Nutrition, Inflammation and Insulin Resistance in End-Stage Renal Disease

NCT04067752

August 26, 2022

Participant Name: _____ Date:_____

Title of Study: Nutrition, Inflammation and Insulin Resistance in End Stage Renal Disease—NaMRI Metabolism

Principal Investigator: __T. Alp Ikizler _____VA Facility: VATVHS Nashville_____

KEY SUMMARY INFORMATION ABOUT THIS STUDY

What key information do you need to know?

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

List of terms

TVHS- VA Tennessee Valley Healthcare System
GCRC- Vanderbilt's General Clinical Research Center
VUMC- Vanderbilt University Medical Center
MRI- Magnetic resonance imaging
DEXA- dual energy x-ray absorptiometry
BIA- body impedance analysis
MUAMC -mid-upper arm muscle circumference

You are being invited to take part in a research study that is being funded by Department of Veterans Affairs. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

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WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn the role of salt storage in the body and its effect on two of these things. These are inflammation (how your body reacts to an injury) and insulin resistance (how your body uses sugar). Your participation in this research will last about ten weeks.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

The benefits to science and humankind that might result from this study are an increased understanding of the role of salt storage in the body and its effect on insulin resistance and inflammation sensitivity which results in protein energy wasting in hemodialysis patients.

For a complete description of benefits, refer to the Detailed Information section of this informed consent form.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The time commitment for the study requires 3 visits to Vanderbilt's GCRC. These visits may be an inconvenience.

For a complete description of risks, refer to the Detailed Consent below.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Alp Ikizler the Nashville VA. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: 615-343-6104

DETAILED INFORMATION ABOUT THE STUDY

WHAT IS THE PURPOSE OF THIS STUDY?

You are being asked to take part in a research study at the VA Tennessee Valley Healthcare System (TVHS) Medical Center because you have kidney disease and are on chronic hemodialysis. Most hemodialysis patients have poor nutritional status. Certain things related to your kidney disease could be making your nutritional status worse. The purpose of this study is to examine the role of salt storage in the body and its effect on two of these things. These are inflammation (how your body reacts to an injury) and insulin resistance (how your body uses sugar).

HOW LONG WILL I BE IN THE STUDY?

We plan to enroll about 20 people like you who are on chronic hemodialysis (CHD). The study requires a total of three study visits at Vanderbilt's General Clinical Research Center (GCRC). You will be in the study about ten weeks. The overall length of the study is about 3 years. All procedures are for research purposes.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

All procedures are for research purposes.

A detailed description of each study procedure will be listed on page 5.

Pre-screening phone call

Prior to each visit we may call you to ask a series of COVID-19 screening questions. Depending on your answers we will continue to confirm your study visit or may postpone your visit.

Screening Visit

The screening visit may take place at Nashville VA or VUMC. We will have one visit to tell you about the study, have you sign the consent form if you wish to participate, and ask you demographic questions such as age and race. We will also talk to you about the medications

you take. When you arrive, you may undergo COVID-19 temperature screening prior to entry into the medical center. You may also be asked COVID -19 screening questions. You will be provided an armband and / or a sticker indicating you have been screened and will need to wear it throughout your visit. You may be required to wear a mask during your visit. If you do not have one, we will provide one to you.

You will also be asked to review and or complete an MRI screening form. This is to ensure it is safe for you to undergo the MRI scan. If there is a possibility that you may have metal in your body, you may be asked to have a screening X-ray exam to confirm the absence of any metal before you can begin the study. This X-ray may happen on another day. The need for this X-ray will be determined by the MRI technologist. About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant.

Study Diet (Week -2 and on-going)

About 2 weeks before your first MRI study day, you will be interviewed for a 2-day random food recall. The interview will last about 15 minutes. You will need to continue a stable diet throughout the study. We will provide a diet diary that can be used to log the foods to ate. This will help to remember what you ate on the recall days.

MRI and additional Study Assessments (Weeks 0, Week 4, and Week 8)

Every four weeks you will be asked to come to the GCRC to undergo an MRI scan, body composition and physical performance tests.

Body composition scans include: DEXA, mid-upper arm muscle circumference (MUAMC) and body impedance analysis (BIA) measurements.

Physical performance tests include simple hand grip test, balance testing, 3-meter walk and 5 repetition sit to stand.

About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant.

Diet Recalls (Weeks 1, 2, 3, 4, 5, 6, 7 and 8)

Every week during the study, you will be interviewed for a 2-day random food recall. Each interview will last about 15 minutes. A diet diary will be provided and can be used to log food ate during the recall days.

Dialysis Sessions-Intervention (3 times a week for 8 weeks)

The dialysis sessions are part of your standard of care dialysis treatments.

After you complete the first MRI study day, you will either undergo dialysis using a low-sodium dialysate or a high-sodium dialysate. The chance that you receive the low-sodium, or the high-sodium dialysate will be determined by something like the toss of a coin. The two dialysate concentrations selected for the study are within the standard of care for clinical practice. The dialysate will be used in all your regularly scheduled dialysis sessions at your dialysis unit for 4 weeks. At that time, we will switch your dialysate sodium concentration to the one you had not been using. This new dialysate will then be used in all your regularly scheduled dialysis sessions at your dialysis unit for another 4 weeks. At each dialysis session we may record your recovery time.

By chance, you will undergo dialysis using either (a) low-sodium dialysate for 4 weeks followed by high-sodium dialysate for 4 weeks, or (b) high-sodium dialysate for 4 weeks followed by low-sodium dialysate for 4 weeks.

Description of Procedures and Timeline of Study

All procedures will be done within about 2 weeks of each of the two dialysis interventions and at the end of the last intervention.

MRI

The MRI scan will take about 1 hour. The MRI is performed by an MRI technician. An MRI scan is taken in a large machine that is shaped like a tunnel. During this type of scan, you will be placed in the scanner foot first. This scan does not use x-rays. Instead, they use a strong magnet and radio waves, like those used in an AM/FM radio to make pictures of your body.

You may not be able to have this scan if you have a device in your body such as aneurysm clips in the brain, heart pacemakers or defibrillators, and cochlear implants. Also, you may not be able to have this scan if you have an iron-based tattoos, pieces of metal (bullet, BB, shrapnel) close to or in an important organ (such as the eye).

Certain metal objects like watches, credit cards, hairpins, writing pens, etc. may be damaged by the machine or may be pulled away from the body when you are getting the scan. Also, metal can sometimes cause poor pictures if it is close to the part of the body being scanned. For these reasons, you will be asked to remove these objects before going into the room for the scan.

