Resistant Hypertension – Pathological Insights from Cardiac Mechanics

"Changes in the Heart and Blood Vessels Due to Poorly Controlled Blood Pressure"

PARTICIPANT INFORMATION SHEET- HIGH BLOOD PRESSURE

We would like to invite you to take part in a research study which is looking at the changes that occur in the heart and blood vessels due to poorly controlled high blood pressure. Before you decide whether to participate, it is important for you to understand why this research is being done and what it will involve. Please take time to read the following information carefully and feel free to ask us if you would like more information about the study or if there is anything that you do not understand. Please also feel free to discuss this with your friends and relatives if you wish. We would like to stress that you do not have to accept this invitation and should only agree to take part if you want to.

This study will be based at Liverpool Centre for Cardiovascular Sciences, (Liverpool Heart & Chest Hospital).

Thank you for reading this.

1. What is the purpose of the study?

People with poorly controlled high blood pressure suffer a high rate of complications, including stroke (brain cells damage due to lack of oxygen), heart and kidney failure. This study will help us to better understand the effects of high blood pressure on the heart and blood vessels. We want to see if having high blood pressure can damage the blood vessels or affect the heart function and the nervous system (part of the nervous system responsible for the control of blood vessels). We will also investigate whether better blood pressure control can improve the functioning of the heart and blood vessels.

2. Why have I been chosen to take part?

You have been invited to take part in this research study because you have high blood pressure.

Our study will invite and include 3 groups of people to participate:

- The first group are patients with so-called resistant hypertension. This means that blood pressure remains high despite the use of three or more blood pressure lowering tablets at the same time, one of which is a water tablet (diuretic). A person with resistant hypertension has a blood pressure that is typically above 140/90 mmHg.
- The second group are patients with controlled hypertension. This means that blood pressure is lowered below 140/90 mmHg by the use of blood pressure lowering tablets.
- The third group are people with normal blood pressure.

All eligible participants should be:

1. Aged above 18 years old
2. Able to voluntarily agree to take part in this research study after being informed about all the procedures involved
3. Participants with resistant hypertension (as described above)
4. Participants with controlled essential hypertension (as described above)
5. Participants with normal blood pressure

Participants with the following conditions will be excluded from the study:

1. Body mass index ≥ 30kg/m^2
2. Moderate to severe heart valve disease
3. Cardiomyopathies (diseases of the heart muscle)
4. Previous myocardial infarction (heart attack) or current symptomatic coronary artery disease (chest pain relieved by the use of medication)
5. Recent (<6 months) stroke (brain cells damage due to lack of oxygen)
6. Active infections or fever
7. Active long time and systemic illnesses (e.g., Type 1 diabetes, lung problems, kidney or liver failure, diseases of the brain and nerves)
8. Atrial fibrillation (irregular heartbeats that affects the heart's upper chambers known as atria)
9. Pregnancy

3. Do I have to take part?

No. It is entirely up to you to decide whether or not to take part in this study. There are no obligations. If you do decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to take part and later change your mind, you are still free to withdraw at any time during the study and without giving a reason. This will not affect the standard of care you receive.

4. What will happen if I take part?

If you choose to take part in this study, then it would mean coming to the Liverpool Heart & Chest Hospital for a scheduled visit that is convenient for you. People with normal blood pressure and controlled hypertension will attend the study on one day only, and people with resistant hypertension will need to come on two separate days.

Before consent

- Once you have read this form, you will be given a follow up telephone call within one week to discuss the information you have received. If you need more time, another phone call will be arranged (a second telephone call is only made if you ask for more time to decide). A researcher will talk to you by phone to make sure that all of your questions have been answered and will take great care to check that you fully understand what is involved in this study before you decide to participate.
- If you agree to participate, we will schedule a visit for you to come to Liverpool Heart & Chest Hospital so we can inform you about the study, gain your signature on a consent form and perform the study related activities in the same visit.

Study preparation

In preparation for the study we will ask you to:

- Avoid eating or drinking anything for at least 6 hours before the study visit.
- Not to drink alcohol or any caffeine or energy drinks such as coffee, coke or red bull for 12 hours (overnight) before the study visit and on the same day of the study visit.

- Not to take your morning blood pressure lowering tablets on the study day. Please bring these tablets with you to take them after the research tests are finished by late morning. This instruction would be completely specific to the tablets for the heart and blood vessels disease of relevance and reviewed by a qualified physician.
- Not to smoke for 6 hours before the study visit and on the day of the study visit (prior to testing).
- Not to exercise on the day before the study visit and on the day of the study visit (prior to testing).

