PARTICIPANT INFORMATION SHEET

MIDAS-HEART STUDY

Full study title: A research study to evaluate the relationship between cardiac microvascular dysfunction, diabetes and cardiac structural and functional abnormalities (MIDAS-HEART)

Chief Investigator: Dr Ify Mordi, Clinical Senior Lecturer and Honorary Consultant Cardiologist

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We need your help to better understand how the function of small blood vessels affects the function of the heart. Therefore, we're inviting you to take part in a research study.

This study is not a drug trial and you won't be asked to take any new treatments. The study tests and blood and urine sampling will take place at Ninewells Hospital. Before you decide whether or not to take part, it's important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully. Talk to others about the study if you want. Contact us if anything isn't clear, or if you'd like more information. Take time to decide whether or not you want to take part.

Why have I been invited to take part

We're inviting you because you're aged over 18 and you fall into one or more of the following groups:

- You're a healthy person with no known heart problem
- You've been diagnosed with heart failure or have changes on a heart scan that can sometimes lead to heart failure.
- You have diabetes (type 1 or type 2)
- You have high blood pressure

Why are we doing this research?

We'd like to invite you to participate in this study to look at the small blood vessels of the heart and how this relates to heart failure (HF). Although medical advances have led to improvements in treatments for some types of heart failure, there are still many things we can improve to help patients live longer, prevent hospital admissions, and improve quality of life. Previous studies have suggested that changes in the small blood vessels of the heart might contribute to changes in heart function that could lead to the heart not pumping as effectively as it should. These changes in the small blood

vessels are known as “microvascular dysfunction”. We are doing the MIDAS-HEART study to determine the role of microvascular dysfunction in the heart and elsewhere in the body on overall heart structure and function.

Both heart failure and diabetes can lead to microvascular dysfunction over time. Most of the treatments we have for these conditions do not specifically target small blood vessel function however, and we don’t fully understand which people are more likely to develop microvascular dysfunction initially and subsequently develop changes in heart function.

Before now, it has been difficult to assess the function of the small blood vessels in the heart. Most tests that we routinely use in the heart only look at the large blood vessels of the heart, however most of the heart’s blood supply is from the small blood vessels (up to 90%). Recently however, we’ve been able to use a special type of heart MRI scan to see how well the small heart blood vessels work. This gives us the opportunity to understand the relationship between small blood vessel function inside and outside the heart, and how this relates to overall heart function. We think that if we can understand the relationship between small blood vessel disease and heart function better, we could potentially develop new, much needed treatments to improve patients’ lives and prevent heart muscle damage.

Do I have to take part?

No, it’s up to you. Deciding not to take part won’t affect the healthcare that you get, or your legal rights.

How many people will be involved in this study overall?

We plan to study approximately 360 people within NHS Tayside.

This includes people with diabetes, heart failure or high blood pressure.

We will also include some people without any of these conditions.

What will happen if I take part?

The first thing we will do is to ask you to is to read the information provided in this leaflet in your own time. You are free to discuss this study with family, friends and anyone else you wish. You can also contact us if you have any specific questions. Once you have read the information, if you are happy to take part in the study then you can contact us to let us know, otherwise we will also contact you to see if you are interested.

If you are happy to take part, we will invite you to the Clinical Research Centre, at Ninewells Hospital in Dundee at a date and time that’s convenient for you. A member of the research team will explain the study and you’ll be able to ask any questions you want to. If you agree to go ahead, you’ll sign a consent form. We will give you a copy of the information sheet and signed consent form to keep.

You can either come on 1 occasion or 2 occasions within 2 weeks. If you come on 2 occasions, the assessments will be spread between the two visits– that is, anything performed on the first visit won’t be repeated on the second visit.

You'll need to make sure you haven't had any caffeine (tea, coffee or other drinks with caffeine in them) from 8pm the evening before. Other than that, you can eat and drink as usual before the visits. If you are having your MRI in the first visit you will be asked to avoid caffeine prior to you signing the consent form. You will be given clear instructions regarding this.

You'll be asked to provide some information about yourself and your health. We will then check that you are eligible to take part in the study.

The tests could be done in any order. If you agree to take part we will ask you to do all of the tests. A list is provided below. We anticipate that the full visit will take around half a day (i.e. a morning or afternoon). We will be able to provide refreshments during your visit.

