be kept in locked cabinets in a secured suite at the Missouri Orthopedic Institute or destroyed.

b. There is potential risk of discomfort from application of the pneumatic tourniquets. This is temporary and occurs during the therapy sessions.

c. Due to the venous pooling from vascular constriction, there is a theoretical risk of increased incidence of blood clots, vascular insufficiency, potential muscle injury, oxidative stress, and possible nerve conduction problems. These theoretical risks have not been demonstrated in previous studies specifically investigating the safety of occlusive therapy (10,11)..

5. Benefits

a. There is a potential benefit to the moderated blood flow group of increased muscle mass, strength, and ability to progress in therapy at an accelerated rate compared with control patients. If this benefit is found in the treatment group, moderated blood flow therapy may be able to be used in all ACL reconstruction patients. The hope is that the increased strength and muscle mass will allow patients to progress in therapy at a safe and accelerated rate, and therefore allow patients to get back to their preinjury activities. Otherwise, there are no further direct benefits to the patient for participation in the study.

6. Payment and Remuneration

a. No compensation for participation in the study.

7. Costs

a. Patients that choose to participate in the study will not incur any additional costs related to the study. Patients will receive the standard of care surgical procedure and postoperative rehabilitation protocols. Any additional lab tests and study related measurements will be at no charge to the patient and will be covered by the Department of Orthopaedic Surgery.

8. References

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