The Association of Ectopic Fat and Cardiovascular Disease in People Living with HIV and General populations: A cross sectional analysis

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Sponsor	University of Liverpool
Joint-sponsor(s)/co-sponsor(s)	
Funder(s)	British HIV Association
Clinical Trials Unit	Clinical Research Facility, Liverpool University Hospitals Foundation Trust
Key Protocol Contributors	Professor Saye Khoo Dr Richard Fitzgerald

Invitation

You are being invited to participate in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read this sheet carefully and discuss it with friends, relatives, and the study team. You may also wish to discuss this with your GP. Ask us about anything that is not clear and take time to decide whether you wish to take part.

What is the purpose of the study?

This study is designed to investigate differences between people living with HIV (PLWHIV) and general populations on how the body utilises and stores energy. This study uses magnetic resonance imaging (MRI) to measure fat around the body organs including the heart and liver. The fat around body organs, also known as visceral fat, is known to be associated with metabolic syndrome and a risk factor for developing heart attacks and strokes.

MRI scans are used frequently in hospitals to diagnose a range of conditions. These scans use radio waves to measure protons in body tissues. The machines can reconstruct tissues using complex algorithms to form composite images of body structures. MRI scans do not use ionising radiation and there is no risk to undertaking an MRI in terms of radiation.

We often use MRI scans to assess the hearts' structure and function. In addition, we can use specific MRI sequences to assess the integrity of heart muscle. Heart MRI is often considered the gold standard imaging technique to assess the heart and heart muscle disease. This study will use multiple MRI sequences to assess the heart and the liver. We are aiming to investigate any changes in heart and liver fat. In addition, we will assess any changes in fat levels within the heart muscle cells whilst also assessing for any change in the way the heart is functioning.

PLWHIV have roughly double the risk of heart attacks compared to general populations. Previous studies have demonstrated that this increased risk may arise from the way in which fat is stored and metabolised in the body. We hope this study will give insight into why HIV-positive individuals have increased risks of heart attacks and how reducing visceral fat may reduce risk. It may lead to further medicines or treatment strategies to reduce the risk of heart attacks in HIV-positive individuals.

Do I have to take part?

It is up to you to decide whether to take part in the study. Participation is entirely voluntary. If you do decide to participate you will be given this information sheet to keep and be asked to sign a consent form. You will receive a copy of the signed consent form to keep. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

What will happen to me if I take part?

You will be invited to undergo an a screening visit. If you agree to take part in this study, we will undergo routine medical history and examination (if required). We will also take a blood test to measure specific biomarkers and to store blood for potential furture research. An ultrasound scan of your liver will be performed (also known as a FibroScan). This will assess for evidence of scarring to the liver and fat around the liver. The ultrasound scan is painless and uses ultrasound waves (there is no risk from radiation from this scan).

We are also conducting a sub-study to assess differences in subcutaneous fat. If you consent then you will undergo subcutaneous fat biopsy. This is a small needle into fat tissue to obtain fat cells. You will then be invited for a MRI at University of Liverpool.

The GP record and inpatient electronic record will be accessed annually by the study team to record new diagnoses. This will occur for up to 5-years of follow up.

Sub-study

The aim of the sub study is to evaluate specific changes within the fat cells in relation to the biomarkers obtained in blood and imaging data generated from the MRI. We will analyse the fat biopsy for activation of certain proteins and genes and how this may relate to health and disease. The fat biopsy requires a small needle to obtain the fat from under the skin. The fat samples are then stored at the University of Liverpool and kept for 10 years. You do not have to consent to the sub study.

Future Studies

If an individual participant gives consent, then a blood sample will be taken and stored at a securely at the nominated biobank. These blood samples may be used in future studies to look at how an individual's genes are related to disease development. There may also be future analysis of how certain proteins are produced from these genes. These samples will

be stored in a dedicated facility at the University of Liverpool for a maximum of 10 years.

By signing the relevant section of the consent form you are agreeing for a sample of your blood to be stored and potentially used in any future research study. There will be no storage of patient identifiable information.

You can still participate in the study if you do not wish for your blood samples to be stored and potentially used in future studies.

What can I expect from the MRI?

The MRI is housed at the Liverpool Magnetic Resonance Imaging Centre (LIMRIC) which is on the University of Liverpool campus. It is on the same geographical footprint as the Royal Liverpool University Hospital. You will be met by a member of the study team to walk across to LIMRIC. There is a waiting room with refreshments available. Once you arrive you will be asked to remove any metal that you may be wearing or carrying. You will complete an MRI safety questionnaire and asked to sign it to ensure that you are safe to have the MRI. Once you have completed the safety form you will be invited to change into a hospital gown (secure lockers provided) and invited into the scanning room.

