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Document:
Informed Consent Form

Official Study Title:
Role of a Novel Exercise Program to prevent Post Thrombotic Syndrome (EFFORT-2)

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Department of Veterans Affairs

Research Consent Form

Participant Name: _____ Date: _____

Title of Study: Role of Novel Exercise Program to Prevent Post Thrombotic Syndrome

Principal Investigator: Brajesh K. Lal, MD 410-328-5840

VA Facility: Baltimore 512

STUDY No: HP 00049880

This is a consent form to take part in a research study conducted by the VA Maryland Health Care System (VAMHCS) Department of Vascular Surgery and is being paid for by the VA Office of Research and Development. Your decision to take part is voluntary and you can choose to withdraw at any time. You may ask questions at any point before or during the study.

As you read this form describing the study, you may ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide.

PURPOSE OF STUDY

The purpose of this study is to determine whether standard treatment alone or standard treatment plus a three month exercise program can lower the risk of long term problems of blood clots in the legs. The study will also investigate the possible ways by which this improvement may occur.

You are invited to take part in this study because you have been diagnosed with a blood clot in the veins of your leg within the last 4 weeks, and you are 18 years of age or older. This study will take place at the VAMHCS. We will enroll 260 patients total over 4 years. The length of time that you will take part in the study is 2 years.

PROCEDURES

In this study, you have an equal chance of receiving either treatment. After you have consented to participate in the study you will be randomized (similar to flipping a coin) to one of the two treatment groups (standard treatment versus standard treatment plus exercise). As a part of this study, you will be required to come in for these follow up visits; 3D Ultrasound testing, blood work, questionnaires and exercise testing.

TREATMENT GROUPS

Standard treatment group

If you are randomized to the standard group, you will receive standard treatment for your blood clots as prescribed by your treating doctor. This usually includes a blood thinning medication, compression stockings and walking as tolerated. These are not research related procedures. However, you will participate in research testing at your follow up visits.

Exercise treatment group
If you are randomized to the exercise group you will receive standard treatment as described above. You will also receive a supervised exercise program for three months as follows:

Supervised Exercise Program
Exercise Phase 1 (Day 1 – Day 7/discharge): If you are admitted to the hospital, we will begin upper body exercise that will last for the first 7 days of your hospital admission or until you can walk safely or until you are discharged if that is earlier than 7 days. You will complete 2 daily sessions of bedside exercise on a portable upper body machine. Each session will consist of three intermittent 30-sec bouts of upper body cycling; and each bout will be followed by a 10 min rest period (repeated 2 times).

If you are unable to perform upper body exercise, you may be asked to use an Food and Drug Administration (FDA) approved neuromuscular electrical stimulation (NMES), for 15-30 minutes daily. Small pads will be placed over the muscles on your legs and then a small amount of electrical current will cause a contraction of your leg muscles. If you are discharged earlier than Day 7, you will go straight to Phase 2 of the exercise program.

Exercise Phase 2 (Day 7/Discharge–Month 1):
Phase 2 will begin immediately after discharge or immediately if you are an outpatient. You will perform aerobic exercise (supervised treadmill walking) at the VA hospital or at the VA exercise facility once a week and will walk twice a week at home. You will also begin stretching exercises before or after walking. Training on the treadmill will start at a very low intensity and progress gradually during the first 3-4 weeks based on your tolerance. You do not have to come to the VA gym on a weekly basis and can choose to exercise at home only. If you choose to exercise at home only, you will be required to walk at least 3 times a week and will receive weekly phone calls to assess safety and compliance.

Exercise intensity will be monitored using wrist heart rate monitors. You will be encouraged to achieve a target heart rate while walking at home and will be given a heart rate monitor capable of storing heart rate data. We will download your heart rate data periodically for review. In addition, we will provide you an exercise logbook to maintain, which will be reviewed weekly by us.

If you are unable to perform walking exercise, you may be asked to use an FDA approved

neuromuscular electrical stimulation (NMES) device for 15-30 minutes daily. You will be taught how to safely use the device to help your muscles contract and take the device home to use. If you become able to perform walking exercise, you will be transitioned to the aerobic exercise described above.

If you have a medical event requiring hospitalization or treatment of some kind, please refrain from the study exercise program until you speak with the study team and/or are given medical clearance by your treating clinician or primary care physician.

Exercise Phase 3 (Month 2-Month 3): You will continue your weekly exercise as before, at the VA Annex once a week, but will extend the walking program at home to 4 days per week. You will continue stretching exercises to improve knee and ankle flexibility. After each aerobic exercise session you will perform stretching exercises. If you choose to exercise at home only, you will be required to walk at least 5 times a week and will receive weekly phone calls to assess safety and compliance.

If you are performing passive exercise using the electrical device, you will continue but increase the frequency to 5 days per week. If you become able to perform walking exercise, you will be transitioned to the aerobic exercise described above.

If you have a medical event requiring hospitalization or treatment of some kind, please refrain from the study exercise program until you speak with the study team and/or are given medical clearance by your treating clinician or primary care physician.

