INFORMED CONSENT FORM

Official title: Reduction of Cardiac Steatosis and Improvement of Diastolic Function by Modulating Metabolic Health in Obese Individuals

NCT number: NCT03448185

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The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research: **Reduction of Cardiac Steatosis and Improvement of Diastolic Function by Modulating Metabolic Health in Obese Individuals**

Funding Agency/Sponsor: American Heart Association
Project Study Title: Novel HFpEF Prevention Strategies In High Risk Individuals: High Intensity Exercise Training Plus Omega-3 Fatty Acids

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Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
The purpose of this study is to determine whether exercise training combined with fish oil, a source of omega-3 fatty acids, can reverse or prevent build up fat within the heart, a condition

known as cardiac steatosis. Prior studies by our research group have shown that excessive accumulation of fat within the muscle of the heart can affect the heart's function. Eventually this can lead to ineffective relaxation and contraction of the heart which makes it difficult for the heart to pump blood efficiently during activities. Obese individuals who have a high amount of visceral fat, or fat around the body's internal organs, are at particularly high risk for developing this type of "fatty heart" syndrome. There are no proven medications to treat or prevent this; however our research has shown individuals who are very fit have less accumulation of fat in their hearts than those who have led a sedentary lifestyle. Other research groups have also shown that omega-3 fatty acids in the form of fish oil can reduce the amount of fat build up around organs. Based on these findings, we would like to know whether exercise training combined with fish oil over 1 year can reverse or prevent further accumulation of fat within the heart muscle in previously sedentary obese individuals.

Why is this considered research?
This is a research study because we would like to learn if exercise in combination with fish oil which is high omega-3 fatty acids, can prevent progression or reverse fat buildup within the heart. To accomplish this we will guide middle-aged obese individuals who also have high amounts of visceral fat through a structured exercise program and compare their hearts and arteries before and after the exercise training program.

The following definitions may help you understand this study:

- Double-blind means neither you nor the researchers will know if you are receiving fish oil or placebo (olive oil).
- Placebo-controlled means that some participants will get a placebo. A placebo looks like the investigational drug but it includes no active ingredients (in this case, a gel capsule filled with olive oil).
- Randomization means you will be placed by chance (like drawing straws) in one of the study groups.
- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being invited to participate in this research study because you are obese (a body mass index greater than 30 kg/m^2) and have high amounts of visceral fat, or fat around the body's internal organs.

Do I have to take part in this research study?"
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
We plan to screen 120 individuals in order to enroll 80 (44 exercise and 36 yoga) participants in this research at UT Southwestern and Texas Health Presbyterian Hospital Dallas

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. All of the procedures are being done solely for the purpose of this study and are not part of standard of care for your condition.

Screening Procedures
To help decide if you qualify to be in this study, the researchers may ask you questions about your health, including medications you take and any surgical procedures you have had, especially since the last time you were in the laboratory. This visit should take approximately 1 to 2 hours.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- Physical exam and medical history;
- Vital signs (including blood pressure, heart rate and body weight)
- Blood tests (1 -2 teaspoons);
- Demographic information (age, sex, ethnic origin)
- Electrocardiogram (EKG), a tracing of the electrical activity of the heart;
- Echocardiogram, a sonogram of your heart and
- Paperwork or files from your cardiologist or doctor that investigators request regarding your heart health

Group Assignment
If the researchers believe you can take part in this study, you will be assigned randomly (like drawing straws) to receive either fish oil with yoga training for one year, fish oil with high intensity exercise training for one year, placebo with yoga training for one year or placebo with high intensity exercise training for one year. You have a 1 in 4 chance of receiving any of the combinations listed above (for example, fish oil with high intensity exercise training).

The group you will be in is decided by a computer program operated by Ms. Beverly Huet, a biostatistician at UT Southwestern. Neither you nor the researchers will be allowed to choose which group you are assigned to.

