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Mechanisms of excess risk in aortic stenosis after aortic valve replacement

Submission date	**Recruitment status**	[X] Prospectively registered
15/03/2021	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
15/03/2021	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/03/2021	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Aortic stenosis (AS) is caused by the narrowing of one of the main heart valves, the aortic valve. When this valve narrows, it restricts blood leaving the heart and flowing to the rest of the body. Replacing the valve is the only treatment for AS. The timing of replacement is currently often too late – half of patients are left with permanent damage to the heart muscle (scarring) and a quarter die within 3.5 years. For patients with scarring, there is currently no treatment. Researchers want to change this and understand why patients who are found to have heart damage are at higher risk of dying.

Who can participate?
Patients with severe narrowing of the aortic valve, and surgical (SAVR) or transcatheter aortic valve implantation (TAVI) have been proposed as the best treatment option

What does the study involve?
The researchers will use a heart scan (MRI) to detect scarring before the valve replacement. After the valve replacement, participants will receive a tiny monitor (paper clip size) injected underneath the skin. This monitor continuously checks the heartbeat rhythm. Participants will be monitored for up to 3 years to see if scarring is linked to abnormal heart rhythms and reduced pumping function (heart failure). If participants die during the study, the monitor will help the researchers to understand what happened to their heart at that time.

What are the possible benefits and risks of participating?
If the MRI scan or the cardiac monitor identify important findings that are not known and will change treatment, the researchers will inform the cardiology or cardiac surgeon as appropriate. For example, the heart monitor may show an irregular heartbeat that requires medicine to prevent a stroke or a slow heartbeat that requires a pacemaker. The information from this study will help improve the understanding of heart disease and in the future may help decide which patients should undergo surgery.

Where is the study run from?
Barts Heart Centre, St Bartholomew's Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2020 to April 2026

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Dr George Thornton
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Contact information

Type(s)
Scientific

Contact name
Dr Thomas Treibel

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04627987

Integrated Research Application System (IRAS)
257307

Protocol serial number
125312

Study information

Scientific Title
Mechanisms of excess risk in aortic stenosis after aortic valve replacement: a prospective single-centre observational cohort study

Acronym
MASTER

Study objectives

The presence of myocardial scar (late gadolinium enhancement [LGE]/extracellular volume [ECV]) or ischaemia (reduced myocardial blood flow) measured by cardiovascular magnetic resonance (CMR) predicts the incidence of:
1. Heart failure death or hospitalisation
2. Burden of nonsustained ventricular tachycardia (NSVT) in patients following aortic valve replacement (AVR) for aortic stenosis (AS)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/01/2020, London - Riverside Research Ethics Committee (Level 3 Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207104 8204; riverside.rec@hra.nhs.uk), REC ref: 19/LO/1849

Study design
Prospective single-centre observational cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Severe symptomatic aortic stenosis

Interventions
An MRI scan is carried out to detect scarring before the valve replacement. After the valve replacement, participants will receive a tiny monitor (paper clip size) injected underneath the skin. This monitor continuously checks the heartbeat rhythm. Participants will be monitored for up to 3 years to see if scarring is linked to abnormal heart rhythms and reduced pumping function (heart failure). If participants die during the study, the monitor will help the researchers to understand what happened to their heart at that time.

The primary objective is to deliver a better understanding of the risk associated with AS cardiomyopathy after aortic valve replacement by identifying whether heart muscle scar (fibrosis) or its precursor, ischaemia (i.e. a mismatch of blood supply and demand), increase hospitalization for heart failure and significant heart rhythm abnormalities (arrhythmias). The primary outcome is heart failure death or hospitalisation for heart failure over a follow-up period of 3 years.

Intervention Type
Device

Phase
Not Applicable

Primary outcome(s)
1. Heart failure death or hospitalisation for heart failure measured using 3 monthly telephone follow up and interrogation of Hospital Episode Statistics (HES) at the end of the study, duration

of follow up is 3 years.
2. Burden of non-sustained VT, assessed using an implantable cardiac monitor via two weekly device downloads for the duration of device longevity (battery life approximately 2 years)

Key secondary outcome(s)
1. All-cause mortality (all-cause and cardiovascular) measured using NHS spine/death registration for 5 years after aortic valve replacement
2. Functional capacity measured using the 6-minute walk test at 6 weeks and 12 months after aortic valve replacement
3. Heart failure symptoms measured using the New York Heart Association (NYHA) functional classification (NYHA) at 6 weeks and 12 months post aortic valve surgery
4. Heart failure symptoms measured using the World Health Organisation Disability Assessment Schedule 2.0 at 6 weeks and 12 months post aortic valve surgery
5. Burden of other serious arrhythmias requiring a change in management, measured using downloads from an implantable device at 2.5 years after aortic valve replacement.
6. Participants with complete heart block, Mobitz 2 atrioventricular (AV) block, and new-onset atrial fibrillation, measured using an implantable device with device downloads at 2 weekly intervals

Completion date
01/04/2026

Eligibility

Key inclusion criteria
1. Able to provide written informed consent
2. Patients with symptomatic, severe AS referred for surgical or transcatheter AVR with one out of the following echocardiographic criteria for severe AS:
2.1. Effective orifice area [EOA] <1.0 cm^2
2.2. Indexed EOA of 0.6 cm^2/m^2
2.3. Peak velocity >4.0 m/s or mean gradient >40 mmHg

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. More than moderate valve disease other than AS
2. Patients that have a conventional contraindication for CMR (non-MR conditional pacemakers /implantable defibrillators, claustrophobia)
3. Renal impairment (creatinine clearance <30 ml/min/1.73m^2)
4. Needle phobic patients that would preclude blood taking

5. Diagnosis of dilated or hypertrophic cardiomyopathy
6. Pregnancy/breastfeeding, eGFR <30 ml/min
7. Inability to complete the protocol, other conditions that would prevent participation in the study.
8. Adenosine stress perfusion will not be performed in those patients with:
8.1. Asthma/COPD of sufficient severity to make adenosine contraindicated
8.2. High-grade conduction disease precluding the use of adenosine
8.3. Patients with known previous allergic reactions to adenosine
8.4. LVEF <40%

Date of first enrolment
01/04/2021

Date of final enrolment
01/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Barts Heart Centre
St Bartholomew's Hospital
King George V Building
West Smithfield
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Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
The British Heart Foundation, the_bhf, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Thomas Treibel (thomas.treibel.12@ucl.ac.uk). The researchers would be prepared to provide anonymised patient-level data to researchers upon reasonable request should this be required. The degree of data sharing and other aspects would be determined on an individual request basis.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No