Lifespan IRB 2
IRBNet ID: 1532110-23
Approved: January 14, 2022
Expiration:
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Research Consent and Authorization Form

Rhode Island Hospital, The Miriam Hospital, EP Bradley Hospital, Newport Hospital, and Gateway HealthCare

Name of Study Participant: _____

Principal Investigator: **Elena Salmoirago-Blotcher, MD, PhD**

Title of Research Study: Heterogeneity and predictors of stress reactivity in takotsubo syndrome - The Broken Heart Study II

Study Key Information

You are being asked to take part in a research study. A research study helps scientists and doctors learn new information to improve medical practice and patient care. This form contains information that will help you decide whether to take part in the research. Taking part in this study is completely voluntary. Even if you decide to take part in the study, you are free to leave at any time if you change your mind. The researcher will explain the study to you and answer any questions you may have. We encourage you to discuss this study with others (your family, friends or other doctors) before you agree to participate in the research. If you agree that you would like to participate in this research study, you will be asked to review and sign this consent. A copy will be given to you.

A. What is the purpose of the research?

In this research study we want to learn more about a condition called “takotsubo syndrome” (TS), also known as “broken heart syndrome” because it is often triggered by acute stress or emotional events.

B. What is experimental/new in this study

We designed this research to study possible triggers of this condition, to determine whether people with this condition are unusually responsive to stress, and to evaluate whether a greater response to stress puts patients at risk of having another TS episode or a heart attack.

C. What do I have to do in this research?

If you decide to join this research study, we will ask you to make 3 study visits. At the first visit, you will undergo a study interview and complete study questionnaires. Two weeks later, you will come back for a second visit, during which we will ask you to recall the stressful event that triggered the TS episode or, if you had no trigger, to recall an event that made you angry. Meanwhile, we will monitor your heartbeat and blood pressure, determine the levels of stress hormones in the blood, and perform an echocardiogram. We will also collect a small sample of hair from a hidden area of your head to measure levels of cortisol, a stress hormone.

You will come back 12 months later for a third and final visit during which we will perform another echocardiogram. It will take you about 12 months to complete this study. The most important potential risks to know about are:

-Rarely, participants may experience chest pain or an irregular heartbeat during the mental stress

-Some questionnaires may make you feel uncomfortable.

D. What are the benefits?

There are no benefits to you from taking part in this research. Others may benefit in the future from the information that is learned in this study.

E. Other things I should know about this research?

If we find out about new information from this research that may affect your health, safety or willingness to stay in this research, we will let you know as soon as possible. The tests done in the study, however, are performed for research purposes only and will not be available to you or your doctor.

F. If I don't want to take part in this research what are my other choices?

This is not a treatment study. You do not have to be in this research study to be treated for takotsubo syndrome. Your healthcare provider has discussed with you what your clinical treatment options are and which clinical treatment(s) might be right for you considering your medical history. These clinical treatment options include medications such as beta-blockers and ACE-inhibitors.

- **Please carefully read this form, additional detail about each item just described is found below.**
- **Please listen to the study team explain the study and this form to you.**
- **Please ask questions about anything that is not clear.**

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1. Nature and Purpose of the Study

The Miriam Hospital is recruiting adults who have been recently admitted with a condition called "takotsubo syndrome" (TS), also known as "Broken Heart Syndrome" because it is often triggered by acute stress or emotional events to take part in a research study. We designed this research to systematically study possible triggers of this condition, to determine whether people with this condition are unusually responsive to stress, and to evaluate whether a greater response to stress puts patients at risk of having another TS episode or a heart attack.
You are being asked to take part in this research project because you have been recently diagnosed with this condition. We expect to enroll 106 subjects into this study. The study is sponsored by the National Heart Lung and Blood Institute (NHLBI).

2. Explanation of Procedures:

This is what will happen if you agree to be in this study. It will take you about 12 months to complete this study. During this time, we will ask you to make 3 study visits. All study visits will be conducted at the Cardiac Research Office located on the 9th floor of the Ambulatory Patient Care building of Rhode Island Hospital, 593 Eddy Street, Providence, RI.