You will hear "hammering", clicking, or squealing noises during the scan. You will be given earplugs to reduce the noise. You will also be told how to alert the staff if you need them.

During the scan, the MRI staff can hear and talk to you. You will also be able to hear the staff. You will be asked to lie very still throughout the scan.

DEXA Scan

We will measure how much fat, bone, and muscle you have. The scan is performed by an Imaging Research Technologist. We will do this by a test called dual energy x-ray absorptiometry (DEXA). You will be asked to lie on a table for 10-15 minutes while a scanner X-rays your body fat, lean muscle, and bone masses. If you are a person who can become pregnant, we will do a pregnancy test before the DEXA to make sure you are not pregnant.

BIA

The body impedance analysis (BIA) test will tell us how much body fat and water you have. A direct member of the study team will perform this test. We will put four electrodes on your body, two on your hands and two on your feet. You will need to lie with your hands at, but not touching, your sides and with your legs separated. We will pass a small electrical current through your body. The current is too small for you to detect and is not painful. This test will take about 5-10 minutes.

Hand Grip Test

During the study, we will also ask you to perform a simple hand grip test. You will squeeze a device with each hand three times. You will be allowed to rest between each squeeze. A direct member of the study team will perform this test.

Physical Performance Battery

We will ask you if you feel safe performing these tasks before we begin. Balance, gait speed and chair speed tests will be completed based on set protocols. You will be asked to stand in three various positions to determine your balance. We will observe and time you walk for a short distance and record the time it takes you to sit and come to a standing position five times. A direct member of the study team will perform this test.

MUAMC

You will have your mid-upper arm muscle circumference (MUAMC) measured. This estimates the circumference of the bone and muscle portions of the upper arm, which in turn helps estimate body fat. Skinfold calipers (a manual measuring device) will be used to measure the back of the upper arm. The circumference (distance around) of your upper arm will also be measured. A direct member of the study team will perform this test.

Physical Activity Monitors

The physical activity monitor is about the size of a watch. It is worn on your non-dominate wrist (for example your left wrist if you are right-handed) or the arm without your dialysis shunt. You will wear this monitor for 4-7 days. You will wear it 24 hours per day, including when you sleep, shower, or do any other activities. We will also provide you a physical activity log to document physical activity during your day.

Diet Recalls

About 2 weeks before your first MRI visit and weekly we will do a 2-day random food recall. We will provide you a diet recall form. This form can be used to write down the foods you ate during the day. This form will be used when we do the recall interview to help remember the foods you ate. The interview will take about 15 minutes of your time. We will provide you the dates to document. A direct member of the study team will perform the diet recall.

Blood Draws and Urine collection

We will also collect up to 70ml (about 4.5 tbsp) of blood over 8 weeks while you are on dialysis. These blood draws will happen at your regular dialysis treatment. We may use some of your monthly labs collected at your dialysis treatment to reduce the amount of blood being collected.

People who can become pregnant will have a blood sample collected before the MRI visits. This is to confirm non-pregnancy status.

Timeline of Study

Title of Study: Nutrition, Inflammation and Insulin Resistance in End Stage Renal Disease—NaMRI Metabolism

Principal Investigator: __T. Alp Ikizler _____VA Facility: VATVHS Nashville_____

Procedure		Weeks -2 to 0	Week 0	Weeks 1,2,3	Week 4		Weeks 5,6,7	Week 8 (end of intervention)
MRI		✓			✓			✓
DEXA		✓			✓			✓
Physical Performance-		✓			✓			✓
Body composition		✓			✓			✓
Physical Activity Monitor		✓			✓			✓
Blood sodium levels			✓	✓	✓		✓	✓
Research labs			✓		✓			✓
Consistent diet		✓	✓	✓	✓		✓	✓
Diet Recalls (weekly)		✓		✓	✓		✓	✓
Dialysis Intervention			✓	✓	✓	✓	✓	

Research procedures being performed at VATVHS Nashville:

VA TVHS Nashville's role in this study is to screen your medical records and to obtain your informed consent with respect to access to you records. The consent/screening visit, blood draws and dialysis treatments will occur at VATVHS. All other parts of this study will be performed at VUMC.

FOR IRB USE ONLY

PI/SC Approval Date:

TVHS Institutional Review Board
Effective Date: August 26, 2022

Research investigational procedures being performed at VUMC:
Vanderbilt's role in this study is to perform the following research activities: screening x-ray (if needed) all and tasks previously discussed above. You will also be asked to sign a Vanderbilt consent form.

WHAT IS EXPECTED OF ME IF I TAKE PART IN THIS STUDY?

- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment. We will be in contact during the study to remind you about appointments.
- Tell the investigator or research staff if you believe you might be pregnant or might have gotten your partner pregnant.
- Complete your diet recalls and activity log diaries as instructed.
- Ask questions as you think of them.
- While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Side effects and risks that you can expect if you take part in this study:

- Reporting to Vanderbilt on a non-dialysis day may be inconvenient.
- Sticking to a standard diet and providing dietary recalls may be inconvenient.
- If you choose to wear the activity monitor, wearing the monitor for about one week three times may be an inconvenience.

- X-ray exam: For subjects who may have metal in their body, this research study involves exposure to radiation from 1 X-ray exam. The total amount of radiation that you might receive by participating in this study is equal to your body receiving 9 months of radiation from your natural surroundings, or about 5% of the amount allowed in a year for people exposed to radiation as part of their work.
- There are no known major risks with an MRI scan. But it is possible that harmful effects could be found out in the future. Even though the tunnel is open, it may bother you to be placed in a tight space (claustrophobia), and to hear the noise made by the magnet during the scan. You will be given earplugs to reduce the noise. You may also feel the table vibrate and/or move slightly during the scan. It may be hard to lie on the table during the scan. If you have any metal pieces in your body, they could move during the scan and damage nearby tissues or organs.
- If you use a transdermal patch (medicated patches applied to the skin), you may need to take it off during the MRI scan. Transdermal patches slowly deliver medicines through the skin. Some patches have metal in the layer of the patch that is not in contact with the skin (the backing). You may not be able to see the metal in the backing of these patches. Patches that contain metal can overheat during an MRI scan and cause skin burns in the immediate area of the patch. Tell the study doctor that you are using a patch and why you are using it (such as, for pain, smoking cessation, or hormones). Ask your doctor for guidance about removing and disposing of the patch before having an fMRI scan and replacing it after the procedure. Tell the MRI facility that you are using a patch. You should do this when making your appointment and during the health history questions you are asked when you arrive for your appointment.
- Having to lie still for 5-10 minutes and having gelled electrodes placed on a hand and foot during the BIA exam may be uncomfortable.
- Having to lie still for 10-15 minutes during the DEXA scan may be uncomfortable.
- The DEXA scan uses x-rays (or radioactivity). If you are a person who can become pregnant, we will do a pregnancy test before the DEXA to make sure you are not pregnant.
- You will be exposed to a small amount of radiation during the DEXA scan. This radiation exposure is not necessary for your medical care and is for research purposes only. The

total amount of radiation that you will receive by participating in this study is equal to your body receiving 26 days of radiation from your natural surroundings.