You will have several ECG stickers placed on your chest area. This allows us to monitor your heart rate whilst you are in the scanner and allows us to time the scan with your heartbeat. You will then have the receiver placed over your chest. This allows us to obtain the detailed images of the heart. You will also be given sound blocking earphones. Once you are set up the scan will begin. You will go into the scanner, and we will start to take the pictures. Some of the images require you to hold your breath for several seconds and the radiographer will talk to you through the headset to advise you on this. The scan usually takes approximately 45 minutes but may last up to an hour in some circumstances. Once the scan is finished the radiographer will come into the room and take the ECG stickers and receiver off. You will then be invited to get changed.

Is there any risk involved with the MRI?

There are no risks involved with the MRI. The scan uses radio waves and therefore there is no radiation administered. Some people may experience a discomfort from lying in the scanner and some people may experience claustrophobia when in the scanner. You will have full communication with the radiographer, so if you feel that you cannot continue with the scan, , we can bring you out the of scanner quickly.

Are there any benefits to taking part?

You will have a full assessment of your visceral fat in the liver and the heart. Visceral fat is a marker for metabolic disease which is a significant risk factor for heart attacks, strokes, dementia, and various forms of cancer. In addition, you will have an assessment of the heart. Heart MRI is considered the gold standard for assessment of the heart structure and function.

You will also be told about any changes in the levels of visceral fat after taking part in the study and any changes to heart structure and function.

This information will be useful as it will give you an overall idea about your risk of future disease and how diet and exercise has affected this risk. In addition, you will receive detailed information on the heart structure and function which some participants may find useful.

Will my taking part in this study be kept confidential?

If you agree to take part then the parent team will forward your contact details, including name, address and telephone number, to the study team to book the study visit. Once the study has finished, we will delete your personal identifiable information in a secure way. The study visit is conducted at the Clinical Research Facility located at Royal Liverpool University Hospital on 4th floor.

All the information collected about you during the study will be kept strictly confidential. All study (clinical) data will be anonymised and you will be identified by a trial identification number. Your anonymised study information will be kept on a secure database at the University of Liverpool. The database used is specifically designed for use in clinical trials and has robust security and its integrity is maintained by dedicated staff.

Data Transparency

University of Liverpool is the sponsor for this study. The University of Liverpool will keep identifiable information about you for 5 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information by contacting a member of the study team as detailed below.

What will happen to the results of the study?

We will combine all the results from the subjects taking part in the study and publish any important results in medical journals. Results presented at scientific meetings may also be viewed at our website http://www.hiv-druginteractions.org/AbstractsAndPosters.aspx. No individuals will be specifically identified in any publication.

Who is funding the study?

The study is funded by the British HIV Association

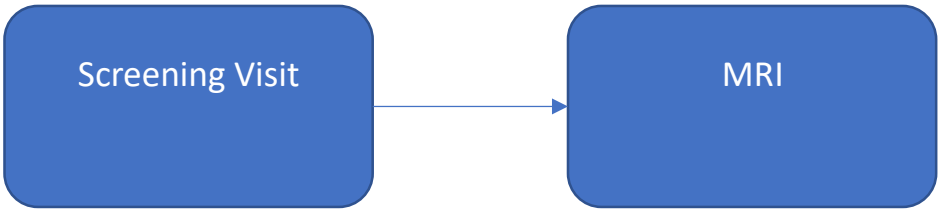
Who has reviewed the study?

This study has been reviewed by the University of Liverpool Research Sponsorship Committee and the Research Ethics Committee for NHS based research

Will I receive financial incentive?

There is no financial reimbursement for this study.

Study Schema



For further information about this study please contact:

Dr Thomas Heseltine, Consultant Cardiologist, Department of Pharmacology, University of Liverpool, 0151 794 5560 or Dr Thomas Heseltine, 0151 706 2000.

Study nurse_____

Telephone number_____ E-

Email_____

Participant Consent Form

Thank you for reading the information about our research project. If you would like to take part, please read and sign this form.

Please initial boxes

1. I confirm that I have read and understand the information sheet dated ..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that I will not benefit financially if this research leads to the development of a new treatment or medical test. ☐

3. I understand how to contact the research team if I need to, and how to get information about the results of the research. ☐

4. I agree to take part in the above sub-study. ☐

5. I agree for my blood sample to stored and used for potential future research projects

.....	.....	.....
Name of subject (BLOCK CAPITALS)	Date	Signature
.....	.....	.....
Name of person taking consent (If different from researcher)	Date	Signature
.....	.....	.....
Name of Researcher	Date	Signature