

**Participant Information and Consent Form**

**Title:** Screening for cardiac amyloidosis in patients with newly identified conduction disease.

**Principal Investigators:** Dr Jithin Sajeev

**Associate Investigators:** Dr Timothy Scully, A/Prof Stephen Ting, A/Prof Andrew Teh, Dr Brendan Wisniowski, Dr Jason Nogic, A/Prof James Hare.

**HREC Reference number:**

**Site:** Box Hill Hospital, 8 Arnold St, Box Hill 3128.

# 1 Would you like to take part in this clinical study?

You are invited to take part in the above study as you are about to have a permanent pacemaker placed due to a problem with the electrical system in your heart. This electrical problem, also known as conduction disease, is a common problem in older adults and is most often due to ageing causing progressive damage to the electrical system. However, there are other rarer causes of conduction disease including autoimmune diseases, infiltrative diseases, heart attacks or medications.

# 2 Why are we doing this research?

Cardiac amyloidosis is an infiltrative condition where proteins produced by your liver or immune system inappropriately deposit into your heart muscles and electrical system. The deposition of these proteins may lead to damage to the muscles of the heart, resulting in heart failure. Alternatively, if these proteins deposit into the electrical system, the first sign of cardiac amyloidosis may be conduction disease.

The aim of our study is to determine what proportion of patients aged 65 or older presenting with electrical problems requiring a pacemaker have underlying cardiac amyloidosis. We estimate around 5% of patients have cardiac amyloidosis.

# 3 Do I have to take part?

If you don’t wish to take part in the clinical study, you don’t have to. If you decide to take part and later change your mind, you are free to withdraw at any stage. If you choose not to take part, or if you choose to take part and then later withdraw, you will still be able to access your usual medical care. Your choice will not affect your relationship with those treating you, or with this institution.

If you choose not to join the study, the study doctor will discuss other options with you.

We must keep any information we collect about you, up until you withdraw. The institution conducting the study, has access to this information so they can check it is correct. If you do not agree with this then we cannot allow you to join the clinical study.

# 4 What is involved in the study?

The screening for cardiac amyloidosis involves two imaging tests and blood tests. The first imaging test is a cardiac pyrophosphate scan, a type of nuclear medicine imaging test, which involves the injection of a radiotracer into the body and then special cameras used to detect where this radiotracer deposits in the body. If a large proportion of this radiotracer deposits in the heart region, this is highly suggestive of cardiac amyloidosis. This test does involve a small dose of radiation, equivalent to that of a standard chest x-ray. Rarely, some patients do have an allergic reaction or feel nauseated by the radiotracer. This test is conducted at Box Hill Hospital, in our nuclear imaging department. The scan takes 2 hours and the results should be available within 2 days.

The second imaging test is a transthoracic echocardiogram, which is an ultrasound of your heart. This is usually conducted for patients with conduction disease and so you may already be booked for this test as it is standard of care. The test is done at Box Hill Hospital and there are no risks associated with an echocardiogram as it is non-invasive and uses ultrasound beams, which have no radiation.

The blood tests are to assess if you have an underlying blood disorder that results in too much immunoglobulins being produced, which can lead to cardiac amyloidosis. There are also two additional blood tests that allow us to determine the degree of cardiac amyloidosis present, if any is detected. These blood tests will be done at the same time as your regular blood tests you will get prior to your pacemaker insertion. No additional blood is required and there are no additional risks associated with these blood tests.

In some situations, the above studies are not adequate to make a diagnosis of cardiac amyloidosis. In some patients, the blood tests may show the presence of an underlying blood disorder, which may be causing cardiac amyloidosis or may be completely unrelated. In these situations, we would encourage patients to meet with a Haematologist at Eastern Health to discuss if a bone marrow biopsy or biopsy of another body part may be helpful in clarifying the diagnosis. There would be no obligation to proceed with further screening tests in this situation. The risks of a bone marrow biopsy include bleeding, pain and infection. A more thorough discussion of the risks and benefits of a bone marrow biopsy would be detailed if you require one.

Alternatively, some patients may have early stages of amyloidosis that are not well seen on the nuclear scan. In this situation, a cardiac MRI would be required to further investigate. A cardiac MRI would be performed at the Victorian Heart Hospital as Eastern Health does not have access to this machine. The risks of an MRI are minimal unless you have pre-existing metal in your body that is not compatible with the MRI scanner. If this is the case, you will not be able to have an MRI. As you will have a new pacemaker after today, you will not be able to have the MRI for 6 weeks as the results of an MRI are unreliable in the first 6 weeks after pacemaker placement. Finally, some patients find the cardiac MRI to be claustrophobic. You are under no obligation to have a cardiac MRI if you wish not to. Not all patients will be required to have an MRI but it is impossible to predict who may require one until the initial screening tests are done.

Finally, in very rare cases, a biopsy of the heart may be required to diagnose cardiac amyloidosis. If you are in this very small group of patients, you would be offered referral to the Alfred Hospital to discuss the procedure of a cardiac biopsy, which is done via a vein in your neck and tubes placed to the heart, there is no surgery required. The risks of a cardiac biopsy include bleeding, pain, infection and potential damage to the heart. A more thorough discussion of the risks and benefits of a cardiac biopsy would be detailed if you require one. There would be no obligation to proceed with further screening tests in this situation.