If you are pregnant or planning on becoming pregnant, you will not be able to enroll in the study. We will check a urine pregnancy test during initial testing (described below).

Study Medication/Intervention
If you decide to participate in this study you will be randomized into one of the four categories:

- 2 gel capsules of fish oil (2 grams) once a day and yoga training for one year or
- 2 gel capsules of placebo once a day and yoga training for one year or
- 2 gel capsules of fish oil (2 grams) once a day and high intensity exercise training for one year or
- 2 gel capsules of placebo once a day and high intensity exercise training for one year

The aerobic-resistance exercise training program consists of an individually tailored training program which uses a variety of aerobic and resistance exercises (running/walking, biking, swimming, weight lifting). The program will begin gradually, with training sessions initially occurring 3 times/week. Over the subsequent few months, the duration, frequency, and intensity of the training sessions will be increased to 5 times/week. Regular interaction with our team ensures that the exercise training proceeds according to plan.

Yoga training consists of a series of exercises designed to improve strength, balance and coordination. This training will be supervised by certified instructors at the Finley Ewing Cardiovascular Center, which is located next door to the Institute for Exercise and Environmental Medicine on Texas Health Presbyterian Hospital's Campus or another, more convenient location that is approved by the research team. Participating in yoga training will allow subjects to have regular interaction with our team of researchers and has significant health benefits, though it may not improve your fitness.

Procedures and Evaluations during the Research

After the initial screening, you will be required to come for 3 more visits. At this time, we will make measurements of your heart and exercise capacity; we call this "Baseline Testing". At 6 months into the intervention, we will some make these same measurements again; we call this "Mid Progress Testing". At the end of your one year of involvement in the study, these tests will be repeated; we call this "Follow-up Testing". Therefore, after the screening, our study involves:

- "Baseline Testing", which is detailed below;
- One year of aerobic-resistance exercise training or yoga training, which was detailed above, with "Mid Progress Testing" at 6 months, which is detailed below; and
- "Follow-up Testing", which is similar to "Baseline Testing" and is detailed below.

An overview of the "Baseline Testing" and "Follow-up Testing" is as follows:

Study Day 1	Familiarization with the procedures, 24-h blood pressure and activity monitor hook up, exercise test with sonogram of your heart. No blood is drawn. Estimated required time: 3-4 hours
Study Day 2	24-hour blood pressure monitoring return, arterial compliance testing, comprehensive cardiac sonogram, exercise test, and body composition measurement. Three finger stick blood samples (<1 teaspoon) are used to measure blood lactate, a byproduct molecule produced during exercise. We will collect 4 tablespoons of blood drawn through an IV during this testing. Urine will also be collected for a urine pregnancy test. Estimated required time: 3.5-4.5 hours
Study Day 3	Magnetic resonance imaging (MRI scanning). No blood is drawn. Estimated required time: 1.5-2.5 hours

An overview of "Mid Progress Testing" is similar to the "baseline" testing and is as follows:

Study Day 1	Arterial compliance testing, comprehensive cardiac sonogram and exercise test. Three finger stick blood samples (<1 cc) are assessed for lactate content as well as 4 tablespoons of blood drawn through an IV will be taken during this testing. Estimated required time: 4-5 hours

As mentioned above in the "Baseline Testing", on day 1 and 2 you will be asked to undergo an exercise test each day, which will examine your fitness and exercise capacity. If you are assigned and agree to participate in the aerobic-resistance exercise training portion of this study, this test will also be used to guide your training program, and serve as a baseline test. The exercise test will be repeated at 6 months to evaluate your progress during the training.

At the end of your one year involvement with the study, these tests will be repeated (referred to as “Follow-up Testing”) to examine how the aerobic exercise training or yoga training has affected your heart's function and your exercise capacity. “Follow-up Testing” includes all of the tests above with the exception of the Study Day 1 Exercise Test. A more detailed description of all the tests and procedures we will perform is included below.

