Principal Investigator: **William K. Cornwell III, MD**
COMIRB No: **17-1042**
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Study Title: **Randomized intervention Of Biventricular pacemakers on ventrIcular function among patients with mechaNical circulatory support devices: the "ROBIN" study.**

Healthy Control Consent Form

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?

Patients with severe heart failure have difficulty completing normal activities of daily living (walking, caring for oneself) because the heart is too weak to pump blood throughout the body. These patients often will need a left ventricular assist device (LVAD), aka "mechanical heart", which helps pump more blood to the body. However, patients still have difficulty completing activities of daily living after insertion of a mechanical heart. We are interested in determining why this is, but in order to understand how the body responds to exercise when someone has a mechanical heart, we also need to better understand how the heart functions during exercise in healthy individuals. In this study, if you choose to participate, you will be a "healthy control". Your information will help us to better understand how a healthy heart responds to exercise.

You are being asked to be in this research study because you are healthy and do not have heart failure. We are interested in defining "normal responses" to exercise to serve as a baseline, or control group.

Other people in this study

For this study, we will be enrolling:

15 patients with advanced heart failure who have a pre-existing CRT-D (a type of defibrillator) device, and have undergone LVAD implantation.

13 patients who are healthy, with no past medical history, to serve as a control group.

What happens if I join this study?

If you join the study, you will be asked to come to the Clinical and Translational

Research Center at the University of Colorado Anschutz Medical Campus. This is the location where all testing will occur
The following are procedures that you will undergo, if you choose to participate:

If you choose to participate, the research visit will include the following:

- A health history and physical examination by the study doctor to confirm that you are healthy and able to participate in the study
- Electrocardiogram: sticky electrodes will be placed on your skin (usually around your chest) to monitor your heart rate and rhythm
- Echocardiogram: we may perform several brief ultrasounds of your heart to help see how your heart is responding to exercise. This is a painless procedure that simply involves holding an ultrasound probe over your chest to look at your heart.
- Brain blood flow (Transcranial Doppler): we will place some small ultrasound probes on your head to measure brain blood flow with exercise.
- Blood pressure monitoring: we will monitor blood pressure by having you wear a small device on your finger. We will also check your blood pressure with an arterial catheter. We may also put on a blood pressure cuff on your arm.
- Arterial catheter: A small arterial line (a thin, soft plastic tube) may be inserted into the radial artery in your forearm, which allows us to continuously monitor your blood pressure. A small amount of lidocaine (numbing medication) will be placed on your skin before the procedure to numb up your skin and remove any discomfort. This procedure would be performed by a physician who is trained in this procedure.
- Cardiac output: We will measure how much blood the heart is pumping by analyzing the air you breathe through a facemask or mouthpiece.
- Ventilation: during exercise, you will breathe into a mouthpiece that monitors how much oxygen you consume and how much carbon dioxide you inhale. This device also measures how fast you breathe.
- Blood Draw: We will draw about 4 teaspoons of blood from either the catheter in your neck and/or in your arm.
- Exercise: you will exercise on a stationary bicycle or, if your study doctor recommends, you will exercise using an arm ergometer. You will perform very easy exercise (mild) for 5-10 minutes, then the exercise will get a little more difficult (moderate) for 5-10 minutes. After that, you will get a short break (about 5-10 minutes). Then, you will exercise for about 10 more minutes, at a more difficult level of exercise, to determine how hard you are able to exercise.
- Right heart catheterization – this procedure involves insertion of a long catheter (soft, plastic tube-like device) through a vein in your neck, that goes into your heart and lungs. This catheter tells us important information about how your heart and lungs are responding to exercise. We will give you numbing medication before the procedure to minimize discomfort. We use ultrasound machines and a fluoroscopy camera to ensure that the catheter is sitting in the appropriate position during the study. There are two types of catheters that will be inserted at different times. The **first catheter** tells us what the pressures are in your heart; the first catheter will only

be in for about 5 minutes. The **second catheter** tells us how your heart functions during activity, and will be in place for the duration of exercise.

- Lactic acid measurement: at each stage of exercise (rest, mild, moderate, peak exercise), we will check how much lactic acid your body is producing. Lactic acid is checked by a small prick of the finger to get a very small sample of blood.
- Six-minute walk test: this test monitors how far you can walk in six minutes at a normal pace
- 10-meter gait speed test: this test measures how long it takes you to walk 10 meters

What are the possible discomforts or risks?
The following are all the procedures, along with possible discomforts/risks:
Electrocardiogram: sticky electrodes will be applied to your skin to measure the heart rate and rhythm. This procedure is painless.