Study day – 1st visit

The study visit will take place in the morning and will last for approximately 3 hours. The visit will be arranged at a time and day that is convenient for you. On the study day, we will explain to you the study procedures and we will answer all your questions and then we will ask you to sign a consent form to participate in this study.

The study will involve the following procedures as shown in (figure 1) below:

1. Clinical assessment (height, weight, hip and blood pressure measurements).
2. Electrocardiogram/ECG (heart tracing) for 10 min: This is a painless, simple medical test to check your heartbeats. Sticky patches will be placed on your chest to record your heart's electrical signals.
3. Vascular tests (tests to study your blood vessels):
    A. Blood vessel function test: We will use ultrasound to look at the blood vessels in your upper arm for 10 minutes. During this time, we will inflate a cuff, (just like one used to measure blood pressure), below your elbow for 5 minutes. This is painless but you may get pins and needles, this will resolve when the cuffs are released.
    B. The stiffness of your arteries will be measured from the recordings of the pulse from your arm. A usual blood pressure cuff will be placed around your arm to measure blood pressure and pulse.
4. Standard Echocardiography test (heart ultrasound scan) that uses sound waves to produce a picture of your heart to assess its structure and function. This is a safe and painless test. We will apply some gel to your chest then a small probe will be moved at different areas across your chest to take pictures of the heart.
5. A blood sample will be taken from a vein in your arm using a small flexible cannula placed by trained researcher. The amount of blood that will be drawn from you is about two tablespoons. We will use it to run a routine blood test at Liverpool Heart and Chest

Hospital laboratory (unless you already had it within the last 6 months). The rest of the blood will be labelled and sent to be processed for later analysis of specific markers of blood vessels function, which will be done at Liverpool Heart and Chest Hospital laboratory, the University of Liverpool laboratory or Liverpool John Moores University laboratory. The blood sample will be stored in the research laboratory at the Liverpool Centre for Cardiovascular Sciences for ten years after which it will be destroyed in accordance with the Human Tissue Authority's Code of Practice. The research facility is kept locked and alarmed at all times and has restricted access.

6. 24-hour blood pressure monitoring (only if you have resistant hypertension). This is done the same way as for the routine diagnosis of blood pressure. We will place a blood pressure cuff around your arm and a small device at your waist to take blood pressure measurements over 24 hours. We will ask you to bring them back on the next day and travel reimbursement will be provided.

After the study tests have been completed, refreshments including snacks, hot and cold drinks will be provided to you.

Study day – 2nd visit (follow up)

Only if you have resistant hypertension, a second visit (follow up visit) will be arranged after 8 weeks of completing the first visit. The follow up visit procedures will be the same as the first study visit.

Coronavirus (COVID-19) safety precautions:

In response to the coronavirus (COVID-19) pandemic, the following safety precautions will be followed in our study:

- We, the research team, will work in line with the current UK government and NHS guidance during the process of conducting the research study, including social distancing (at least 1 metre), the use of gloves/face masks/gowns and equipment sterilisation procedures.
- All study equipment/tools will be continuously cleaned and sterilised.
- You are advised **NOT TO ATTEND** hospital if you have coronavirus symptoms or have been in contact with a person who has coronavirus.
- If you need to be accompanied, you are allowed to bring **ONLY ONE** relative/carer/accompanying person with you to the appointment. The same safety precautions will be applied to the accompanying person.

- Upon arrival at the research venue, you will be advised to follow some key instructions: clean your hands using hand sanitiser or water and soap (will be available in the study area), wear a face mask, maintain safe distance (at least 1 metre) between you and others and avoid touching your eyes, nose and mouth.