Electrocardiogram or EKG (Screening Day; Study Day 1, 2).
Sticky electrodes will be applied to your skin to measure the heart's electrical signals.

Echocardiogram (Screening Day; Study Day 1, 2).
An ultrasound camera will take a picture of your heart; similar to the "sonar" used by fishermen to locate fish underwater. We will also use the Doppler principle of ultrasound (the reason why a fire engine sounds higher as it comes toward you and lower as it goes away) to measure the velocity of blood flow.

Blood Pressure (Screening Day; Study Day 1, 2).
Your blood pressure will be monitored using a cuff placed on your upper arm that is inflated and deflated periodically.

Arterial Compliance Test (Study Day 2).
To determine the flexibility of your arteries we will obtain blood pressure measurements through several different non-invasive techniques and take pictures of your arteries using an ultrasound machine. The arteries that we will examine include the arteries in your wrist, elbow, neck, groin, and stomach. During this process you will be lying on a bed relaxing. There is no risk associated with this procedure.

Body Composition Measurements (Study Day 2).
In order to determine your body's muscle, fat, and water composition we will obtain detailed measurements of height, weight, skinfold thickness, etc., using measuring tape and calipers. Calipers are small devices that measure the thickness of skin folds. There is no risk with this procedure, though some individuals experience some pinching from the calipers. We will also measure your body volume underwater to provide another measurement. There is no risk associated with this procedure, though you will get wet from being under water, and some people experience mild discomfort when asked to hold their breath underwater. Alternatively, we may also measure your body composition using a special X-ray scan called DEXA which is commonly used to measure bone density and screen for osteoporosis. A DEXA scan can also provide information on your body’s muscle, fat and water composition and involves lying flat on a table for 5 – 10 minutes while the scanner makes its measurements. Prior to a DEXA, we will perform a routine pregnancy test to ensure that you are not pregnant before undergoing the scan.

Exercise Tests (Study Day 1, 2).
Cycling or walking/running tests will be performed on a treadmill or on a bike. During the exercise test we will continuously record an EKG (electrocardiogram, see above) and also perform another ultrasound of your heart. This test is to see how your heart function responds to exercise. A second test will be performed to assess your exercise capacity. A qualified physician will directly supervise the test in a lab equipped to handle any problem. Exercise rarely causes any problems in normal subjects but in patients with known or hidden heart disease, the test may cause chest pain, dizziness, or bouts of irregular heart rhythm. Your pulse and blood pressure will be recorded during the test.

Activity Monitoring (Period between Study Days 1 and 2).
We will either ask you to fill out a questionnaire about your daily activities or have you carry a small device around your wrist and waist for a few days. This device uses a device that measures the movement of your body, like a fancy pedometer or step counter, to monitor your body motion and will help us to better estimate how active you are.

Finger Blood Pressure (Study Day 2).
In order to continuously monitor your blood pressure during the experiment, a small blood pressure cuff will be placed on one of your fingers. Occasionally, some people experience some mild discomfort in the finger after a prolonged period of inflation. If this is the case with you, we can easily deflate the cuff to give the finger a rest.

24-hour Blood Pressure (Period between Study Day 1, 2).
Your blood pressure will be monitored using a cuff placed on your upper arm that is inflated and deflated periodically and linked to a little 'tape recorder', which you will be asked to carry via a belt for 24 hours at home during a day with normal activities.

Blood Samples (Screening Day Base Line Study Day 2, Mid Progress, and Follow-up Testing).
To measure the concentration of "heart hormones" we will obtain approximately 4 tablespoons of blood from a venipuncture blood draw. The total amount of blood drawn during the entire course of this study is about 180 ml, or 12 tablespoons.

