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A feasibility study for a randomised controlled trial of two different preservative fluids for heart transplantation.

Submission date
12/09/2023

Recruitment status
Recruiting

Registration date
27/11/2023

Overall study status
Ongoing

Last Edited
18/11/2025

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Donor hearts are injected with a preservative fluid to protect them during transport to the transplant recipient. Currently, there are two different fluids used for this purpose in the UK, St Thomas' solution and Custodiol-HTK. St Thomas' is the standard fluid used in most UK transplants. Some animal studies and data from previous transplants have suggested that Custodiol-HTK may preserve the heart better. However, it is not known if this is true, because no one has ever tested this in a controlled way in humans. This study aims to conduct a randomised controlled trial (RCT) - the gold standard in research - to compare the two fluids. To test whether there is truly a difference, data from around 450 patients will need to be collected. This will take a long time. Therefore, this study will first test if enough patients will consent to take part in the study to make it realistically possible. This is called a feasibility study.

Who can participate?
Adult patients scheduled to be heart transplant recipients aged over 18 years old

What does the study involve?
All UK heart transplant recipients will be asked whether they wish to be involved in the trial. If they do, they will be randomly allocated with hearts that have received either Custodiol-HTK or St Thomas' solution before they are transplanted. This will be done for 50 hearts, which should take less than 1 year. The primary aim of the project is to see if more than two-thirds of eligible heart transplant recipients consent to take part and go on to receive a heart that has been correctly randomised.

What are the possible benefits and risks of participating?
Conducting this feasibility study will hopefully prove that it is possible to conduct the RCT. By conducting the RCT the question: "Which preservative fluid should we use in heart transplantation?" can be answered, and, if one is shown to be better, change practice in the UK, saving the lives of transplant recipients.

Both of the preservative solutions involved in this trial have been extensively used and researched in the field of cardiac surgery. They have both also been used in cardiac transplantation around the world for nearly 50 years and have shown to have excellent safety profiles. They both hold MHRA approval for the specific use of myocardial preservative solutions in cardiac transplantation. Although St Thomas' solution is the most used in the UK, as it forms part of the UK standard cardiac retrieval protocol, surgeons can currently choose to use Custodiol-HTK according to their preference. Transplant recipients would not normally be informed which solution has been used. As a result, there is not thought to be any additional risk to participants as a result of taking part in this trial, beyond the risks that they are informed of when consenting to receive a cardiac transplant. The outcomes of recipients will be monitored to assess if there is a difference between the two solutions, as outlined in the secondary aims of this feasibility study.

Where is the study run from?
Royal Papworth Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2023 to September 2026

Who is funding the study?
Heart Research UK (UK)

Who is the main contact?
randdenquires@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Group inbox account

Contact details
Royal Papworth Hospital
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY
+44 (0)1223 638000
papworth.fcustos@nhs.net

Type(s)
Principal investigator

Contact name
Dr Marius Berman

ORCID ID
https://orcid.org/0000-0002-9144-5376

Contact details
Royal Papworth Hospital
Cambridge Biomedical Campus
Cambrigde
United Kingdom
CB2 0AY
+44 (0)1223 638000
marius.berman@nhs.net

Type(s)
Scientific

Contact name
Dr Luke Williams

ORCID ID
https://orcid.org/0000-0002-2744-6446

Contact details
F-CUSToS Trial Manager
Royal Papworth Hospital
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY
+44 (0)1223 638289
luke.williams5@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007011

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
P03062, IRAS 1007011, CPMS 56717

Study information

Scientific Title
Feasibility study for randomised controlled trial of Custodiol-HTK vs St Thomas' solution for cardioplegia and cold static storage of UK donor hearts in cardiac transplantation (F-CUSToS)

Acronym
F-CUSToS

Study objectives
The study team aim to conduct a randomised controlled trial (RCT) - the gold standard in research - to compare two fluids used to preserve donor hearts during heart transplantation. We want to see if one of the fluids can reduce the rate of primary graft dysfunction, which is when the heart fails immediately after being transplanted. Data from approximately 450 patients will be required to test whether there is truly a difference. This will be difficult and take a long time. Therefore, this study will first test if enough patients are willing to take part in the study to make it realistically possible. This is called a feasibility study. This intends to assess what proportion of eligible patients consent to take part and, for those that do, what proportion are enrolled properly in the study and receive the correctly allocated treatment. This will help the team to decide whether the RCT is feasible to conduct in the future.

The secondary objectives of this trial are to assess the overall methodology of the study to see if it can or should be improved for the RCT and to assess whether any difference between the two fluids is seen, even with the small number of patients (50) that will be included in the feasibility study. All aspects of the trial conduct will be assessed and data will be collected on clinical outcomes after transplant, such as the development of primary graft dysfunction (heart failure in the first 24 hours), death within 30 days and post-operative complications.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/11/2023, South Cambridge REC (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8084, (0)207 104 8194; cambridgesouth.rec@hra.nhs.uk), ref: 23/EE/0224

Study design
Randomized controlled single-blind study

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Organ preservation during cardiac transplantation

Interventions
Donor cardiac organ retrieval will proceed according to the nationally standardised protocol, as set by the National Organ Retrieval Service (NORS). The only change to the protocol will be the randomisation, using SealedEnvelope, to receive either Custodial-HTK or St. Thomas' solution. Donor hearts included in the study will be randomly allocated on a 1:1 basis to receive either Custodiol-HTK or St Thomas' solution as cardioplegia and preservative solution during the organ retrieval process.

For the Custodiol-HTK (treatment) arm:
Following cross-clamping of the ascending aorta, at least 3.5L of cold Custodiol-HTK will be perfused into the aortic root, over at least 10 minutes at a perfusion pressure of 40-50mm Hg. The heart will then be stored in 2L of cold Custodiol-HTK solution for transport.

For the St Thomas' Solution (Control arm):
Sterile Concentrate for Cardioplegia Infusion (SCfCI) will be diluted by adding 20ml of SCfCI to 1 litre of Ringers solution. Following cross-clamping of the ascending aorta, the correct volume of reconstituted SCfCI will be perfused into the aortic root according to the donor weight as outlined below:
- Donor weight 30-70 Kg: administer 1 litre of reconstituted SCfCI solution
- Donor weight >70 Kg: administer 1.5 L of reconstituted SCfCI solution
- At the request of the recipient transplant surgeon, it is permissible to change the above doses depending on logistics and/or donor physiology.
The delivery pressure will be 60-90 mmHg and the heart will be stored in 2L of cold 0.9% sodium chloride solution, as is standard practice according to the UK NORS protocol.

Participants (recipients of donor cardiac allografts that have received one of the above treatments as part of the random allocation process) will be blinded to their treatment allocation. It is not possible to blind the healthcare staff involved in the transplant process as the solutions have different volumes and methods of administration and are different colours. Healthcare staff who look after the recipient but are not directly involved in the transplant retrieval or implant procedures should not be informed of the treatment allocation.

The duration of treatment is from the point of perfusion via the aortic root at the donor hospital until the perfusate is washed out prior to transplantation into the recipient. The safety reporting will cover the 24-hour post-surgery upon admission to recovery from theatres. The patient will then be followed up until 30 days after surgery.

Discussion of the primary outcome:
The primary outcome will measure the proportion of eligible hearts randomised that receive the correct intervention. This is a composite outcome. For the purpose of this study, eligible hearts are defined as hearts from DBD donors, where an offer has been made to a recipient at a UK transplant centre. The composite outcome therefore includes the proportion of hearts where both donor family and recipient consent to take part in the study and where randomisation occurs according to the protocol and the heart is preserved in the allocated preservative solution. We feel this composite outcome provides the best estimate of the feasibility of the larger trial. A proportion of two-thirds will be considered reasonable, as it would indicate approximately 90 patients per year being recruited.
A power calculation for a superiority trial based on the development of primary graft dysfunction as the primary outcome, with an estimated effect size difference of 12% absolute risk reduction in PGD between the two solutions (or 15 cases of primary graft dysfunction prevented per year) gives a sample size of 450 for a power of 80%. Approximately 140 adult DBD heart transplants are performed in the UK each year. We therefore estimate the larger trial taking a maximum of 5 years to complete.

