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Coronary artery stents in heart failure with preserved ejection fraction

Submission date
02/05/2025

Recruitment status
Recruiting

Registration date
03/06/2025

Overall study status
Ongoing

Last Edited
30/04/2026

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Heart failure with preserved ejection fraction (HFpEF) is a serious medical condition where the heart muscle stiffens and is unable to properly pump blood around the body. The main symptoms are difficulty breathing, tiredness and leg swelling. HFpEF can be linked to other medical conditions such as high blood pressure, diabetes, kidney failure and obesity as well as age. It is more likely to affect women and people of non-White ethnicities than other types of heart failure. There are very few treatments for HFpEF.
Half of people with HFpEF have coronary artery disease, blockages in the blood vessels which supply the heart. These blockages are thought to be the cause of heart failure. Stents are small metal tubes that are used to unblock arteries in a keyhole operation so that blood can flow normally. Research shows that they are a good treatment for heart attacks and angina in patients without heart failure. They are quite safe, with a 1 in 200 risk of a major complication and 1 in 10,000 risk of dying from a planned stent procedure.
We think that stents will help people with HFpEF and coronary artery disease but need research to prove this. This study will help us to answer this question. The team running the study is an equal partnership of doctors, researchers and patients.
The REPRIEVED trial aims to find out if treating people with HFpEF and coronary artery disease with stents improves their quality of life and blood supply to their heart.

Who can participate?
Patients aged 18 years and over with a diagnosis of HFpEF and coronary artery disease

What does the study involve?
Participants are randomly allocated to one of two groups:
Intervention group: Participants will receive percutaneous coronary intervention (PCI) as per current standard of care.
Control group: Participant will undergo a placebo PCI procedure that involves placement of a thin tube to image the blood vessel but does not involve placement of an actual stent.

What are the possible benefits and risks of participating?
Possible risks:
There are some risks that it is important to be aware of if you decide to take part in this study.

Some people who have not had a previous angiogram will be asked to have a CT coronary angiogram of their coronary arteries. This will allow us to see if they have coronary artery disease and if they can take part in the trial. All people taking part in the study will have a coronary angiogram and you may have a stent procedure (depending on the treatment group you are assigned to). All of these procedures can be extra to those that you would have if you did not take part in this study. These procedures use ionising radiation to form images of your body and provide treatment. Ionising radiation may cause cancer many years or decades after the exposure. In patients with your current clinical condition, the chance of this happening to you is extremely small.
A coronary angiogram can involve a special wire called a pressure wire study procedure. This procedure involves putting a thin tube (catheter) through the arm or groin to take pictures of the coronary arteries and measure how well they function. A special dye (called contrast) is injected during the procedure. The procedure is in regular use to assess patients with angina or heart attacks across the National Health Service (NHS). It is performed by specially trained heart doctors (cardiologists) called interventional cardiologist. It is done using local anaesthetic and with medication to make people sleepy.
For all people receiving treatment including those in the placebo group, the risks of an angiogram and pressure wire study include minor bleeding (1 in 50 procedures), major bleeding (1 in 500 procedures), bleeding round the heart (1 in 2000 procedures), damage to the blood vessels (1 in 1000 procedures), heart attack (1 in 1000 procedures), stroke (1 in 2000 procedures) allergic reaction to contrast dye (1 in 1000 procedures) and damage to the kidneys from injected contrast dye (1 in 2000 procedures). The risk of death from a planned test such as this is around 1 in 10,000 procedures. The overall risk of a major complication is around 1 in 400 procedures. This means that 99.75% of patients will not have a complication.
In the people who receive the stent procedure, there will be an additional step where stents are placed within the coronary arteries. Balloons are used to stretch open the narrowings, and stents (small expandable metal tubes) are used to hold them open. The risks of these procedures are the same as for the angiogram but occur slightly more often as the procedure is more complex. The specific increased risks are of heart attacks (1 in 500), stroke (1 in 1000), damage to the kidneys (1 in 500) and death (1 in 2000). The overall risk of a major complication is around 1 in 200 procedures. This means that 99.5% of people will not have a complication.
After the procedure, people will receive medication to thin their blood. Aspirin will be prescribed to all people who take part as this is needed to treat their coronary artery disease. A second medication, called clopidogrel, will be prescribed to people who take part and receive stents. This is to stop blood clots from forming inside the stents for 12 months. These medications are routinely given to people who have stents inserted for heart attacks or angina. Taking both of these medications together increases the risk of bleeding. It is common that people notice that they bruise more easily when taking clopidogrel. The risk of major bleeding from taking aspirin and clopidogrel, as opposed to aspirin alone, is 1 in 100 over 12 months. There is no increased risk of life-threatening bleeding. People who do not receive stents will not take clopidogrel (and instead they will receive a placebo tablet).

Possible benefits:
As we do not know whether the use of stents is helpful, we cannot say whether or not there will be a direct benefit to you. The information that we get when people take part may benefit people living with HFpEF and coronary artery disease in the future.
The trial will give us a better understanding of how well stent procedures work to treat people with these heart conditions. If it does work, then it could be used in the NHS in the future. If the stent procedures does not work well in this setting, then we will still have learned important information about what research needs to be done in the future to improve treatments for people living with HFpEF and coronary artery disease.

Where is the study run from?
The study is being run by the London School of Hygiene & Tropical Medicine (LSHTM) Clinical Trials Unit (CTU) (UK)

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

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

Who is the main contact?
REPRIEVED Clinical Trials Unit, REPRIEVED@lshtm.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)

330189

Central Portfolio Management System (CPMS)
56787

National Institute for Health and Care Research (NIHR)
159715

Study information

Scientific Title
REvascularisation for heart failure with PReserved ejection fraction and Ischaemia: EValuation of Efficacy and mechanistic Description (REPRIEVED)

Acronym
REPRIEVED

Study objectives
Efficacy:
1. In patients with heart failure with preserved ejection fraction (HFpEF) and coronary artery disease, treatment with percutaneous coronary intervention (PCI)is associated with superior quality of life, measured with the Kansas City Cardiomyopathy Questionnaire - Overall Summary Score (KCCQ-OSS), compared to a placebo procedure.

Mechanistic:
1. In patients with HFpEF and coronary artery disease, the severity of symptoms correlates with the extent of myocardial ischaemia measured by coronary flow reserve (CFR).
2. Treatment of epicardial coronary disease by PCI will improve CFR.
3. The change in quality of life following PCI correlates with the change in CFR.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/05/2025, London - Riverside Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8150, (0)207 104 8243; riverside.rec@hra.nhs.uk), ref: 25/LO/0277

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Heart failure with preserved ejection fraction (HFpEF) and coronary artery disease

Interventions
Patients with HFpEF and coronary artery disease will be randomised 1:1 using an online randomisation system to either PCI (intervention group) or placebo procedure (control group) using an online randomisation system in permuted blocks of varying size and stratified by recruiting site.

Intervention group: Participants will receive percutaneous coronary intervention (PCI) as per current standard of care.
Control group: Participant will undergo a placebo PCI procedure that involves placement of a thin tube to image the blood vessel but does not involve placement of an actual stent.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Primary efficacy:
Quality of life measured using KCCQ-OSS at 6 months

Primary mechanistic:
CFR measured using pressure wire at 6 months

Key secondary outcome(s)
Secondary outcomes:
1. All-cause death and hospitalisation for heart failure at 6 months
2. Efficacy of blinding assessed using standard tools at discharge
3. ICHOM standard outcome set for heart failure at 6 months
4. Individual components of the KCCQ (including total symptom score and clinical summary score) at 6 months
5. Health status measured using New York Heart Association (NYHA) functional class at 6 months
6. NT-pro-BNP measured using blood test/assay at 6 months
7. Difference in left ventricular ejection fraction (LVEF) and diastolic function (mitral E/e') measured at 6 months

Secondary mechanistic:
Change in invasively measured fractional flow reserve (FFR), CFR and microvascular resistance from pre- to post-PCI in all target coronary arteries measured during the PCI procedure

Completion date
31/08/2029

Eligibility

Key inclusion criteria
1. A diagnosis of HFpEF, defined by the European Society of Cardiology (ESC) criteria, as:
1.1. Symptoms of heart failure (New York Heart Association (NYHA) class II-IV)
and
1.2. Left ventricular ejection fraction >=50%
and
1.3. One or more of the following objective signs of left ventricular diastolic dysfunction:
1.3.1. Invasively measured left ventricular end diastolic pressure >=15 mmHg at rest or >=25 mmHg on exercise (directly measured or estimated via pulmonary capillary wedge pressure)

1.3.2. Estimated pulmonary artery systolic pressure > 35mmHg or tricuspid regurgitation velocity >2.8 m/s on echocardiography
1.3.3. Left atrial volume index >34ml/m2 in patient in sinus rhythm or left atrial volume index >40 ml/m2 in atrial fibrillation
1.3.4. Relative left ventricular wall thickness >0.42
1.3.5. Left ventricular mass index >=95 g/m2 in females or >=115 g/m2 in males
1.3.6. Mitral E/E' ratio > 9
and
1.4. NT-pro-BNP >125 pg/ml in sinus rhythm or >365 pg/ml in atrial fibrillation

plus

2. Significant coronary artery disease defined as:
2.1. Functionally significant disease in at least one major proximal epicardial coronary artery (British Cardiovascular Intervention Society Jeopardy Score >=4) with a fractional flow reserve (FFR) <=0.80 measured with FFR, estimated with computational fluid dynamics during invasive angiography (e.g. VFR) or CT-FFR.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Age <18 years
2. People without capacity to provide informed consent
3. PCI contraindicated or not feasible on coronary angiography or screening CTCA
4. Contraindication to clopidogrel/dual antiplatelet therapy
5. Recent acute myocardial infarction or coronary revascularisation (within 90 days)
6. Enrolment in another interventional study which may affect study outcomes
7. Severe chronic obstructive pulmonary disease (GOLD stage >=3)
8. Haemoglobin <=80 g/L
9. Other cardiac diagnosis as a cause for HFpEF (hypertrophic cardiomyopathy, untreated severe left sided valvular disease, cardiac amyloidosis)

Date of first enrolment
23/03/2026

Date of final enrolment
31/05/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
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SE1 7EH

Study participating centre
King's College Hospital
Denmark Hill
London
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SE5 9RS

Study participating centre
Royal Bournemouth Hospital
Castle Lane East
Bournemouth
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Study participating centre
Mid and South Essex NHS Foundation Trust
Prittlewell Chase
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SS0 0RY

Study participating centre
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Agamemnon Street
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Study participating centre
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West Smithfield
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EC1A 7BE

Study participating centre
Leeds General Infirmary
Great George Street
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LS1 3EX

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Organisation

Guy's & St Thomas' NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes:

Results and Publications

Individual participant data (IPD) sharing plan

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?
Study website	Study website	11/11/2025	11/11/2025	No	Yes