Carbon Monoxide Blood Volume and Hemoglobin Mass (Study Day 2).
In order to measure the total amount of hemoglobin (protein in the blood that carries oxygen) and myoglobin (protein in the muscle that transports oxygen into the muscle cell) in your body, we will use a procedure called Carbon Monoxide (CO) Rebreathing. During this procedure, a blood sample is taken before and after a small amount of CO has been absorbed into the bloodstream and the concentration of CO in the blood is measured. We will do this test at the end of study day 3, so no extra IVs or needle sticks will be required. The test involves sitting comfortably in a semi-reclining position for about 30 minutes and breathing through a mouthpiece for about 5 minutes. The test begins by breathing through your nose. You are then asked to hold your breath out and a nose clip is placed on your nose and valves are then used to switch the mouthpiece over to a self-contained "rebreathing" circuit initially containing 100% oxygen and a small portion of CO. The rebreathing circuit is a closed system from which you will breathe in and out during the test. It contains a carbon-dioxide (the waste product in the air you breathe out) absorber so that the air that you breathe in will always be 100% oxygen. A small amount (about 1/4 cup) of CO is introduced into the re-breathing circuit and re-breathed for 2 minutes after the nose clip is placed on your nose. A venous blood samples are taken from your IV 4 and 6 minutes after you stop breathing on the mouthpiece. Some subjects may experience slight discomfort due to breathing through a mouthpiece for the required duration of the test. The total amount of CO introduced into the rebreathing circuit is harmless and is similar to passive sitting for 3-4 hours in a 'smoky' environment such as a nightclub. Your body will completely washout the CO from your blood in about 8-9 hours.

Cardiac Output (Study Day 1, 2).
We will measure the heart's pumping capacity by analyzing the air you breathe through a mouthpiece connected to a bag full of air and small concentrations of harmless gases, including helium and acetylene.

MRI Scanning (Study Day 3).
A picture of your heart will be taken by a MRI scanner, which applies a magnetic field and then processes the response of your body into images. This magnetic field is not harmful and you will feel nothing during the exam. There is no radiation associated with magnetic resonance imaging, and no known risk to the procedure. You will be positioned inside a large, doughnut-shaped magnet for the cardiac imaging, have ECG leads attached, and be given headphones. Initial MRI cardiac scanning will be done to determine positioning. The exam will require that you lie rather motionless for about 90 minutes on a table. Some people get somewhat claustrophobic (anxious because of the small space within the magnet) during this procedure, but we will be right in the next room and talking to you by intercom the whole time. If this feeling of anxiety becomes too severe, we will simply discontinue the test. In addition to the routine imaging of the size and structure of your heart, this study will also use magnetic resonance imaging and spectroscopy (MRI&S) to measure fat in your liver, skeletal muscle and heart. 1-3 teaspoons of blood will be drawn by a nurse before the imaging to measure fats in your blood.

If you should have metal in your body (i.e., prosthesis, pacemaker, pin, or any other metal containing material) you may not be allowed to have this scan done because the magnetic field may cause movement of the metal parts in your body. Therefore, it is very important that you tell us about any metal in your body.

Training: Training will begin with you working out 3 times/week for thirty minutes each session. If you are randomized to the exercise group, you will be asked to continue training 3 times/week as the program progresses however the intensity of each session will be harder. The goal is to have you perform at least 2 sessions of high intensity of training per week. We will start you off fairly lightly (60-75% max heart rate) and will gradually increase the intensity (85-95% max heart rate during some sessions) over the first 6 months. Training will consist of a variety of different exercises and will take place in a variety of places. Once you achieve your target training level after 6 months, the training will remain constant for the rest of the study, which will last a total of 12 months. In order to re-evaluate your fitness level, exercise testing will take place at six months. Since the success of this study depends greatly on your conformity to your training program it is very important that you follow the training program dependably.

Journal: You will be asked to complete a training journal during the course of the study. The training information should include mode (type of exercise), frequency, duration, and intensity of exercise along with general comments on how you felt during the workout. This journal is particularly important as our ability to regulate and safely prescribe an exercise program for you for the length of this study depends on your ability to accurately report any discomforts that may surface during the training and other general feelings such as: did the exercise feel good or bad, was the workout too easy or hard, etc.