Both Groups will take part in research testing detailed below. See table on page 4 for frequency of testing.

1. **Blood Sampling (10 minutes)**
   Blood samples will collected to determine if there is inflammation in your body, and to determine if there are any changes in your clot breakdown ability. We will draw 10 teaspoons of blood at various times in the study (see chart on page 3) The blood samples will be de identified and the plasma and serum will be stored for analysis at Baltimore VA Medical Center. We will not use samples for biological or genetic development for any commercial products. While you are in this study, blood will be taken from you that may be useful for research analysis. These samples will be stored for a time period at the Baltimore VA Medical

Center until all research analysis are complete and will only be accessible to the PI and study team

(Please initial one of the statements below)
_____I agree to have my blood stored for research analysis

_____I DO NOT agree to have my blood stored for research analysis

Genetic tests may be performed on your blood samples to examine genes (DNA) that may influence blood clots and related health problems. All samples will be coded to ensure anonymity and confidentiality. You will not be provided with the results of these genetic tests as they are research tests of unproven clinical significance. You may participate in the research even if you do not agree to genetic testing. Please initial below to indicate whether or not you agree to have genetic tests run on your coded, anonymous stored samples.

(Please initial one of the statements below)
_____I agree to have my samples used for genetic tests.

_____I DO NOT agree to have my samples used for genetic tests.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

2. **3D Ultrasound test (being performed at University of Maryland Medical Center (UMMC): 30 minutes**
   You will be positioned on a cushioned table and gel will be applied to the skin on your legs. An ultrasound machine will be moved over your legs to take images.

3. **Questionnaires (15 minutes)**: You will be asked to complete two questionnaires related to your quality of life, which will take approximately 5 minutes each. We will inspect your legs for evidence of chronic problems related to the blood clot.

4. **Exercise testing (30 minutes):** This test shows us how your body responds to exercise. You will be asked to complete a 400 meter walk in the hallway. This takes several minutes. We will measure the distance you walk and the time it takes to finish the test. We will also measure the strength of your calf muscles using a small hand held device. You will be asked to push your foot against the device as hard as you can and your strength will be recorded.

5. SCHEDULE OF TESTS:

Test	Baseline	1 Month	3 Month	6 Month	1 Year	2 Years
Consent	**X**					
Questionnaires	**X**		**X**	**X**	**X**	**X**
3D Duplex Ultrasound (Location UMMC)	**X**	**X**	**X**	**X**	**X**	**X**
Exercise Testing	**X**		**X**		**X**	**X**
Blood Sampling	**X**	**X**	**X**			

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?

If you take part in this research, you will be responsible for coming to each follow-up appointment for a period of 2 years. **POTENTIAL RISKS/DISCOMFORTS**:
There will be no change to the standard treatment prescribed by your doctor and your doctor will decide on the type and duration of the medication used to treat your blood clot. If you are assigned to the exercise group, you will receive the study exercise program in addition to standard treatment. You will complete the following tests regardless of which group you belong to:

- **Ultrasound;** This non-invasive test will be performed while lying down with minimal discomfort. There may be risks to the subject or to the embryo or fetus, if the subject is or becomes pregnant which are currently unforeseeable.
- **Questionnaire**: There are no risks.
- **Blood sample collection**: You may experience pain, bruising and bleeding.
- **Exercise Testing and Training**: Exercise is associated with the risk of cardiovascular complications such as chest pain, heart attack, or sudden death and complications related to stress and strains of muscles, twisted ankles, or falls. The risk is increased in people who have heart disease, poor circulation to the legs, or stroke. Studies have shown that exercise after a blood clot in your leg does not increase the risk of it travelling to your lungs. In fact, it may reduce that risk. To minimize this risk, if soreness does develop, you will be instructed on how to stretch and ice the sore muscles to relieve the soreness. Monitoring by trained personnel during exercise training limits the risk for these occurrences.
- **Neuromuscular Electrical Stimulation (NMES):** If you use NMES, risks include skin irritation and muscle soreness. The risk of skin irritation will be reduced by giving you training sessions in the beginning where we can watch and check you to make sure that you are correctly using the NMES unit. The risk of muscle soreness will also be reduced by slowing increasing the amount of time and strength of stimulation, starting at a low level and slowly increasing as tolerated.

POTENTIAL BENEFITS

You may or may not benefit by taking part in this study. There is no guarantee that you will receive direct benefit from your participation in this study. However, the study could find that exercise enhances clot break down and that it prevents post clot problems. This knowledge gained will provide additional treatment options to enhance completeness of recovery. Therefore,

this study could provide highly significant information with minimal risks.

ALTERNATIVES TO PARTICIPATION
The alternative to participation in this study is to use only standard treatment for patients with deep vein blood clots.

COSTS TO PARTICIPANTS
You will not be charged for any treatments or procedures that are performed for research purposes in this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study..

PAYMENT TO PARTICIPANTS

You will be compensated for your time in this study according to the following schedule and will receive a total of $240.

