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Does the introduction of a national pre-implantation biopsy histopathology service increase numbers, and improve outcomes, of kidney transplants performed in the UK?

Submission date
22/01/2018

Registration date
30/01/2018

Last Edited
01/04/2022

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
There is a great shortage of kidneys for transplantation. All kidneys from deceased donors carry risk to the recipient (risk of not working, or of disease transmission), but donor age is strongly associated with poor function and early failure of the kidney transplant. This is important; because the majority of the pool of potential UK deceased donors are now over 60 years old. Thus, if we can improve our identification of kidneys from older donors that are better 'quality', we can maximise numbers of transplants performed without compromising transplant outcomes. The use of urgent kidney biopsy (analysis of a small portion under the microscope) to identify age-related damage has been reported to aid selection of those kidneys from older donors that are good enough 'quality' for transplantation. This approach has not been widely adopted in the UK, because the exact impact that the extra information provided by biopsy has on transplant numbers and on transplant outcomes is not clear, and its cost effectiveness remains unproven. Our study will evaluate whether providing an urgent 24 hour National Biopsy Service increases the number and function of kidneys transplanted from donors aged over 60 years. The study is a national trial: every four months a randomly-chosen group of UK kidney transplant centres will be offered access to the National Biopsy service (a 'stepped-wedge randomised cluster trial'). By the end of the trial, all UK centres will have access, and we will then compare results for each centre from before and after the biopsy service was made available, as well as evaluating the cost of providing the service. We anticipate that this comparison will show that biopsy availability increases the use of kidneys from elderly donors by about 11%, which equates to an additional 120 kidney transplants performed in the UK per year.

Who can participate?
Kidneys offered for transplantation from deceased donors aged ≥60 years.

What does the study involve?
A biopsy can be requested by the transplanting surgeon (at the time of organ offer) on a kidney which meets the inclusion criteria and none of the exclusion criteria. All kidneys are from

deceased donors aged > 60 years old at the time of death. The result of the biopsy provide additional information on the quality of the organ, allowing a better assessment of whether it is transplantable. The biopsy result are discussed with the potential recipient, before they consent to undergo their kidney transplant. Follow-up of kidney transplant recipients are performed as per standard practice, and all data is obtained from the UK Transplant Registry which is held by NHS Blood and Transplant.

What are the possible benefits and risks of participating?
The main potential benefits are increased number of kidneys available for transplantation (i.e. reduced waiting time for a kidney transplant) and improved outcomes for those kidneys which are transplanted. The main potential risks of the intervention are biopsy-related complications. Currently, 85% of deceased-donor kidneys are biopsied at retrieval for future experimentation (by the national QUOD bioresource, sponsored by NHSBT in close collaboration with all academic centres in the UK: http://www.quod.org.uk), and to date, there have been no reported losses of organs due to biopsy complications. Moreover, the choice of biopsy technique (punch biopsy) has been made following consultation with renal histopathologists and transplant surgeons; this technique is expected to further limit the risk of complications, as well as limit inter-observer differences in the quality of biopsy performed. There is a small risk that the biopsy service may lead to a reduction in the number of kidneys transplanted, because more kidneys are discarded following biopsy analysis. By the nature of the trial design, it will not be possible to ascertain diminished kidney usage until formal analysis of data after the trial is completed.

Where is the study run from?
NHS Blood and Transplant Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
October 2017 to March 2023

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

Who is the main contact?
PITHIA@nhsbt.nhs.uk

Study website
http://www.pithia.org.uk/

Contact information

Type(s)
Public

Contact name
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Contact details

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CB2 0PT

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
34408

Study information

Scientific Title
Pre-Implantation Trial of Histopathology In renal Allografts (PITHIA)

Acronym
PITHIA

Study objectives
Provision of a national 24/7 pre-implantation biopsy service results, at reasonable cost, in transplantation of a greater proportion of kidneys offered from donors aged ≥60, and/or improves kidney transplant function at one year post-transplant. Numbers of deceased donor kidney transplants performed annually in the UK are consequently significantly increased or improved in quality.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridge South Research Ethics Committee, 07/12/2017, ref: 17/EE/0481

Study design
Non-randomised; Both; Design type: Screening, Surgery, Other, Validation of investigation /therapeutic procedures

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
The trial information sheet will be available on www.pithia.org.uk.

Health condition(s) or problem(s) studied
Surgery for renal failure

Interventions
Access to national histopathology service: the service is implemented according to the trials stepped-wedge cluster randomised design. Once a centre has access to the service, they can request a kidney biopsy at the time that an organ is offered from a deceased donor aged ≥60. The transplant centres can use the service at their discretion. If the organ is transplantable, the recipient undergoes their transplant as per standard practice. There areno additional visits or investigations for the recipients – follow-up data (up to one year post-transplant) will be taken from the UK Transplant Registry. Transplant activity at each of the centres are monitored throughout the trial.

Intervention Type
Other

Primary outcome measure
1. Proportion of kidneys that are transplanted on first offer.
2. Estimated glomerular filtration rate (eGFR) measured at 12-15 months after transplant.

Secondary outcome measures
Primary and secondary outcome data will be measured using data from the UK Transplant Registry, which is held by NHS Blood and Transplant:
1. Proportion of kidneys utilised
2. Total number of kidney transplants performed, overall and by centre
3. Proportion of kidneys discarded after retrieval, out of all retrieved kidneys
4. Number and proportion of ‘single’ vs ‘dual’ kidney transplants performed
5. Absolute number of kidneys transplanted (per centre and per time period) that were not accepted on first offer
6. Biopsy utilisation and fidelity, defined as the proportion of kidneys that are biopsied in concordance with the education plan, out of all kidney biopsies.
7. Kidney Donor Profile Index (KDPI) of transplants performed
8. Cold ischaemia time (CIT), defined as the total time between perfusion of the donor kidneys with cold preservation fluid during retrieval, and reperfusion with recipient blood at implantation.
9. 12-month patient survival
10. 12-month graft survival (censored for patient death)
11. Proportion of kidneys diagnosed with primary non-function
12. Proportion of kidneys diagnosed with delayed graft function (defined as the use of dialysis during the first postoperative week)

Overall study start date
01/10/2017

Completion date
31/03/2023

Eligibility

Key inclusion criteria
Kidneys offered for transplantation from deceased donors (DCD* and DBD**) aged ≥60 years

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 2306; UK Sample Size: 2306

Key exclusion criteria
Kidneys offered as a component of a multi-organ transplant.

Date of first enrolment
01/03/2018

Date of final enrolment
31/01/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
NHS Blood and Transplant Clinical Trials Unit
Long Road
Cambridge
United Kingdom
CB2 0PT

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Research Governance
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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

Planned publication in a high-impact peer reviewed journal – late 2021. The trial protocol and Statistical Analysis Plan will be published.

Intention to publish date
31/03/2024

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	17/01/2019	17/06/2019	Yes	No
HRA research summary			28/06/2023	No	No