During the study, you will:

- Attend a first study visit between 2 and 4 weeks after discharge from the hospital. The first visit can be scheduled up to 12 weeks after discharge if needed. During this visit we will first obtain your informed consent to participate. We will then confirm that you are eligible to participate in the study. If you are not eligible, you will not be enrolled in the study. Next, you will undergo a detailed interview to determine possible factors that might have triggered the TS episode (such as stress, depression, and/or anxiety) and complete a series of questionnaires. The interview will be tape-recorded and reviewed by study staff for quality assurance purposes; recordings will be destroyed immediately once we examined the interview accuracy. We will also measure your blood pressure and your body weight and height. This visit will take approximately 1 and ½ hour to complete.
- Attend a second study visit 1-2 weeks later. We will ask you to recall an event that made you angry (mental stress). You will be instructed by study staff to mentally place yourself back in the situation, and then make a 5-minute speech about the incident, talking about the event and your thoughts and feelings during the event. Before, during, and after mental stress, we will monitor your heartbeat and blood pressure, we will draw blood (4 tablespoons in total) three times over a period of approximately one hour to determine the levels of stress hormones in your blood, perform an echocardiogram, and apply a Holter monitor. To collect blood, we will insert a small intravenous catheter in your arm; this will allow us to collect blood 3 times with only one needle stick. The catheter will be removed before you go home. An echocardiogram is a procedure routinely done to evaluate the function of the heart. It is a non-invasive procedure which takes real time pictures of the

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heart using ultrasounds, similar to that done to monitor a fetus' health during pregnancy. A Holter monitor is a non-invasive test which collects information on your heartbeat in real time, similar to an electrocardiogram. Electrodes are applied to your chest and the heartbeat is recorded for approximately 30 minutes. We will also collect a small sample of your hair (a 1-inch, pencil-width sample from a hidden area of your head) to measure levels of hair cortisol, a stress hormone.

- This visit will last 3 hours.
- Attend a third and final visit 1-year since enrollment in the study, during which you will undergo another echocardiogram. This visit will take about 1 and ½ hour to complete.
- The Echocardiogram data will be analyzed at the UMass Memorial Medical Center. The Blood Sample data will be analyzed at the Yale Medical School Lab.
- No personal information will be transferred to this lab. Study data have a unique study ID number which is NOT associated with any personal information.
- We will ask to collect information from your medical record about your medical history, medications, and heart procedures up to 1 year after you enroll in the study.
- You will be compensated a total of $ 200 for your participation in this research ($ 50 at visit 1, $ 75 at visit 2, $ 75 at visit 3). Compensation will be provided as cash on the day of the visit once you have completed all the procedures planned for that visit.

Your identifiable private information or identifiable biospecimens that have been collected as part of the research will not be used or shared with other researchers for future research studies.

If we find out about new information from this research that may affect your health, safety or willingness to stay in this research, we will let you know as soon as possible. The tests done in the study, however, are performed for research purposes only and will not be available to you or your doctor.

<u>Costs for participating in this study</u>

Some of the services you will receive are being performed only because you are participating in this research study. Examples of these 'research only' services include echocardiograms, blood tests, and all study visits. These services will be paid for by the study and will not be billed to you or your health insurance company.

<u>Contact Information:</u>

You can call us with any concerns or questions about the research. If you have questions about the study or concerns about side effects/problems, you can contact the Principal Investigator, Dr. Elena Salmoirago-Blotcher at **401-793-8325 during office hours (9 am - 5 pm).**

