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Improving function of transplanted kidneys

Submission date
10/02/2016

Recruitment status
No longer recruiting

Registration date
10/02/2016

Overall study status
Completed

Last Edited
26/05/2023

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
In a healthy person, the kidneys are responsible for filtering out the waste products and excess water in the blood, and converting them into urine. If the kidneys suddenly stop working (acute kidney injury) or are suffering from severe, long-term disease of the kidneys (chronic kidney failure) then the body is unable to get rid of the waste products building up in the blood. Eventually, the kidneys are no longer able to support the body's needs (end stage renal disease) and so a treatment to replace the work of the failed kidneys is needed. Kidney transplantation is the best treatment for end-stage renal disease. Ideally, kidneys are donated by healthy, living donors however an ongoing organ donation shortage means that sometimes they need to be taken from a patient whose heart has stopped (donation after circulatory death, DCD). Using kidneys from DCD donors is very risky as the kidney could become damaged when it is connected to the blood supply in the recipient, after going without oxygen before the transplant (ischaemic reperfusion injury) causing it to not work properly (graft failure). In order to avoid this, the way that the kidney is stored between donation and transplantation is very important. Normally, the kidney is packed in ice before transplantation (cold storage), however this technique can still result in tissue damage and graft failure. Ex-vivo normothermic perfusion (EVNP) is a new technique where the kidney is warmed in a blood-based solution for a short period just before transplantation. The aim of this study it to find out whether EVNP technique can help to improve the function of transplanted kidneys in comparison to those kept using the cold storage technique.

Who can participate?
Adult patients having their first or second kidney transplant from a DCD donor.

What does the study involve?
Participants are randomly allocated to one of two groups. Following kidney harvest (removal from the donor), the kidneys are either kept in cold storage (emerged in a solution and packed with ice) or prepared for EVNP and placed in a protective, blood-like environment which is rich in oxygen. Participants in the first group receive a kidney which has been stored using the cold storage technique between donation and transplantation. Those in the second group receive a kidney which has been stored using the EVNP technique between donation and transplantation. Participants in both groups are followed up after 12 months in order to determine the graft failure rate for each of the different techniques.

What are the possible benefits and risks of participating?
Participants in the EVNP group may benefit from a better chance that their kidney transplant is successful in the long-run, however this is not certain. There are no specific risks of taking part in this study, however there is a risk with all kidney transplants that it may be unsuccessful, as well as a small <1% risk that the kidney may be damaged by the procedure.

Where is the study run from?
1. Addenbrookes Hospital, Cambridge (UK)
2. Freeman Hospital, Newcastle (UK)
3. Guy's Hospital, London (UK)

When is the study starting and how long is it expected to run for?
February 2016 to March 2021

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

Who is the main contact?
1. Mrs Hailey Austin (public)
2. Mr Matt Stark (scientific)

Study website
https://urldefense.proofpoint.com/v2/url?u=https-3A__www.evnp.org.uk&d=DwIDaQ&c=vh6FgFnduejNhPPD0fl_yRaSfZy8CWbWnIf4XJhSqx8&r=UYLCdmZKkJczcKmY7S

Contact information

Type(s)
Public

Contact name
Ms Sarah Hosgood

Contact details
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
20266

Study information

Scientific Title
A randomised controlled trial of Ex-Vivo Normothermic Perfusion versus static cold storage in donation after circulatory death renal transplantation

Acronym
EVNP

Study objectives
The aim of this study is to evaluate the effectiveness of ex-vivo normothermic perfusion (EVNP) in improving the function of transplanted kidneys.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England - Cambridge Central Research Ethics Committee, 17/11/2015, ref: 15/EE/0356

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Kidney transplantation

Interventions
After the identification of a suitable DCD kidney and matched recipient, the patient will be called into the transplant centre. Once assessed and the inclusion criteria met, the patient will be given the patient information sheet and the trial explained to them in full. Informed consented will be taken by a qualified member of the research team after the patient has been given an appropriate length of time to read the information sheet. Randomisation will be performed after the transplant recipient and kidney have both arrived in the transplanting centre and a final decision to proceed with transplantation has been made. The randomisation will be performed by sealed envelope online created using a generated randomisation

sequence. A member of the transplant research team will access this. In cases where paired kidneys from the same donor are transplanted in the same centre, one kidney from the pair will be randomly allocated to CS and the other to EVNP. In these cases the randomisation will also determine which kidney (right or left) will be transplanted first.