We cannot promise you any personal benefits from this research. It is possible that potential benefits of participating includes earlier diagnosis of cardiac amyloidosis if you have this condition. There is a large body of evidence to suggest that the diagnosis of cardiac amyloidosis is often missed and patients do have better outcomes if the diagnosis is reached earlier in the disease process. You would also have access to the amyloidosis clinic at Eastern Health to guide both follow up and treatment options. This would only be required if cardiac amyloidosis is identified during the screening process. The risks of participating in this trial is the risks detailed above with the screening tests. Most patients who choose to participate will only be required to have the additional nuclear bone scan but it is impossible to identify who may require the more invasive screening tests. By taking part, you may be helping other people in the future by improving our understanding of which patients with conduction disease should be screened for cardiac amyloidosis.

Your enrolment in this study is voluntary, if you don’t wish to take part you don’t have to. You will receive the best possible care whether or not you take part. If you do choose to participate but later change your mind, you can withdraw from the study at any time.

This project is being undertaken by the Department of Cardiology, Eastern Health. Ethical aspects of this research have been approved by Eastern Health Human Research Ethics Committee in accordance with National Statement on Ethical Conduct in Human Research (2023).

# 5 Who is conducting and paying for this research?

Some of the tests, medication and or treatments used in this study may be part of standard care used to maintain your health even if you did not take part in the study. You will be responsible for the cost of this standard care in the usual way (health insurance, Medicare and your personal contribution depending on your circumstances).

All treatment, medication and study-related tests will be provided at no cost to you. You should ask the study doctor to explain any payments for which you may be responsible.

# 6 What if something new comes up during the study?

If we find something new about an intervention while the study is under way, the study doctor will discuss with you what it means and whether you want to continue in the study. If you decide to continue in the clinical study, we will ask you to sign an updated consent form.

# 7 What will happen to the confidential information about me?

As part of the study we will need some of your personal details (name, gender, age and address) and medical history including your current medications. We will keep all personal information confidential and securely stored.

All of the collected data will be coded. No personal information about you, such as your name and address will leave the clinic, and in all study information sent out from the clinic you will be identified with a code number only.

# 8 What are my responsibilities during the study?

If you agree to participate in this study, you agree to be responsible for participating in the initial screening tests of a nuclear bone scan and blood tests according to our instructions. You also agree to comply with the other conditions in this document. If you cannot, or do not wish to accept this responsibility, then we cannot accept you as a participant in the study.

# 9 Can I have other medicines or procedures during this clinical study?

You must tell us about any procedures or medicines you may be using. This is in your interest as well as important for the study, because they may interact or interfere with the tests. You must tell us about any prescription or over-the-counter medications, vitamins or herbal remedies you are taking.

# *10 Will you be doing any genetic tests?*

As a separate part of our research, we will be undertaking some genetic tests for those that are diagnosed with cardiac amyloidosis. We will give you information about that sub-study on a separate document for you to consent to the genetic tests. You do not have to participate in the tests if you do not wish to do so.

# 11 What happens if I suffer severe side effects as a result of my participation in this study?

If you suffer any complications as a result of this study, please contact us as soon as possible. In case of an emergency, contact 000.

# 12 Will you pay me to participate in this study?

There is no reimbursement or payment for this study.

# 13 What happens when the study ends?

Once the initial screening tests of the blood tests and the nuclear scan are completed, one of the research members will contact you to explain the results of the test. If the initial screening tests have reached a conclusion, you will be informed of whether you have evidence of cardiac amyloidosis or no evidence of cardiac amyloidosis. If you have no evidence of cardiac amyloidosis, that is the end of your participation in the trial and there will be no further obligation on your part. If you do have evidence of cardiac amyloidosis, you will be offered genetic testing to determine the subtype of cardiac amyloidosis you have and follow up with our amyloid specialist clinic. You do not have to follow up at our amyloid clinic and may choose to seek external opinion/follow up. Additionally, you do not need to have genetic testing if you would prefer not to. Your GP will also receive written correspondence at the end of the trial explaining the results of your screening test. All study results will be available to you on request.

# 14 Will the results of the study be published?

To protect your privacy, no information will be published that could identify you as a participant in this study. The intention of this study is to gather data however the data will be de-identified. This may take some time and should be discussed with the study doctor.

# 15 Who do I contact if I have a question or complaint?

We have included several contacts for you below. Who you contact depends on what information you need:

**Further information and who to contact**

 The person you may need to contact will depend on the nature of your query.  If you want any further information concerning this project or if you have any problems which may be related to your involvement in the project, you can contact the researcher.

**Research contact person**

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

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| --- | --- |
| Name | Dr Timothy Scully |
| Position | Associate Investigator  |
| Telephone | 0401 397 550 |
| Email | tgraemescully@gmail.com |

**Complaints contact person**

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

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| Name | Eastern Health Office of Research and Ethics |
| Position | Manager |
| Telephone | 03 9895 3398 |
| Email | ethics@easternhealth.org.au |

**Reviewing HREC approving this research** **and HREC Executive Officer details**

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| --- | --- |
| Name | Eastern Health Human Research Ethics Committee |
| Position | Chairperson |
| Telephone | 03 9895 3398 |
| Email | ethics@easternhealth.org.au |



**Consent Agreement**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

**Declaration by Participant – for participants who have read the information:**

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| Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

**Declaration - for participants unable to read the information and consent form:**

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| Witness\* to the informed consent processName (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older. |

**Declaration by Doctor**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

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| --- |
| Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |