Quantification of Peripheral Hematopoietic Progenitor Cell Circulation Following Repeated Acute, Vascular Restriction Resistance Exercise Using the Delfi Tourniquet System

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE OF PROJECT: Quantification of Peripheral Hematopoietic Progenitor Cell Circulation Following Repeated Acute, Vascular Restriction Resistance Exercise Using the Delfi Tourniquet System

INVESTIGATOR: Tyler Opitz, DPT, SCS, CSCS

CO-INVESTIGATORS: James Andrews, MD
Adam Anz, MD
Jessica Jewell MAT, L/ATC, CSCS
Steve Jordan, MD

RESEARCH SITE(S): Andrews Research and Education Foundation

SPONSOR: State of Florida

INVESTIGATOR CONTACT INFORMATION:

Andrews Research & Education Foundation (AREF)
1020 Gulf Breeze Pkwy
Gulf Breeze, FL 32561
(850) 916-8702

Baptist Physicians Group
1020 Gulf Breeze Pkwy
Gulf Breeze, FL 32561
(850) 916-8700

Quantification of Peripheral Hematopoietic Progenitor Cell Circulation Following Repeated Acute, Vascular Restriction Resistance Exercise Using the Delfi Tourniquet System

INTRODUCTION:
In order to decide whether you wish to participate in this research study, you should understand why the study is being done, how the study will be run, the types of study procedures involved, your time commitments, and the possible risks and/or benefits to make an informed decision. This process is known as "informed consent."

This written consent form provides detailed information about the research study. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. Before you decide to take part in this study, you may want to think about it more, or discuss it with family or friends. You can take a copy of this form home with you before making your decision. Your participation in this study is voluntary. You should not join this research study until all of your questions are answered to your satisfaction.

If you wish to participate in this research study, you will be asked to sign this consent form. You will be asked to sign before any study procedures are done. You will be given a copy of this consent form to keep for your records.

PURPOSE OF THE RESEARCH STUDY:
You are being asked to participate in research being conducted by the Andrews Research & Education Foundation (AREF). The purpose of this study is to quantify the cellular content *(in vitro)* of mobilized hematopoietic stem cells and CBC data extracted from peripheral blood before exercise and at 0-, 20-, 40-, and 60-minute intervals following exercise. The purpose of this study is to examine how slowing down blood flow to the legs, called blood flow restriction (BFR), during exercise by applying compression to your legs, affects the way stem cells are released into the blood stream. It is hoped that the results of this study will lead to a better understanding of how stem cells can be collected from the blood to be used in medical procedures and treatments.

SELECTION OF SUBJECTS:
If you decide to be in this study, you will be one of up to 30 people in this research study. You are asked to be in this research study because you are healthy and between the ages of 18 and 45 years old. You will not be able to participate if you are unable to complete 20 minutes of intense exercise or have a medical history of any of the following medical conditions: uncontrolled hypertension, diabetes, autoimmune disorders, blood disorders, disorders requiring immunosuppression, cancer, an ongoing infectious disease, use of steroids, or significant cardiovascular, renal, hepatic or pulmonary disease, or if using tourniquet bands on your legs would not be medically appropriate.

RESEARCH PROCEDURES:
If you choose to participate you will attend a familiarization session, 12 treatment sessions and final session. A summary of activities you will complete at each session is below.
Familiarization Session:

- You will undergo a standard physical exam, including answering questions about your medical history. You will also be asked to rate your physical activity level by filling out the questionnaire called the Tegner Activity Level Scale.

- The Delfi BFR tourniquet system will be introduced to the subject. Subjects will become familiarized with the pressure that the tourniquet system will produce on their legs during the experimental testing session.
- The study team will find the one repetition maximum (1-RM) for each exercise (Figure 1). This process will be performed by the physical therapist trained in the use of the exercise equipment. The resistance of each exercise will be modified as needed until the physical therapist finds the suitable amount of weight required for the subject to be able to perform one and only one repetition. The progression for obtaining a 1-RM weight will be repeated for each exercise (seated leg extension, semi-reclined leg press, seated hamstring curl.)
- The study team will answer any questions the subject may have about any of the exercises or the Delfi tourniquet system.

