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Splanchnic Nerve Block for Therapy of Chronic Heart Failure (Splanchnic III)

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DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Splanchnic Nerve Blockade as Treatment of Chronic Heart Failure

CONCISE SUMMARY

This study aims to test the effects of a nerve block on heart congestion and shortness of breath symptoms among patients with heart failure. You may be eligible for this study because you have heart failure and are scheduled to have a right heart catheterization performed.

You will undergo planned hemodynamic testing during the right heart catheterization procedure in the cath lab. The hemodynamic testing measures the pressures from your heart.

The research study will require the injection of a mixture of an anesthetic drug (ropivacaine) with botulinumtoxin (Botox) on one side of your heart. This mixture will be injected into the space around a nerve, called the splanchnic nerve, which controls the blood vessels in your intestines. This drug will be delivered using a long needle placed between your ribs, in the mid region of your back. The placement of the needle will be performed by an anesthesiologist experienced with the needle placement, with the assistance of x-ray guidance. The ropivacaine/Botox mixture is a nerve blocking medicine and will stop working on its own after about 6 months.

After the block, you will go home. You will be retested with a catheterization and/or a supine bike at 2, 4, 8 weeks. Study participation also includes a call at 48 hours, 1 week, 6 and 12 months following your splanchnic nerve block procedure.

The risks associated with the nerve block include local bleeding, pain and infection. The most serious complications include a pneumothorax (collapsed lung) and with use of Botox, potentially excessive weakness, difficulty swallowing and breathing, and aspiration pneumonia (pneumonia that develops from inhaling food or liquid into your lungs). There is also risk associated with the catheterization that is done at Week 4 for research purposes. Risks of a right heart catheterization (RHC) include pain and bruising. Rare risks of RHC include rhythym disturbances, clotting, heart attack and even death. The expected benefit is a short and long term drop in your heart pressures and improvement in shortness of breath and related symptoms.

If you are interested in learning more about this study, please continue reading below.

You are being asked to take part in this research study because you have chronic heart failure. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this

research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Dr. Dr. Marat Fudim will conduct the study and it is funded by a grant from the National Institutes of Health (NIH).Portions of Dr. Fudim's and his research team's salaries will be paid by this grant.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, ***Dr. Marat Fudim*** will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to test an investigational procedure using a pair of drugs in patients with chronic heart failure. Heart failure presents a big problem to the person affected by it and to the whole health care system. Patients with heart failure tend to be re-admitted to the hospital frequently with fluid overload, shortness of breath and leg swelling. The investigators want to test an intervention that targets an unexplored mechanism to reduce congestion and improve symptoms. We want to understand if a temporary block of the splanchnic nerves (nerves to the abdomen), which has been found to cause vasoconstriction resulting in an increase in blood volume and congestion in your heart. We believe that if we block the action of the splanchnic nerve, it will reduce congestion in your heart and allow you to breathe better.

A splanchnic nerve block is not usually done in patients with chronic heart failure. In this study, the splanchnic nerve block is considered investigational. The investigators will be using a mixture of ropivacaine and Botox to block your splanchnic nerve in an effort to reduce your heart failure symptoms. Both ropivacaine and Botox are traditionally used for other medical purposes. Ropivacaine is a local anesthetic (numbing medication) normally used to prevent the feeling of pain before, during, or after surgery, a medical procedure, or childbirth. Botox is a neurotoxin produced by bacterium, which will block nerves from producing a flaccid paralysis (weakness or paralysis and reduced muscle tone). Since Botox can reduce muscle tone it has been used commonly to reduce lines and wrinkles from a person's face. It has also been used medically to treat conditions such as neck spasms, overactive bladder and lazy eye. Both of these drugs interact with the the brain, spinal cord and major nerves by inhibiting nerve impulses and in this study, they will together inhibit the splanchnic nerve actions on the abdomen.

Recently, we conducted a study using ropivacaine, as an intervention to block the splanchnic nerve, on patients with acute and chronic heart failure. There were changes in heart pressures and symptomatic benefit to the patient. In all cases the nerve block was <24 hours in duration. We would like to explore whether patients with chronic heart failure would directly benefit from the intervention, if the effects of the block have a prolonged duration, up to 6 months.

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HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
The maximum amount of people that will take part in this study will be 10 at Duke University Medical Center.

WHAT IS INVOLVED IN THE STUDY?
If you agree to be in this study, you will be asked to sign and date this consent form.

Some of these procedures and tests are standard for patients with heart failure, and are not investigational. If you have already had these tests performed before, they may be used for the study if your study doctor determines they do not need to be repeated for study purposes.

Your participation in this study is strictly voluntary. If you do not sign this consent form, you will continue to receive care, but not as a part of this study. Declining to participate will not have any adverse effects on your care, incursion of any penalty, or withholding of benefits to which you are entitled. If you volunteer for the study but change your mind, you simply need to inform the study staff. We will provide you contact information to notify us of this decision. If you are unable to reach the study staff, you can inform your primary treatment team and they will facilitate notifying the study team. If you withdraw from the study, you will return to your usual care without repercussion.

Pre-Procedure Testing (Day 1):
You will have the following tests and procedures done before undergoing the right heart catheterization with cardiopulmonary testing:

- Physical exam and medical history
- Vital signs (blood pressure, heart rate, respiratory rate and oxygen level). This will include measuring your blood pressure while you are in a reclined position, in a seated position, in a standing position (orthostatic vitals). Document whether you have shortness of breath while lending forward (Bendopnea).
- Shortness of Breath Questionnaires: questions asked about your shortness of breath and how you are breathing while resting.
- EQ-5D-3L Quality of Life Questionnaire which will allow you to rate your health-related quality of life about your mobility, self-care, usual activities, pain and discomfort, anxiety and depression, on how severe of a symptom.
- Blood and urine tests:
- 6-Minute Walk Test: to measure your exercise capacity and endurance.
- Testing your lungs for fluid content using **ReDS** unit, which emits radiofrequency waves to measure fluid content.
- Measurement of lung impedance (**CardioSet** device), which will determine the intra-thoracic blood volume.

- **InBody** will measure the fluid content of your body. It uses either clip-on or stick-on electrodes on your fingers and/or ankles and is worn for approximately one hour. The technology is called impedance.
- An investigational device called the **VO2 Master Pro** will be used to measure oxygen consumption during rest and exercise. This device is a mask that will be worn for approximately one hour and will transmit data to a device.
- Oxygen saturation of the brain using non invasive patches on the temples.
- Arterial stiffness (**Sphygmocor** device) using a brachial cuff. A cuff will be applied to your arm, similar to a blood pressure cuff, and a hand held probe will be placed on your groin and arm. The cuff will inflate and will measure pulse wave changes in your blood vessels.
- **WHOOP strap 3.0** (an investigational device). The WHOOP strap 3.0 will measure heart rate and heart rate variability and will be worn for approximately one hour. This device is a wrist watch.
- A device called **PhysioFlow** will monitor cardiac output noninvasively using electrodes applied to your chest that will be worn for approximately one hour.
- Two investigational devices called **PortaLite** and **MOXY** will measure oxygen concentration during exercise. The device consists of a small and flexible probe. The probe is the only part of the device in contact with the patient's skin.
- **Blood volume analysis:** Administration of a small amount of plasma protein, albumin, containing a small amount of radioactive iodine (injected through the PIV). An initial blood sample will be drawn from one PIV and a small amount of radioactive iodine mixed with a plasma protein will be injected into the other PIV. After a short wait for the radioactive iodine to circulate throughout your body, five more blood samples will be drawn from the peripheral intravenous (PIV) line over about half an hour. In total, about 15 milliliters (3 tablespoons) will be collected.
- **MUGA scan** is a non-invasive imaging method to evaluate the function of your heart. This scan will produce images/pictures of your heart beating. We will also take pictures of your abdomen. This test will help our research team determine more information about the health of your cardiac ventricles and blood distribution.
- **Scintigraphy (radiation scan),** is a diagnostic test that detects emitted radioisotopes absorbed by the body. It is used with a computer to capture this radiation with external detectors to form two-dimensional images.

On the day of the procedure, you will arrive to the Duke University Cath Lab. After you have been checked in, the cath lab nurse will obtain a PIV for you before procedure lab draw. We will then perform the blood volume analysis procedure. The radioactive iodine labeled albumin protein (blood volume solution) will be administered through your PIV line. Blood samples will be withdrawn before administration of the blood volume solution and 12, 16 and 20 minutes after administration. The blood samples will be processed at the Duke Nuclear Laboratory or sent to Daxor for further processing. If

sent to Daxor, the blood samples will be given a deidentified label. Your age, gender and weight, which are needed to calculate your total blood volume, will be shared with Daxor.

Following the injection of the blood volume solution, you will then be injected with technetium99 (a contrast drug used during the MUGA scan). You will then be placed under a scintigraphy camera, which will pick up the counts of radiation over your chest and abdomen. We will record your resting counts over both your chest and abdomen. You will perform up to 5 minutes of low resistance leg exercise while laying on a stepper placed at bed end. Counts will be recorded over both your chest and abdomen during exercise.

A member of the study team will perform additional assessments, such as, vital signs, shortness of breath questionnaires before and after the 6-Minute Walk Test, lung fluid content, lung impedance and arterial stiffness. We will also use the non-invasive devices to measure your heart rate variability before during and after the hemodynamic testing.

Eligibility Procedure:
You will have the following additional tests to determine you eligibility:

- Right heart catheterization done as part of your usual medical care
- Echocardiogram, a picture of the heart using sound waves
- Cardiopulmonary exercise test, used to assess the performance of your heart and lungs at rest and during exercise

You will undergo the planned catheterization procedure that will be done as part of your routine medical care. The physicians will use your arm or your neck to access your veins. Patients who are having routine catheterization outside of this study may also have vein access through their leg. If vein access cannot be obtained through your arm or neck then you will be unable to continue in this study.

If the pressure measurements from your heart meet study inclusion criteria, you will proceed with study-related activities. You will first be asked to perform the Valsalva maneuver, in which you blow through a syringe for 30 seconds. This procedure is designed to put mild pressure on the abdomen and restrict venous blood return to your heart. This will cause a temporary drop in your heart pressures. This is used as a standard of care procedure to test the autonomic nerve tone.

We will ask you to exercise (pedal on a bike) in a supine, or flat on your back, position. This is called an invasive cardiopulmonary exercise. It will be done with a catheter in your heart. You will petal the bike, using your best effort, for about 2-5 minutes, before stopping to rest. The catheter remains in your heart to measure pressures while you exercise to provide us with detailed information about its exercise ability.

If your cardiologist has not ordered the exercise test as part of your routine investigation, we will add an exercise component to your study. If patients do get an exercise test ordered by the cardiologist it is typically only one exercise test at a time.

After the initial results from the right heart catheterizations with cardiopulmonary testing are complete, your eligibility will be evaluated based on the hemodynamic results (pressures in your heart) at rest and during stress. These results will indicate whether you are congested. It will also let the investigator know if your heart functions well. You will not be included in the study if it is determined that heart functions well or if the medical team is concerned about complications based on your results. The information and blood samples that were collected and not yet processed will be discarded/destroyed.

Splanchnic Block Procedures:
Once the necessary clinical information is obtained and satisfies all criteria, the investigator will begin the splanchnic nerve blockade procedure. Under x-ray guided technology, the investigator will require the injection of lidocaine with epinephrine at the location of the splanchnic nerve. This solution is injected first to ensure the proper location. Once the proper location has been confirmed, ropivacaine 10 cc (approximately 2.5 teaspoons) and Botox 75-125 units (approximately 0.25 teaspoons) solution will be placed into the space around the splanchnic nerve,. These drugs will be delivered using a long needle placed between your ribs in the mid-region of your back. The placement of the needle will be performed by an anesthesiologist experienced with the needle placement, with the assistance of x-ray guidance. The ropivacaine/Botox mix is a numbing medicine and will stop working on its own after 6 months.

The nerve block will be administered only on one side of your back. After the anesthetic is delivered, you will be kept in the catheterization lab so that the blood pressures in the various parts of your heart can be monitored for 60 minutes. The catheters used to monitor these pressures will be the same as those required for your medically necessary procedure, but they will be left in place longer.

Additional Tests and Monitoring:
We will carefully monitor your urine output for 3 hours before and 3 hours after your procedure. In addition, both before and after the investigational procedure, we will ask you to complete a 6-minute walk test (test of how far you can walk in 6 minutes) and a questionnaire about symptoms of shortness of breath. You will also receive blood tests. While blood is always drawn as part of your routine care, we will remove some extra blood from you (~15 ml- approximately 3 teaspoons) for the purposes of our study. Blood will be collected before your catheterization procedure and at the end of it. Blood collected at the end of the procedure is purely investigational and not part of routine care. Blood will be drawn from the catheter that is in your body and will not require extra blood draws.

