Principal Investigator: Jayashri Aragam, MD

Title: Exercise Training in Heart Failure: structural and functional cardiac remodeling

Intervention Patient version 7/13/15

1. Purpose of study: This is a research study to better understand the impact of exercise training on changes in the heart as well as functional capacity. Participating in exercise for patients with heart failure has been shown to be beneficial at decreasing symptoms of heart failure however the mechanisms that create that change are still unclear. This study will look specifically at how exercise creates changes within the hearts filling ability, the heart's pumping strength as well as the hearts ability to rebuild.

This study is a complementary study to the approved protocol "Exercise Therapy to Reduce Heart Failure Symptoms; sorting mechanisms of benefit" by (Exercise Therapy) Site-PI Daniel Gottlieb, Prime-PI Daniel Forman which is focused primarily on peripheral mechanisms of exercise intolerance in older patients with HF with reduced ejection fraction (HFrEF), and the related benefits of exercise training on skeletal muscle gene expression. This study builds on what will be collected as part of that study and adds to it by looking at the mechanics of the heart.

You have been asked to be a part of this study because you have been told by your doctor that you have a diagnosis of heart failure and are currently enrolled in the approved exercise intervention protocol "Exercise Therapy". The length of your participation within this study will be approximately 17 weeks. Study visits will take place at the West Roxbury campus of the VA Boston Healthcare System (VABHS). Before starting the intervention for the Exercise Therapy study and after the completion of the Exercise Therapy study you will complete a visit to the West Roxbury campus where you will have an echocardiogram performed as part of this study.

Please note that several assessments that you will have completed as part of the Exercise Therapy protocol will be shared with the current study staff as part of the project to reduce your burden of having to repeat those tests. The assessments that will be shared are 1) cardiopulmonary exercise stress test, 2) 6minute walk test, 3) Breathing tests, 4) questionnaires looking at quality of life, and 5) the intervention group you have been assigned to as well as your adherence to the exercise intervention group (number of sessions you complete).

We will recruit approximately 60 subjects to this study that are taking part in Exercise Therapy study. We will also recruit 15 patients who will only undergo assessments pre and post 12-weeks of standard clinical care. This study is being sponsored by the Veterans Health Administration Rehabilitation research and Development.

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2. Description of the study, procedures to be used, and how long it will last:
Your participation in this study will involve a total of 2 (1 baseline and 1 post) assessment visits over a 17 week period of time the baseline and posts tests are exactly the same.

Baseline and post testing will involve one visit to the West Roxbury campus where you will have an echocardiogram done which will take about 90 minutes.

Echocardiogram: An echocardiogram uses sound waves to produce images of your heart. This commonly used test allows us to see how well your heart is pumping blood. During the test, you will be given a hospital gown to wear. You will be asked to remove your clothing from the waist up. A cardiac sonographer will place three electrodes (small, flat, sticky patches) on your chest. The electrodes are attached to an electrocardiograph monitor (ECG or EKG) that charts your heart's electrical activity. The sonographer will ask you to lie on your left side on an exam table. He or she will place a wand (called a "sound-wave transducer") on several areas of your chest. The wand will have a small amount of gel on the end, which will not harm your skin. The gel is used to help produce clearer pictures. You may be asked to change positions several times during the exam in order for the sonographer to take pictures of different areas of your heart. You may also be asked to hold your breath at times during the exam. You should feel no major discomfort during the test, although you may feel coolness from the gel on the transducer and a slight pressure of the transducer on your chest. The test will take about 60 minutes.

In the small chance the echocardiography technician is unable to get a clear image of the heart which is in less than 10% of people a contrast agent called Definity may be used that allows for better imaging of the heart. For the contrast to be administered an IV may be placed in your arm.

If the echocardiogram indicates that you have any unexpected medical concerns, your doctor will be immediately notified, and you may not be able to continue in the study.
Please note that all other testing and exercise interventions you will complete are part of the Exercise Therapy study and were outlined in the IFC's you signed as part of that study. If you have questions on that study please contact study staff at 857-364-5811 or the site-PI Dr. Gottlieb at 857-203-6375.

Please note that discomforts, inconveniences and risks are covered in the following sections.

3. Reasonably foreseeable discomforts or inconveniences of the study:

a. Difficulty completing the 1 assessment visits pre and post.
b. During the echocardiogram there is a small chance that the pressure of the transducer and heat generated by the ultrasound may create some discomfort. Precautions will be taken to minimize these possibilities.
c. In the instance that you require contrast during the echo an IV line will be used during the echo contrast administration and it will be maintained for the 30 minutes of recovery to insure access in the small chance of reaction. Any time an IV is placed there is a small chance of bruising and infection. Standard precautions will be followed in cleaning and sterilizing the area.

4. Reasonably foreseeable risks of study:
a. There is a rare chance (1:10,000) that patients may be allergic to the microscopic bubble contrast (lipid shell and gas), thus allergies will be confirmed via patient medical charts and verbally with the patient prior to the injection of the contrast agent. Allergic reactions are most likely to occur within 30 minutes of the injection of the contrast. These reactions can include breathing problems (shortness of breath), heart problems (changes in rhythm), chest pain, jaw tightness, feeling of faintness, seizures, and headaches. Special efforts will be taken to reduce risks by watching each subject for 30 minutes after the echo contrast agent additionally patients will be instructed to let staff know if they begin to experience any of these symptoms.

The treatment or procedure may involve risks that are currently unforeseeable.

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

If you are or became pregnant, the particular treatment or procedure might involve risks to the embryo or fetus, which are currently unforeseeable.

