The Effects of Preoperative Blood Flow Restriction Training in Patients Undergoing ACL Reconstruction

Protocol Version 2.0:
October 28, 2022

Principle Investigator:
Dr. Lawrence Wengle
Resident Physician, Division of Orthopaedic Surgery, University of Toronto

Primary Supervisor:
Dr. John Theodoropoulos
Staff Orthopaedic Surgeon, Mount Sinai Hospital, Toronto, ON

Introduction

Quadricep femoris (QF) muscle function is an integral factor in the rehabilitation and overall outcome after lower extremity injury or surgical intervention. Atrophy of this muscle group is a common finding in patients undergoing anterior cruciate ligament (ACL) reconstruction. This is due to the immobility prior to surgery, vascular ischemia caused by a tourniquet intra-operatively and inability to perform high load strength training in the early post-operative period[1]. A deficit in QF muscle strength can result in excessive joint loading and be a contributing factor in the early onset of osteoarthritis of the knee[2]. It should be noted that a loss of strength in this primary knee extensor mechanism muscle group can persist for up to 2 years after surgery[3]. Thus, the reduction of QF atrophy and maintenance of strength during an intervention such as an ACL reconstruction has large implications for the overall post-operative outcome and natural history of the knee joint.

In order to combat the challenges of muscle atrophy for patients with an ACL injury, blood flow restriction (BFR) training has been shown to have beneficial effects in the post-operative period specifically. The process of using BFR therapy involves the application of an extremity tourniquet to occlude venous outflow and restrict arterial inflow. Thus, an anaerobic environment is created to promote muscle hypertrophy by having cells upregulate cell signalling, protein synthesis and ultimately myogenic proliferation[4]. The use of BFR during lower extremity rehabilitation has shown that its simultaneous use with low load resistance training can have similar hypertrophic effects to isolated high load resistance training[5]. This is ideal for patients who are initially unable to perform high intensity exercises shortly after an ACL reconstruction surgery, but are attempting to reduce overall QF atrophy.

However, the use of BFR in the pre-operative period has yet to be well established. Preconditioning with an ischemic environment may provide an effective way to reduce QF atrophy with low load exercises while awaiting surgery. Additionally, having a period of sensitization with anaerobic conditions prior to surgery, may provide some resistance to the damaging effects of a tourniquet intra-operatively. The limited studies that have attempted to use BFR therapy prior to ACL surgery have had short intervention periods, small sample sizes and outcome variables that have not assessed overall clinical outcome[6]. If BFR in the pre-operative setting can be shown to provide beneficial effects, it will be a valuable tool in maximizing the overall outcome of patients undergoing ACL reconstruction.

We are proposing a prospective feasibility study to assess pre-operative BFR in patients awaiting ACL reconstruction. This study will serve the following: (1) to determine if BFR improves strength testing prior to surgery and (2) to determine if BFR reduces QF muscle group atrophy prior to surgery. As a result of this study, we will also be collecting preliminary results on pre-operative clinical and quality of life scores. If this study shows encouraging results, it will serve as a template for a more comprehensive randomized control trial.

Specific Aims

To determine if pre conditioning with blood flow restriction training in patients awaiting ACL surgery

1. Improves QF muscle strength testing
2. Reduces QF muscle group atrophy

Hypothesis

Preconditioning with Blood Flow Restriction Training in patients requiring ACL reconstruction has a beneficial effect on clinical outcomes prior to surgery.

Methods/Study Design

Group Allocation:

- Patients will be randomized into 1 of 2 groups:
  - **BFR Group**: BFR Physiotherapy Pre Operatively (16 patients)
  - **Non-BFR Group:** Same Physiotherapy protocol without BFR intervention Pre Operatively (16 patients)
- This was not a balanced randomization.