The day of the procedure, we will ask you to delay the administration of your morning dose of diuretics (for example, furosemide, Lasix, hydrochlorothiazide, Bumex, bumetanide). This is so we can determine the impact of the procedure on your kidney function. You will return to your regularly scheduled diuretics 3 hours after the procedure.

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As part of the study, Dr. Fudim and his study team will send your blood for study-related laboratory tests to a laboratory vendor (Mayo Clinic and Inter Science Institute) which specialize in analyzing blood samples for hormone levels in your blood. Blood samples will only be labeled with a subject identifier (study ID). By signing this consent form, you authorize Dr. Fudim to send your blood to the Mayo Clinic and Inter Science Institute and their designated affiliates.

Week 2, 4, 8 Follow Up:
The study procedures of the first day will be repeated at 2 weeks following the splanchnic nerve block. At week 2 you will repeat a supine bike exercise. There will not be a heart catheterization procedure, so invasive pressures will not be measured at Week 2. If a Cardiomems is in place we will measure pressures non-invasively.

You will then return at week 4 for a repeat catheterization with exercise similar to the initial study day. This catheterization is performed for research purposes only.

At week 8 we will repeat the exercise without catheterization again

If you have a Cardiomems in place we will access your hemodynamic data and review your hemodynamic tracings for the 2 months before the nerve block (if available) and through the 12 months after.

You will also have the blood volume procedure repeated before the right heart catheterization procedure or review of your Cardiomems device, at the Week 4 visit. The study doctor will administer a small amount of plasma protein containing a small amount of radioactive iodine. An initial blood sample will be drawn and a small amount of radioactive iodine mixed with a plasma protein will be injected. After a short wait for the radioactive iodine to circulate throughout your body, three more blood samples will be drawn over about half an hour. In total, about 15 milliliters (3 teaspoons) will be collected. You will not have the blood volume procedure at the 1-2 month follow up visit.

After blood collection is complete, you will perform some low degree of exercise on a bike attached to the table in the radiology scanner. We will take pictures of your abdomen and chest before and after the exercise. There is no additional Xray exposure. We are simply measuring the radioactivity emitted from your body and trying to understand where and how much blood is located in your abdomen. This activity will be done at baseline and at 1 months.

Before, during and after obtaining the hemodynamic heart values, the study team will perform additional tests. We will measure you vital signs including orthostatic vitals and bendopnea. You will have additional blood samples drawn before and after the procedure. These blood samples will measure functional/diagnostic and hormone levels. A vest will be applied to your chest and will

measure non-invasively what the lung fluid content is in your lungs. We will also use a technology, CardioSet, InBody and PhysioFlow to measure lung and belly fluid, and heart rate variability.

A cuff will be applied to your arm, similar to a blood pressure cuff, and a hand-held probe will be placed on your groin and arm. The cuff will inflate and will measure pulse wave changes in your blood vessels. The technology used for this is tonography using the Sphygmocor device.

You will be allow to go home after all your tests and procedures have been completed.

At 48 Hours, 1 Week, 6 Months and 12 Months Phone Follow Up:

A member of the study team will contact you by telephone ask you about your current health state and any possible adverse events you may have experienced since your last visit.

HOW LONG WILL I BE IN THIS STUDY?
Your active participation in this study will last for only 2 months. We will contact you several times, up to 12 months, after your procedure, by phone. If you have been admitted to an outside hospital, we will ask for permission to review the outside hospital and Duke Hospital medical records over the 12 months after the study.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

Clinically relevant results of this research will be communicated with you. The potential new information gained will come from the cath lab procedure. The knowledge gained can be of value to your doctor as well.

WHAT ARE THE RISKS OF THE STUDY?
By participating in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

Splanchnic Nerve Blockade
Injection of **ropivacaine** in your back may cause some, all or none of the side effects listed below.

More likely side effects include:
- local pain at injection site for hours to days,
- slight bleeding or bruising at injection site
- orthostatic hypotension (light-headedness on standing) for up to several hours.
- Also, commonly reported is gastrointestinal dysmotility (mild abdominal cramping, diarrhea or constipation) for up to several hours.

Less Likely complications include:

- collapsed lung**,**
- damage to the nerve between ribs causing pain,
- prolonged dizziness with standing for months
- puncture of the aorta, which could cause bleeding into the space around the lungs or the abdomen.
- Further damage to the disc between vertebrae and paralysis of lower extremities due to spinal cord trauma or damage to one of the arteries supplying the spinal cord.

