ISRCTN19413194 https://doi.org/10.1186/ISRCTN19413194

Timing an intervention for aortic stenosis with remote patient monitoring

Submission date
27/02/2023

Recruitment status
No longer recruiting

Registration date
12/05/2023

Overall study status
Completed

Last Edited
10/09/2024

Condition category
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The most common form of heart valve disease is a narrowing of the aortic valve known as aortic stenosis (AS). The narrowing is developed over years, and so affects mainly older adults. Symptoms may not be noticed until the narrowing is severe. The most common symptoms experienced are tiredness, shortness of breath, chest tightness, dizziness and collapse. Currently, there are no medications that prevent AS. For people with severe AS who develop symptoms, the only treatment is aortic valve replacement. Some people with severe AS who display no symptoms (termed asymptomatic) are recommended 6-monthly hospital-based clinic visits and once symptoms appear, the aortic valve is replaced. We rely on these people to self-report the development of symptoms, but the symptoms can be confused with getting older and so not be flagged, leading to delays in valve replacement and possibly poor outcomes. Some researchers and doctors believe if people with severe asymptomatic AS report their symptoms, levels of activity (Timed Up and Go Test) and health status (quality of life) in between their regular hospital appointments by completing some questionnaires and a test on their smartphone it would be helpful. This is known as remote monitoring. If the report shows that the person is developing symptoms, action can hopefully be taken sooner than waiting for the next clinical appointment. Remote monitoring in people with severe asymptomatic AS is a new concept. This is a pilot study, and the results can be used to plan a much larger clinical trial, which will help show if APRAISE-AS reporting in the NHS is better for patients.

Who can participate?
Adult patients with a diagnosis of severe asymptomatic AS, able to give written consent and access an app-based programme

What does the study involve?
Participants are randomly allocated into two groups. Those in one group are allocated to be followed up as per the standard of care. Those in the second group are randomised to be followed up as per standard of care and provided with access to the APRAISE-AS app to facilitate self-reporting of symptoms. We will look at the functionality of the self-reporting of symptoms within this cohort of participants to inform a future trial design.

What are the possible benefits and risks of participating?
The APRAISE-AS trial is led by a team of experienced researchers, who have an excellent track record of running clinical trials. Participants are followed up as per routine care and in addition, a group of patients are randomised to use the APRAISE-AS app to self-record their side effects. There are no related side effects or harms because of app use to facilitate self-reporting of symptom data. Therefore, there is no reason to anticipate any safety concerns arising from this intervention with APRAISE-AS.

Where is the study run from?
The Heart and Lung Centre at The Royal Wolverhampton NHS Trust (UK)

When is the study starting and how long is it expected to run for?
July 2021 to March 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) Central Commissioning Facility (CCF); Grant Codes: NIHR202810 (UK)

Who is the main contact?
Dr Nazish Khan, (Chief Investigator), nazish.khan@nhs.net

Contact information

Type(s)
Principal investigator

Contact name
Dr Nazish Khan

ORCID ID
https://orcid.org/0000-0003-4483-7390

Contact details
Department of Cardiology (Queen Elizabeth Hospital Birmingham)
Nuffield House
University Hospitals Birmingham NHS Foundation Trust
Birmingham
United Kingdom
B15 2TH
+44 (0)121672000
nazish.khan@nhs.net

Type(s)
Scientific

Contact name
Dr Mary Nulty

Contact details
Birmingham Clinical Trials Unit (BCTU)
Institute of Applied Health Research

College of Medical and Dental Sciences
Public Health Building
University of Birmingham
Birmingham
United Kingdom
B15 2TT
+44 (0)121 415 9112
apraiseas@trials.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
272195

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 55477, IRAS 272195

Study information

Scientific Title
A pilot study to assess the safety, effectiveness and practical utility of remote patient monitoring to guide the timing of valve intervention in patients with asymptomatic severe aortic stenosis (APRAISE-AS)

Acronym
APRAISE-AS

Study objectives
The primary aim of this study is to pilot the trial protocol and assess the feasibility and potential refinement of the trial design prior to undertaking a larger RCT investigating whether proactive reporting of symptoms, definitive disease-specific PROMs and assessment of frailty in addition to standard care can be used to help inform the timeliness of valve intervention in patients with asymptomatic sAS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/12/2022, West Midlands – Black Country Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8019; blackcountry.rec@hra.nhs.uk) ref: 22/WM/0214

Study design
Prevention device validation of investigation/therapeutic procedures

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Remote monitoring of patients with aortic stenosis

Interventions
Remote patient monitoring:
The AS App & Clinician's Portal has been developed via a process of participatory design in collaboration with our patients and clinicians and will collect both subjective and objective data on a patient's health and well-being following their diagnosis of asymptomatic severe AS. This information will be presented to the healthcare team via a bespoke platform which allows near real-time surveillance of the patient's healthcare data. Thereby facilitating clinical prioritisation of patients who demonstrate early warning signs of decompensation or symptom deterioration to allow for escalation of treatment and/or earlier intervention.