The primary endpoint will be analysed once recruitment ceases, after 50 patients have successfully been recruited. This is anticipated to be not more than 18 months from recruitment beginning.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
St Thomas' solution, Custodiol-HTK

Primary outcome(s)
The proportion of eligible hearts randomised that receive the correct intervention, once recruitment ceases after 50 patients have successfully been recruited. This is anticipated to be not more than 18 months from recruitment beginning.

Key secondary outcome(s))
The following secondary endpoints will be analysed 30 days after the final recruited patients undergoes their transplant:
1. Dataset completion rate
2. The development of Primary Graft Dysfunction, according to the 2014 ISHLT Consensus Definition
3. Cardiac Power Output Index at admission to ICU and at 6h post-operation
4. 30-day mortality
5. Time to death within the limits of the study
6. Development of postoperative complications: Dysrhythmias; myocardial infarction; stroke; transplant rejection; infection (from any source); venous thromboembolism; 30-day re-admission; hyponatraemia (Na<125mEq/L)
7. Length of ICU stay
8. Length of hospital stay

Completion date
20/09/2026

Eligibility

Key inclusion criteria
1. Age over 18 years old
2. Listed for a heart transplant in the UK
3. All categories of listing including urgent and super-urgent
4. All pathologies leading to the requirement for heart transplant
5. Second, third or subsequent heart transplants within the same individual will be eligible provided this subsequent transplant does not occur in an emergency setting during the same hospital admission as the index heart transplant. The index transplant would remain eligible for inclusion in the trial in this case.
6. Patients who are simultaneously enrolled in other trials will be considered eligible to take part in this study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Recipients under the age of 18 years old at the time of transplantation (patients listed when under the age of 18 will be eligible if their transplant is conducted on or after the date of their 18th birthday, provided that they have also provided consent to take part in the trial on or after the date of their 18th birthday)
2. Emergency re-transplant patients, where the re-transplant occurs within the same admission as the index transplant
3. Patients who receive hearts procured from donation after circulatory death (DCD) donors. These patients are excluded from the study because the process of organ retrieval from DCD is very different, involving ex situ perfusion of the beating heart with oxygenated blood, rather than maintenance of the heart in the cold arrested state with a preservative solution. The system for doing this ex situ perfusion is called the organ care system (OCS). Currently approximately 10% of UK heart transplants are performed using a DCD heart
4. Patients who receive hearts from DBD donors procured using the organ care system device or normothermic regional perfusion (NRP). This rarely occurs
5. Patients receiving a heart-lung block or a multi-visceral transplant

Date of first enrolment
21/08/2025

Date of final enrolment
21/08/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Queen Elizabeth Hospital
Edgbaston

Birmingham
England
B15 2TH

Study participating centre
Golden Jubilee Hospital
Agamemnon Street
Clydebank, near Glasgow
Scotland
G81 4DY

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
England
M23 9LT

Study participating centre
Harefield Hospital
Hill End Road
Harefield
Uxbridge
England
UB9 6JH

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

Study participating centre
Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus

Cambridge
England
CB2 0AY

Sponsor information

Organisation
Papworth Hospital NHS Foundation Trust

ROR
https://ror.org/01qbebb31

Funder(s)

Funder type
Charity

Funder Name
Heart Research UK

Alternative Name(s)
HRUK

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 will be available upon request from the Sponsor, Royal Papworth Hospital (Papworth.randdenquiries@nhs.net). Only anonymised data will be shared. The data requested will be reviewed by the Sponsor and released for a specified time period where reasonable applications are made by appropriate individuals or organisations.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	03/07/2023	25/09/2023	No	Yes
Protocol file	version 2	30/01/2025	18/11/2025	No	No