

# Myocardial work in severe aortic stenosis

<b>Submission date</b> 17/11/2022	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 12/12/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 06/11/2024	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Aortic stenosis (AS) is a debilitating, degenerative form of valve disease whereby the aortic valve (AV) becomes thickened and restricted over time. As the aortic valve leaflets do not open sufficiently in people with AS, there is a risk of developing heart failure and premature death due to the stress experienced within the main pumping chamber of the left ventricle (LV).

AS is the most common type of valvular heart disease in the western world and more prevalent in the elderly population where one in eight people over the age of 75 years have moderate or severe AS. Patients who have significant AS have a considerably reduced quality of life due to symptoms such as breathlessness, chest pain and fatigue. Transthoracic echocardiography (TTE) is a non-invasive ultrasound imaging test, regarded as the gold standard technique for assessing the severity of AS by measuring the speed of blood through the narrowed aortic valve. Another benefit of using TTE is the ability to visualise and assess the function of the LV which is directly connected to the AV. Optimal timing for replacing the AV with a prosthetic alternative is important as those who develop symptoms associated with a restrictive AV are at higher risk of developing long-term complications such as early death following the procedure. While we can assess LV function using a parameter known as ejection fraction (EF) derived by TTE, there are inherent limitations using this method including it not being a particularly sensitive measurement to subtle changes in heart function and problems in accuracy and reproducibility when repeating measurements.

Myocardial Work (MW) is a new parameter which has recently been developed within TTE. This new technique has been identified to be a more sensitive measurement of assessing LV function by dividing the LV into segments and evaluating how well the heart contracts and combining this information with resting blood pressure. MW allows for a more detailed and sensitive look at how the heart is responding to the increased demands caused by AS by the formation of pressure-strain loops of each segment heart muscle. However, there are no current studies that evaluate whether MW before AV replacement can predict short and long-term outcomes. Therefore, this study intends on evaluating MW in severe AS patients prior to their already scheduled transcatheter aortic valve intervention (TAVI) and determine if this new measurement predicts re-hospitalisation for heart failure and survival. The aims of the study are to determine if MW is a better predictor of outcomes compared to current measurements such as EF and

myocardial strain. Secondary outcomes are to establish if the percentage change in MW following valve replacement predicts outcomes and whether changes in blood pressure measurement related to patient position significantly alter MW results.

Who can participate?

Adult patients with severe AS

What does the study involve?

MW will be evaluated in severe AS patients prior to their already scheduled TAVI. A TTE will also be performed following the implantation of the new prosthetic valve prior to hospital discharge to repeat MW measurements and provide details of any complications that have arisen during the procedure. This TTE will provide all the standardised measurements performed by staff within the hospital and therefore will reduce the burden in the department. These patients will also receive an echocardiogram at 6 weeks and 12 months post-TAVI to look at the change in MW as a part of their standard follow-up. The same patients will also be followed-up after hospital discharge at regular intervals every six months via telephone appointment or email to enquire about any hospital readmissions or death for three years.

What are the possible benefits and risks of participating?

As this is a non-invasive, observational study using echocardiography. The possible benefits are to future patients with severe AS to determine if MW is a more sensitive marker of outcomes compared to current methods used in clinical practice. There are no risks to patients being involved in the study.

Where is the study run from?

Newcastle Hospitals Trust, which is a large tertiary TAVI centre, as a part of a PhD project (UK)

When is the study starting and how long is it expected to run for?

November 2022 to November 2027

Who is funding the study?

The PhD is funded by Newcastle University (UK) in collaboration with Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

Who is the main contact?

Peter Luke, [peter.luke@newcastle.ac.uk](mailto:peter.luke@newcastle.ac.uk) (UK)

## Contact information

### Type(s)

Principal Investigator

### Contact name

Dr Mohammad Alkhalil

### ORCID ID

<http://orcid.org/0000-0002-3088-8878>

### Contact details

Freeman Hospital  
Freeman Road

High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE 7 7DN  
+44 (0)191 2236161  
mohammad.alkhalil@nhs.net

**Type(s)**

Scientific

**Contact name**

Mr Peter Luke

**ORCID ID**

<http://orcid.org/0000-0002-5756-5243>

**Contact details**

Room M.1.038  
Biomedical Science, Nutritional and Sport Science  
Newcastle University  
Newcastle upon Tyne  
United Kingdom  
NE1 7RU  
+44 (0)7845199255  
[peter.luke@newcastle.ac.uk](mailto:peter.luke@newcastle.ac.uk)

## Additional identifiers

**EudraCT/CTIS number**

Nil known

**IRAS number**

313577

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

IRAS 313577

## Study information

**Scientific Title**

Can the use of echocardiographic derived myocardial work predict outcomes in patients with severe aortic stenosis prior to transcatheter aortic valve intervention

**Study objectives**

Does Myocardial work, an echocardiography-based diagnostic tool, better predict survival, and major adverse clinical endpoints (myocardial infarction, stroke, re-hospitalisation for heart failure) compared to existing methods observed in echocardiography such as ejection fraction and myocardial deformation imaging?