Echocardiogram/ultrasound: You may undergo several very brief echocardiograms of your heart, which will require you to lie/sit still while the ultrasound probe is passed over your chest or neck. These tests tell us how hard the heart is beating, or how much certain blood vessels are pumping blood to the body. This procedure is painless.

Brain blood flow (Transcranial Doppler): A gel-covered probe may be placed on your temple. Sound waves will be used to record how much blood is going to the brain during activity. This procedure is painless.

Blood pressure monitoring: Your blood pressure will also be monitored by applying a normal blood pressure cuff to your arm.

Blood Draw: We will draw about 4 teaspoons of blood from the catheter in your neck and/or arm. You may feel a tingling sensation while the blood is being drawn.

Arterial catheter: A small arterial line (a thin, soft plastic tube) may be inserted into the radial artery in your forearm, which allows us to continuously monitor your blood pressure. A small amount of lidocaine (numbing medication) will be placed on your skin before the procedure to numb up your skin and remove any discomfort. This procedure would be performed by a physician who is trained in this procedure. There is a very small risk of infection, but this risk will be minimized by this procedure being performed using sterile technique, and again, by a physician who is trained in this procedure.

Cardiac output: We will measure how much blood the heart is pumping by analyzing the air you breathe through a facemask or mouthpiece. This method is harmless and is frequently used in clinical and laboratory settings to check cardiac output. This facemask/mouthpiece will also allow us to measure how much oxygen your body is consuming and how much carbon dioxide your body is producing.

Ventilation: An elastic belt placed around your rib cage will be used to measure our breathing rate. Also, a small, soft nasal cannula (plastic nose piece) will be placed into your nose to measure how much carbon dioxide you are breathing out.

Exercise: you will be asked to perform mild and moderate levels of exercise on a stationary bicycle or treadmill, as well as a short period of maximal exercise. It is possible that you may experience fatigue or shortness of breath during exercise. These sensations are temporary and will resolve soon after discontinuing exercise. You will be permitted to stop exercising if at any time you feel that you are no longer able to exercise.

Right heart catheterization: It is very important for us to understand how the heart functions to provide blood to the body with exercise. Along these lines, we need to know how pressures and blood volume change in your heart with exercise. If you are a healthy volunteer, it is still important for us to do this procedure, because we need to be able to define normal responses (in healthy individuals).

This procedure will be performed in the cardiac cath lab on the 3rd floor of the hospital before any other procedures are performed on the day of testing. The procedure will be performed by a cardiologist who is experienced with this technique. You will be asked to lie flat on a table. Lidocaine (numbing medication) will be applied to your skin to minimize discomfort. We will locate a vein in your neck or upper arm that leads back to your heart. Using an ultrasound probe, we will insert a small needle into the vein. Thereafter, a catheter and wire will be inserted into the vein. Once the catheter is in position, we will advance a longer catheter into your heart, using fluoroscopy to guide the catheter into the correct position. This **first catheter** tells us what the pressures are in your heart. This catheter will be in place for about 5 minutes. Then,we will remove this catheter, and put in the **second catheter**, which tells us how your heart functions during exercise. This catheter will be in place for the remainder of the study. The catheter will be secured into position by application of tegaderm (a thick tape-like substance that holds catheters in place). At the end of the study, the catheter will be removed.

While this procedure is almost always well tolerated, there are some risks that you should be aware of:
*Pain/discomfort: if this occurs, it will be at the site of the skin where we insert the needles/catheters. This risk will be minimized by applying lidocaine to the skin before the procedure begins.

*Bleeding: if this occurs, it will be at the site of the skin where we insert the needles/catheters. This risk is minimized by using an ultrasound probe to ensure that the needles/catheters are going into the correct position.

*Pneumothorax: this is a very rare complication that involves partial collapse of the lung and results from incorrect positioning of the needle. This risk is minimized by using an ultrasound probe to ensure that the needles/catheters are going into the correct position. The risk of this complication is well less than 1% when using ultrasound-guidance.