Risks that are not known:

Because this study is being done for research only, there may be risks that we do not know about at this time. If new risks become known, you will be informed of these risks.

If you are a person who can become pregnant, you will have a blood test to make sure that you are not pregnant before you receive treatment in this study

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this research consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

The benefits you might get from being in this study. You will receive no direct benefits from participating in this study. However, benefits to science and humankind that might result from this study are an increased understanding of the role of salt storage in the body and its effect on insulin resistance and inflammation sensitivity which results in protein energy wasting in hemodialysis patients.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

If you do not wish to participate in this study, you would receive the same follow up and treatment plan as you would if you were to participate in this study.

You are not required to take part in this research study. Your participation is entirely voluntary. You can refuse to participate now, or you can withdraw from this study at any time after giving

your consent without affecting your healthcare/services or other rights. This will not change your regular medical treatment.

Could you be removed from the study if you decided to take part?

The investigator(s) may stop your participation in this study without your or your legal authorized representative's consent for reasons such as: it will be in your best interest; you do not follow the study plan; or you experience a study-related illness or injury. You may be withdrawn from the study if laboratory tests suggest that it is not safe for you to continue. If you are removed from the study, you will be told the reason why.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Taking part in this study will involve collecting private information about you. This information will be protected in the following ways:

This study is happening at both Nashville VA and VUMC. Your data may be combined with data collected at VUMC. You will also be asked to sign a VA HIPAA authorization and VUMC consent document.

This study involves access of Protected Health Information (PHI) for research as listed: (for a full list of PHI see HIPAA Authorization)
Information from your VA Health Records such as Demographic Information such as name, age, race, contact information, and medical records.

During the course of this study, your research data will be stored as follows:
Sensitive Research data (hard copy such as signed consent form, case reports forms):

- In a locked office at VA TVHS Arce Building
- Coordinator's office at Vanderbilt in Medical Center North

- Electronic sensitive research data (computer spreadsheets/CFRs/code linking to PHI)
  - PI's research folder on VA TVHS Server;

- VA's RedCap database

During the course of this study, the de-identified research specimens will be stored at VATVHS Nashville. They will be stored in a secure lab in the Acre Building. Your samples will be stored until the study is complete.

We may look at information collected in your medical record prior to the week 0 visit and continue to view information in your records up to 2 years after the last study at Vanderbilt. This is so we may view your medical chart before and after you complete the study. If we need to view your medical chart before or after this time period, we will contact you for your consent.

Upon completion of the recruitment/study phase of the study data will be exported from the VA redcap database to be analyzed.

Your medical records will be maintained according to this medical center's requirements and the Privacy Act of 1974. All information obtained about you during the research study will be kept as confidential as legally possible and will be accessible only to the investigators and members of the research team, the sponsor (when applicable), and any appropriate government agency. Research records, like any other hospital records, may be inspected by federal regulatory authorities, including the VA Office of Research Oversight, the VA TVHS Research Compliance Officer, Vanderbilt University Medical Center, state regulatory authorities, and legally authorized parties.

Personal private Identifiers might be removed from data collected during the study. After removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative. Your identification will not be known.

We will include information about your study participation in your medical record.

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.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

You will not be charged for any procedures that are part of this study. Your dialysis sessions are considered standard of care and you would still receive these treatments regardless of participating in the study. These dialysis sessions are NOT being done for research purposes. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

Will you be compensated for your time and inconvenience?

You will not be paid for joining this study.

We will compensate you $75 for each of the MRI study visits (maximum of $225). If you drive, you will be reimbursed for mileage.

If you chose to withdraw, you will be compensated for the activities you have completed. Your payment will be paid via check.

This compensation is to help cover the cost of time and inconvenience. The amount that you are reimbursed is commensurate with the time and inconvenience incurred that you otherwise would not have incurred. You must agree to the release of personally identifying information such as your name, address and social security number to the VA Tennessee Valley Healthcare System so that you may receive your money.

Your payment will be issued from the Austin Financial Service Center which will generate the IRS Form 1099 regardless of the amount of your participation compensation.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury is due to non-compliance by a study participant with study procedures or if the research is conducted for VA under contract with an individual or non-VA institution.

Compensation may or may not be available to you under applicable state and federal law in the event that you suffer physical injury or illness arising from this study. By agreeing to participate in this study you are not waiving or giving up your legal rights to seek compensation.

If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document, you are not giving up your right to make a legal claim against the United States.

If you should have a medical concern or if you feel you have been hurt by being a part of this study, please feel free to contact the Principal Investigator, Dr. Alp Ikizler, at 615-343-6104. You may also call the Nephrology answering service at 615-343-7592 after hours)

DO I HAVE TO TAKE PART IN THE STUDY?

You are not required to take part in this research study. Your participation is entirely voluntary. You can refuse to participate now, or you can withdraw from this study at any time after giving your consent without affecting your healthcare/services or other rights. This will not interfere with your regular medical treatment if you are a patient.

Contact the principal investigator at the contact number above if you want to be withdrawn from the study. Deciding to not be part of the study will not change your regular medical care in any way.
The PI may continue utilizing all data collected up to the point of your withdrawal.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The investigator(s) may stop your participation in this study without your or your legal authorized representative's consent for reasons such as: it will be in your best interest; you do not follow the study plan; or you experience a study-related illness or injury. You may be withdrawn from the study if laboratory tests suggest that it is not safe for you to continue. If you are removed from the study, you will be told the reason why.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have questions about this study, wish to express concerns or complaints about the research, or to report a research-related injury, you can contact:

Principal Investigator Dr. Alp Ikizler at this phone number 615-343-6104 or
After hours (24h access) number at this phone number: 615-343-7592.

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the VA Tennessee Valley Healthcare System (VATVHS) Institutional Review Board Office at (615) 873-6076 or the Research and Development Service Office at (615) 873-8066.This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the primary investigator Dr. Alp Ikizler at this phone number 615-343-6104 if you have questions, complaints, or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

In the event new information becomes available that may affect the risks and/or benefits associated with this study or your willingness to participate in it, you and your physician will be notified so you can make a decision whether or not to continue your participation in this study.