Inclusion Criteria:

- Sagittal Knee instability caused by ACL tear requiring surgical reconstruction
- Minimum 4 weeks since the time of injury
- Age 18 to 50 years
  - Range of motion required
    - Active extension deficit <5º, Active flexion > 120º
  - No previous surgery to affected knee

Exclusion Criteria:

- Functional impairment (neuro disease, gait abnormality, ambulatory aids at baseline)
- Severe spine or lower limb injuries
- Comorbidities including cardiovascular, respiratory or metabolic disease, blood coagulation disorders, current smoker

Outcome Variables:

- Primary: **Objective Quadricep** (extension) **and Hamstring** (flexion) **Strength**
  - Biodex Isokinetic testing
  - Measured in **Peak Torque** (FT-LBS)
  - Both flexion and extension measured at:
    - 60 degrees / second (indicative of **strength)**
    - 80 degrees / second (indicative of **endurance)**
  - Both the affected leg (ACL injury) and unaffected leg (CONTROL) were measured

- Secondary Outcomes:
  - Clinical Score
    - Organ Specific: (i.e. KOOS – Knee Injury and Osteoarthritis Outcome Score)
    - General Quality of Life: (i.e. SF-12 Score)
  - Clinical Exam: Thigh circumference (mm) – measured 10 cm superior to patella

- Independent Group Measures:
  - Patient Demographics: Age, Sex, Weight, Leg dominance, Injured leg side

BFR Cuff Details:

- 14 cm wide contoured pneumatic tourniquet cuff (Delfi VariFit Contour Thigh Cuff)
- Placed around proximal thigh, connected to portable pressure regulating system (Delfi Portable Tourniquet System)
- Inflated to 80% LOP (Limb Occlusion Pressure) – measured at initial visit via ultrasound probe or photoplethysmography probe

BFR Exercise Protocol: *To be completed at Mt. Sinai Hospital*

- Patient will perform a total of 12 sessions prior to surgery (3 sessions/week x 4 weeks)
- Patients will perform single leg knee extension exercise in a closed kinetic chain on a leg-press machine.
- Non injured leg will not perform any exercises but will act as control and be measured for strength and clinical outcome
- Patients in the non BFR group will perform the same protocol but there will be no inflation of their tourniquet during testing
- Load will be individually set to 15% 1RM for warm up and 25% 1RM for intervention
    - Warmup: 10 to 15 reps at 15% 1RM workload, no BFR occlusion
        - Rest: 30 seconds
    - 1st Set: cuff inflated to 80% LOP, patient completes 30 reps at 25% 1 RM
        - Rest: 30 seconds
    - 2nd Set: cuff remains inflated to 80% LOP, patient completes 15 reps at 25% 1RM
        - Rest: 30 seconds
    - 3rd Set: cuff remains inflated to 80% LOP, patient completes 15 reps at 25% 1RM
        - Rest: 30 seconds
    - 4th Set: cuff remains inflated to 80% LOP, patient completes 15 reps at 25% 1RM
        - Session complete, cuff deflated.
- Load Progression
    - If patient's are able to complete all 75 repetitions (30-15-15-15) on two consecutive sessions, their load will be increased by 20 lbs at the subsequent session

Biodex Testing Protocol

- **Warm-up:** Stationary bike x 3-min

- **Biodex Set-up:** tall sitting with waist and thigh strap in place to secure limb, axis of movement through knee joint (1" above head of fibula)

- **Movement:**
    - Knee Extension (quadriceps kicking UP)
    - Knee Flexion (hamstrings pulling DOWN)

- **Muscle Activation:**
    - machine moves limb through a 70 degree range of movement while patient actively kicks up and down to get used to the pattern for the test
    - patient starts at 50% intensity x 5 reps and builds up slowly until they are ready to perform the test at 100% effort

- **Test:**
    - 5 repetitions @ **60** degrees/sec (heavy resistance) – **indicative of strength**
    - 10 repetitions @ **180** degrees/sec (lighter resistance) – **indicative of endurance**

- **Effort:** 100% for all 15 reps on both limbs

- **Results:** compared via print-out after the test and submitted for study

Intervention Timeline:

- Pre Op Period:
    - Phase One: Begins at time of initial consultation until 4 weeks pre operatively
        - This time allows for patient to reduce effusion, normalize range of motion prior to BFR intervention
    - Phase Two: Intervention period begins 4 weeks prior to surgery
        - 3 Sessions/week = 12 sessions total
        - Baseline Biodex testing completed at time = 0 weeks (4 weeks pre op)
            - This ensures patient is cleared for intervention to begin.
        - Pre-Operative Biodex testing completed at time = 4 weeks
            - This will be done prior to surgery once the physiotherapy protocol is completed.

Recruitment Strategy and Patient Screening:
All patients presenting to participating orthopaedic surgeons between the ages of 18 to 50 years with a diagnosis of an ACL injury requiring surgery will be screened. Potentially eligible patients will be approached by the site investigator to speak with a study coordinator to discuss participating in the trial. The study coordinator will be the one obtaining informed consent and no study related procedures will be done prior to subject signed the consent form.