Study design: A randomised controlled trial (RCT) has been chosen as the most robust method of evaluating the effectiveness of the intervention. This is a single-centre, prospective, two-arm, RCT in which 66 participants with asymptomatic sAS will be recruited and assigned to either the intervention arm (app-based proactive surveillance plus standard care) or control arm (current standard of care, clinic-based watchful waiting).

Identification of Participants: Participants will be identified for eligibility following a diagnosis of asymptomatic severe AS and will be approached for recruitment prospectively from new referrals seen in outpatient clinics or following identification at the ward level. In addition, all patients with asymptomatic severe AS remain under the care of the multidisciplinary Heart Team and as per current recommendations are reviewed in an outpatient clinic every 6 months. It will be possible for the Cardiovascular Research Team (pharmacist/nurses) to review the current caseload of patients with aortic valve disease and screen against the inclusion/exclusion criteria for the identification of potentially eligible participants. Participants deemed to be eligible for recruitment will be approached by a member of the clinical care team and will be given a patient information sheet (PIS) for review and an appropriate period (usually 24 hours) over which to assimilate the information contained within the PIS prior to deciding to participate. For those patients identified following the screening of the existing out-patient caseload, a study letter and PIS will be sent to them ahead of their next clinic appointment, with a view to seeking consent during their consultation.

Study duration: The study will run over 26 months. Patient recruitment will take place over 8 months and patient participation and follow-up will cease 12 months from the time of enrolment. Data analysis and write-up will take place over 6 months.

Study outcome measures: The primary aim of this study is to pilot the trial protocol and determine potential refinement of the trial design prior to undertaking a multi-centre RCT to investigate whether proactive reporting of symptoms, definitive disease-specific PROMs and assessment of frailty in addition to standard care can be used to help inform the timeliness of valve intervention in patients with asymptomatic severe AS.

The pilot study will capture both quantitative and qualitative data which will:
- Assess the integrity of the study protocol (including the inclusion/exclusion criteria, uptake and use of the patient app and clinician's portal, and training of staff and participants in the administration and assessment of the intervention).
- Assess the randomisation procedure as well as recruitment and retention rates.
- Assess adherence to and acceptability of the intervention in addition to completeness of data collection including self-reporting by the participants and following remote surveillance by the clinical team.
- Inform selection of the most appropriate outcome measures for a full-scale multi-centre randomised controlled trial.
The pilot trial is not powered to detect differences in clinical outcomes, but it allows for an assessment of whether there may be any issues in terms of the completion of the data collection for the proposed outcomes measured that will be collated in the main RCT. The following outcome data will be collected:
- Symptoms assessed using the established and validated NYHA and CCS classification to determine the degree of dyspnoea/fatigue/palpitations/angina and syncope] at baseline and on a weekly basis until 12 months in those assigned to the intervention arm. For those assigned to the standard care arm, these data will be collected at baseline, 6 months and 12 months.
- Frailty/functional capacity as determined by the "timed up and go" will be undertaken at baseline, every 2 weeks via the app until 12 months. For those assigned to the standard care arm, these data will be collected at baseline, 6 months and 12 months.
- PROM data (quality of life) will be captured from the app and collected at baseline, monthly via the app until 12 months in those assigned to the intervention arm. For those assigned to standard care, these data will be collected at baseline, 6 months and 12 months
Assessment and Follow-Up: Participants assigned to the control arm will be managed as per the current standard of care. Data relating to their symptoms will be collected at baseline and each 6-monthly clinic visit and they will be advised to contact the service should they develop symptoms in between clinic appointments.

For participants assigned to the intervention arm, a member of the research team will install and provide access to the app on their own or a Trust sourced device. Over a 12-month period, participants will use the app to self-report information relating to:
- Symptoms (dyspnoea/fatigue/palpitations/angina/syncope) on a weekly basis
- Frailty/functional capacity (timed up and go test) every 2 weeks
- Disease-specific PROMs (KCCQ) once a month

The app will provide notifications to complete data entry should the participant not do so within 24 hours of the scheduled date/time. All data uploaded will be relayed to a clinician's portal from where it will be viewed by a healthcare professional involved in the patient's care.

