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Cytokine removal in kidney transplantation

Submission date
31/10/2023

Recruitment status
Recruiting

Registration date
06/02/2024

Overall study status
Ongoing

Last Edited
17/06/2025

Condition category
Surgery

[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
When kidneys are removed from an organ donor they are normally stored on ice until they are ready to be transplanted. A kidney can be preserved safely at a low temperature in these conditions. However, there is some degree of deterioration and the longer the kidney is left in this condition the more it deteriorates.
We have developed a technique that may improve the quality of the kidney. This involves placing the kidney on a machine and passing a warmed, oxygen-rich solution containing red blood cells through it. This is called warm perfusion. Under these conditions the kidney can start to function again and produce urine.
We have trialled warm perfusion in kidney transplantation with no adverse effects. From our research we know that whilst being perfused, kidneys release cells that cause inflammation. In a small number of patients, we want to test whether adding a specialised filter to the machine has any beneficial effects. The filter may be able to remove the molecules that cause inflammation and so improve the condition of the kidney. The results of this small study may be used to design a larger clinical trial to test the use of the filter in warm perfusion in a larger number of patients.

Who can participate?
You are able to participate if you are aged over 18 years, are on renal replacement treatment (dialysis) and are on the waiting list for a first or second kidney transplant in the East of England. You are unable to participate if you are younger than 18 years, are pre-dialysis, are receiving a third or subsequent kidney transplant, or are recieving a kidney along with another organ (e.g. dual kidney transplant, simultaneous pancreas-kidney transplant). We are unfortunately unable to facilitate participation for patients waitlisted outside the East of England region.

What does the study involve?
You will be prepared for surgery in the normal way. Standard care involves keeping the transplant kidney under cold storage in ice until the time of the transplant operation.
If you consent to take part in this trial then the transplant kidney will be taken out of ice and will undergo warm perfusion. It will be placed on a machine and warmed with an oxygenated blood-based solution before it is transplanted. Kidneys that are perfused will be randomly assigned to one of two groups. In one group a special filter will be added to the perfusion circuit to reduce the risk of inflammation. In the other group the kidney will be perfused without the special filter in the circuit. These treatments are not part of standard care.
Should there be any problem with the warm perfusion procedure then the kidney can be quickly

removed from the perfusion machine and returned to cold storage in ice before transplantation. While you are still in surgery we will take a small tissue biopsy from the kidney after transplantation. Although there is a small risk of causing bleeding from the kidney biopsy site (less than 5%) your surgeon will be able to repair the bleeding site if this happens. Genetic analysis will be carried out on the biopsy tissue from the transplanted kidney. The analysis will look at the expression of genes involved in inflammation. The results of this genetic analysis will not be fed back to you.
If you take part in the study you will be asked to provide a few additional blood and urine samples for analysis. Blood and urine samples will be taken at the start of surgery and then at 2 and 5 days after transplant. The samples are needed to measure levels of inflammation in your body before and after transplantation. This is to test whether adding a filter into the circuit during warm perfusion can reduce the inflammatory response and reduce injury.
Follow-up after transplant will follow normal standard care which usually involves clinic visits at least twice a week for six weeks and then weekly for a further six weeks.
The data collected from the study will be stored in a secure database. Tissue, blood and urine samples will be stored within secured laboratories only accessed by the transplant research team. Samples will only be transferred outside the research site in a pseudonymised format (with identifiable information removed) and will only be analysed at labs within the UK. Once the samples have been analysed, they will be disposed of as per Human Tissue Authority guidance.

What are the possible benefits and risks of participating?
This study is being performed to test whether the specialised filter added during warm perfusion can improve the condition of the kidney. The first step is to assess whether this is practical before carrying out a larger trial. We cannot guarantee that this will improve the outcome of your kidney transplant but it will help us to improve future techniques of kidney preservation. This may enable us to transplant more kidneys in the future.
There are no potential side effects to you. This technique of warm perfusion is applied to the kidney only, before it is transplanted. There is a small risk that the kidney might be damaged during the assessment and therefore could not be transplanted. This has not happened in our experience of 200 cases so far but it remains a potential risk.

Where is the study run from?
The research is being organised by the Transplant Research Team, Department of Surgery, University of Cambridge and carried out at the Addenbrooke's Transplant Unit, Cambridge University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
December 2022 to June 2026

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

Who is the main contact?
Dr Sarah Hosgood, sh744@cam.ac.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
322728

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 322728

Study information

Scientific Title
A randomised pilot study to assess the safety and feasibility of adding a Cytosorb filter during kidney normothermic machine perfusion.