Sample Size Estimation
Estimation of minimal sample size with a statistical power level of ≥0.80 (β-error ≤20%) was calculated based on the expected mean difference of our primary outcome measure (maximal voluntary isometric contraction, MVIC). The estimated minimal number of subjects for each treatment arm was 13 and 20% was added to account for loss to follow up. In total, 16 patients will be recruited to each pathway for a total of 32 individuals.

Budget

Item	Notes	Hours	Cost (per hour)	Cost
Delfi BFR Cuffs	Two sets of Delfi BFR Equipment	Nil	Nil	$1600
Biodex Testing	1 on 1 strength assessments (30 min x 64 sessions)	32	$120	$3840
Physiotherapy	1 on 1 Physiotherapy (30 minute session x 384 sessions)	192	$100	$19,200
Data Collection and Analysis	Patient data collection and statistical analyses	200	Nil	Nil
			TOTAL	**$24,640**

Study Facilities and Locations

- Each patient will complete twelve (12) physiotherapy sessions at the ***Rehab & Wellbeing Centre, Mount Sinai Hospital, 600 University Avenue, 20th floor Toronto, ON, M5G 1X5***

- Additionally, each patient will complete two (2) Biodex strength testing assessments at ***Cleveland Clinic Canada – Sport Medicine, 150 Eglington Ave East, Toronto, ON, M4P 1E8***

Research Team

- Principle Investigator: Dr. Lawrence Wengle, MD
    - Resident Physician, Division of Orthopaedic Surgery, University of Toronto
- Primary Supervisor: Dr. John Theodoropoulos, MD, FRCSC, MSc
    - Division of Orthopaedic Surgery, Mount Sinai Hospital, Toronto, ON
- Co-Supervisor: Dr. Marcel Betsch, MD, MBA
    - Clinical Fellow, University of Toronto Orthopaedic Sports Medicine
- Biodex Strength Testing Supervisor: Paul Papoutsakis, Athletic Therapist
    - Cleveland Clinic Canada – Sport Medicine Clinic, Toronto, ON
- Clinical Supervisor: Katrina Dekirmendjian, PA
    - Rehab & Wellbeing Centre, Mount Sinai Hospital, Toronto, ON

Significance

To date, the benefits of BFR for patients awaiting ACL surgery during the pre-operative period is extremely limited. This study will provide:

- The largest sample size to date for pre-operative BFR intervention in ACL patients
- High quality outcome testing in the form of Biodex isokinetic quadriceps strength testing
- An intervention protocol that involves the most BFR sessions per patient in the literature

If patients demonstrate favourable results prior to their surgery, this will provide some insight into the benefits BFR can have in patients awaiting ACL reconstruction.

References

1. Buckthorpe M, La Rosa G, Villa FD. Restoring Knee Extensor Strength after Anterior Cruciate Ligament Reconstruction: A Clinical Commentary. *Int J Sports Phys Ther.* 2019;14(1):159-172.

2. Oiestad BE, Holm I, Gunderson R, Myklebust G, Risberg MA. Quadriceps muscle weakness after anterior cruciate ligament reconstruction: a risk factor for knee osteoarthritis? *Arthritis Care Res (Hoboken).* 2010;62(12):1706-1714.

3. Kilinc BE, Kara A, Camur S, Oc Y, Celik H. Isokinetic dynamometer evaluation of the effects of early thigh diameter difference on thigh muscle strength in patients undergoing anterior cruciate ligament reconstruction with hamstring tendon graft. *J Exerc Rehabil.* 2015;11(2):95-100.

4. DePhillipo NN, Kennedy MI, Aman ZS, Bernhardson AS, O'Brien LT, LaPrade RF. The Role of Blood Flow Restriction Therapy Following Knee Surgery: Expert Opinion. *Arthroscopy.* 2018;34(8):2506-2510.

5. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. *Eur J Appl Physiol.* 2002;86(4):308-314.

6. Zargi T, Drobnic M, Strazar K, Kacin A. Short-Term Preconditioning With Blood Flow Restricted Exercise Preserves Quadriceps Muscle Endurance in Patients After Anterior Cruciate Ligament Reconstruction. *Front Physiol.* 2018;9:1150.