ISRCTN87042095 https://doi.org/10.1186/ISRCTN87042095

Reducing 'bubbles' (gaseous micro-emboli) circulating in the blood system during open heart surgery

Submission date 19/05/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/06/2022	**Overall study status** Ongoing	
Last Edited 09/01/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
After heart surgery, some people can experience mild problems which affect their brain. These can include short-term difficulties with thinking, attention, and memory. A recent study found about one in five people over 65 years of age who had heart surgery experienced these problems. In people over 80 years of age who had heart surgery, one in three people had these difficulties temporarily. Surgeons believe that the brain problems that are sometimes seen in patients after heart surgery are caused by tiny nitrogen-rich air bubbles getting into the blood when it is circulated in the heart and lung machine. These tiny air bubbles are also known as gaseous micro-emboli.

An artificial lung (part of the heart and lung machine) has been developed that limits the supply of oxygen entering the circulating blood and removes some of the nitrogen in the blood. This in turn helps the tiny air bubbles dissolve, as nitrogen in the air bubbles flows into the circulating blood and is removed from the heart-lung machine. Using this type of artificial lung is known as hypobaric oxygenation. We are doing this study to see if there are any differences in the number and type of air bubbles circulating in the bloodstream during heart surgery using the artificial lung that uses hypobaric oxygenation versus the standard, commonly used artificial lung in the heart and lung machine.

Who can participate?
People aged 40 years and over who are having either a coronary artery bypass graft (CABG), aortic valve replacement (AVR) or AVR and CABG at the same time

What does the study involve?
After you have read the study Patient Information Sheet, if you decide to take part in the study, you will be asked to sign a consent form. Everyone who joins the study will be put into one of two groups: In one group the artificial lung that uses hypobaric oxygenation will be used in the heart and lung machine during surgery. In the other group, the commonly used artificial lung will be used in the heart and lung machine during surgery. Before your operation, a member of your research team will take an extra blood sample (approximately 15mls, enough to fill a

tablespoon). Blood samples will be taken from a small tube in one of your blood vessels that has been inserted to help monitor you during your operation, and not because you are taking part in this study. This blood sample will be analysed to determine the amounts of certain proteins, known to be indicators of brain injury and inflammation, circulating in your blood prior to the operation.

Everything about your operation will be the same as if you weren't in the study. The only difference is that during your surgery either the artificial lung that uses hypobaric oxygenation or the commonly used artificial lung will be used in the heart and lung machine. During your operation, an ultrasound machine will be used to look at the tiny air bubbles that enter your bloodstream and how quickly the blood is flowing in the main artery in your head. Sensors will be placed on your temples once you have been anaesthetised and before the operation begins. These sensors will be removed before you leave the operating theatre.

After your operation, four more blood samples will be taken by a member of the research team at 1, 4, 12, and 24 hours after your operation through small tubes inserted in your blood vessels that are already in place. The maximum amount of blood that we may take after your operation is 80mls (this is about enough to fill an egg cup). These blood samples will again be analysed to determine the amounts of the proteins known as indicators of brain injury and inflammation that are circulating in your blood. We will also collect information from your medical notes about any complications you may have experienced and how well you have recovered following your heart surgery. 30 days after your operation you will be contacted by a member of your research team, by phone or video call, to see how you have been since you left hospital after your operation. After you have had your 30-day follow up you will have completed the study.

What are the possible benefits and risks of participating?
There are no known risks or benefits from having heart surgery using either the conventional oxygenator in the heart and lung machine or the one that uses hypobaric oxygenation. The oxygenator that uses hypobaric oxygenation has a CE mark.

Where is the study run from?
Bristol Trials Centre

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

Who is funding the study?
British Heart Foundation

Who is the main contact?
Professor Gianni Angelini
g.d.angelini@bristol.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Barbara Warnes

Contact details
Bristol Trials Centre
University of Bristol
1-5 Whiteladies Road
Bristol
United Kingdom
BS8 1NU
+44 (0)117 455 3108
Home-trial@bristol.ac.uk

Type(s)
Scientific

Contact name
Ms Amelia Lowe

Contact details
Research and Innovation
Education & Research Centre Level 3
Upper Maudlin Street
Bristol
United Kingdom
BS2 8AE
+44 (0)117 342 0233
R&DSponsorship@uhbw.nhs.uk

