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CROSS sectional versus invasive imaging in patients with Heart Failure

Submission date 22/08/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 30/09/2024	**Overall study status** Ongoing	
Last Edited 04/09/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Each year in the UK at least 60,000 patients are diagnosed with heart failure. Coronary artery disease (narrowing of the blood vessels supplying the heart) is the most common cause of heart failure. It is important to identify coronary artery disease because these patients have an increased risk of dying and may respond less well to modern treatments. Invasive coronary angiography (described below) is often done as the first-line test to identify coronary artery disease in a fifth of patients with heart failure in the UK. However, it is known from work with our patient and public involvement groups and patient charities (including the British Society for Heart Failure Patient Group and Cardiomyopathy UK) that most patients would prefer to avoid invasive coronary angiography if possible. This trial aims to establish if it is possible to reduce the need for invasive angiography in patients with newly diagnosed heart failure.

Who can participate?
Patients presenting with a new diagnosis of heart failure and not known to have coronary artery disease

What does the study involve?
They will be randomly assigned (equal chance) to one of three tests:
1. Invasive coronary angiogram (current NHS practice)- A specialised X-ray test where dye is injected directly into the heart arteries via the groin or wrist. It carries a small risk of serious complications such as stroke. The test exposes patients to radiation and is expensive (NHS tariff up to £1563). Furthermore, there are long waiting lists for the test following many cancellations due to the COVID-19 pandemic.
2. CT coronary angiography - this test is quick, non-invasive and cheaper than invasive angiography (NHS tariff up to £310). It has a high accuracy for the detection of coronary artery disease but can be challenging in certain patient groups such as elderly patients or those with irregular heart rhythms. It also exposes patients to a small dose of ionising radiation.
3. Stress cardiovascular MRI - This test is non-invasive and cheaper than invasive angiography (NHS tariff up to £596) and provides additional information on the structure and function of the heart. The accuracy of this test for detection of coronary artery disease is unproven in patients with heart failure. It does not expose patients to ionising radiation.

The recruitment strategy aims to maximize the inclusion of patients who have been underrepresented in heart failure trials, such as elderly individuals, ethnic minorities, and socio-economically disadvantaged patients. Efforts will be made to reduce barriers to participation, and collaboration with the NIHR Ethnic Minority Research Inclusivity Group will help create a YouTube video explaining the trial's rationale and the importance of participation. The video will be presented in plain language and made available in multiple languages.

The trial is designed to minimize inconvenience for patients by eliminating the need for additional hospital visits. Follow-up will be conducted remotely, primarily through the review of electronic health records. Surveys exploring patient experiences will be sent via online platforms, text messages, or post, based on patient preference. The trial will also assess whether the tests provide good value for money for the NHS.

If the trial shows that non-invasive imaging tests are as effective as invasive angiography, it could lead to a significant reduction in the number of angiographies performed annually in the NHS. This could result in improved patient experience and cost savings without compromising the health outcomes of patients with heart failure.

What are the possible benefits and risks of participating?
Although direct benefits to participants cannot be guaranteed, the information gained might help the treatment of future patients. Participants will have more contact with medical staff and have more opportunities to ask questions and be informed about their health. All tests in this trial are standard NHS care so there are no additional research tests or additional risks to participating in the study. There is however a small burden of patient time to complete the consent form and questionnaires at baseline, 6 months and 12 months. To minimise inconvenience, questionnaires will be offered in a variety of formats including telephone, postal and online.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
April 2024 to August 2029

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
p.swoboda@leeds.ac.uk
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Study website
https://medicinehealth.leeds.ac.uk/directories0/dir-record/research-projects/1838/cross-sectional-versus-invasive-imaging-in-patients-with-heart-failure-cross-hf

Contact information

Type(s)
Scientific, Principal Investigator

Contact name

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
332073

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2024-NCT25, CPMS 57653

Study information

Scientific Title
CROSS sectional versus invasive imaging in patients with Heart Failure

Acronym
CROSS-HF

Study objectives

To establish whether, in patients with heart failure, a strategy of non-invasive imaging with computed tomography coronary angiography (CTCA) or stress cardiovascular magnetic resonance (CMR) is non-inferior to invasive coronary angiography (ICA) in terms of major adverse cardiovascular events (MACE), patient reported outcome measures, and cost-effectiveness.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/08/2024, West of Scotland REC (Ground Floor Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, United Kingdom; +44 141 314 0212; WoSREC3@ggc.scot.nhs.uk), ref: 24/WS/0108

Study design
Multicentre open-label randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records

Study type(s)
Diagnostic, Quality of life

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Heart failure

Interventions
Participants will be randomised (online) 1:1:1 ratio to either invasive coronary angiogram (ICA), non-invasive imaging with computed tomography coronary angiography (CTCA) or stress cardiovascular magnetic resonance (CMR). Each test is expected to take between 1 h 20 minutes and 1 h 45 minutes. Participants will be asked to complete up to 3 questionnaires at baseline, 6 months and 12 months but completion of each questionnaire is expected to take no more than 20 minutes. Follow-up by review of medical records at NHS sites will be up to 4.5 years and longer-term follow-up through remote data linkage for up to 10 years.

Intervention Type
Procedure/Surgery

Primary outcome measure
Time to first major adverse cardiovascular event (MACE) measured from randomisation for a minimum of 12 months:
MACE defined as any of:
1. All cause death

2. Myocardial Infarction (MI)
3. Heart Failure Hospitalisation

Secondary outcome measures
Measured using patient records:
1. Total MACE events (MACE is defined as all-cause mortality, MI and heart failure hospitalisations)
2. Total (first and recurrent) HF hospitalisations
3. KCCQ-CSS at 6 and 12 months
4. Total Cardiovascular (CV) deaths
5. Total all-cause mortality

Overall study start date
01/04/2024

Completion date
01/08/2029

Eligibility

Key inclusion criteria
1. Onset of symptoms ± signs of heart failure in the past 12 months AND
2.1. Non-elective heart failure hospitalisation (where heart failure was the primary reason for hospitalisation in the opinion of the investigator) OR
2.2. Outpatients with LVEF ≤40% OR
2.3. Outpatients with LVEF >40% and NT-proBNP >300ng/L (sinus rhythm) or >600ng/L (AF)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
3000

Key exclusion criteria
1. Previous investigations for coronary artery disease (CAD), where CAD was identified as the cause of heart failure
2. Clear alternative cause of heart failure (e.g. cardiac amyloidosis or hypertrophic cardiomyopathy)
3. Severe valvular heart disease thought to be the main cause of heart failure
4. Comorbid conditions with lifespan of less than a year (in the opinion of the investigator)

Date of first enrolment
01/10/2024

Date of final enrolment
01/04/2028

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Pinderfields Hospitals NHS Trust
Trust Hq, Rowan House
Pinderfields General Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4EE

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
Glasgow
United Kingdom
G12 0XH

Study participating centre
Northumbria Healthcare NHS Foundation Trust
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Kettering General Hospital NHS Foundation Trust
Rothwell Road
Kettering
United Kingdom
NN16 8UZ

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
James Paget University Hospitals NHS Foundation Trust
Lowestoft Road
Gorleston
Great Yarmouth
United Kingdom
NR31 6LA

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

Study participating centre

Airedale NHS Foundation Trust
Airedale General Hospital
Skipton Road
Steeton
Keighley
United Kingdom
BD20 6TD

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Barnsley Hospital NHS Foundation Trust
Gawber Road
Barnsley
United Kingdom
S75 2EP

Study participating centre
Glenfield Hospital NHS Trust
Groby Road
Leicester
United Kingdom
LE3 9QP

Sponsor information

Organisation
University of Leeds

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LS2 9JT
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Sponsor type
University/education

Website
https://www.leeds.ac.uk/

ROR
https://ror.org/024mrxd33

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

Publication and dissemination plan

The success of the trial depends upon the collaboration of all participants. For this reason, credit for the main results will be given to all those who have collaborated in the trial, through authorship and contributorship. Uniform requirements for authorship for manuscripts submitted to medical journals will guide authorship decisions. These state that authorship credit should be based only on substantial contribution to:
• conception and design, or acquisition of data, or analysis and interpretation of data
• drafting the article or revising it critically for important intellectual content
• and final approval of the version to be published
• and that all these conditions must be met (www.icmje.org).

All collaborators will be listed as contributors for the main trial publication, giving details of roles in planning, conducting and reporting the trial. The CROSS-HF team should be acknowledged in all publications, as should the funder NIHR. Other key individuals will be included as authors or contributors as appropriate and at the discretion of the CROSS-HF TMG. Any disputes relating to authorship will be resolved by the TSC.

The Chairs and Independent members of the TSC will be acknowledged, but will not qualify for full authorship, in order to maintain their independence.

To maintain the scientific integrity of the trial, data will not be released prior to the first publication of the analysis of the primary endpoint, either for trial publication or oral presentation purposes, without the permission of the Trial Oversight Committee. In addition, individual collaborators must not publish data concerning their participants which is directly relevant to the questions posed in the trial until the first publication of the analysis of the primary endpoint.

The funder, the NIHR, has adopted an open access policy for all funded research which means that an electronic copy of all peer-reviewed published papers must be accessible via the UKPMC website.

Intention to publish date

30/03/2030

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	01/08/2024	06/09/2024	No	Yes