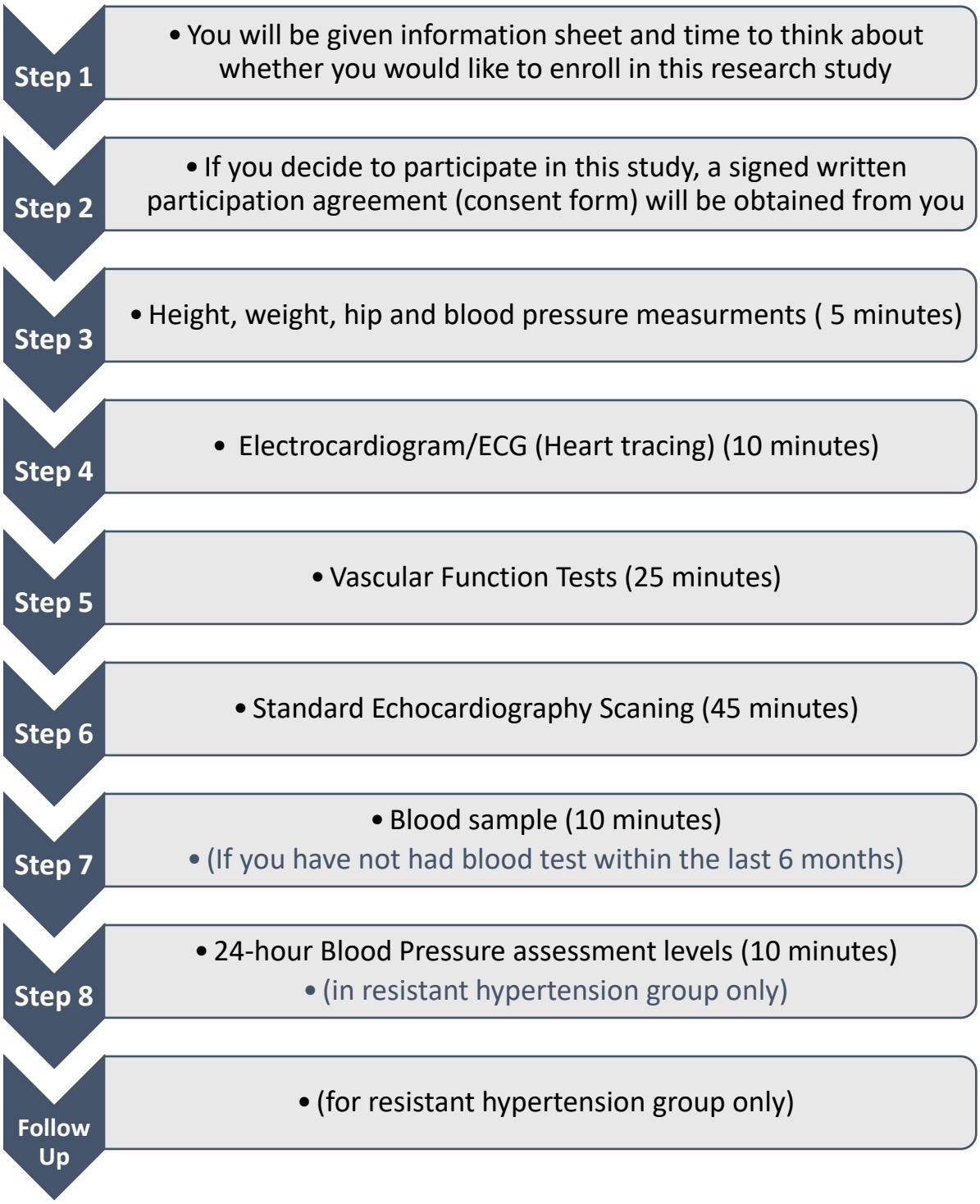

Figure 1: Study Procedures Flowchart (total time ~ 3 hours)

5. Who the researchers are?

The research team consists of:

- Professor Gregory Y H Lip (Consultant Cardiologist, Professor of Cardiovascular Medicine, Liverpool Centre for Cardiovascular Science, University of Liverpool)
- Mrs Azhar Akhmimi (PhD student, Liverpool Centre for Cardiovascular Science, University of Liverpool)
- Dr Alena Shantsila (Tenure Track Fellow, Liverpool Centre for Cardiovascular Science, University of Liverpool)
- Dr David Oxborough (Reader in Cardiovascular Physiology, Clinical Cardiac Physiologist, Liverpool Centre for Cardiovascular Science, Liverpool John Moores University)
- Dr Tori Sprung (Senior Lecturer Physical Activity and Cardiovascular Physiology, Liverpool John Moores University)

6. Expenses and /or reimbursement

Prepaid parking tickets and public transport tickets will be provided and this including the travel reimbursement for returning the blood pressure monitoring device. After the study tests have been completed, refreshments including snacks, hot and cold drinks will be provided.

7. Are there any risks in taking part?

Study procedures are carried out by trained researcher who have experience with all the procedures described. However, there might be minor issues that you may or may not face such as:

- You may experience some discomfort and/or get a small bruise when the blood sample is taken from your arm.

The following precautions are in place to ensure your safety and minimise the risks. All blood samples will be collected by experienced clinical research staff under hygienic conditions. If you experience any distress following participation you are encouraged to inform the researcher and you are still free to withdraw at any time during the study and without giving a reason.