Group 1: Participants receive kidneys perfused with a packed red blood based solution mixed with a priming solution for 60 minutes immediately before transplantation (Ex-vivo Normothermic Perfusion, EVNP). The EVNP circuit has been designed using paediatric cardiopulmonary bypass technology (Medtronic, Watford, UK) and consists of a centrifugal blood pump (Bio-pump 560), a heat exchanger, a venous reservoir (Medtronic), 1/4 inch PVC tubing and an Affinity membrane oxygenator (Medtronic). The hardware includes a speed controller, a TX50P flow transducer and a temperature probe (Cole-Parmer, London, UK). Two infusion pumps are also incorporated into the system. Kidneys will be perfused at a set mean arterial pressure (75 mmHg). The blood based solution is oxygenated and warmed to 32–37C. The renal blood flow (RBF) will be monitored continuously during EVNP. Intra-renal resistance (IRR) will be calculated (mean arterial pressure/RBF) every 5 min until the end of perfusion. The total urine output will be recorded. Blood gas analysis will be used to measure the acid base balance pre and post EVNP.

Groups 2: Participants receive a kidney which has been emerged in a solution and placed in crushed ice in an insulated transport box until implantation (static cold storage).

Tissue samples from the transplant kidney, blood and urine samples from the transplant recipients and samples of the blood based perfusion solution and urine from the kidneys during EVNP will be collected to assess injury markers. During the transplant procedure a biopsy will be taken prior to transplantation then 30 minutes after reperfusion. Routine daily blood samples will be collected from the patients to monitor kidney function during their hospital stay. Some samples will be stored and used to measure kidney injury and recovery. After discharge patients will be monitored as normal during routine clinic visits. Patients will visit the transplant clinic and be seen by a member of the transplant team at 1, 3, 6 and 12 months post-transplant. At 3 months post-transplants patients will be asked to undergo a renal transplant biopsy performed under local anaesthetic and ultrasound guidance. This is not mandatory. A trained member of staff will perform this on the day ward within the hospital. Renal function, and any complications will be recorded at each visit using the electronic case report forms. Patients will be followed up as normal practice for the duration of their functioning transplant kidney. Blood and urine samples from the recipient will be used for routine biochemistry and haematology. A sample of blood and urine will also be kept for analysis of injury markers. Samples will be collected from the patient pre transplant, 6h, 24h, 48h and 72h post-transplant.

Intervention Type
Other

Primary outcome measure
Delayed graft function rate is determined by the need for dialysis in the first 7 days post-transplant.

Secondary outcome measures
1. Primary non-function (PNF), defined as the permanent lack of allograft function from the time of transplantationincluding graft losses due to irreversible rejection and vascular thrombosis, is recorded along with the cause at the end of the trial (12 months)
2. Duration of DGF is measured by recording the number of sessions and days that the recipient

requires dialysis after transplantation in days
3. Functional DGF (fDGF), defined as <10% fall in serum creatinine for 3 consecutive days, is measured using blood analysis in the first week post-transplant
4. Creatinine reduction ratio (CRR2 = creatinine day 1 – creatinine day 2/ creatinine day 1) is measured using blood analysis on day 2
5. Creatinine reduction ratio (CRR 5 = pre transplant creatinine - creatinine day 5/ pre-transplant creatinine) is measured using blood analysis on day 5
6. Length of hospital stay is measured as the number of days the recipient remains in hospital after the transplant
7. Biopsy-proven acute rejection rates is measured through examination of kidney biopsy samples when acute rejection is suspected
8. Serum creatinine and eGFR is measured using blood and urine analysis at baseline (pre-transplant), 1, 3, 6 and 12 months
9. Patient survival (time from transplant to death) is measured in days
10. Allograft survival (time from transplant to graft loss or return to dialysis) is measured in days

Overall study start date
01/03/2015

Completion date
19/03/2021

Eligibility

Key inclusion criteria
1. Patients undergoing DCD kidney transplantation (Maastricht Categories III & IV)
2. DCD donor aged 18 years or over
3. Transplant recipients aged 18 years or over
4. First or second kidney transplant recipients

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Total final enrolment
338

Key exclusion criteria

1. DCD donors aged under 18 years
2. DCD donors in Maastricht Categories I & II
3. Third and subsequent kidney transplant recipients
4. Multi-organ transplants e.g. simultaneous pancreas-kidney transplantation
5. Dual kidney transplants
6. Paediatric en-bloc kidney transplants
7. Organ preservation by hypothermic machine perfusion

Date of first enrolment
13/02/2016

Date of final enrolment
04/02/2020

Locations

Countries of recruitment
England

United Kingdom

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

Study participating centre
Freeman Hospital
Freeman Road
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation trust & University of Cambridge

Sponsor details
Research Services Department
Box 277
Addenbrooke’s Hospital Hills Road
Cambridge
England
United Kingdom
CB2 2QQ

Sponsor type
Hospital/treatment centre

Website
www.cuh.org.uk

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Kidney Research UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
On completion of the trial the results will be published in a peer reviewed journal. The results will also be presented at national and International meetings.

Intention to publish date
31/07/2022

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	23/01/2017		Yes	No
Results article		25/05/2023	26/05/2023	Yes	No
HRA research summary			28/06/2023	No	No