At this time, we do not plan to disclose any research results or individual results.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.

FUTURE USE OF DATA AND RE-CONTACT

Your data and/or specimens will be retained indefinitely for future use. Once the study is complete the data and specimens will be stored in the locations described above.

Your information or bio-specimens (blood or urine) could be used for future studies or by another investigator for future research studies without your or your legally authorized representative's consent. Should this happen information that could identify you will be removed.

TISSUE BANKING

Your data and/or specimens will be retained indefinitely for future use. Once the study is complete the data and specimens will in the locations described above. Your information or bio-specimens (blood or urine) could be used for future studies or by another investigator for future research studies

All procedures in this study are being done for research purposes rather than for diagnosis, and the results will not be routinely examined for abnormalities. However, in the event an abnormality is detected by the investigators, you may be encouraged to consult your physician.

Your data could be used for future studies or by another investigator for future research studies without your or your legally authorized representative's consent. Should this happen information that could identify you will be removed. Data may be used in future studies related to kidney disease and other associated diseases (diabetes, cardiovascular disease, etc.)

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

A member of the study team has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

Title of Study: Nutrition, Inflammation and Insulin Resistance in End Stage Renal Disease—NaMRI Metabolism

Principal Investigator: __T. Alp Ikizler _____VA Facility: VATVHS Nashville_____

By signing this document below, you voluntarily consent to participate in this study You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it.

I agree to participate in this research study as has been explained in this form.		
_____ Participant's Name	_____ Participant's Signature	_____ Date

FOR IRB USE ONLY

PI/SC Approval Date:

TVHS Institutional Review Board
Effective Date: August 26, 2022

Department of Veterans Affairs	**VA RESEARCH CONSENT FORM** Hemodialysis version (full study) **Version Date: 7-27-2022**

Title of Study: **ID#**: **1395515**	Nutrition, Inflammation and Insulin Resistance in End Stage Renal Disease—NaMRI Metabolism		
Principal Investigator:	T. Alp Ikizler, MD	**VAMC: (626)**	Tennessee Valley Healthcare System (VA TVHS)
Participant Name:		**Date:**	

KEY INFORMATION

What key information do you need to know?

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List of terms

TVHS- VA Tennessee Valley Healthcare System
GCRC- Vanderbilt's General Clinical Research Center
MRI- Magnetic resonance imaging
DEXA- dual energy x-ray absorptiometry
BIA- body impedance analysis
MUAMC -mid-upper arm muscle circumference
IV- venous catheter
D20- glucose

PURPOSE OF THE STUDY AND EXPECTED TIME OF PARTICIPATION

What is the study's purpose and how long will you be in the study?

You are being asked to take part in a research study at the VA Tennessee Valley Healthcare System (TVHS) Medical Center because you have kidney disease and are on chronic hemodialysis. Most hemodialysis patients have poor nutritional status. Certain things related to your kidney disease could be making your nutritional status worse. The purpose of this study is to examine the role of salt storage in the body and its effect on two of these things. These are inflammation (how your body reacts to an injury) and insulin resistance (how your body uses sugar).

This study is funded by the Department of Veterans Affairs. It is expected that your overall participation in this study will last 3-10 weeks. This research study is anticipated to last 4 years for Aim 1 and 3 years for Aim 2.

DESCRIPTION OF THE PROCEDURES

What will you be asked to do?

Aim 1 requires one separate overnight study visit at Vanderbilt's General Clinical Research Center (GCRC).
Aim 2 requires a total of three overnight study visits at the GCRC. At each visit, we will measure your metabolism (how your body uses protein and calories). We will also examine your insulin resistance. You will be in the study about three weeks for Aim 1 and about ten weeks for Aim 2.

Aim 1 is the first study visit for Aim 2. You have the option of deciding to only do Aim 1 now, but later changing your mind to do Aim 2. If you change your mind, you may not have to repeat the first set of pre-study assessments nor the first overnight study visit.

Which Aim of the study do you want to do? (Please place your initials in the space in front of your response.)
____ Aim 1 only
____ Aim 1 and Aim 2
____ Aim 2 (having already completed Aim 1)

Pre-screening phone call

Prior to each study visit, we will call you to ask a series of COVID-19 screening questions. Depending on your answers we will continue to confirm your study visit or may postpone your visit.

Screening Visit

We may have one visit to tell you about the study, have you sign the consent form if you wish to participate, and ask you demographic questions such as age and race. We will also talk to you about the medications you take. When you arrive, you will undergo COVID-19 temperature screening prior to entry into the medical center. You will also be asked COVID-19 screening questions. You will be provided an armband and or sticker indicating you have been screened and will need to wear it throughout your stay. You will be required to wear a mask during your visit. If you do not have one, we will provide one to you
You will also be asked to complete an MRI screening form. This is to ensure it is safe for you to undergo the MRI scan. If there is a possibility that you may have metal in your body, you will have a screening X-ray exam to confirm the absence of any metal before you can begin the study. This X-ray may happen on another day. About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant.. This screening visit is being done for research purposes.

Aim 1 (all being done for research purposes)

A full detailed description of each of the procedures will be on page 4.

Pre-Study Diet (Week -2)
About 2 weeks prior to starting the study, you will be interviewed for a 2-day random food recall. The interview will last about 15 minutes. In addition, you will not have to change your diet, but you will be asked to eat a stable diet for 2 weeks prior to the metabolic clamp study(part of the study looking at inflammation (how your body reacts to an injury) and insulin resistance (how your body uses sugar).

Pre-Metabolic Clamp Study Assessments (Weeks -2 to 0)
Within about 2 weeks of the metabolic clamp study, you will be asked to come to the GCRC to undergo a series of tests. You may be asked you not to eat about 4-6 hours before this appointment. We will obtain an MRI, DEXA, and body impedance analysis (BIA) measurements, as well as perform a simple hand grip test. You will also undergo a physical performance battery test and have your mid-upper arm muscle circumference (MUAMC) measured. You will be asked to wear a physical activity monitor and complete a physical activity log for about 1 week. You may also be asked to complete a breathing test. About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant. You may also be asked to have a COVID test 48-72 hours prior to your GCRC admission. This test will be performed at one of the Vanderbilt testing stations.
In the event of scheduling issues these activities may be performed within about 2 weeks after the metabolic clamp study (excluding COVID test).