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3. Discomforts and Risks

- No serious side effects have been reported during the mental stress protocol even in high-risk and older patients. There are no risks associated with the collection of a small hair sample to measure hair cortisol levels.
- Rarely, participants experience an abnormal heartbeat or chest pain. These symptoms usually go away quickly once the mental stress is over. But if they persist, you may need monitoring or treatment in a hospital.
- Your blood pressure may increase or decrease during mental stress, which can cause you to feel dizzy or faint. This problem usually goes away once the mental stress is stopped; it usually doesn't require treatment.
- Should you experience these symptoms, the mental stress will be immediately stopped and you will be referred to your doctor.
- There is a minor risk of skin irritation (redness, itching) from the patches used to monitor your heart rate during the echocardiogram and the Holter. These are usually mild and do not require treatment.
- We may find a condition on your Echocardiogram which previously was not known. If we find out about new information that may affect your health, safety or willingness to stay in this research, we will let you know as soon as possible. The tests done in the study, however, are performed for research purposes only and will not be available to you or your doctor.
- In the unlikely event of a serious side effect, the Research Assistant will page Dr. Abbott (study cardiologist) or the cardiologist on call for advice. If symptoms appear to be severe or in the rare case of a cardiac arrest, a code blue will be called and you will be admitted to the Emergency Department of RIH for immediate treatment.
- Study staff will be trained in cardiopulmonary resuscitation and an automated external defibrillator will be available in the room in the unlikely occurrence of a cardiac event.
- Blood samples will be collected by a well-trained phlebotomist (this is a person with special expertise in drawing blood). Blood will be taken by inserting a needle into a vein in your arm and withdrawing a sample of blood (4 tablespoons), the same procedure you have probably experienced at a regular doctor visit. You may experience mild discomfort associated with blood sample collection, including pain during blood drawing and some bruising. In rare circumstances you may experience fainting or local infection. These risks may be minimized by having a well-trained phlebotomist do the blood draw.
- The study questionnaires or the study interview may make you uncomfortable. You may refuse to answer any of those questions and you make take a break at any time during the interview or when completing the questionnaires.
- Another risk of being in this study is a loss of your personal information. This is very unlikely to happen, and we will do everything to make sure that your information is protected.

4. Benefits

You will not receive any direct benefit from your participation in this study. We hope that the information we get from this study on takotsubo syndrome may help people with this condition in the future.

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5. Alternative Therapies

This is not a treatment study. You do not have to be in this research study to be treated for takotsubo syndrome. Your healthcare provider has discussed with you what your clinical treatment options are and which clinical treatment(s) might be right for you considering your medical history. These clinical treatment options include medications such as beta-blockers and ACE-inhibitors.

6. Refusal/Withdrawal

It is up to you whether you want to be in the study. You are not required to enroll or participate. If you decide to participate, you can always change your mind and quit at any time. If you decide not to be in the study, or if you quit later, you will still be able to get the health care services you normally get. If you join, but later the researcher or your doctor feels being in the study is no longer good for you, they may choose to take you out of the study before it is over. If new information becomes available that might change your mind about whether you want to stay in the study, the researcher will share this information with you as soon as possible.

Reasons the researchers would take you out of the study even if you wanted to stay in:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

Follow-up after Withdrawal of Consent

If you leave the study, it would still be useful for us to know how you do during the 12 months following your enrollment. We would appreciate if you would permit us to get follow-up information about your health from your doctor or your medical record.

_____ If I withdraw from the study, you have my permission to collect information about my health from my doctor or medical record

_____ I do not give my permission for you to continue to collect information about me if I stop participating in the study.

_____ _____

Signature of study volunteer Date

You have the right to change your mind at any time regarding follow-up after withdrawal. If you decide to quit the study please tell the head researcher Dr. Elena Salmoirago-Blotcher at 401-793-8325.

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7. Medical Treatment/Payment in Case of Injury

A research injury is any physical or mental injury or illness caused by being in the study. If you are injured by a medical treatment or procedure you would have received even if you were not in the study, that is not a research injury. To help avoid research injury and added medical expenses, it is very important to follow all study directions carefully. If you do experience a research injury, Lifespan or the study doctor can arrange medical treatment for you. Such treatment will be paid for as described below.

The Sponsor (NHLBI) does not offer compensation in case of injury. If you have insurance and have a research injury that is not covered by the study, it is possible that some or all the cost of treating you could be billed to your insurer. If your health insurance will not cover such costs, it is possible you would have to pay out of pocket. In some cases, Lifespan might be able to help you pay if you qualify for free care under Lifespan policy. However, Lifespan has no policy to cover payment for such things as lost wages, expenses other than medical care, or pain and suffering.

8. Rights and Complaints

Signing this form does not take away any of your lawful rights. If you have any complaints about this study or would like more facts about the rules for research studies, or the rights of people who take part in research studies, you may contact the Director of the Lifespan Office of Research Administration, at (401) 444-6246.