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 07/11/2022, Health Research Authority London – Chelsea (London Centre, 2 Redman Place, HRA, E20 1JQ, UK; +44 (0)207 104 8029; chelsea.rec@hra.nhs.uk), ref: 22/LO/0675

### **Study design**

Observational investigation study

### **Primary study design**

Observational

### **Secondary study design**

Cohort study

### **Study setting(s)**

Hospital

### **Study type(s)**

Diagnostic

### **Participant information sheet**

See trial outputs table

### **Health condition(s) or problem(s) studied**

Severe aortic stenosis prior to transcatheter aortic valve intervention

### **Interventions**

A standard transthoracic echocardiogram and non-invasive blood pressure will be performed prior to transcatheter aortic valve intervention (TAVI) to assess myocardial work. This is a non-randomised, single-centre, observational trial following up patients with severe aortic stenosis post-TAVI for 3 years using echocardiography to measure myocardial work. Each patient recruited into the study will be followed up at 6-month intervals for 3 years by their preferred contact details (email, post or telephone) and have a transthoracic echocardiogram prior to TAVI, post-TAVI, 6 weeks and 1-year post-TAVI (4 echocardiograms in total for each participant). For those who have a different valve, their myocardial work will be compared to see if there is a statistically significant difference in myocardial work and whether this influenced outcomes at 3 years. Changes in blood pressure in the sitting and the left lateral decubitus position due to change will be directly compared for each participant to determine if myocardial work significantly changes with patient positioning.

### **Intervention Type**

Procedure/Surgery

**Primary outcome measure**

1. Myocardial work measured using echocardiography assessed immediately before transcatheter aortic valve intervention (TAVI), immediately post-TAVI, and at 6 weeks and 12 months post-procedure.
2. Survival and incidence of major adverse clinical endpoints measured by contacting patients by telephone, post or email at 6 monthly intervals up to 3 years, and by echocardiograms performed at 6 weeks and 12 months. Mortality will be reviewed by assessing patient medical records prior to contacting patients at six-month intervals.

**Secondary outcome measures**

1. Myocardial work results in seated and supine patients measured using non-invasive blood pressure and echocardiography prior to and post TAVI (before hospital discharge), 6 weeks and 12 months post-TAVI
2. Post-procedure Myocardial work results in patients with differing valve types measured using echocardiography. Evaluating percentage change in myocardial work in severe aortic stenosis patients before the valve implantation and compare to myocardial work following the TAVI using echocardiography to see if percentage change predicts mortality and hospitalisation at end of study follow-up at 3 years.

**Overall study start date**

01/11/2022

**Completion date**

01/11/2027

**Eligibility****Key inclusion criteria**

1. Severe aortic stenosis with a peak velocity ( $>4.0\text{m/s}$ ), mean gradient ( $>40\text{mmHg}$ ) and an aortic valve area  $<1.0\text{cm}$  on transthoracic echocardiography requiring a transcatheter aortic valve intervention.
2. Patients with low-flow aortic stenosis (peak gradient  $<4.0\text{m/s}$  with AVA  $<1.0\text{cm}^2$ ) who require a TAVI will also be invited to participate

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

140

**Total final enrolment**

**Key exclusion criteria**

1. Age under 18 years old
2. Mild or moderate aortic stenosis ( $<4.0\text{m/s}$ ), mean gradient ( $<40\text{mmHg}$ ), and aortic valve area  $>1.0\text{cm}^2$
3. Suboptimal image quality which does not allow for quantitative left ventricular function assessment by Biplane Simpson, myocardial deformation imaging and myocardial work
4. Poorly controlled arrhythmias or more than moderate mitral regurgitation
5. Unable to tolerate a transthoracic echocardiogram
6. Do not provide consent

**Date of first enrolment**

30/11/2022

**Date of final enrolment**

30/11/2024

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

**The Newcastle upon Tyne Hospitals NHS Foundation Trust**

Freeman Hospital

Freeman Road

High Heaton

Newcastle upon Tyne

United Kingdom

NE7 7DN

**Sponsor information****Organisation**

Newcastle upon Tyne Hospitals NHS Foundation Trust

**Sponsor details**

Freeman Hospital

Freeman Road

High Heaton

Newcastle upon Tyne

England

United Kingdom

NE7 7DN  
+44 (0)191 2086000  
nuth.nuthsponsorship@nhs.net

**Sponsor type**

Hospital/treatment centre

**Website**

<https://www.ncl.ac.uk/medical-sciences/study/postgraduate/postgraduate-research-programmes/>

**ROR**

<https://ror.org/05p40t847>

## **Funder(s)**

**Funder type**

University/education

**Funder Name**

Newcastle University

**Alternative Name(s)**

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Universities (academic only)

**Location**

United Kingdom

**Funder Name**

Newcastle upon Tyne Hospitals NHS Foundation Trust

**Alternative Name(s)**

Newcastle upon Tyne Hospitals NHS Trust

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Local government

## Location

United Kingdom

# Results and Publications

## Publication and dissemination plan

The data will be collected for a PhD qualification with the intention of publication in a high impact peer-reviewed journal. The specific details of which journal and what data will be published is currently unknown.

## Intention to publish date

01/12/2028

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Peter Luke - peter.luke@nhs.net, the type of data that will be shared is Individual participant data that underlie the results reported in this article, made available immediately following publication with no end date, to researchers who provide a detailed methodically sound proposal in order to achieve the aims in the approved proposal. The data will be available following a data access agreement. All data will be completely anonymised.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version 3.0	18/10/2022	29/11/2022	No	Yes
<a href="#">HRA research summary</a>			28/06/2023	No	No