As already confirmed with the MHRA, the app is not a medical device since it does not provide clinical decision support; this will be highlighted to the patient during the consent and set-up process. Information on symptom guidance and advice regarding patient self-management (from currently recommended websites), will also be displayed within the app and can be viewed prior to completing each questionnaire.

Patients will receive automated reminders prior to submitting a self-assessment via the app and 24 hours after a failure to submit their report if necessary. For the management of mild /moderate symptoms information will be available from currently recommended websites and can be accessed via the app. Severe symptoms noted by the patient will trigger an email alert to the clinical team (dedicated monitored email inbox) and a simultaneous patient notification advising them to contact their clinical team during office hours (or to use a standard NHS

support mechanism outside of these hours). The clinical team will monitor for notifications and respond in line with standard care recommendations. Actions taken in response to an alert will be logged in the patient's electronic healthcare record by a member of the cardiovascular research team.

All study staff/patients will be invited to complete a trial process questionnaire at the end of the study, which will evaluate aspects surrounding:
- Data collection forms/questionnaires
- Randomisation procedure
- Acceptability of the intervention (e.g. for patients using the mobile app rating score (MARS) tool
- Appropriateness of the frequency of APRAISE-AS reporting, alert thresholds, and management

Sample size: Since this is a pilot study a formal sample size calculation has not been performed. To obtain estimates of the parameters needed for sample size determination, in line with published recommendations for pilot studies, 30 patients are required. Assuming a loss to follow-up rate of 10% over the 12-month follow-up period, the study will require 33 patients to be randomised to each group, with a total of 66 patients overall. This will also allow for the estimation of recruitment and retention rates with 95% CI maximum widths of 20% and 25%, respectively.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
APRAISE-AS app

Primary outcome(s)
Primary measures are measured using data from the app at the conclusion of the follow-up period:
1. Assess the utility of the "app" measured using quantitative app usage data and data completeness recorded in the app and qualitative interview data
2. Assess engagement with the intervention
3. Recruitment rate per month
4. Number of withdrawals and losses to follow up (with reasons)

Key secondary outcome(s))
Secondary outcomes measured using medical records and the data populated within the case report form (CRF), unless otherwise stated:
1. Time to heart valve replacement over 12 months follow up
2. In-hospital mortality over 12 months follow up
3. Mortality at 30 days post-randomisation
4. Mortality at 12 months post-randomisation
5. Incidence of stroke over 12 months follow up
6. Incidence of myocardial infarction over 12 months follow up
7. Left ventricular ejection fraction (LVEF) at 6 and 12 months
8. Incidence of unplanned hospital admissions over 12 months follow up
9. Number of health-related contacts due to symptom development and/or deterioration during

study enrolment over 12 months follow up
10. Quality of life measured using the patient-reported outcome measure Kansas City Cardiomyopathy Questionnaire (KCCQ) score captured from the app and collected at baseline, monthly via the app until 12 months in those assigned to the intervention arm. For those assigned to standard care, these data will be collected at baseline, 6 months and 12 months.
11. Frailty/functional capacity measured using the Timed Up and Go (TUG) test score self-reported by patients in the interventional arm every two weeks and at 6 and 12 months for patients assigned to standard care, over 12 months follow up

Secondary outcomes post heart valve replacement only measured using medical records and the data populated within the case report form (CRF):
1. Incidence of major bleeding (as defined in Valve Academic Research Consortium clinical outcomes) over 12 months follow up
2. Incidence of vascular access site or access-related complications over 12 months follow up
3. Incidence of acute kidney injury over 12 months follow up
4. Incidence of conduction disturbances over 12 months follow up
5. Incidence of arrhythmias over 12 months follow up

Completion date
16/03/2025

Eligibility

Key inclusion criteria
1. Patients diagnosed with asymptomatic sAS of a native valve
2. Aortic valve area <1cm2 and mean pressure gradient >40mmHg and left ventricular ejection fraction (LVEF) >50% (in the last 6 months)
3. Able to give written informed consent
4. Aged ≥18 years old
5. Able to access and use app-based programmes (using the English language)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
38

Key exclusion criteria

1. Lack of capacity to understand the nature of the study and possible consequences as assessed by their attending clinician
2. Significant disease of other valves e.g. mitral stenosis/regurgitation
3. Co-morbidities that in the opinion of the cardiac surgeon/cardiologist preclude successful valve intervention e.g. life expectancy of fewer than 2 years

Date of first enrolment
19/01/2023

Date of final enrolment
01/09/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Sponsor information

Organisation
University of Birmingham

ROR

https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request
nazish.khan@nhs.net

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		10/06/2024	11/06/2024	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes