19. Appendix 1. Sample Informed Consent Form

Consent To Participate As A Research Subject In Medical Research

Evaluation Study of Congestive heart failure and Pulmonary-artery catheterization Effectiveness (ESCAPE)

You are being admitted to the hospital for treatment of worsening heart failure and the need to adjust your medicines. You are being asked to take part in a research study. Your primary cardiologist has given approval for you to be enrolled in this study, but you must read the following and ask as many questions as you need to, so that you understand what participation would involve, before you agree to be a volunteer.

Background and Purpose of the Study

Patients with worsening heart failure are treated with several medicines, which aim to help relieve the symptoms of heart failure and improve heart pressures and blood flow through the heart. Doctors and medical professionals have two ways to adjust medicines when patients come to the hospital with symptoms of worsening heart failure. One is to use your symptoms and physical signs. The other, in addition to your symptoms and physical signs, uses an instrument called a pulmonary-artery catheter (PAC) to measure the pressures and blood flow of the heart. A PAC is a thin, flexible tube that is inserted into a vein in the neck, and then pushed forward through this vein into the place where blood vessels enter the heart. The PAC stays in place for 2 to 5 days. When patients are treated for heart failure in the hospital, the PAC is often used to measure the pressures and blood flow in the heart.

The purpose of this study is to compare these two ways to adjust medicines that improve the pressures and blood flow in the hearts of people with worsening heart failure. It will be important to know, in the long term, which method is better for managing patients suffering from heart failure.

This study will enroll 500 patients at 22 heart-failure centers in the United States. The National Heart, Lung, and Blood Institute, part of the National Institutes of Health (NIH), is sponsoring the study.

Procedures

If you agree to participate in this study:

You will be randomly assigned (as if by coin-toss) to one of the two treatment groups. If you are assigned to the group that uses a PAC, you will have the PAC placed, and it will remain in place for 2 to 5 days. The machine used to place the PAC uses fluoroscopy (a type of X-ray that helps the physician guide the PAC to the exact spot where it needs to be). The study physician also will ask you about your symptoms and perform a physical exam. If you are not assigned to the PAC group, no PAC will be placed, but you still will be asked about your symptoms and receive the physical exam. There is a 50/50 chance you will receive a PAC. Some study procedures will be performed in the hospital (at admission and as you are about to leave the hospital) and some will occur during visits to the clinic, which will occur roughly at 7 days (if you have been discharged), 14 days, 1 month, 2 months, 3 months, and 6 months.

Blood samples will be taken to measure levels of two hormones, atrial natriuretic peptide and brain natriuretic peptide, produced by your heart and brain, respectively. This will be done four times in the study: when you enroll, when you are discharged from the hospital, and at 3 months and 6 months after you enroll. A **total** of about 10 tablespoons of blood will be taken over the 6 months.

If you enroll, you will be asked questions about living with your heart-failure symptoms and your desire for better health. These questions take about 10 minutes to answer the first time they are asked. These questionnaires will then be repeated at 1 month, 3 months, and 6 months.

You also will be asked to complete a heart-failure questionnaire that takes about 15 minutes. This questionnaire will be given seven times during the study: at enrollment, at discharge, and at 2 weeks,

1 month, 3 months, and 6 months after enrollment.

You will have an echocardiogram (a test that uses sound waves to measure heart function) three times during the study: at enrollment, at discharge, and at 3 months.

You will be asked to perform an exercise test on a bicycle (or a treadmill) with a mouthpiece to measure oxygen use. You will be encouraged to exercise until you are tired, but you can stop at any time. You will do this test at enrollment, at discharge, and at 3 months. The exercise test is the same test that is performed as part of the standard care and evaluation of patients with heart failure.

You will be asked to do a 6-minute walk at enrollment, at discharge, at 3 months, and at 6 months. We will ask you to walk in a specified area for 6 minutes. You may stop to rest if needed.