Type(s)
Principal Investigator

Contact name
Prof Gianni Angelini

ORCID ID
http://orcid.org/0000-0002-1753-3730

Contact details
University of Bristol
Bristol Royal Infirmary
Bristol Heart Institute
Level 7
Marlborough Street
Bristol
United Kingdom
BS2 8HW
+44 (0)117 342 3145
g.d.angelini@bristol.ac.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number
305038

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 52419, IRAS 305038

Study information

Scientific Title
Hypobaric oxygen during cardiopulmonary bypass to reduce gaseous micro-emboli during cardiac surgery: a randomized controlled trial

Acronym
The HOME Study

Study objectives
The HOME study will test the hypothesis that hypobaric cardiopulmonary bypass (HCPB) virtually eliminates gaseous mircoemboli (GME) formation during CPB in patients undergoing cardiac surgery. Surgeons believe that the brain problems that are sometimes seen in patients after heart surgery are caused by these GME getting into the blood when it is being circulated in the cardiopulmonary bypass machine and blocking the blood vessels in the brain.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/04/2022, North of Scotland Research Ethics Service (Summerfield House, 2 Eday Road, Aberdeen, Scotland, UK, AB15 6RE; +44 (0)1224 558 458; gram.nosres@nhs.scot), Ref: 22/NS/0038

Study design
Randomized interventional single-centre single-blind parallel-group placebo-controlled

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cardiothoracic Surgery

Interventions
The HOME study is a single centre, single blind parallel two-group placebo-controlled RCT in which only the participants and outcome assessors will be blinded to the treatment allocation. The HCPB and conventional (CCPB) systems require different heater-cooler units to operate so it is not possible to blind the surgical clinical care team to the intervention allocation. The outcome assessors will be blinded to the intervention allocation.

40 participants will be recruited over 12 months at the Bristol Heart Institute NHS Hospital. Adults undergoing elective or urgent isolated coronary artery bypass grafting (CABG) or aortic valve surgery (AVR) with or without an associated CABG procedure (AVR±CABG) will be approached to take part.

Potential participants will be identified by the research team and will sent or given an invitation letter and HOME Study PIL to read before they attend the hospital for their surgery. The invitation letter and PIL have been approved by a PPI group that contains patients who have had direct experience with heart surgery.

Potential participants will have time to read the PIL and discuss their participation with others outside the research team if they wish. Most patients will have at least 24 hours to consider whether to participate. In a few cases, this time interval may be as little as 12 hours, for example for patients admitted for urgent planned surgery without prior notification to the waiting list coordinator. Despite the short notice, it is important to include these patients for the applicability of the trial findings since about 40% of patients having cardiac surgery are admitted as urgent cases.

Potential participants will be seen or contacted by a member of the local research team who will answer any questions and take informed consent if the patient decides to participate. Consent will be obtained face to face at a clinic appointment or remotely by telephone/video call.

Details of all patients approached for the trial and reason(s) for non-participation (e.g. reason for ineligibility or patient decline) will be documented. Participant eligibility will be assessed in full as close to randomisation as possible. Everyone who joins the study will be put into one of two groups, depending on the type of surgery they are having, either CABG or AVR (with or without CABG at the same time). In one group hypobaric oxygenation will be used in the cardiopulmonary bypass machine during surgery (Intervention=HCPB). In the other group, the conventional oxygenator will be used in the cardiopulmonary bypass machine during surgery (control=CCPB). Everything else about the operations will be the same as if the participants were not in the study.

During surgery, participants will have transcranial doppler ultrasound (TCDU) of the medial cerebral artery to measure the frequency and type of GME in circulation and cerebral blood flow. In addition, blood samples will be taken to analyse various known biomarkers of brain injury (S100) and the inflammatory response (interleukins 6, 8, and 10 and TNF alpha) before the operation begins and 1, 4, 12 and 24 hours after the operation has been completed.

Patients will be followed up at 30-days post-surgery with a phone or video call to collect information on any adverse events since leaving the hospital. The trial will run over 24 months. 6 months set up, 12 months recruitment and 6 months to analyse and report the findings.