Study objectives
It is hypothesised that adding a Cytosorb filter to the circuit during ex-vivo normothermic machine perfusion of human deceased-donor kidneys prior to transplantation, will reduce the inflammatory and immune response in the kidney after transplantation.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 28/07/2023, HRA Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8000; approvals@hra.nhs.uk), ref: IRAS 322728

2. Approved 23/05/2023, NHSBT RINTAG (500 North Bristol Park, Filton, Bristol, BS34 7QH, United Kingdom; +44 300 123 23 23; Lucy.Roberts2@nhsbt.nhs.uk), ref: Study 148

Study design
Interventional Phase I (safety and feasibility) randomized pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment, Safety, Efficacy

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

Health condition(s) or problem(s) studied
Kidney transplantation from deceased donors.

Interventions
Prospective kidney transplant recipients on the waiting list at a single centre (Cambridge University Hospitals NHS Foundation Trust), who are eligible to participate in this study, will be approached for consent. A total sample size of 20 patients will be recruited.

Consenting participants will be randomised in a 1:1 ratio, to each of the two study groups:
1. Normothermic machine perfusion (NMP)
2. Normothermic machine perfusion with a Cytosorb filter (NMP+C)

Randomisation will be performed after the transplant recipient and kidney have both arrived in the transplant centre and a final decision to proceed with transplantation has been made. The randomisation will be performed by an independent company that will use a sealed envelope system created using a computer-generated randomisation sequence. The patients and doctors caring for the patients after surgery will be blinded to the groups.

The intervention with be 6 hours and follow-up will be 3 months post-transplant.

Intervention Type
Device

Pharmaceutical study type(s)
Device

Phase
Phase I

Drug/device/biological/vaccine name(s)
Cytosorb filter

Primary outcome measure
Inflammatory and immune gene expression measured in cortical biopsy from the kidney 60 minutes post-transplant

Secondary outcome measures
1. Rates of delayed graft function, defined as the requirement for dialysis in the first 7 days post-transplant
2. Duration of delayed graft function, measured from the first to the last episode of dialysis post-transplant
3. Incidence of primary non function, defined as a non-functioning graft up to 3 months post-transplant
4. Graft function at 3 months post-transplant measured by levels of serum creatinine and estimated glomerular filtration rate (eGFR)
5. Incidences of biopsy-proven rejection measured by histopathology up to 3 months post-transplant
6. Complications (infection, re-operation due to bleeding) recorded up to 3 months post-transplant
7. The length of hospital stay post-transplant
8. Levels of inflammation/immune and injury markers measured in the perfusate and urine collected from the kidney during NMP (pre, 2, 4 and 6 h). Samples will be analysed using ELISA techniques
9. Isolation of peripheral blood mononuclear cells blood samples collected pre-transplant and on day 1 and day 5 post-transplant
10. Biomarkers of kidney injury measured by ELISA using plasma samples collected from the patients on day 1 and day 5 post-transplant

Overall study start date
01/12/2022

Completion date
01/06/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 17/06/2025:
1. Patients receiving a kidney from donation after brain death (DBD) and/or donation after circulatory death (DCD) donor ≥50 years
2. Transplant recipients aged ≥18 years
3. Patients undergoing a 1st or 2nd kidney transplant
4. Patients who have given written informed consent

Previous inclusion criteria:
1. Patients receiving a kidney from donation after brain death (DBD) and/or donation after circulatory death (DCD) donor ≥50 years
2. Transplant recipients aged ≥18 years
3. Patients undergoing a 1st or 2nd kidney transplant
4. Patients who have given written informed consent
5. Patients who are receiving renal replacement therapy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
100 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
Current exclusion criteria as of 17/06/2025:
1. Patient receiving a kidney from DCD and DBD donor <50 years old
2. Patients receiving a 3rd or subsequent kidney transplant
3. Patients receiving multi-organ transplants e.g. simultaneous pancreas-kidney transplantation
4. Patients receiving dual kidney transplants
5. Paediatric en-bloc kidney transplants
6. Kidneys with complex vascular anatomy

Previous exclusion criteria:
1. Patient receiving a kidney from DCD and DBD donor <50 years old
2. Patients receiving a 3rd or subsequent kidney transplant
3. Patients receiving multi-organ transplants e.g. simultaneous pancreas-kidney transplantation
4. Patients receiving dual kidney transplants
5. Paediatric en-bloc kidney transplants
6. Patients that are pre-dialysis
7. Kidneys with complex vascular anatomy

Date of first enrolment
01/01/2025

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
University of Cambridge

Sponsor details
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Sponsor type
University/education

Website
http://www.cam.ac.uk/

ROR
https://ror.org/013meh722

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 1223 348490
cuh.research@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.cuh.org.uk/

ROR
https://ror.org/04v54gj93

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
On completion of the study, the data will be analysed and tabulated and a Final Study Report prepared. The results will be presented locally and nationally, and written up as a manuscript for publication in a peer-reviewed journal.
The data will be owned by the University of Cambridge.
Participants that request the results will be provided with the Final Study Report and or the published manuscript.
The study protocol, full study report, will be made publicly available on the trial registry database when the trial has been completed.

Intention to publish date
01/02/2026

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