Polar Heart Rate Monitor: You will be asked to wear a strap around your chest and a device around your wrist, which records your heart rate during your exercise training. This is to assure that your training is adequate for your fitness level.

Procedures for storing of extra or left over samples
We will retain whatever blood is left over after all the analyses are complete in case other blood tests become available that might be useful to explain the effects of aging on the heart. The samples will be kept in the freezer in the biochemistry lab at the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas labeled with your code and study date. Only the Principal investigator will have access to these samples.

The tests performed in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your heart to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the tests done in this study are not for medical purposes, we will not issue official reports of the results. However we will provide you with a summary of the key findings that you can show to your doctor, and would be pleased to provide whatever further details that you or your doctor might wish.

How long can I expect to be in this study?
Your participation in this study will end following completion of your repeat cardiovascular testing, which should take place roughly two years after your initial testing. On occasion, training may be delayed due to injury, illness or personal matters. If this is the case, your enrollment in the study may last longer than two years as we attempt to complete the training and testing.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Medical Procedures

1. Risks

a) Electrocardiogram: There is no risk associated with an electrocardiogram.

b) Echocardiogram: There is no risk associated with an echocardiogram

c) Blood Pressure Measurements (all forms): There is no risk associated with BP measurements

d) Body Composition Measurements: There is no risk associated with body composition measurements performed by the methods of measuring height, weight, and measuring skinfold thickness using measuring tape and calipers. Radiation risks associated with the DEXA scan are detailed below in the section titled “Body Composition Measurements (Study Day 2).

e) Activity Monitoring: There is no risk associated with activity monitoring

f) Heart Rate Monitoring: There is no risk associated with heart rate monitoring

g) Cardiac Output Monitoring: There is no risk associated with monitoring cardiac output.

Patch adhesives placed for many of these tests may be cold and sticky; shaving of hair to get the patches to stick may be required. You may develop a rash or redness where the patches were attached. This mild rash often goes away without treatment.

2. Risk from radiation:

This research study includes exposure to radiation from diagnostic tests (DEXA scan) in addition to that which you would receive from standard care. The additional radiation dose you will get is about 1 % of the average radiation dose from all sources (natural background radiation, consumer appliances, radon gas, medical tests, etc.) that a person in the United States receives each year. We wish to keep radiation exposure as low as possible, therefore, if you have been a subject in another project involving radiation during the previous 12 months, you should discuss it with the physician in charge of this study.

Any women with an intact uterus, regardless of age, must have a negative urine pregnancy test. Women with total hysterectomies or post-menopausal women with documented FSH levels >35mlU/ml are exempt from pregnancy testing. Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be limited to the first ten days after a woman who can become pregnant (age 10-50 years) has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UT Southwestern. This policy applies unless there is an important medical reason requiring radiation outside this time frame.

Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

(1) surgical sterilization (vasectomy), or

(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a urine pregnancy test will be done and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or “tubes tied”),

(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),

(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or

(4) an intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

3. Risks from exercise testing: With any type of exercise testing, there exists the possibility of injury or discomfort. Hard exercise may cause strain or injury to the muscles, bones and joints. During testing, the risk of having a heart attack or even dying goes up slightly, however the risk during any given session in an apparently healthy person like yourself is less than 1/100,000 tests. Exercise tests may also occasionally be accompanied by abnormal blood pressure, nausea, fainting, muscle soreness, joint and bone injury, and in rare instances, heart attack, stroke, or death. Every precaution will be taken to minimize these risks by evaluating your health and fitness status throughout the study.

4. Magnetic resonance imaging and spectroscopy:
There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure

at any time . You may also experience some discomfort and fatigue from lying still during imaging. If you have any metal clips or plates in your body, you should tell the investigator. MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

5. Exercise Training

When performed as instructed, moderate intensity exercise training carries minimal risk. This risk is no greater than unsupervised exercise and is primarily composed of musculoskeletal injury.