8. Are there any benefits in taking part?

While there are no immediate benefits for those people participating in the project, it is hoped that the results that we get from this study will help us to understand more details about the patients who do not respond to blood pressure-lowering tablets (resistant hypertension patient group) and possibly improve future treatment of these patients. During the course of the study if we find anything of clinical importance, we will inform your GP so appropriate action can be taken.

9. Will my participation be kept confidential?

Yes, all of your personal information, study data and appropriate documentation will be kept secure and will be accessible only to the members of the research team and will not be shared with anyone outside the research team.

10. How will my data be used?

The University processes personal data as part of its research and teaching activities in accordance with the lawful basis of 'public task', and in accordance with the University's purpose of advancing education, learning and research for the public benefit.

Under UK data protection legislation, the University acts as the Data Controller for personal data collected as part of the University's research. The Principal Investigator Professor Gregory Lip acts as the Data Processor for this study, and any queries relating to the handling of your personal data can be sent to [Principal Investigator / Email: Gregory.Lip@liverpool.ac.uk , Tel.: 01517065735/ 0151794 9020].

Further information on how your data will be used can be found below:

We will be using information from you and/or your medical records in order to undertake this study. This means that we are responsible for looking after your information and using it properly.

All the information that we collect about you during the course of the research will be kept strictly confidential. This information will be will be anonymized (identified according to a code number) known only to those directly involved with this project. All information will be kept securely on a locked desk/filing cabinet and/or a locked room at the Liverpool Centre for Cardiovascular Science at Liverpool Heart and Chest Hospital. All data entered into an electronic database will be password protected, with limited access to members of the research team.

Your data will be stored for 10 years after the completion of the study [until 2030] on secure Liverpool Centre for Cardiovascular Science server at Liverpool Heart and Chest Hospital.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways so that the research is 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. With your permission, your GP will be informed that you are taking part.

You can find out more about how we use your information by contacting [The researcher Azhar, Tel: 07469072318].

11. What will happen to the results of the study?

The results will be summarised and reported in a dissertation/thesis and may be submitted for publication in an academic or professional journal. If the result of the research will be published, you will not be identified in any report or publication. A lay summary report of the study results will be sent to your home address or provided to your email address, if you allowed to contact you for access to feedback on the study results.

12. What will happen if I want to stop taking part?

You are under no obligation to take part in this study; your medical care will not be affected in any way. You can withdraw from the study at any time without any pressure, and it will not affect your usual care in any way. If you decide to withdraw, please contact the study team (please see contact details below).

If you decide to withdraw from the study or you lose the capacity to consent during the study, your identifiable data or blood sample already collected with consent will be retained and used in the study. No further data or tissue would be collected, or any other research procedures carried out on or in relation to the participant.

13. Who is organizing the study?

The research study is being organised by the University of Liverpool, Liverpool Centre for Cardiovascular Science.

14. What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please feel free to let us know by contacting [Principal Investigator, Tel.: 01517065735/ 0151794 9020] and we will try to help. If you remain unhappy or have a complaint which you feel you cannot come to us with then you should contact the Research Governance Officer at ethics@liv.ac.uk. When contacting the Research Governance Officer, please provide details of the name or description of the study (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make.

The University strives to maintain the highest standards of rigor in the processing of your data. However, if you have any concerns about the way in which the University processes your personal data, it is important that you are aware of your right to lodge a complaint with the Information Commissioner's Office by calling 0303 123 1113.

15. Who can I contact if I have further questions?

If you have more questions, or you do not understand something in this information letter, please contact our study team who will do their best to answer your questions (please see contact details below). Alternatively, you can speak to Dr Rajiv Sankaranarayanan (Consultant Cardiologist), Tel: 01515292721, Email: Rajiv.Sankaranarayanan@liverpoolft.nhs.uk.

Contact Details of Researchers:

Principal Investigator:

Professor Gregory Y H Lip (Consultant Cardiologist, Professor of Cardiovascular Medicine)

Address: Liverpool Centre for Cardiovascular Science, Institute of Ageing and Chronic Disease, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool, L7 8TX

Tel.: 01517065735/ 0151794 9020, Email: Gregory.Lip@liverpool.ac.uk

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Thank you for taking the time to read this Patient Information Sheet and considering whether to take part in the study.

NOTE: PLEASE KEEP THIS INFORMATION SHEET IN A SAFE PLACE