Testing Sessions (12):

- You will be asked to refrain from consumption of alcohol and caffeine for 12 hours before testing and strenuous exercise 24 hours prior to testing.
- You will be advised to avoid the consumption of non-steroidal anti-inflammatory drugs (NSAIDS) in response to muscle soreness. NSAIDS include but are not limited to ibuprofen, high dose aspirin, naproxen, and diclofenac.
- The research team will collect height, weight, and seated blood pressure.
- You will then have 6 cc of blood collected via forearm/arm vein access once 15 minutes of rest in the sitting position have elapsed.
- You will then, under the supervision of an individual trained in BFR, undergo a BFR session. The Delfi Personalized Tourniquet System (PTS) (Delfi Medical Innovations Inc., Vancouver, BC) is the BFR system that will be utilized. Bilateral proximal thigh bands will be applied and inflated to a pressure of 80% of occlusive pressure as determined by the automated tourniquet. The three exercises (seated leg extension, semi-reclined leg press, seated hamstring curl) will be formatted with 4 sets of 30-15-15-15 repetitions per exercise. The resistance will be set as 30% of one repetition maximum (1-RM).
- After the BFR session concludes, additional 6 cc blood draws will be obtained immediately post-exercise and after 20-minute, 40 minute, and 60 minutes have elapsed. You will be offered the insertion of a peripheral intravenous blood draw or multiple percutaneous blood draws.

Final Session

- The final session will take place no sooner than six weeks after the first experimental session and within five days of the twelfth and final experimental session.
- Within the seventh week following completion of the familiarization session, you will be brought in for a blood draw post-BFR. You will be asked to refrain from strenuous exercise 24 hours leading up to the final session. You will also be asked to refrain from the consumption of alcohol and caffeine for 12 hours before the blood draw.

- You will be advised to avoid the consumption of non-steroidal anti-inflammatory drugs (NSAIDS) in response to muscle soreness. NSAIDS include but are not limited to ibuprofen, high dose aspirin, naproxen, and diclofenac.
- The research team will collect height, weight, and seated blood pressure.
- You will then have 6 cc of blood collected via forearm/arm vein access once 15 minutes of rest in the sitting position have elapsed.

RISKS AND DISCOMFORTS:
This study includes the risks relating to blood draws, moderate exercise, and vascular occlusion. The risks of taking blood include pain, bruising at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting. It is possible that during the exercise the following might occur: abnormal blood pressure, fainting, dizziness, disorders of heart rhythm, and in very rare instances heart attack, stroke, or even death. There are also risks of bodily injury including, but not limited to, injuries to the muscles, ligaments, tendons, and joints of the body from exercise. You may experience discomfort from the Delphi leg bands, and may experience muscle soreness and fatigue from the exercise protocol. These risks will be minimized by ensuring you are physically able to safely perform the exercises in this testing session and by having trained staff to take the blood samples.
There is a small risk of the disclosure of your protected health information, which will be minimized where possible including removing all identifiable information from data collection sheets and storing study information in secure locations as described in more detail below.

ALTERNATIVES:
There are no known alternatives available to you other than not taking part in this study.

BENEFITS:
There are no direct benefits for subjects who participate in the study. Indirect benefits include additional medical care and physical therapy care not associated with any medical procedures or injury. Results from the study may help clinicians to develop a better understanding of BFR and its effects on blood metabolites and the mobilization of peripheral hematopoietic progenitor cells (aspirational benefit).

CONFIDENTIALITY:
All patient protected health information and other confidential information is protected by state and federal law, unless you allow it to be disclosed. During the course of this study, your information will be identified by a letter-number combination. Any new information that might develop during the project will be provided to you if that information might affect your willingness to participate in the project. Pictures of you will be taken only if you sign below where it states: “I am willing to have photographs taken of the inside of my knee for use in presentations or publications.”

All information and data collected during this research will be recorded on the appropriate forms and stored in a locked room in the AREF research facility. In addition, all subject data forms, including

summary information and spreadsheets, will be scanned and stored in a secure password protected folder on a laptop that only the study investigators will have access to, and will be permanently deleted following publication of any and all manuscripts written as a result of this research. Records related to this study will be retained in a secure location for as long as required by applicable law, but no less than a period of 3 years after the completion of the study. At this time, all records will be properly destroyed.

