ISRCTN15444108 https://doi.org/10.1186/ISRCTN15444108

The study investigates how machine preservation methods protect and repair donor livers, and aims to understand which methods work best and why, so more of these higher-risk livers can be safely used for transplants

Submission date 07/04/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 23/04/2026	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 07/05/2026	**Condition category** Digestive System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

There are not enough donated livers for everybody who needs one, and as a result, thousands of patients worldwide are waiting for liver transplants, with many dying while waiting for a life-saving organ. One reason for this shortage is that some usable livers from donors who are considered of high-risk are being thrown away out of concern that they might not work well after transplantation due to a problem called ischaemia reperfusion injury (IRI).

The discarded organs are mostly those coming from donors who have died due to cardiac arrest (called 'donation after circulatory death' or DCD), with only 27% of them being used in the UK. The quality of these DCD organs could be improved by changing how they are preserved after being removed from the donor. The most commonly used strategy is still to remove the livers and put them in an icebox ('static cold storage' or SCS). The alternative approaches, which are more complex and expensive but can also improve the quality of the DCD livers, involve using machines to pump fluids through the livers ('machine perfusion' or MP).

Three MP methods are being used in patients: 1) normothermic regional perfusion (NRP), which involves pumping the donor's blood through the liver after the donor has died but the liver is still in the donor's body; 2) normothermic machine perfusion (NMP), in which the liver is pumped with blood outside of the donor's body; and 3) hypothermic machine perfusion (HOPE), which is also used outside of the donor's body by pumping cold fluid into the liver. HOPE and NRP have been shown to improve how well DCD livers function after transplantation. NMP can also improve the quality of the DCD livers, but its main advantage is that it allows confirming that the donated liver functions well before proceeding with the transplant. Until now, there has not been a proper comparison of these methods, and we do not understand well the mechanisms through which MP improves the quality of the DCD livers.

The plan is to conduct a study where 36 DCD human livers will be split into three groups: SCS, NRP, and HOPE. After that, they will be put in NMP to confirm that they are good enough to be transplanted and to study the mechanisms through which NRP, SCS and HOPE work.

Who can participate?
Adult patients listed for elective liver transplantation.

What does the study involve?
This study tests three different ways of preserving donor livers from donors after circulatory death before transplantation. Donor livers are randomly assigned to standard cold storage, bloodbased regional perfusion in the donor, or oxygenated cold perfusion after retrieval, before all livers undergo normothermic machine perfusion and transplantation, where possible.

What are the possible benefits and risks of participating?
Benefits and risks not provided at time of registration

Where is the study run from?
Kings College Hospital, UK.

When is the study starting and how long is it expected to run for?
March 2025 to December 2026.

Who is funding the study?
King's College Hospital NHS Foundation Trust, UK.
Medical Research Council, UK.

Who is the main contact?
Prof Alberto Sanchez-Fueyo, sanchez_fueyo@kcl.ac.uk

Contact information

Type(s)
Principal investigator, Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
328606

Central Portfolio Management System (CPMS)
58963

Medical Research Council (MRC) grant code
MR/X019470/1

Study information

Scientific Title
Mechanistic evaluation of machine perfusion strategies in donation after circulatory death liver transplantation

Acronym
iMAPS

Study objectives
Primary objective: To determine the effect of different preservation strategies on the development of mitochondrial damage following reperfusion.

Secondary mechanistic and exploratory objectives:
1) To determine the effect of different preservation strategies on mitochondrial integrity using alternative analytical strategies.
2) To assess the overall cellular metabolic and redox state during NMP and after reperfusion in the transplant recipient.
3) To determine how the different preservation strategies impact on the levels of inflammatory mediators during NMP.
4) To determine the influence of the different preservation strategies on biomarkers of liver damage and function during NMP.
5) To compare the applicability of different preservation strategies in DCD liver transplantation.

Secondary clinical objectives:
1) To determine the impact of the 3 different MP strategies on clinical outcomes up to 12 months following transplantation.
2) To develop objective means to assess the quality and suitability for transplantation of DCD livers.
3)To compare the applicability of different preservation strategies in DCD liver transplantation.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/11/2023, West Midlands - South Birmingham Research Ethics Committee (2 Redman Place Stratford, London, E20 1JQ, United Kingdom; +44 0207 104 8000; southbirmingham.rec@hra.nhs.uk), ref: 23/WM/0226

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Device feasibility

Study type(s)

Health condition(s) or problem(s) studied
The patient population consists of adults listed for elective liver transplantation

Interventions
Open-label, prospective, three-arm, phase II randomized clinical trial investigating the effects of 3 different preservation techniques on pre-defined functional and mechanistic endpoints in DCD liver transplantation.

Consecutive circulatory death donors (DCD) assigned to recipients consented to participate in the trial will be randomized to one of three arms (n=12 per arm):
Arm 1 (Static cold storage: SCS). The donor liver will be flushed in situ with 4 °C UW preservation solution (or HTK) through the aorta and portal vein, retrieved, and transported to the transplant centre in an icebox.
Arm 2 (Normothermic regional perfusion: NRP). The donor aorta and inferior cava vein will be cannulated, followed by descending thoracic aorta cross-clamp and initiation of perfusion (Cardiohelp device) with the donor's own blood at 37 °C for 2 h (while monitoring pump flow, venous O2 saturation, lactate and ALT), followed by in-situ flush with 4 °C preservation solution as in the SCS arm.
Arm 3 (Hypothermic oxygenated perfusion: HOPE). The liver will be retrieved and preserved as in the SCS arm. Then, on arrival to the transplant unit, the portal vein and hepatic artery will be cannulated, and the liver perfused with hypothermic oxygenated solution (VitaSmart device) for 2 h.
All livers, regardless of their allocated Arm, will then be perfused under normothermic machine perfusion conditions for at least 4 h before transplantation.
Primary analysis will be as per protocol and include all livers that are perfused under normothermic machine perfusion (NMP) conditions for at least 4 h. A secondary analysis including recipient outcomes will include only livers actually transplanted.
The overall study duration will be up to 30 months. The study participant recruitment phase will last up to 18 months. Patient follow-up will be 12 months. Clinical outcome data will be collected up to 5 years post-transplant.

Intervention Type
Device

Phase
Phase II

Drug/device/biological/vaccine name(s)
NRP (normothermic regional perfusion), SCS (static cold storage) and HOPE (hypothermic perfusion)

Primary outcome(s)
1. Ischaemia-Reperfusion injury (IRI) damage measured using a surrogate post-transplant clinical endpoint of IRI damage up to 12 months post-transplant, such as reperfusion syndrome, early allograft dysfunction (assessed by the Model for Early Allograft Function (MEAF) and Liver Graft Assessment following Transplantation (L-GrAFT) scores), clinically relevant non-anastomotic biliary complications, comprehensive surgical complication index, Clavien-Dindo complication grade, and graft/patient survival. Clinical outcome data up to 5 years post-transplant will be collected if required, at 12 months post transplant

2. Mitochondrial function in DCD livers measured using changes in mitochondrial complex I enzyme activity in liver tissue samples at 30 minutes and 4 hours after initiation of normothermic machine perfusion (NMP)

3. Quality and suitability for transplantation of DCD livers measured using associations between biomarkers of liver damage and function collected from liver tissue, perfusate, and recipient blood and post-transplant clinical outcomes, with samples collected at before NMP, at 30 minutes and 2 hours during NMP, and at 2 hours post-reperfusion in the recipient

Key secondary outcome(s)
1. Oxidative damage to mitochondrial DNA (mtDNA), genomic DNA (gDNA), and cardiolipin in liver tissue, measured using quantitative assays of oxidised mtDNA, gDNA, and cardiolipin, at before NMP, 30 min and 2 h after initiating NMP, and 2 h after reperfusion in the recipient

2. Metabolic and transcriptional profiles of liver and bile duct tissue, measured using targeted metabolomics of polar and nonpolar metabolites and bulk RNA sequencing at before NMP, 30 min and 2 h after initiating NMP, and 2 h after reperfusion in the recipient

3. Immune activation and cellfree nucleic acid release during NMP, measured using quantification of immune cell subsets and inflammatory cytokines in perfusate, singlecell RNA sequencing of liver tissue, and measurement of mtDNA and cellfree DNA (cfDNA) in perfusate, at before NMP, 30 min and 2 h after initiating NMP, and 2 h after reperfusion in the recipient

4. Liver injury, function, and bile composition during NMP, measured using data collected on sequential perfusate biochemical markers (AST, ALT, bilirubin, alkaline phosphatase, LDH, lactate), bile production and bile pH, bicarbonate and glucose concentrations, liver and bile duct histology, and perfusate proteomics, at one time point

5. Posttransplant ischaemiareperfusion injury and graft outcomes, measured using data collected on surrogate clinical endpoints including reperfusion syndrome, early allograft dysfunction assessed by MEAF and LGrAFT scores, clinically relevant nonanastomotic biliary complications, Comprehensive Complication Index, Clavien–Dindo complication grade, and 6-month graft and patient survival, at one time point

6. Associations between biomarkers of liver damage and function during NMP and posttransplant clinical outcomes measured using statistical association analyses between biomarker data and clinical endpoints at one time point

7. Use of retrieved livers by preservation strategy measured using the proportion of livers retrieved and subsequently transplanted for each preservation strategy at one time point

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Donor inclusion criteria:
1. DCD category III donors considered for abdominal organs-only retrieval
2. Donor age ≥18 years
3. Retrieval procedure allocated to the recruiting site's NORS team
4. Donor liver accepted for a patient on the recruiting site's transplant waiting list via the standard offering process
5. Donor BMI <35kg/m2
6. Predicted cold ischaemic time <8 hours
7. Donor family has given consent to use donated liver for research

Recipient inclusion criteria:
1. Recipients 18 years of age or older
2. Listed on an elective transplant waiting list
3. Suitable to receive a DCD graft based on the liver listing MDT
4. Willing and able to consent for the study participation

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
Donor exclusion criteria (at the time of randomisation):
1. Donor is HIV, hepatitis B (HBV HbsAg) or hepatitis C (HCV RNA) positive
2. Any medical condition that, in the opinion of the principal investigator, would interfere with safe completion of the trial

Donor exclusion criteria (at the time of retrieval):
1. Liver weight >2.5 kg
2. Macroscopic evidence of advanced fibrosis
3. Functional donor warm ischaemia (defined as a period between the systolic blood pressure <50mmHg and aortic cold flush) >30 minutes
4. Any other clinical issue that in the opinion of the surgical team constitutes a contraindication to proceed with transplantation

Recipient exclusion criteria:
1. High-risk surgical candidates (e.g. presence of extensive portomesenteric thrombosis, previous complex upper abdominal surgery)
2. Patients undergoing liver re-transplantation or multi-organ transplantation
3. Patients receiving super-urgent transplantation for acute and acute-on-chronic liver failure

Date of first enrolment
25/03/2025

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Kings College Hospital
Denmark Hill
London
England
SE5 9RS

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
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CB2 0AU

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital
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NW3 2QG

Study participating centre
University Hospitals Birmingham NHS Ft
Queen Elizabeth Hospital
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B15 2TH

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Organisation
King's College Hospital NHS Foundation Trust

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 4	21/07/2025	07/04/2026	No	No