*Arrhythmias: occasionally the heart catheter will bump up against the wall of the heart, causing you to have a "skipped beat" or making your heart go into an abnormal rhythm, which can cause chest discomfort. This risk will be minimized by performing the procedure with fluoroscopy, to ensure the catheter is going into the correct position. We will also be watching your heart rate, rhythm and blood pressure continuously. Finally, the procedure will only be performed by an experienced cardiologist who is familiar with this technique.

*Cardiac tamponade: this is a very rare complication that involves fluid buildup around your heart that impairs the ability of the heart to pump blood. This risk will be minimized by performing the procedure with fluoroscopy, to ensure the catheter is going into the correct position. We will also be watching your heart rate, rhythm and blood pressure continuously. Finally, the procedure will only be performed by an experienced cardiologist who is familiar with this technique. The risk of this complication is well less than 1% when the above-noted safety measures are implemented.

*Pulmonary artery rupture: this is a very rare complication that involves damage to the main artery in the lung. This risk will be minimized by performing the procedure with fluoroscopy, to ensure the catheter is going into the correct position. We will also be watching your heart rate, rhythm and blood pressure continuously. Finally, the procedure will only be performed by an experienced cardiologist who is familiar with this technique. The risk of this complication is well less than 1% when the above-noted safety measures are implemented.

*Radiation exposure: there is a very small amount of radiation exposure that will be experienced during insertion of the catheter. The typical amount of radiation exposure is <7mSv. For comparison, the average amount of radiation exposure per year that results from standing outside is around 3-4mSv.
If you are female and premenopausal, a urine pregnancy test will be performed prior to this study to ensure that you are not pregnant. If you are found to be pregnant, no further studies will be performed.

Lactic Acid measurement: at several times during the study, we may need to perform a "finger stick" to measure the amount of lactic acid your body is producing. Lactic acid is a very common byproduct of exercise and it is important for us to gauge how much lactic acid is produced during these studies.

Blood pressure monitoring: we will ask you to wear a small device on your finger that measures your blood pressure. The device will very gently squeeze your finger –

sometimes people report that this is slightly uncomfortable. If you experience any discomfort, we can change the finger that is being measured, or will stop the procedure.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

What are the possible benefits of the study?
You will be able to see your cardiovascular fitness level (how "fit" you are, using gold-standard exercise testing equipment), but will receive no other direct benefit from participating in this study.

This study is designed for the researcher to learn more about heart failure symptoms after the insertion of a LVAD. This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Who is paying for this study?
This research is being sponsored by the National Institutes of Health (NIH) and the National Heart, Lung and Blood institute (NHLBI) through a K23 Mentored Career Development Grant (Grant # 1K23HL132048-01), of which Dr. Cornwell is the primary investigator.

Will I be paid for being in the study? Yes.
You will be paid $100 for participating in this study.

Please note: all participants in the study will be reimbursed for any travel-related expenses (e.g. gasoline, bus-fare) as well as reimbursement for parking costs.

Will I have to pay for anything?
No. You will not need to pay for anything.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call Dr. William K. Cornwell immediately. His phone number is 303-724-2085.
We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Dr. William K. Cornwell. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Cornwell at 303-724-2085. You may also call the research coordinator of this study, Greg Coe, at 720-848-7333 You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Cornwell with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.
A description of this clinical trial will be available on 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.

You can also talk to a Subject Advocate at the Clinical Translation Research Center (CTRC). The phone number there is 720-848-6662.

A Certificate of Confidentiality has been obtained from the Federal Government for this study to help insure your privacy. This Certificate means that the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative or other proceedings. But, if you request disclosure, we can release the information.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA)

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.
The institutions involved in this study

- University of Colorado Hospital
- University of Colorado Denver

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Primary Investigator of this study:
William K. Cornwell III, MD
Mail Stop B130
Academic Office One
12631 E. 17th Ave, Rm 7107
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:.

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.

- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

Information about you that will be seen, collected, used and disclosed in this study:

- De-identified demographic Information (age, sex, ethnicity)
- Research Visit and Research Test records
- Blood samples and the data with the samples.

What happens to Data that are collected in this study?

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data collected from you during this study are important to this study and to future research. If you join this study:

- The data given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data collected from you.
- If data are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.
- Collected data may be discussed or presented at research meetings. Results of research may be printed in journals but your name will always be kept private.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____

Witness Signature:_____ Date_____

Witness Print Name:_____

Witness of Signature ☐

Witness of consent process ☐