HIPAA and PROTECTED HEALTH INFORMATION:
We know that information about you and your health is private. We are dedicated to protecting the privacy of that information. Because of this promise, we must get your written authorization (permission) before we may use or disclose your protected health information, also called "PHI," or share it with others for research purposes.

You can decide to sign or not to sign this authorization section. However, if you choose not to sign this authorization, you will not be able to take part in the research study. Whatever choice you make, about this research study will not have an effect on your access to medical care.

The United States government has issued a privacy rule to protect the privacy rights of patients ("Privacy Rule"). This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your health information. This section describes your rights and explains how your health information will be used and disclosed for this study.

During this study, the researchers will need to use personal health information about you. Your personal health information is health information about you that could be used to identify you because it includes information, such as your name, address, telephone number, photograph, date of birth, social security number, new and existing medical records, or the types, dates, and results of various tests and procedures. This may include information in your medical record and information created or collected during the study. By signing this consent, you are agreeing to allow the research personnel to use your personal health information to carry out this study.

By signing this document, you also allow the research staff to disclose your personal health information to outside entities who may be directly involved in completing the study project. The study data that the researchers send to these entities will not include your name, address, or social security number, but instead, will be designated with a code number. However, your medical records can be reviewed or copied at the study site by regulatory authorities or other oversight bodies, including the Baptist Hospital Institutional Review Board. The purpose of these reviews is to make sure the study is being conducted properly and that the data is being collected correctly, or for other purposes allowed by law.

Your personal health information may no longer be protected by the Privacy Rule once it is disclosed, your personal health information will be kept as confidential as possible under the law; however, absolute confidentiality cannot be guaranteed.

If you cancel this authorization, the researchers will no longer use or disclose your personal health information under the authorization for this study, unless it is needed to preserve the scientific integrity of the study. Information obtained before you cancel this authorization may still be used by the researchers.

COST AND COMPENSATION:
There will be no cost to you for participating and you will not receive any money for participating in this research. In the unlikely event of an emergency, the AREF will provide basic first aid medical treatment. However, if you were to require additional medical care as a result of participating in this study, you would need to contact your personal physician at your own expense.

The Investigators, the employers of the Investigators, and the Research Site does not have programs for compensating subjects for injury or complications related to human subjects' research. Any treatment will be at your expense.

Participants will be provided a stipend for their time spend participating in this study. A $20.00 gift card will be provided at each of the 14 sessions: (Introductory, 12 Experimental, Final).

VOLUNTARY PARTICIPATION/WITHDRAWAL:
Taking part in this study is voluntary. Your medical treatment, costs of treatment and eligibility for benefits will not be affected if you decide not to sign this Consent Form or participate in the study. In the event new information becomes available that may affect your willingness to participate in this study, this information will be given to you so that you can make an informed decision about whether or not to continue your participation.

QUESTIONS:
It is your right, as a research participant, to ask questions at any time regarding the procedures involved and any aspects of this study including the potential benefits or risks. For any questions you may have for the researcher, you may contact them at (850) 916-8590.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact the Baptist Hospital Institutional Review Board* at (850) 469-2227. The IRB will not be able to answer some types of questions, such as questions about appointment times.
*The IRB is a group of individuals who independently review research

STATEMENT OF CONSENT TO PARTICIPATE IN THIS RESEARCH STUDY:
By signing this consent form I agree to and acknowledge the following statements:

Quantification of Peripheral Hematopoietic Progenitor Cell Circulation Following Repeated Acute, Vascular Restriction Resistance Exercise Using the Delfi Tourniquet System

I agree to participate as a subject in this study and for my protected health information to be released as described in this consent.

I understand that my participation is completely voluntary, and that I may withdraw at any time without prejudice by sending a written request to the researcher at the Sports Medicine Research Lab, Andrews Research and Education Foundation, 1020 Gulf Breeze Pkwy, Gulf Breeze, FL 32561.

I have read and understand the above information and have been given the opportunity to discuss it and ask questions.

I understand that this authorization does not have an expiration date.

I have received a copy of this authorization form for my records.

I have been informed that I may contact the investigators by phone at (850) 916-8796 in order to answer any questions that I may have at any time during my participation.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

PHOTOGRAPH CONSENT:

Please indicate your preference below with regard to photographs to be taken of you during your participation:

_____ I am willing to have photographs taken of the inside of my knee for use in presentations and/or publications.

_____ _____
Signature of Participant Date