The trial may be stopped early if there is a failure to recruit sufficient patients to meet the target sample size. There are no known expected adverse events from the trial intervention in this trial population, so we do not anticipate that the trial will be stopped on grounds of safety. Both bypass machines are routinely used as 'standard of care' so we do not anticipate that the trial will be stopped early based on a failure to deliver the intervention as allocated.

Bias arising from the randomisation process will be prevented by generating a random sequence of allocations and concealing randomised allocations until participants are enrolled and sufficient information has been recorded to uniquely identify them.

Bias due to deviations from the intended interventions will be minimised by blinding participants. The patient information leaflet (PIL) and the process of obtaining informed consent will describe the uncertainty about the effects of HCPB vs conventional CPB. Therefore, in the event of inadvertent unblinding of a participant, he or she should not have a strong expectation that any one method should lead to a more favourable result.

Bias in measurement of the outcomes will be minimised by blinding outcome assessors and using objective outcome measures; measurements of GME and blood biomarkers cannot be influenced by the operator/analyst.

Bias due to missing data will be minimised by using established methods developed in the Bristol Trials Centre to maximise the quality and completeness of the data (e.g. regular monitoring of data, detailed querying of data inbuilt into the study database, offering alternative methods for participating in follow-up (e.g. postal, online or telephone). Follow-up for the primary outcome, measured intraoperatively, should be complete for all patients.

Bias in selection of the reported result will be minimised by pre-specifying study outcomes and following a detailed analysis plan which will be prepared in advance of any comparative analyses of the study data.

Any instances of non-adherence to the assigned intervention will be fully documented and reviewed at study meetings and an action plan for maximising adherence drawn up as appropriate. Data will be analysed by intention to treat (i.e. according to the treatment allocation, irrespective of future management and events), and every effort will be made to include all randomised patients.

Intervention Type
Procedure/Surgery

Primary outcome measure
Frequency of gaseous micro-emboli measured continually during the operation by transcranial doppler ultrasound of the middle cerebral artery

Secondary outcome measures
1. The markers of inflammation and oxidative stress tumour necrosis factor (TNF)-alpha, interleukins (IL)-6, IL-8, IL-10 and S100 protein levels in blood serum measured by MILLIPLEX MAP Human Neurodegenerative Disease Magnetic Bead Panel 4 - Neuroscience Multiplex Assay at baseline, 1, 4, 12 and 24 hours after the operation

2. Serious adverse events (SAEs) experienced by participants up to 30 days after the operation, including hospital readmissions in the 30 days after being discharged home from the initial heart surgery, measured by a follow-up phone call with the patient and by accessing the patient's medical records if required

Overall study start date
03/11/2021

Completion date
30/09/2025

Eligibility

Key inclusion criteria
1. Age > = 40 years
2. Having elective or urgent CABG or AVR (with or without an associated CABG procedure AVR±CABG) via a partial or full sternotomy using using central aortic perfusion cannulae CPB.

Participant type(s)
Patient

Age group
Adult

Lower age limit
40 Years

Sex
Both

Target number of participants
Planned Sample Size: 40; UK Sample Size: 40

Key exclusion criteria
1. History of clinical stroke within 3 months prior to randomization
2. Cardiac catheterisation within 3 days of the planned surgery
3. Cerebral and/or aortic arch arteriography or interventions within 3 days of the planned surgery
4. Active endocarditis at time of randomisation
5. Planned concomitant aortic procedure such as root replacement
6. Clinical signs of cardiogenic shock or treatment with IV inotropic therapy prior to randomization
7. Myocardial infarction in the previous 4 days
8. Participation in an interventional (drug or device) trial
9. Unable to provide written informed consent
10. Prisoner

Date of first enrolment
17/04/2023

Date of final enrolment

08/01/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Trials Centre
University of Bristol
1-5 Whiteladies Road
Clifton
Bristol
United Kingdom
BS8 1NU

Sponsor information

Organisation
University Hospitals Bristol and Western NHS Foundation Trust

Sponsor details
Research and Innovation
Education & Research Centre Level 3
Upper Maudlin Street
Bristol
England
United Kingdom
BS2 8AE
+44 (0)117 342 0233
R&DSponsorship@uhbw.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.uhbristol.nhs.uk/

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (BHF); Grant Codes: CH/1992027/7163

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

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
30/09/2026

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

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?
HRA research summary			28/06/2023	No	No