Metabolic Clamp Study Day (Week 0)
You will undergo a one-day metabolic clamp study (part of the study looking at inflammation (how your body reacts to an injury) and insulin resistance (how your body uses sugar) as described below. **Aim 2**

Study Diet (Week -2 and on-going)
About 2 weeks prior to starting the 8-week study, you will be interviewed for a 2-day random food recall. The interview will last about 15 minutes. In addition, you will not have to change your diet, but you will be asked to eat a stable diet for 2 weeks prior to the first metabolic clamp study. You will need to continue the stable diet throughout the 8-week study. This is being done for research purposes.

Pre-Metabolic Clamp Study Assessments (Weeks -2 to 0, Week 4 and Week 8)
Within about 2 weeks of the first metabolic clamp study (and as close as possible to the next two metabolic clamp studies), you will be asked to come to the GCRC to undergo a series of tests. You may be asked to come to this visit in a fasted state (about 4-6 hours). We will obtain an MRI, DEXA, and BIA measurements, as well as perform a simple hand grip test. You will also undergo a physical performance battery test and have your mid-upper arm muscle circumference (MUAMC) measured. You will be asked to wear a physical activity monitor and complete a physical activity log for about 1 week. You may also be asked to complete a breathing test. About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant. You may also be asked to have a COVID test 72-48 hours

prior to your GCRC admission. This test will be performed at one of the Vanderbilt testing stations. This is being done for research purposes.

Metabolic Clamp Study Day (Week 0, Week 4 and Week 8)
You will undergo three one-day metabolic clamp studies as described below. These clamp studies will be done for research purposes.

Diet Recalls (Weeks 1, 2, 3, 4, 5, 6, 7 and 8)
Every week during the 8-week study, you will be interviewed for a 2-day random food recall. Each interview will last about 15 minutes. This is being done for research purposes.

Dialysis Sessions (3 times a week for 8 weeks)
After you complete the first metabolic clamp study, you will either undergo dialysis using a low-sodium dialysate or a high-sodium dialysate. The chance that you receive the low-sodium, or the high-sodium dialysate will be determined by something like the toss of a coin. The two dialysate concentrations selected for the study are within the standard of care for clinical practice. The dialysate will be used in all of your regularly scheduled dialysis sessions at your dialysis unit for 4 weeks. At that time, we will switch your dialysate sodium concentration to the one you had not been using. This new dialysate will then be used in all of your regularly scheduled dialysis sessions at your dialysis unit for another 4 weeks. At each dialysis session we may record your recovery time. While the dialysis session is part of your standard of care the high vs low sodium dialysate concentrations are being done for research purposes.

By chance, you will undergo dialysis using either (a) low-sodium dialysate for 4 weeks followed by high-sodium dialysate for 4 weeks, or (b) high-sodium dialysate for 4 weeks followed by low-sodium dialysate for 4 weeks.

Description of Procedures and Timeline of Study

MRI
The MRI scan will take about 1 hour. This will be done within about 2 weeks of the metabolic clamp study. An MRI scan is taken in a large machine that is shaped like a tunnel. This scan does not use x-rays. Instead, they use a strong magnet and radio waves, like those used in an AM/FM radio to make pictures of your body.
You may not be able to have this scan if you have a device in your body such as aneurysm clips in the brain, heart pacemakers or defibrillators, and cochlear implants. Also, you may not be able to have this scan if you have an iron-based tattoos, pieces of metal (bullet, BB, shrapnel) close to or in an important organ (such as the eye).
Certain metal objects like watches, credit cards, hairpins, writing pens, etc. may be damaged by the machine or may be pulled away from the body when you are getting the scan. Also, metal can sometimes cause poor pictures if it is close to the part of the body being scanned. For these reasons, you will be asked to remove these objects before going into the room for the scan.
You will hear “hammering”, clicking, or squealing noises during the scan. You will be given earplugs to reduce the noise. You will also be told how to alert the staff if you need them.

During the scan, the MRI staff is able to hear and talk to you. You will also be able to hear the staff. You will be asked to lie very still throughout the scan.

DEXA Scan

We will measure how much fat and muscle you have. This will be done within about 2 weeks of the metabolic clamp study. We will do this by a test called dual energy x-ray absorptiometry (DEXA). For the DEXA, you will lie on a bed for 10-15 minutes while a scanner X-rays your body fat, lean muscle, and bone masses. If you are a person who can become pregnant we will do a pregnancy test before the DEXA to make sure you are not pregnant.

BIA

The body impedance analysis (BIA) test will tell us how much body fat and water you have. We will put four electrodes on your body, two on your hands and two on your feet. You will need to lie with your hands at, but not touching, your sides and with your legs separated. We will pass a small electrical current through your body. The current is too small for you to detect and is not painful. This test will take about 5-10 minutes.

Hand Grip Test

During the study, we will also ask you to perform a simple hand grip test.

Physical Performance Battery

We will ask you if you feel safe preforming these tasks before we begin. Balance, gait speed, and chair speed tests will be complete based on set protocols. Various movements will be complete to determine your balance. We will observe you walk for a short distance and record the time it takes you to sit and come to a standing position five times.

Physical Activity Monitors

The physical activity monitor is about the size of a watch. It is worn on your non-dominant wrist. You will wear this monitor for 4-7 days about 2 weeks before or after the metabolic clamp study day. You will wear it 24 hours per day, including when you sleep, shower or do any other activities. We will also provide you a physical activity log to document physical activity during your day.

Diet Recall Form

We will ask you to complete a diet recall form. The form is to ease patients to remember their diet and to increase the accuracy of diet recalls. You will be given the forms 1 -2 weeks before your clamp study to be completed at home. You will document one set on a weekday and one set on the weekend. You will review the form either in person or via phone with a study coordinator.

Breathing test

You may be asked to breathe into a "metabolic cart" for about 20 minutes. This machine measures the oxygen and carbon dioxide content of your breath. This lets us know how much energy you use. A non-restrictive clear hood will be placed over your head that has a tube which allows air (oxygen) in and air (carbon dioxide) out.

MUAMC

You will have your mid-upper arm muscle circumference (MUAMC) measured. This estimates the circumference of the bone and muscle portions of the upper arm; which in turn helps estimate body fat. Skinfold calipers (a manual measuring device) will be used to measure the back of the upper arm. The circumference (distance around) of your upper arm will also be measured. For this procedure, you will be asked to stand and have your arms hanging loosely at your sides. The procedure should take about 10 minutes.

Metabolic Clamp Study

The metabolic clamp studies will happen at the GCRC. Each study will be scheduled on a non-dialysis day. You will come to the GCRC the night before each study and spend one night. We will provide you dinner and a snack. You will be asked not to eat or drink anything after about 10 PM. You will only be allowed to drink water after that. About 1 teaspoon of blood will be collected to confirm non-pregnancy status for people who can become pregnant.