9. Confidentiality and Research Authorization for Use and Disclosure of Your Health Care Information.

Your research records will be treated as private health care records and will be protected according to Lifespan privacy practices and policies that are based on state and federal law. Federal law requires us to get your permission to use or disclose (release your information to someone outside of Lifespan) your health information for research purposes. If you sign this form, you agree to be in this research study and you permit the use and disclosure of your health information for the purpose of conducting the research, providing treatment, collecting payment and running the business of the hospital. This permission has no expiration date. You may withdraw from the study at any time. However, if you do not want the researchers to use or disclose any further information in this study, you must cancel permission in writing and may do so at any time. If you cancel your permission, you will stop taking part in the study and no new information will be collected about you. However, if you cancel your permission, it will not apply to actions already taken or information already collected about you by the hospital or the researchers before you canceled your permission.

Generally, the entire research record and any medical records held by the hospital may be used for research purposes. The following people or businesses/companies might use, release, or receive such information:

- The researcher and their support staff
- The study sponsor (The National Heart, Lung and Blood Institute)
- Doctors, nurses, laboratories and others who provide services to you or the sponsor in connection with this study
- The company or section of the U.S. government that is paying for the study and others they hire to oversee, administer, or conduct the research
- The United States Food and Drug Administration, the Department of Health and Human Services, the Office of Inspector General, the Office of Civil Rights, European Medicines Agency
- People who volunteer to be patient advocates or research volunteer protectors
- Members of the hospital's administrative staff responsible for reviewing, approving and administering clinical trials and other healthcare or research activities
- Accrediting Organizations

There are times when the law might require or permit Lifespan to release your health information without your permission. For example, Rhode Island law requires researchers and health care workers to report abuse or neglect of children to the Department of Children, Youth and Families (DCYF) and to report abuse or neglect of people age 60 and older to the Department of Elderly Affairs.

All researchers and health care providers are required to protect the privacy of your health care information. Other people and businesses/organizations that are not health care providers are not required by law to do that, so it is possible they might re-release your information.
You have the right to refuse to sign this form and not participate in the research. Your refusal would have no effect on your treatment, charges billed to you, or benefits at any Lifespan health care site. If you do not sign, you will not be able to enroll in the research study and will not receive treatment as a study participant.

If you decide to quit the study after signing this form (as described in Section 6: Refusal/Withdrawal), no new information will be collected about you unless you gave us permission to do so. However, the hospital or the researchers may continue to use information that was collected before you quit the study to complete analysis and reports of this research. You will not be allowed to see or copy the information described in this form if the research is open. You may see and copy the information when the study is completed.

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

Contact for Future Studies:

Your participation in **any research** is completely voluntary and you should feel no pressure to participate if you are contacted about another research study.
Please check and initial one of the options below regarding future contact about other research done by us or other researchers we are working with (collaborators).

_____ ☐ Yes, I may be contacted about participating in other research projects studying Takotsubo syndrome or related conditions. I give permission for my contact information (name and mailing address and/or phone number) to be given to other researchers working with the study investigator.

_____ ☐ No, I do not want to be contacted about other research projects. **Do not** give my contact information to the staff of any other research studies

SIGNATURE

I have read this informed consent and authorization form. ALL OF MY QUESTIONS HAVE BEEN ANSWERED, AND I WANT TO TAKE PART IN THIS RESEARCH STUDY.

By signing below, I give my permission to participate in this research study and for the described uses and releases of information. *I also confirm that I have been now or previously given a copy of the Lifespan Privacy Notice.*

This informed consent document is approved for use with a valid IRB stamp at the top of each page. The document expires for use on the date listed within the IRB stamp. DO NOT sign this document after this expiration date.

If the expiration date is blank, this document does not expire.

The Researcher is required to provide a copy of this consent to you.

Signature of Adult Study Participant	Date (MM/DD/YEAR)	Time when signed

Signature of researcher or designate	Date(MM/DD/YEAR)	Time when signed

☐ **A copy of this complete (note total number of pages in footer) signed consent form has been given to the participant.**