Risks

Risks associated with participating in the study include the possibility of skin bruising from the taking of blood samples as well as having momentary discomfort. There is a slight risk of infection (1/1000). The risks associated with the insertion of a PAC include infection (1/1000), bleeding (1/1000), a blood clot (1/1000), collapsed lung (less than 1/1000), or heart-rhythm problems (less than 1/1000).

To place the PAC in the correct position, fluoroscopy, X-ray, or both are required. The amount of radiation you will receive for this study has been carefully calculated. The National Committee on Radiation Protection has set "occupational radiation exposure limits." The limits are defined as the "dose of radiation that in light of the present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his/her lifetime." The risks of this amount of occupational exposure for any scientist, radiologist, or technologist who is exposed to radiation nearly everyday, are considered very small, and at these levels, which have been in effect since 1957, there is no indication of harmful effects to the worker or any offspring. We estimate that the maximum exposure that you will get from the combination of these studies is about 1% of the amount allowed by current exposure limits per year. This radiation dose is what you would receive from this study only; it does not include any exposure you may have received or will receive from other tests.

Benefits

You may not receive any benefit from participating in this study, but other patients with heart failure may benefit from the overall findings of the study in the future. Many heart-failure patients participating in studies such as this one are thought to benefit from participation, regardless of the treatment to which they are assigned. This may be due to the extra care they receive during participation.

Alternative Therapy

If choose not to participate in this study, you will continue to receive the standard treatment for heart failure. This may or may not include the use of a PAC, as decided by your doctors.

Significant Findings

As the study continues, we will let you know about any major developments that could affect your willingness to participate. We will provide you with the relevant information so that you can consider whether to continue in the study.

Confidentiality

The confidentiality of study records that identify you will be maintained within _____ (name of the hospital). Your identity will masked if material from your records is used for publication or education. However, authorized representatives from the U.S. Food and Drug Administration (FDA) and the National Heart, Lung, and Blood Institute may inspect the records.

For Women of Childbearing Potential

Some procedures in this study could be harmful to a developing fetus. If you are a woman of childbearing potential, we will perform a pregnancy test to be certain that you are not pregnant. The pregnancy test will involve taking about 1 teaspoon of blood. We also might request a urine sample

from you. If you are sexually active, you must certify that you are using an acceptable form of birth control, such as hormonal contraceptives (birth-control pills), an intrauterine device (IUD), or barriers with spermicide throughout the study.

By signing this consent form, you are agreeing to use an acceptable form of birth control during the study. If you have any questions about this subject, do not hesitate to ask your doctor or the person who is requesting that you participate in the study. During the study, if you think that you might have become pregnant, please notify the study doctor immediately.

You also cannot participate in this study if you are breastfeeding. If you are found to be pregnant or nursing, you will be withdrawn from the study without your consent.

Costs

Both study methods of adjusting medicines are considered standard care for patients with heart failure. Whichever method you receive, your care will be billed as part of standard care to your insurance. All medicines given are those typically used to treat heart failure. The echocardiograms, exercise test, and blood tests performed as part of the study will be provided free.

Voluntary Statement of Understanding And Agreement

Participation in this research is voluntary. You can withdraw your consent and stop participating in this study any time, and this will not affect your regular treatment or medical care in any way. If you decide to end your participation at any time, please notify Dr. _____ at _____ or Dr. _____ at _____, who will explain how to withdraw from the study.

I have read the above and have been given an opportunity to talk about participating in this study and to ask questions. I know that I can contact _____ or _____ to answer any questions I have during the study, and the Office of Risk Management for _____ at _____ if I have any questions about my rights as a research subject. I agree to participate with the understanding that I can withdraw at any time without affecting my regular care. I have been given a copy of this form for my records.

_____	_____
Patient	Date
_____	_____
Parent or Guardian (if patient is less than 18 years old)	Date
_____	_____
Person Obtaining Consent	Date