Patients undergoing this procedure have a small risk (<1%) risk of developing local anesthetic systemic toxicity. Symptoms include non-specific central nervous system effects (altered mental status, agitation, seizures) and cardiac arrest. While we expect that the nerve block will improve your symptoms such as shortness of breath, we cannot exclude that the nerve block will make you feel worse.

Injection of **Botox** in your back may cause some, all or none of the side effects listed below.

- Bruising and pain at the injection site
- Swelling and/or tenderness at the injection site
- Rash
- Flu-like symptoms
- Headache
- Nausea
- Redness
- Temporary muscle weakness

Serious reactions include the following:

- Allergic reaction (anaphylaxis)
- Prolonged dizziness
- Paralysis
- Fainting
- Arrhythmias

If the Botox spreads beyond the treatment site of administration, it can cause botulism-like signs and symptoms, which include the following:

- Breathing problems
- Severe muscle weakness
- Trouble swallowing
- Speech disorders
- Botox has a block box label issued by the FDA because of its potentially life-threatening side effect.

<u>Risks of Right Heart Catheterization</u>

The risk associated with this procedure, which requires the insertion of a tube (a catheter) into the arteries of your body. The following are possible risks of the catheterization procedure:

Uncommon < 10% (less than 1 in 10 chance), temporary and not severe unless otherwise stated

- Nausea or vomiting
- Complications associated with the use of any pain or anxiety medication during or after the procedure
- Complications at catheter insertion site in the groin (thigh)
    - Pain
    - Bruising
    - Hematoma (collection of blood outside a blood vessel)

Rare < 1% (less than 1 in 100 chance), temporary and not severe unless otherwise indicated

- Heart rhythm disturbances, including bradycardia (a slowed heart rate)
- Embolism - A blood clot or other substance is moved from the wall of your blood vessels, which travels downstream into small vessels, blocking blood flow and causing temporary or permanent damage to organs in the body. Clots are known to cause pulmonary embolism and may ultimately lead to incapacitation or death.
- Complications at catheter insertion site in the groin (thigh)
    - Pseudoaneurysm (injury to the artery wall resulting in a build-up of blood under the skin)
    - Arteriovenous fistula (an abnormal connection or passageway between an artery and a vein)
- Vascular complications requiring surgery

Very Rare <0.1% (less than 1 in 1000 chance)

- Complications at catheter insertion site in the groin (thigh)
    - Infection
    - Significant bleeding
- Cardiopulmonary arrest
- Heart Attack
- Death

Female Reproductive Risks

Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. This will be done as part of clinical routine and not part of the study, for your initial catheterization. The pregnancy test that will be taken at the 4 week time point, will be part of the study.

Risks of Radiation from Imaging Tests

If you take part in this research, you may have one or more medical imaging tests which use radiation. These tests help the study doctor assess your medical condition and assess the effects of treatments. The study doctor will decide which tests you will have. The number of tests you will have depends upon how long you stay in the research study. To give you an idea about how much radiation you will get each time a test is done, we will make a comparison with an every-day situation. Everyone receives a small amount of unavoidable radiation each year called the 'natural background'. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. The chart below shows the tests that may be used in the research, and the amount of time in the natural background that gives an amount of radiation that is about equal to the amount of radiation each time you have the test.

A possible health problem seen with radiation exposure is the development of cancer later in life. This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research is also shown in the chart. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all.

Test	'Natural Background Time' Equivalent for Each Time This Test is Done	Extra Cancer Risk Each Time This Test is Done
	0 Minutes	Negligible
Right Heart Catheterization	2 Months	Minimal
I-131 Albumin Blood Volume Study	2 Months	Minimal
MUGA Scan	2 Years	Very Low

RADIATION THERAPY: This research includes radiation therapy treatments. The test(s) in the table above will give you a small amount of additional radiation. However, the additional radiation from those tests is a very small fraction of the radiation from the therapy treatments, and are not expected to add any significant side effects or risk.

You may have a number of nuclear scans and fluoroscopy studies that are part of the regular care for your condition, and you would have them whether or not you participate in this

research. These studies will not add to the risk of the research. However, if you have concerns about the overall radiation exposure, you should discuss them with your physician.

Risks of Scintigraphy
There are not any risk associated with the use of the scintigraphy. It is just a device that measure the emitted radiation from the body.

Risks of Drawing Blood
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Drug and Food Interactions
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

Risks of Washout
There will be a brief period (<12 hours), where you will go without your regularly scheduled diuretic. During this washout period, your symptoms of shortness of breath may get worse. Please discuss the washout period with the study doctor.