The next morning, if you have not already completed the breathing test, you may be asked one time to breathe into a "metabolic cart" for about 10-20 minutes. We will also measure the rate at which blood flows through your arm or leg. Afterwards, dialysis needles will be placed in your shunt. Blood will be drawn to collect baseline data. We will also collect a sample of your breath. An IV will be started with a solution that has combination of glucose and amino acid solution. We call this a ‘tracer’. Amino acids are the building blocks of proteins. Your dialysis access will be used to do this procedure. The infusion will continue through the whole study. A venous catheter (IV) will be placed in the arm without your access. The catheter IV will be used to draw blood at specific time points.

During the first two hours of the study, we may measure again the rate at which blood flows through your arm or leg.

Two hours after starting the tracer, we will have a ‘sampling period’. During the sampling period we will draw blood every 5 minutes for 30 minutes. Also, during this time, you will be asked two times to breathe into a bag for several breath cycles.

After the ‘sampling period’, insulin supplementation will be started at a set rate. The amino acid supplementation may be started at the same time or may be delayed. During this time small amounts of blood will be drawn every 5 minutes. This is to check your blood glucose levels. Every 10 minutes we will check the amino acid levels. The infusion will run for about 1-3 hours. After the insulin begins, your glucose level will be adjusted to a normal range. This will be maintained at that level by providing you a glucose infusion (D20) as needed.

After 90-180 minutes (depending on how quickly your blood sugars stabilize), we will sample your blood for 30 minutes. Again, during this time you will be asked two times to breathe into a bag for several breath cycles. We may collect another set of samples if the amino acid infusion was delayed. Potassium levels will be checked every 30 minutes to monitor any changes.

If your potassium is low, we will give you potassium through your vein.

If you urinate during the study, we will collect a sample of your urine. After the study is completed, all infusions except for glucose will be discontinued. You will be allowed to eat after the study. The glucose solution will be gradually decreased over time. Your blood glucose will be checked every 15 minutes. Once your blood glucose level is stable, the glucose solution will be discontinued. The IV catheter and your dialysis access needles will be removed.

We may perform a short post-study dialysis treatment at the GCRC or at one of the outpatient dialysis clinics. This will depend on your clinical status (labs and fluid intake). This will be determined by a doctor or a nurse practitioner. This dialysis treatment is not for research. This treatment will not take place of your normal dialysis treatment. You will receive standard discharge instructions including contact information before leaving the GCRC. We will follow up with you within about 1 week of the metabolic clamp study visit.

Arm/Leg Blood Flow

We will measure the rate at which blood flows through your arm or leg one or two times. This involves placing three blood pressure cuffs on your arm. The cuffs send an electronic signal to a computer that estimates the rate at which blood flows through your arm.

Heart Monitoring

We will monitor your heart rhythm and rate during the metabolic clamp study. This will be done by placing sticky pads (electrodes) on your chest. The sticky pads are connected to wires (leads) that hook up to a machine. This way we can monitor your heartbeat and heart rhythm.

Breath Samples

You will be asked to breathe into a breath collection bag at specific times during the metabolic clamp study. We will collect the air you breathe out.

Blood Draws and Urine collection

In total, a little less than a cup of blood will be obtained during each metabolic clamp study visit.
We will also collect 30ml (about 2 tbsp) of blood over 8 weeks while you are on dialysis to check your blood sodium levels.
People who can become pregnant will have a blood sample collected at consent/screening, before the DEXA, as well as the overnight study visit. This is to confirm non-pregnancy status.

Timeline of Study

Procedure	Aim 1	Aim 2					
	Screening	Weeks -2 to 0	Week 0	Weeks 1,2,3	Week 4	Weeks 5,6,7	Week 8
Blood collection	✓		✓	✓	✓	✓	✓
X-ray exam (if needed)	✓						
Pregnancy test	✓	✓	✓		✓		✓
Diet recalls		✓		✓	✓	✓	✓
Activity Monitor		✓			✓		✓
Breathing test		✓		✓		✓	
MRI		✓			✓		✓
COVID-19 testing (48-72h prior to admission)			✓		✓		✓
DEXA		✓			✓		✓
BIA		✓			✓		✓
Hand grip		✓			✓		✓
Physical Performance Battery		✓			✓		✓
MUAMC		✓			✓		✓
Metabolic clamp study			✓		✓		✓
Blood flow measurement			✓		✓		✓

*Breathing test will happen either before OR during the metabolic clamp study day. Aim 1 you will complete 1 breathing test and Aim 2 you will complete 3.

Optional Procedure:

Muscle Biopsy (muscle sample): The muscle biopsy is for research purposes only. If you have a dialysis shunt in your thigh you will not be able to complete this procedure. The biopsy will give us more information on how your body handles nutrients. Before and after the metabolic clamp study, a muscle biopsy will be taken from the mid-thigh area. The first biopsy will use one thigh muscle and the second biopsy will use the other thigh muscle. Lidocaine will be used to numb the area where the biopsy will be done. A small incision (about an inch) will be made in the skin. A special needle will be used to withdraw the muscle tissue. The amount will be about the size of a pencil eraser. Any bleeding will be stopped with a pressure dressing.

Do you consent to the Muscle Biopsy part of the study? (Please place your initials in the space in front of your response.):

____ Yes ____ No

Research procedures being performed at VATVHS Nashville:
VA TVHS Nashville's role in this study is to screen your medical records and to obtain your informed consent with respect to access to you records. The consent/screening visit, some blood draws and dialysis treatments will occur at VATVHS. All other parts of this study will be performed at Vanderbilt.

Research investigational procedures being performed at Vanderbilt University Medical Center:
Vanderbilt's role in this study is to perform the following research activities: screening x-ray (if needed), some blood draws, all and parts of the pre-metabolic assessments and all procedures associated with the metabolic clamp study including the optional muscle biopsy. You will also be asked to sign a Vanderbilt consent form.

DESCRIPTION OF THE DISCOMFORTS, INCONVENIENCES, AND/OR RISKS

What are the side effects and risks you can expect if you take part in this study?

