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Investigation of the safety and feasibility of preservation of kidneys for up to 24 hours at normal body temperature prior to transplant

Submission date
21/01/2021

Recruitment status
No longer recruiting

Registration date
28/01/2021

Overall study status
Completed

Last Edited
19/05/2025

Condition category
Urological and Genital Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims

This study aims to demonstrate the safety and feasibility of using a new device for preserving kidneys before transplantation. The current standard of care is for kidneys to be transported from the donor hospital to the recipient on ice (Static Cold Storage, SCS). Whilst cooling the organ slows the rate of metabolism and deterioration, it prevents assessment of the kidney in a functioning state and does not prevent deterioration. SCS affects kidneys from elderly donors and those with other illnesses such as high blood pressure most severely, and these donors are accounting for an increasing number of transplants. The median waiting time for a kidney transplant in the UK is 829 days, with around 250 patients dying on the waiting list each year. An improved method of preservation would increase the proportion of available organs that could successfully be transplanted, decreasing waiting time and the number of deaths on the waiting list.

Researchers have developed a device that perfuses kidneys with oxygenated perfusate (fluid) at normal body temperature (normothermic perfusion, NMP). They have demonstrated that kidneys that have been rejected for transplantation can be preserved in this manner for up to 24 hours. This study would bring this technology into clinical practice, starting with short duration perfusions of 2 hours and increasing up to 24 hours. Kidneys that are deemed suitable for transplantation will be transported to the Oxford Transplant Centre in the usual manner (SCS). Those that are appropriate for the study will be perfused for increasing lengths of time, then transplanted. The researchers will assess the safety and feasibility of this technique, and simultaneously study the clinical outcomes and function of NMP-preserved kidneys; compare this to historical matched controls; examine the effects of NMP on the kidney; identify markers during preservation that may predict future kidney function; and characterise the perfusion system.

Who can participate?

Patients on the waiting list to receive a kidney transplant at the Oxford Transplant Centre, and who are matched to an eligible kidney.

What does the study involve?
The study involves applying the new perfusion technology to the kidney for between 2 and 24 hours before the transplant. This compares to standard treatment, where the kidney would remain on ice. As a part of the study the researchers will take some additional blood and urine samples on top of those expected as part of standard care. They will also follow up how the patient and kidney are doing from transplant until discharge (or for the first 7 days after the transplant), and again at 30 days, 3 months, and 1 year after the transplant.

What are the possible benefits and risks of participating?
Similar preservation technology has been used in other trials of kidney transplantation, but only for up to 1 hour. The researchers are aiming to increase this preservation time up to 24 hours, and the effects of this on the kidney are unknown. There is a small risk that machine malfunction could damage the kidney. The kidney will be constantly monitored, and if there is any sign of a problem it will be returned to ice (the standard preservation technique) and transplanted as soon as possible.
The researchers will take daily blood and urine samples as part of the study, which may be inconvenient and cause bruising. However, whilst an inpatient after kidney transplantation daily blood tests are part of routine care. The researchers will take an extra 5-10 ml (1-2 teaspoons) where possible at the same time as routine blood tests, keeping the number of extra tests needed to a minimum. They will arrange follow-up visits to coincide with routine clinic appointments, where possible, to minimise the inconvenience this poses.
It is likely that there will be no direct benefit as a result of participating in this study. It is possible that the kidney will be in a better condition after this form of preservation than it would have been after storage on ice only.

Where is the study run from?
Oxford Transplant Centre (UK)

When is the study starting and how long is it expected to run for?
December 2018 to January 2024

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

Who is the main contact?
Mr Richard Dumbill
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
271359

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 47500, IRAS 271359

Study information

Scientific Title
Normothermic Kidney Perfusion Phase 1

Acronym
NKP1

Study objectives
Prolonged (2-24 hour) normothermic ex-vivo perfusion of the kidney is safe and feasible in the clinical setting.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/12/2020, Northwest - Greater Manchester South (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8221; gmsouth.rec@hra.nhs.uk), REC ref: 20/NW/0442

Study design
Non-randomized; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Renal failure

Interventions
This study investigates the use of extended-duration normothermic machine perfusion (NMP) prior to transplantation of the kidney. This process involves circulating blood, oxygen and nutrients through the kidney at normal body temperature (37 degrees) - rather than keeping the kidney on ice, which is the current standard of care. As such, the study intervention is applied to a human kidney that is retrieved for transplantation, rather than to an individual patient.

When a suitable donor organ becomes available, meets all inclusion criteria, and is allocated to a recipient who has previously been provided with verbal and written information regarding the study then a clinically-qualified member of the research team will approach the patient on arrival at the Oxford Transplant Centre to discuss the study and to take written informed consent. If the patient is not willing to proceed with the study at this stage, then organ preservation will be carried out using conventional techniques (Static Cold Storage) and transplanted as soon as possible, in line with the usual local protocol.

On arrival to hospital after being called in for transplant, the recipient will be assessed for fitness to proceed according to local procedures. If a recipient is deemed unfit for transplant at the time of admission, they will no longer be active on the transplant waiting list and as such will be excluded from the trial. Pre-operative assessment and investigations will not differ between trial patients and those receiving standard care, aside from a single blood sample and a single urine sample that will be taken following the induction of anaesthesia, at the time of transplant. The study cohort will consist of the first 36 consecutive eligible transplants who undergo transplantation with a normothermically perfused kidney.