- $20 after completing baseline testing
- $30 after completing 1 month testing
- $30 after completing 3 months testing
- $40 after completing 6 months testing
- $60 after completing 1 year testing
- $60 after completing 2 years testing

MEDICAL TREATMENT AND COMPENSATION FOR INJURY
Every reasonable safety measure will be used to protect your well-being. If you are injured as a result of taking part in this study, the VA Maryland Health Care System (VAMHCS) will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures. This care may be limited by local or federal law.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:

DURING THE DAY: Research Coordinator at 410-605-7000 ext. 4854 and
AFTER HOURS: Dr. Brajesh Lal, Study PI at 410-328-5840

The VA does not normally provide any other form of compensation for injury. However, by signing this form, you have not waived any legal rights or released the VAMHCS or its agents

from liability for negligence.

CONFIDENTIALITY AND ACCESS TO RECORDS

Taking part in this study will involve collecting private information about you including your social security number. Your social security number will be used to access your VA medical records and may also be used for payment purposes for your participant in this research study. More information related to the use and disclosure of your individually identifiable health information will be further outlined in the "Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research".

All efforts will be made to limit your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may access your information include the University of Maryland IRB, Office of Human Research Protection, VA Office of Research Oversight, VA Office of the Inspector General, the study sponsor, VA Office of Research and Development, and the VAMHCS Office of Research Compliance.

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

Loss of confidentiality will be minimized by storing data in a secure location such as a locked office and locked cabinet or electronic data will be password-protected. If you consent to take part in this study, all measures to protect the confidentiality of your study records, your identity and personal health information will be strictly taken to the extent permitted by the appropriate laws and/or regulations. Your study records and identity will not be made public.

You will be provided with additional privacy information and a consent form regarding data protection called Authorization to Use and Disclose Personal Health Information for Research. This form must be sign by you.

Your research records and/or identifiers will be retained in accordance with the VA records control schedule. The "records control schedule" is a set of rules set by the federal government that states when federal agencies are allowed to dispose of records. The VA must follow these rules.

Everyone using study information at the VAMHCS will work to keep your personal information confidential. Your personal information will not be given out unless required by law or authorized by you in the VAMHCS "HIPAA Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research". However, if your information is disclosed to other entities, the VAMHCS no longer has control of that information. Please see the HIPAA Authorization for this study for further details.

If you are a patient in the VAMHCS, the results of your medical tests for this study may be included in your medical record. Your medical and research records will be kept strictly confidential to the fullest extent permitted by law.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. Your participation will not affect the way you now pay for medical care at the VAMHCS.

If you decide to stop taking part, if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator Dr. Brajesh Lal at 410-605-7000 ext. 4854

If you choose to have your blood samples destroyed please contact the investigator Dr. Brajesh Lal at 410 -605 -7000 ext.4854

There are no adverse consequences (physical, social, economic, legal, or psychological) of your decision to withdraw from the research. If you decide to withdraw, we would encourage an orderly termination of participation, including a written withdrawal request.

We will notify you of any significant new findings, which develop during the study,

which may affect your willingness to participate in the study.

CAN I BE REMOVED FROM THE RESEARCH?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include failure to follow instructions of the research staff or the signed consent form and if the person in charge decides that the research study is no longer in your best interest. The sponsor can also end the research study early. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

The VA Maryland Health Care System (VAMHCS) has designated the University of Maryland Baltimore (UMB) Institutional Review Board (IRB) to review this research study.

If you wish to confirm that this study is in fact IRB approved and is being conducted at the VAMHCS, you may contact (Research Coordinator) at 410-605-7000 extension 4854 [

Please read the University's statement below.

(Minimal Risk Studies)

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research all rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research participant.

The research described in this consent form has been classified as minimal risk by the IRB of the University of Maryland Baltimore. The IRB is a group of scientists, physicians, experts, and other persons. The IRB's membership includes persons who are not affiliated with UMB and persons who do not conduct research projects. The IRB's decision that the research is minimal risk does not mean that the research is risk-free. You are assuming risks of injury as a result of research participation, as discussed in the consent form.

If you are harmed as a result of the negligence of a researcher, you can make a claim for compensation. If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the staff of the UMB Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

You may also contact the VAMHCS Human and Animal Research Protections Officer (HARPO). The contact information for the HARPO is:

VAMHCS Human and Animal Research Protections Officer
Baltimore VA Medical Center
10 North Greene Street, Mail Stop 151
Baltimore, MD 21201
410-605-7000, extension 6512
Room 3D-158

The VAMHCS Human and Animal Research Protections Officer may contact you in the future to ask you about your experiences with this research study.

Department of Veterans Affairs

Research Consent Form

Participant Name: _____ Date: _____

Title of Study: Role of Novel Exercise Program to Prevent Post Thrombotic Syndrome

Principal Investigator: Brajesh K. Lal, MD 410-328-5840

VA Facility: Baltimore 512

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____ _____

Participant's Signature Participant Please Print Your name

Date: _____

_____ _____

Investigator or Designee Obtaining Consent Signature

Investigator or Designee Obtaining Consent Please Print your name

Date: _____