Risk of Withholding Medication
We will need to take you off oxygen, if you are receiving it, during administration of the shortness of breath questionnaire. You will answer questions about shortness of breath several times over the course of study participation. We will monitor oxygen levels in your blood closely to see if your oxygen saturation drops below 90%, which is considered to be the lower limit of normal. In that case, you will be re-started on oxygen.

Risk of Echocardiography
There are not many anticipated risks associated with the echocardiographic evaluation of your heart during the study. However, some risks may include pressure on your chest from the probe that the technician uses to create pictures of your heart. Please tell the technician if you feel any pain or discomfort. We will use standard ultrasound technology.

You could, however, possibly have a skin reaction from the application of the ultrasound gel. An allergic reaction to the ultrasound gel is an uncommon problem.

6-Minute Walk Test:
There are some risks associated with taking the 6 minute walk test. During the 6 Minute Walk Test, you may experience difficulty breathing, shortness of breath, chest pains, dizziness, and or light headedness.

You may also fall during the 6-minute walk. Your doctor and the study team will take all precautions possible to avoid and minimize these risks. Should any of these occur, your doctor may treat you with medicine and/or provide you with oxygen.

Cardiopulmonary Exercise Test:
The cardiopulmonary exercise test is done as routine evaluation for heart failure. This might not been ordered as part of your test initially, but will be added on as part of the clinical study as it gives detailed information on the exercise ability and the limitations of exercise. This test will require you to exercise to your maximum, and is not associated with additional risks due to the exercise. The main risk during this procedure is related to the catheter being in the heart to record your pressures. These risks include bleeding and infection. The catheter will be inserted as part of routine care and should not present any additional risk inherent to the exercise test.

Risks of ReDS Vest and Cardioset Devices and InBody and PhysioFlow
There is minimal risk associated with the ReDS vest as some may find wearing and the fitting of the device uncomfortable. Risks are associated with a mild rash where the electrodes are attached to your skin. Other devices are patches only, they emit a low electrical current that you will not feel and wont endanger your body or an implanted electrical device should you have one.

Risks of Questionnaires
There are no physical risks associated with questionnaires for this study. There is, however, the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in this study at any time.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be direct medical benefit to you. You may experience rapid relief of your heart failure symptoms, including shortness of breath and fatigue; however, these improvements may only be temporary. Furthermore, we hope that in the future the information learned from this study will benefit other people with your condition.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
You do not have to be in this study to receive treatment for your heart failure. If you decide not to be in this study, your primary team will proceed with the standard of care treatment of your heart failure, which typically involves drug treatment.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

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Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to the Duke Translational Research Institute and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, the Duke University Health System Institutional Review Board, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

As part of this study, you will be asked to have certain tests, x-rays, and/or procedures performed. Some of these tests, x-rays and/or procedures would have been done as part of your regular care. The study doctor will use these test results both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to the research data office at Duke**.** Results of tests and studies done solely for this research study and not as part of your regular care will also included in your medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record may be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS?
You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your

insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with Dr. Fudim. At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

The Duke University Grant has agreed to pay for services and procedures that are done solely for research purposes such as the Week 4 right heart catheterization. Please talk with the Dr. Fudim or the study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible.

We will monitor your DUHS patient care charges to make sure that costs are directed appropriately. If you have any questions or concerns about appropriate billing, contact your study team coordinator so that he/she can help find a resolution.

WHAT ABOUT COMPENSATION?
You will be receive up to $300 for your expenses related to your participation (parking, gas, and time).

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Marat Fudim at 919-681-2549 during regular business hours and at 919-970-8372 after hours and on weekends and holidays

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Fudim in writing and let him know that you are withdrawing from the study. His mailing address is PO box 17969, 27715 Durham. No further action will be required on your part once you have withdrawn from the study.

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Splanchnic Nerve Blockade as Treatment of Chronic Heart Failure

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. Reasons why this might occur include an unsafe drop in blood pressure, worsening symptoms, new infection, or any condition whereby participation in the study poses a risk to your health. If this occurs, you will be notified and your study doctor will discuss other options with you.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Marat Fudim at 919-681-2549 during regular business hour,s and at 919-970-8372 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Splanchnic Nerve Blockade as Treatment of Chronic Heart Failure

STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Printed Name of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time
_____	_____	_____
Printed Name of Person Obtaining Consent	Date	Time