Study transplants will be conducted in three stages with perfusions of increasing duration. Interim reports will be drawn up as each stage approaches completion. An initial group of 12 patients will receive kidneys that have undergone between two and six hours of NMP; the second group of 12 patients will receive kidneys that have undergone between 2 and 12 hours of NMP, and the final group of 12 patients will receive kidneys that have undergone between 2 and 24 hours of NMP. This sample size and step-wise increase in perfusion duration have been chosen in view of the primary end-point being assessment of safety and feasibility. 36 perfusions of increasing duration would provide sufficient evidence that the technique is safe, and would also permit exploratory analyses of markers of organ function to guide future studies into organ assessment, efficacy, and graft utilisation.

Perfusions will be performed with urinary recirculation, guided by local experience of this technique. The researchers will take a range of samples including perfusate and urine during perfusion, a pre-perfusion and post-reperfusion biopsy, and blood and urine samples immediately before, and on the days following transplantation as detailed in the protocol. The frequency and type of sample taken from the recipient will not differ in general from routine care after transplantation - daily blood tests are the standard of care. However, additional blood (approximately 10 ml, in addition to 10-15 ml required for routine clinical care) will be drawn for tests investigating novel biomarkers. The researchers will take daily samples whilst the patient remains an inpatient up to day 7 post-transplant. Should the patient be discharged earlier than

day 7 and attend a routine follow-up clinic appointment within 7 days of the transplant, the researchers will also use this visit as an opportunity to collect data, blood, and urine samples. Additional follow-up data will be collected at 30 days, 3 months, and 1-year post-transplant.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
OrganOx Metra (kidney prototype)

Primary outcome(s)
30-day graft survival, defined as a functioning graft in a patient who does not require chronic dialysis, assessed clinically at 30 days

Key secondary outcome(s))
1. Graft survival, defined as a functioning graft in a patient who does not require chronic dialysis, assessed clinically at 3 and 12 months
2. Patient survival assessed clinically at 30 days, 3 months, 12 months
3. Use of dialysis in the first 7 days post-transplant, assessed as incidence (i.e. number who required dialysis / total number) and frequency (i.e. number of dialysis sessions required per time period), assessed clinically in the first 7 days post-transplant
4. Incidence of functional delayed graft function, defined as a failure of serum creatinine to fall by at least 10% per day for the first 3 days
5. Creatinine reduction ratio assessed using (serum creatinine day 2 - serum creatinine day 1) / serum creatinine day 1 on Day 2
6. Total proteinuria each day measured as milligrams of urinary protein by 24-hour urine collection on postoperative days 1-4
7. Total urine production assessed using 24-hour collection on postoperative days 1-4
8. Incidence of Primary Non-Function (PNF), defined as persistent dialysis dependence at 3 months post-transplant
9. eGFR assessed using CKD-EPI formula at 30 days, 3 months, and 12 months
10. Creatinine gradient assessed at month 12, using (serum creatinine month 12 - serum creatinine month 3)
11. Proteinuria as a binary variable defined using published KDIGO cut-offs and quantitated by protein-creatinine ratio, at 30 days, 3 months and 12 months
12. Incidence of acute rejection, defined as biopsy-proven acute rejection diagnosed in accordance with the Banff criteria at 12 months post-transplant
13. Histology assessed using Reummuzi scoring and KIM-1 immunohistochemistry pre-perfusion and post-reperfusion
14. Serial measurement of injury biomarkers including LDH and NGAL using biochemical assay on postoperative days 1-4

Completion date
12/01/2024

Eligibility

Key inclusion criteria

Donor criteria:
1. Kidneys from deceased donors aged above 16 years
2. DCD or DBD
3. Accepted for transplantation according to local criteria
4. Cold ischaemia time (CIT) prior to NMP no greater than 10 hours

Recipient criteria:
1. Male or female, aged 18 years or older
2. On waiting list for kidney transplantation at Oxford Transplant Centre, Oxford
3. Provided informed consent for participation in the study
4. Able and willing to comply with all study requirements (in opinion of investigator or deputy)
5. Fit to proceed with kidney transplantation

Matched controls criteria:
1. Kidneys from donors aged 16 years or over
2. DBD or DCD
3. Recipients underwent transplantation of a deceased-donor kidney on or after 01/10/2016

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
36

Key exclusion criteria
Donor criteria:
1. Donor kidneys that would not be accepted according to local criteria
2. Donor kidneys accepted as a pair for dual transplant
3. CIT greater than 10 hours prior to initiation of NMP

Recipient criteria:
1. Not willing or unable to provide informed consent
2. Recipients aged less than 18 years
3. Participation in an investigational study likely to affect on interpretation of the trial data
4. Undergoing living donor kidney transplantation
5. Undergoing dual kidney transplantation
6. Undergoing transplantation of other organ(s) in addition to the kidney
7. Substantial risk of transplant not proceeding – e.g. risk of positive cross-match (in opinion of Investigator and/ or implanting surgeon)

8. Other significant disease or disorder which, in the opinion of the Investigator, may: (i) put the participant at risk by participating in the study; (ii) influence the result of the study; (iii) affect the participant's ability to participate in the study

Matched controls criteria:
1. Underwent transplantation of other organ(s) in addition to the kidney
2. Underwent dual kidney transplantation
3. Underwent living donor kidney transplantation
4. 12-month eGFR not available

Date of first enrolment
05/11/2021

Date of final enrolment
12/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Transplant Centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200022

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during the study are not expected to be made available due to concerns over confidentiality - this is because of the low patient numbers involved in the trial, and highly specialised nature of the treatment/intervention.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/05/2025	19/05/2025	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version V1.0	23/10/2020	28/01/2021	No	No
Protocol file	version 2.0	23/08/2021	02/11/2021	No	No
Protocol file	version 4.0	20/10/2023	11/03/2024	No	No