BASIC EXAMINATIONS AND QUESTIONNAIRES

- We'll ask you about your **medical history.**
- We'll measure your height and weight.
- We'll carry out a **clinical examination**. This will be a brief general clinical examination where we will listen to your heart and lungs using a stethoscope and check for any signs of ankle swelling.
- You'll **complete between 1 and 3 questionnaires** about how your life is impacted by your health. There is one general questionnaire, a questionnaire for people with diabetes and a questionnaire for people with heart failure. You will only have to answer questionnaires related to you e.g. if you do not have diabetes you will not have to answer the diabetes questionnaire. The questionnaires are:
  1. Kansas City Cardiomyopathy Questionnaire (KCCQ) – this questionnaire asks 15 questions about how your heart failure symptoms may be affecting your life.
  2. Diabetes Treatment Satisfaction Questionnaire (DTSQ) – this questionnaire asks 8 questions about how you feel your diabetes treatment and glucose control.
  3. A general health questionnaire (EQ-5D-5L) – this asks you to rate how you feel about 5 aspects of your health and life in general. You will also be asked to rate your general health on a scale from 0 to 100.

BLOOD AND URINE SAMPLING

- We'll take a **blood sample** (of approximately 50mls, or 5 tablespoons). To do this a research nurse will insert a needle through the skin into one of your veins. Before this is put in the area will be swabbed clean. The needle will be removed after the sample has been taken and the area will be cleaned again and a plaster put on. You'll also be looked after while the sampling is being done and the nurse or doctor will stay with you at all times. Some of the blood samples will be analysed to measure your full blood count, kidney function, diabetes control (HbA1c) and heart stress markers (NTproBNP). With your consent remaining blood will be stored anonymously for future research.
- We'll ask you to give a **urine sample**. You'll do this in private. Some of the urine will be analysed to measure levels of protein in the urine (a marker of the function of the small blood vessels in the kidney). With your consent remaining urine will be stored anonymously for future research.

ECG, ECHOCARDIOGRAM AND MRI SCAN OF HEART

- We'll perform a **heart tracing (ECG)**. This is the same as a routine ECG test.
- We'll carry out a **heart scan (echocardiogram, an ultrasound test)**. You may have had one performed before as part of your clinical care. We'll put some stickers and some cold jelly on your chest before we take pictures by placing a probe on your chest. Sometimes people only have symptoms related to heart issues when they exert themselves, so as part of this test we'll perform this scan while you are lying down, and also after some exercise on a bicycle. You will perform the exercise for a set period based on your age, however the exercise is not to tire you out, and you will be able to stop exercising at any point if you wish. The test lasts around 30-45 minutes.
- We'll carry out an **MRI scan of your heart (cardiac MRI)**. The MRI gives us very detailed pictures of the heart. The MRI scanner is quite noisy, and some people can find it a little tight, particularly if they are claustrophobic. During this scan you'll have 2 drips inserted via a needle into your arm. One of these will be used to give a dye (contrast) that shows certain aspects of heart function, and the other will give a medication called adenosine. Adenosine lets us look at the small blood vessels of the heart. The adenosine drip is given for around 2-3 minutes. Some people feel a little uncomfortable when adenosine is used – for example you may feel a little short of breath or have some chest tightness. This is very short-lasting however, and once the adenosine is stopped these feelings pass within a minute. We will be monitoring you throughout the scan. **It is important that you do not take any caffeine from the night before the MRI scan.**
  If you have a continuous glucose monitor (CGM), you will have to take it off prior to the MRI scan and apply a new one afterwards.
  The MRI scan will last approximately 1 hour.

EYE PHOTOGRAPHY

- We will take a **photograph of the back of your eyes**.

SKIN BLOOD VESSEL TEST

- We will study the function of the **small blood vessels in your skin**. Two medicines will be used for this test. The first medicine is called Acetylcholine (Ach). Our body naturally has acetylcholine. It carries messages from your brain to your body through nerve cells. The second medicine is sodium nitroprusside (SNP). It dilates blood vessels. We will put two sticky rings (one filled with Ach and another filled with SNP) on your forearm and use a laser light to measure blood flow in your skin while Ach and SNP are applied to your skin. You might experience a mild tingling sensation but there should not be any pain. This test takes around 15 minutes. If you have had this test within the previous 6 months you will not need this again.

ACCESS TO YOUR MEDICAL RECORDS

- We'll ask you to allow us to **follow up your clinical care** for up to 5 years by reviewing your medical records. We will look to see whether you have had any heart-related issues over this period. You will not need to be recontacted for this.

OTHER TESTS THAT WILL BE DONE FOR SOME PEOPLE FOR SAFETY REASONS

- If there is concern that you may have had metal in your eyes at any point in your life, we may ask you to have **an x-ray of your eyes** before the MRI to make sure it is safe for you to enter the scanner.
- **CGM DOWNLOAD FOR PEOPLE WITH DIABETES** If you have a **continuous glucose monitor** we will, with your permission, download data on your glucose measurements over the previous 6 months.

All tests will either be performed in the Clinical Research Centre, Ninewells or the Division of Cardiovascular Research, Ninewells Hospital.

Follow up visit

You may also be asked if you would be willing to come back for a repeat assessment in approximately 2 years. Exactly the same tests will be done once again.

If you agree, we will recontact you at that time and will ask your permission to store your contact details so that we can get in touch with you again.

The research team will get in touch with you about a month before the repeat tests are due and will arrange a date and time. If your health status changes or you no longer wish to have a repeat visit please let us know.

What about travel expenses?

This is a charity funded project so you won't receive any payment for taking part but you can claim reasonable expenses for transport. The Clinical Research Centre in Ninewells has dedicated parking spaces for research patients, alternatively we may be able to organise a taxi for you to attend.

Is there anything I need to do or avoid?

The only thing you need to do is **not** have caffeine at breakfast or the evening before you come for each of the visits. You should wear clothing that is light or easily removable. We will provide you with a gown to wear for scans.

When you have joined this study please continue to manage your health conditions such as diabetes, heart failure or high blood pressure in your usual way unless your GP or other specialist advises otherwise.

What are the possible benefits of taking part in the study?

We already know that heart failure and diabetes are major public health issues worldwide. There may not be any direct benefits to you immediately from taking part in the study, however the information we obtain will be useful for us to understand the problems patients with heart disease and/or diabetes have. In future any study findings we make might be useful in understanding why heart failure develops and in developing new treatments for heart failure. The results of this study will be of interest to those involved in providing healthcare and may influence the way we use existing treatments and the advice we give.

If we do identify something that may impact on your clinical care we will tell you and your GP immediately. If you are interested we will send you a summary of the full study results by email or post – please let us know at any point.

What are the possible risks of taking part?

Please tell your study doctor or a member of the research team about any side effects or health problems you have while taking part.

The blood test will be no different to any you may have had before. If possible we will take blood at the same time as putting in a drip for your MRI scan so that we only need to do it once. The blood sampling has a very small risk of infection because we will make a hole in your skin. You can reduce the risk by keeping the area clean. There may be some bruising or redness of the area around the needle entry however this does not usually cause any issues. In rare instances some people faint or feel wobbly. We will stop the procedure if you faint or experience any distress so please tell us straight away if you can feel this coming on.

The echocardiography test can sometimes be a little uncomfortable as we occasionally need to press on your chest with the probe to get good pictures, but generally patients manage this without any problems. If you find that the exercise is too much (during the echo scan), you will be able to stop immediately.

During the ECG or testing the function of the small blood vessels in your skin, your skin may react to the sticky electrode patches. Any skin irritation usually disappears when the patches are removed. Please let us know if you have experienced a reaction before to the sticky patches.

An MRI scan is a safe and painless test that can provide detailed pictures of organs and other structures inside your body. Rarely, you may develop reactions to the contrast agent (dye) and adenosine. You may feel a little short of breath or have a tight chest during the infusion of adenosine and this feeling will pass very quickly once the infusion is stopped.

It is possible that we could identify findings that will affect your current clinical care, however, if we do, with your consent, we will let your GP or any other appropriate doctor know. This applies to both physical and mental health concerns – although the questionnaires are not designed to diagnose any specific mental health issues, if there are any concerns identified we would treat these in the same way as a physical health problem.

If at any point you have concerns, as well as discussing with the research team you can also discuss them with your GP or other relevant doctor (e.g. cardiologist).

What will happen if I don't want to carry on with the study?

You can withdraw your consent to take part in this research at any time. You're under no obligation to complete the study.

You can withdraw without this in any way affecting your future medical care or your relationship with medical staff looking after you. If you wish to withdraw, you simply need to inform a member of the research team.

With your permission, any data collected prior to withdrawal will be stored anonymously for analysis purposes. Contact details for the research team can be found on the last page of this information sheet.

What will happen to my blood and urine samples?

The blood and urine samples will be stored in the laboratories of the University of Dundee. With your consent, the samples may be used in other approved research projects. The samples will be destroyed after 10 years from the date the study ends.

Will my GP be informed?

With your permission only, we will write to your GP to let him/her know that you are taking part in this study. We may ask you to visit your GP if we decide you might need this.

What will happen to the results of the study?

When the study is finished, we will write the study results for publication in an open scientific access journal. This scientific publication will be available right across the world but will not include any information or results that could identify you. The results of the study will be stored in a locked dataset. Any results or information that could identify you will not be passed on to third parties.

What about future research?

Some of the information and blood and urine samples we collect may be stored and used for future research. After the study there may be some extra blood and urine that we wish to store for future research. This will be stored in the Division of Cardiovascular Research and registered with the Tayside Biorepository. This research will always use anonymous information. Results may be shared anonymously with other researchers and collaborators, including commercial organisations. You will never be able to be identified.

Who has sponsored and organized this study?

This study has been sponsored by the University of Dundee and is organized by Dr Ify Mordi. The study is funded by the British Heart Foundation, the leading heart disease charity in the UK.

Who has reviewed this study?

This study has been reviewed and approved by the University of Dundee and the East of Scotland Research Ethics Committee who are responsible for reviewing research which is conducted in humans. The Research Ethics committee does not have any objections to this study going ahead.

Will my taking part in the study be kept confidential?

It is a requirement that your records in this research, together with any relevant medical records, be made available for examination by regulatory authorities, monitors from the study Sponsor, the University of Dundee.

Any information we collect about you and your healthcare records, and the results we obtain will remain strictly confidential. All information will be held on a secure database that will be accessible only to staff directly involved in the project. Your personal details (name, address, date of birth, etc.) will be held separately from the other information collected. Your details will not be given to any third party, nor will it appear in any report or publication that arises from this study.

Insurance

The University of Dundee holds Clinical Trials indemnity cover which covers the University's legal liability for harm caused to patients/participants.

What if something goes wrong?
If you are concerned about your participation in the study you have the right to discuss your concern with a researcher involved in the study or a doctor involved in your care.
If you have a complaint about your participation first of all please talk to the researcher.
If you are not satisfied, you can make a formal complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside.

Complaints and Feedback Team
Ninewells Hospital Dundee DD1 9SY
Freephone: 0800 027 5507
Email: TAY.feedback@nhs.scot

If you think you have come to harm due to taking part in the study there are not any automatic arrangements to get financial compensation. You might have the right to make a claim for compensation. If you wish to make a claim, you should think about getting independent legal advice but you might have to pay for your legal costs.

How will we use information about you?

We will need to use information from you and your medical records for this research project. This information will include your:

- Age
- Gender

- Ethnicity
- Medical health records (including previous and future details of your medications, blood test results, details from relevant clinic letters (for example cardiology or diabetes clinics) and hospital admissions)
- CHI number

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

The University of Dundee is the sponsor of this research and is responsible for looking after your information. We will keep all information about you safe and secure by:

- Ensuring all identifiable electronic information is password-protected
- Only approved users will have access to identifiable information
- Any paper records will be stored in secure, locked rooms

Your data will not be shared outside the UK.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. We will keep your anonymised study data for a maximum of 15 years. The study data will then be securely archived or destroyed.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Your information will be kept safe and secure by the research team at the University of Dundee, in line with the General Data Protection Regulations (GDPR) (see https://www.gov.uk/government/publications/guide-to-the-general-data-protection-regulation) and the Data Protection Act 2018 (see https://www.gov.uk/data-protection).

Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at **www.hra.nhs.uk/patientdataandresearch**
- by asking one of the research team
- by sending an email to **xxxxxxxxxx**, or
- by ringing us on xxxxxxxxxx.

If you have further questions?

If you would like to discuss this study with someone who is independent of the study please contact Dr Anna Barnett (NHS Research Scotland Diabetes Network) on 01382 383455 or a.l.z.barnett@dundee.ac.uk.

You can also contact the Patient Advice and Support Service for free, confidential and independent advice for patients of the NHS in Scotland at https://www.cas.org.uk/pass or you can telephone them on 0800 917 2127.

Contact details for the research team?

If you have any questions regarding this study, you can write or telephone at the addresses shown below:

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Telephone: 01382 383199

Thank you for taking the time to read this information and considering helping us with our study.