- Inconvenience of reporting to the GCRC the night before each of the metabolic clamp studies.
- Eating a recommended diet and providing dietary recalls may be inconvenient.
- Fasting for 8 hours may be inconvenient.
- Wearing the activity monitor for one week may be an inconvenience.
- X-ray exam: For subjects who may have metal in their body, this research study involves exposure to radiation from 1 X-ray exam. The total amount of radiation that you might receive by participating in this study is equal to your body receiving 9 months of radiation from your natural surroundings, or about 5% of the amount allowed in a year for people exposed to radiation as part of their work.
- There are no known major risks with an MRI scan. But it is possible that harmful effects could be found out in the future. Even though the tunnel is open, it may bother you to be placed in a tight space (claustrophobia), and to hear the noise made by the magnet during the scan. You will be given earplugs to reduce the noise. You may also feel the

table vibrate and/or move slightly during the scan. It may be hard to lie on the table during the scan. If you have any metal pieces in your body, they could move during the scan and damage nearby tissues or organs.

- If you use a transdermal patch (medicated patches applied to the skin), you may need to take it off during the MRI scan. Transdermal patches slowly deliver medicines through the skin. Some patches have metal in the layer of the patch that is not in contact with the skin (the backing). You may not be able to see the metal in the backing of these patches. Patches that contain metal can overheat during an MRI scan and cause skin burns in the immediate area of the patch. Tell the study doctor that you are using a patch and why you are using it (such as, for pain, smoking cessation, or hormones). Ask your doctor for guidance about removing and disposing of the patch before having an MRI scan and replacing it after the procedure. Tell the MRI facility that you are using a patch. You should do this when making your appointment and during the health history questions you are asked when you arrive for your appointment.
- Having to lie still for 2 minutes and having gelled electrodes placed on a hand and foot during the BIA exam may be uncomfortable.
- Having to lie still for 10-15 minutes during the DEXA scan may be uncomfortable.
- The DEXA scan uses x-rays (or radioactivity). If you are a people who can become pregnant , we will do a pregnancy test before the DEXA to make sure you are not pregnant.

  Aim 1 subjects: You will be exposed to a small amount of radiation. The radiation dose that you will receive from this procedure is about the same amount that you will get over a period of 6 days from natural background radiation as you go about your usual activities.

  Aim 2 subjects: You will be exposed to a small amount of radiation. The radiation dose that you will receive from this procedure is about the same amount that you will get over a period of 18 days from natural background radiation as you go about your usual activities.
- The insulin infusion during the metabolic clamp study can lower blood potassium levels. If this drops too low, your heart rhythm may be affected. We will closely monitor potassium levels and place you on a machine that monitors your heart to decrease this risk and to observe any complications. If a decrease in potassium occurs, it will be replaced intravenously.
- Replacing the potassium may cause slight burning or irritation and your heart rhythm may be affected. We will monitor your heart to decrease this risk. We may adjust the rate of replacement as needed.
- There is a small risk of low blood sugar. If this occurs, you may experience any of these symptoms: feeling lightheaded, headache, fast heartbeat, sweating, blurred vision, hunger, and rarely seizures. We will check blood sugar every 5 minutes. If the blood sugar level drops below normal, it will be restored intravenously.

- Inconvenience of having gelled electrodes placed on the chest and being connected to a heart monitor during the metabolic clamp study. The gelled electrodes used for ECG monitoring may cause skin irritation.
- The IV placed in your forearm may cause a slight bruise and carries a risk of infection which is rare.
- Breathing through a mouthpiece may be inconvenient for you and may make you feel lightheaded or dizzy.
- The blood pressure cuffs placed on the forearm/leg may be uncomfortable when inflated. For each blood flow test, one cuff will remain inflated up to 2 minutes. Another cuff will be inflated/deflated about 9 times over 2 minutes. The third cuff will remain uninflated.
- Inhaling and exhaling into the breath sample bag may be an inconvenience, but it does not pose any risk.
- The tracers used in the metabolic clamp studies are not radioactive and do not present any additional risk. The D20 and amino acid supplementation also do not present any additional risk.
- The fistula needles placed in your arm or leg carry a risk of infection or clotting. These risks are rare. Your access will be cleaned before inserting the needles.
- The lidocaine used for local anesthetic prior to IV insertion or muscle biopsy may cause numbness, burning and/or local rash or irritation, if you are allergic. There is a risk that lidocaine may cause problems with heart rhythm. This is unlikely given the amount you will receive.
- Optional Muscle Biopsy. The muscle biopsy may cause muscle soreness, bruising, infection or a small blood-filled bump (hematoma) at the biopsy site. There is a small chance that some slight bleeding may also occur. The soreness may last as long as 48 hours.

Risks that are not known:
Because this study is being done for research only, there may be risks that we do not know about at this time. If new risks become known, you will be informed of these risks.

- If you are a person who can become pregnant you will have a blood test to make sure that you are not pregnant before you receive treatment in this study

ANTICIPATED BENEFITS RESULTING FROM STUDY PARTICIPATION

What are the good effects that might result if you take part in the study?

a) The benefits to science and humankind that might result from this study are an increased understanding of the role of salt storage in the body and its effect on insulin resistance and inflammation sensitivity which results in protein energy wasting in hemodialysis patients.

b) The benefits you might get from being in this study. You will receive no direct benefits from participating in this study.

ALTERNATIVE PROCEDURES/OTHER TREATMENT AVAILABLE

What are the other treatments you could get if you decide not to take part in the study?

If you do not wish to participate in this study, you would receive the same follow up and treatment plan as you would if you were to participate in this study.

You are not required to take part in this research study. Your participation is entirely voluntary. You can refuse to participate now, or you can withdraw from this study at any time after giving your consent without affecting your healthcare/services or other rights. This will not change your regular medical treatment.

The investigator(s) may stop your participation in this study without your or your legal authorized representative's consent for reasons such as: it will be in your best interest; you do not follow the study plan; or you experience a study-related illness or injury. You may be withdrawn from the study if laboratory tests suggest that it is not safe for you to continue. If you are removed from the study, you will be told the reason why.

Could you be removed from the study if you decided to take part?
The study doctor may stop your involvement in this study without your consent for reasons such as: it will be in your best interest or you do not follow the study plan. If you are taken out of this study, you will be told the reason why.

DESCRIPTION OF STUDY RELATED COSTS

Will there be any cost if you take part in the study?

You will not be required to pay for any treatment received or blood test done solely for the purpose of this research study. Some veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this study. You will be charged co-payments for any routine treatment of hemodialysis treatments you will continue to pay these co-pays.

Will you be compensated for your time and inconvenience?
You will not be paid for joining this study.
You will receive $200 for each set of the pre-clamp study procedures and metabolic clamp study (maximum of $600).
If you choose to participate in the optional muscle biopsy you will be compensated $100 for each biopsy (maximum of $600).
The total amount that you will be compensated to complete all three metabolic clamp studies and all six optional muscle biopsies is $1,200.
If you drive, you will receive mileage based on current IRS travel rates.