6. Fish Oil medication: There is minimal risk from ingesting fish oil/omega-3 at the doses provided in this study. Fish oil at prescription level doses have been used by thousands of patients with very few serious adverse reactions. Some individuals who have a history of bleeding disorders or very low platelets may be at increased risk of suffering minor bleeding (gingival bleeding, skin bruising). Rarely, allergic reactions may occur to the medications contained within the fish oil gel capsules including GI distress or rash. If this occurs, notify study investigators immediately.

7. Loss of Confidentiality

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

8. Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. You will have a total of 4 tablespoons of blood collected because you are in this research study (all the tests combined).

9. Risks of Carbon Monoxide Blood Volume Measurement

There is minimal risk with carbon monoxide blood volume measurement. The amount of carbon monoxide given is a very small amount and would be equivalent to the amount inhaled during a few hours in a bar or restaurant that allows smoking.

10. Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?

Only experienced and highly trained personnel will perform any of the procedures used during this study. During testing you will be very closely monitored both by a cardiologist as well as by a critical care trained nurse.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illnesses while you are on study even if you do not think they are related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?

If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?

If you agree to take part in this study, there may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research. The tests performed on your heart will provide information that may be useful as baseline data for the future. A previously unknown condition that should receive medical attention may occasionally be discovered. The combined results from studies in patients and normal subjects will give us a better understanding of the effects of exercise on the function of the heart.

What options are available if I decide not to take part in this research study?

You do not have to take part in this study.

Will I be paid if I take part in this research study?
Yes. Texas Health Presbyterian Hospital Dallas will compensate you for participating in this study. You will be paid $150 after completion of the "Baseline Testing" involving the MRI, cardiac sonograms and exercise tests. As this testing is repeated at the conclusion of the study which usually takes one year, you will be paid an additional $150 after completion of the "Follow-up Testing" which involves similar testing as "baseline testing." You will also be paid $100 after the successful completion of every quarter of training. Therefore, if you complete all of the testing, you will be paid a total of $700 over roughly one year. If you don't complete all study procedures, you will be paid according to the number of procedures you complete.

Your Social Security Number (SSN) will be given to Texas Health Presbyterian Hospital in order to process your payment as required by law. This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

You may be eligible to be reimbursed for your transportation to and from the research center (for example cab or bus fare), or child care expenses. In order to receive reimbursement, please discuss these needs ahead of time so that we can help make the best possible arrangements. You will need to turn in all your receipts to the research coordinator.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, Fish Oil, gym or yoga studio membership or Monitoring/Follow-up Procedures described above).

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately. Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas, or Texas Health Presbyterian Hospital Dallas. You retain your legal rights during your participation in this research

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care. If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. The researchers may decide to take you off this study if:

- The researchers believe that participation in the research is no longer safe for you.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Information about you that is collected for this research study will remain confidential unless you give your permission to share it with others, or if we are required by law to release it. You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The American Heart Association;
- Texas Health Presbyterian Hospital Dallas; and
- The UT Southwestern Institutional Review Board.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Are there procedures I should follow after stopping participation in this research?
Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return any unused study materials, including the investigation drug, placebo gel capsules, your training journal and/or the Polar heart rate monitor.
- Return to the research center for tests that may be needed for your safety.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

There are no known risks to stopping the nutri-ceutical Fish Oil, exercise training or yoga training pre-maturely.

Whom do I call if I have questions or problems?
For questions about the study, contact Satyam “Tom” Sarma, M.D. at 214-345-4619 during regular business hours or page him at 214-786-4658 after hours and on weekends and holidays. For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES: YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.
Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____

Participant's Name (printed)

_____ _____

Participant's Signature Date/Time

_____

Name of person obtaining consent (printed)

_____ _____

Signature of person obtaining consent Date/Time