5. Expected benefits of study: There are no known direct benefits to you for being in this study.

6. Other treatment available: This is not a treatment study and therefore, will not alter any treatment you are receiving at the VA.

7. Use of research results and Confidentiality: Information collected for the purpose of this research study will be kept confidential as required by law. The results of this study may be published for scientific purposes, but your records or identity will not be revealed unless required by law.

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Information about you is protected in the following way. All information that is collected will be stripped of any information that would reveal your identity. Paper data will be stored in secure, locked file cabinets in a locked study office at the VABHS JP campus. Data will be identified only by the study participant number assigned to you. The data will also be coded and computerized. Electronic data will be stored in a password-protected file on a password-protected computer. Only the study staff will have access to the data. Finally, all staff involved in this study will be trained to understand the importance of maintaining the confidentiality of study participants.

Your research records will be kept indefinitely or until the law allows their destruction in accordance with the VA Record Control Schedule (www1.va.gov/VHAPUBLICATIONS/RCS10/rcs10-1.pdf). Records will be destroyed, when allowed, in the following manner.

- Paper records will be shredded
- Electronic records will be destroyed in a manner in which they cannot be retrieved.
- Digital images (scans,) will be destroyed in a manner in which they cannot be retrieved.

Your research records and the information within them will not be used for any purpose other than that described in this study as approved by the IRB.

8. New Findings: You will be told of any significant new findings that come to light during the course of this study and that may relate to your wanting to stay in the study.

9. Special circumstances: A veteran subject will not be required to pay for medical care and services received as a subject in an approved VA research study. Some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services (including, but not limited to, dental services, supplies, medicines, orthopedic and prosthetic appliances, and domiciliary or nursing home care) provided by the VA that are not part of this research study.

Subjects who enroll into this study have the potential to receive a total of $200 for completing the study in whole. For the baseline assessments, you will receive $100. For the post exercise assessment visit you will be paid $ 100. Additionally you might be eligible for a potential total of $25 for travel compensation based on how far away you live. You can choose to withdraw from the study at any time, but will only

receive payment for the visits you have completed. If you withdraw from the study before all visits are completed, the researchers still may use the data they have already collected.

You have the choice to receive payment for participation in the study by check or cash. If you receive payment by check, you consent to the release of personally identifying information about you including your name, address, and social security number to the VA so that we may provide compensation to you. You can expect to receive a check within 2-6 weeks. The government may garnish the compensation against outstanding debts a veteran has to the federal government. Alternatively, if you receive payment in cash, you consent to the release of personally identifying information about you including your name, address, and the last 4 of your social security number to the Fiscal Office of the VA Boston Healthcare System so that we may provide compensation to you. If payment is made to you by the VA (whether by check or cash voucher), an IRS Form 1099 will be generated regardless of the amount you are paid.

10. Rights of Recourse: In the event that you are injured as a result of your being in this research study, you will receive medical care, including emergency treatment. This care or treatment is governed by federal law and VA policy. You would also have the right to file any legal action, as in any instance of alleged negligence.

11. Study Monitoring: You consent to the access of your VA research and medical records that may identify you by persons approved for this purpose. Such access may be by the Human Studies Subcommittee and Research Oversight Committees of this hospital, the VA, federal agencies, national research oversight and accreditation organizations. You may expect the same confidentiality from these persons that is given to you by the Investigator and his/her research staff.

12. RESEARCH SUBJECT'S RIGHTS: I have read or have had read to me all of the above.
The study person named below has explained the study to me and answered all of my questions. I have been told of the discomforts and risks of the study. I have been told of other choices of treatment that I could have.

I understand that if I have any medical questions about this research study, I can call
Dr. Jayashri Aragam at ***617-323-7700 x6838*** during normal working hours.

Subject's Name: _____ , _____ **Date:** _____
Last First

Soc. Sec. No. _____

(If research requires documentation in the medical record in accordance with VHA handbook 1907.1 the entire SSN must be obtained. If research does not require documentation in the medical record the SSN should not be obtained)

VA Boston IRB # _____
Approval Period: _____

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I understand that if I have any general questions about this research study, I can call **Dr. Jayashri Aragam** at ***617-323-7700 x6838*** during normal working hours.

I understand that if I have any medical problems that might be related to this study that **during the day** I can call **Dr. Jayashri Aragam** at **617-323-7700 x6838**and **after hours I can call** the cardiology fellow on call by calling the Medical Center operator at (617)323-7700 and asking for the fellow on call for cardiology.

I understand that, if at any point during or after this study I have any questions about my rights as a research subject or I want to discuss problems, complaints, concerns, and questions about the research, obtain information, or offer input, I may contact the Research Compliance Officer at (857) 364-4182.

I understand that my participation in this study is voluntary, that I do not have to take part in this study and that, if I do take part, I may withdraw from the study at any time. I also understand that, if I refuse to take part or if I decide to withdraw, I will not suffer any penalty, loss of rights, or loss of VA or other benefits that I have a right to receive.

I voluntarily consent to be in this study. I will receive a signed copy of this consent form.

Subject's Signature	**Month Day Year**	**Name (print)**
Signature of Person Obtaining Consent	**Month Day Year**	**Name (print)**

Subject's Name: _____ , _____ **Date:** _____
Last First

Soc. Sec. No. _____

(If research requires documentation in the medical record in accordance with VHA handbook 1907.1 the entire SSN must be obtained. If research does not require documentation in the medical record the SSN should not be obtained)

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