The payment will be submitted for payment once you have completed the study. If you chose to withdraw, you will be compensated for the activities you have completed. Your payment will be paid via check.
You are also being asked to sign a VUMC consent document. If you have already completed the metabolic clamp study but did not complete the breathing test we will compensate you $25 by gift card to return and complete one breathing test. This will be provided to you from VUMC (you will also be asked to sign an updated VUMC consent to reflect this compensation)
This compensation is to help cover the cost of time and inconvenience. The amount that you are reimbursed is commensurate with the time and inconvenience incurred that you otherwise would not have incurred. You must agree to the release of personally identifying information such as your name, address and social security number to the VA Tennessee Valley Healthcare System so that you may receive your money.
Your payment will be issued from the Austin Financial Service Center which will generate the IRS Form 1099 regardless of the amount of your participation compensation.

MEDICAL TREATMENT FOR RESEARCH-RELATED INJURY

What if you get injured from taking part in the study?
Every reasonable safety measure will be used to protect your well-being. The VA has the authority to provide medical treatment to participants injured by participation in a VA project. VA medical facilities will provide necessary medical treatment to you as a research participant if you are injured as a result of your participation in this study.

Compensation may or may not be available to you under applicable state and federal law in the event that you suffer physical injury or illness arising from this study. By agreeing to participate in this study you are not waiving or giving up your legal rights to seek compensation.

COMPENSATION FOR RESEARCH-RELATED INJURY

Will there be any payment available if you are injured as a result of the study?
If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document, you are not giving up your right to make a legal claim against the United States.

CONFIDENTIALITY AND PRIVACY

How will your information (data) be protected and who will have access to it?

Your medical records will be maintained according to this medical center's requirements and the Privacy Act of 1974. All information obtained about you during the research study will be kept as confidential as legally possible and will be accessible only to the investigators and members of the research team, the sponsor (when applicable), and any appropriate government agency. Research records, like any other hospital records, may be inspected by

federal regulatory authorities, including the VA Office of Research Oversight, the VA TVHS Research Compliance Officer, Vanderbilt University Medical Center, state regulatory authorities, and legally authorized parties.

Your permission to allow access to your medical information and a description of your rights under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) is addressed in a separate HIPAA Authorization document. By signing the separate HIPAA Authorization form, you agree to allow access, use and disclosure of your personal health information as described in the HIPAA Authorization form. By signing the consent form, you are voluntarily choosing to participate in the study as described in this consent form.

This study involves access of Protected Health Information (PHI) for research as listed: (for a full list of PHI see HIPAA Authorization)
Information from your VA Health Records such as Demographic Information such as name, age, race, contact information, and medical records.

During the course of this study, your research data will be stored as follows:
Sensitive Research data (hard copy such as signed consent form, case reports forms):

- In a locked office at VA TVHS Arce Building
- Coordinator's office at Vanderbilt in Medical Center North

- Electronic sensitive research data (computer spreadsheets/CFRs/code linking to PHI)
  - PI's research folder on VA TVHS Server;
  - VA's RedCap database

During the course of this study, the de-identified research specimens will be stored at VATVHS Nashville. They will be stored in a secure lab in the Acre Building. Your samples will be stored until the study is complete.

We may look at information collected in your medical record prior to the pre-metabolic assessment visit and continue to view information in your records up to 2 years after the last metabolic clamp study at Vanderbilt. This is so we may view your medical chart before and after you complete the study. If we need to view your medical chart before or after this time period, we will contact you for your consent.

Upon completion of the recruitment/study phase of the study data will be exported from the VA redcap database to be analyzed.

Will you be given any information after you take part in the study?

In the event new information becomes available that may affect the risks and/or benefits associated with this study or your willingness to participate in it, you and your physician will be notified so you can make a decision whether or not to continue your participation in this study.

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.

What will happen to your information (data) at the end of the study?

Your data and/or specimens will be retained indefinitely for future use, as applicable to this protocol). Once the study is complete the data and specimens will in the locations described above. At this time, we do not plan to disclose any research results or individual results.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.

At the end of the study your VA information will be retained in your research record in accordance with Veterans Health Administration (VHA) and Federal Records Control Schedule policies.

How will your information be used in the future?

Your information or bio-specimens (blood or tissue) could be used for future studies or by another investigator for future research studies without your or your legally authorized representative's consent. Should this happen information that could identify you will be removed.

CONTACT INFORMATION

Who do you call for any questions, or in case you are injured?

If you have questions about this study, wish to express concerns or complaints about the research, or to report a research-related injury, you can contact:

Principal Investigator Dr. Alp Ikizler at this phone number 615-343-6104 or
After hours (24h access) number at this phone number: 615-343-7592.

If you have general questions about giving consent or your rights as a participant in this study or wish to discuss problems or concerns, offer input, or you want to make sure this is a valid VA study, or request information you can call the VA Tennessee Valley Healthcare System (VATVHS) Institutional Review Board Office at (615) 873-6076 or the Research and Development Service Office at (615) 873-8066.You may also contact the VATVHS Patient Advocate at (615) 873-7225 to discuss problems or concerns and ask questions not related to the consent process, offer input, or request information.

Statement of Volunteerism

Do I have to take part in this study?

You are not required to take part in this research study. Your participation is entirely voluntary. You can refuse to participate now, or you can withdraw from this study at any time after giving your consent without affecting your healthcare/services or other rights. This will not interfere with your regular medical treatment, if you are a patient.

What happens if you start the study and decide to stop later?
Contact the principal investigator at the contact number above if you want to be withdrawn from the study. Deciding to not be part of the study will not change your regular medical care in any way.
The PI may continue utilizing all data collected up to the point of your withdrawal.

STATEMENT & SIGNATURE OF PERSON AGREEING TO PARTICIPATE IN THIS RESEARCH STUDY:

Signatures. I agree to participate in this research project as described in this consent form. I will be given a signed copy of this consent form for my records. I have read or have had this consent form read to me.

- This study has been explained to me and all of my questions have been answered by the person obtaining consent. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. If I have questions later, I understand I can contact the researcher or a member of the research team.
- If I do not take part in this study, my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.
- I have been told my rights as a research subject, and I voluntarily consent to participate in this study. I have been told what the study is about and how and why it is being done. All my questions have been answered.
- A copy of this consent form will be forwarded to the VA Tennessee Valley Healthcare System Research Compliance Office.

SIGNATURES: (Note: ALL signatures and dates of signature below *are required* for legally effective research consent and HIPAA authorization.)

Study Participant Name (Print)	Study Participant Signature	Date