In house Pre-implantation Oxygenated Hypothermic Machine Perfusion Reconditioning after Cold Storage versus Cold Storage alone in ECD Kidneys from Brain Dead Donors

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Objective of this study is to compare 1-year garft survival after hypothemic machine perfusion with oxygentaed perfusion solution versus static cold storage of extended criteria kidneys from DBD donors.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON41997

Source
ToetsingOnline

Brief title
COPE-POMP

Condition

- Nephropathies
- Renal and urinary tract therapeutic procedures

Synonym
End stage kidney failure/End stage renal disease

Research involving
Human

Sponsors and support

Primary sponsor: Oxford University
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Extended donor criteria, Kidney, Machine perfusion, Transplantation

Outcome measures

Primary outcome

The primary outcome for this study is Graft survival at 12 months after transplantation.

Secondary outcome

- Patient and (death censored) graft survival at day 7, 3, 6 and 12 months after transplantation. eGFR defined by the MDRD equation at day 7, 3, 6 and 12 months after transplantation.
- Delayed graft function defined as the need for dialysis in the first 7 days after transplantation and preceding the return of kidney function.
- Slow graft function based on functional DGF defined as the absence of decrease in the serum creatinine level of at least 10% per day for at least 3 consecutive days in the first 7 days after transplantation.
- Primary non-function defined as the continued need for dialysis at 3 months after transplantation.
- Comparison of biopsy proven acute rejection between the 2 groups.
- Quality of life measures (EQ-5D-5L) at consent, 3 and 12 months, length of hospital stay (including ICU) and need/length for dialysis treatment

Study description

Background summary

Renal transplantation remains the therapy of choice for patients with end stage renal disease. However, the number of patients waiting for a kidney graft continues to increase and far exceeds the availability of donor grafts (1-3). A large number of deceased organ transplants manifest a degree of early dysfunction leading to the clinical syndrome of Delayed Graft Function (DGF) (4,5). DGF represents a significant problem in clinical kidney transplantation affecting up to 30% of all deceased donor graft recipients (6). This has an impact on short-term management, including the requirement of hemodialysis treatment and is associated with an increased risk of acute rejection. Moreover DGF has been shown in multivariate analyses to increase the incidence of chronic nephropathy and later graft loss (4). The shortage of donor organs has led the transplant community to accept an increasing number of older and more marginal donor grafts for transplantation (7). Kidneys from these donors are particularly vulnerable for the development of DGF and have decreased long term graft survival. One important modifiable risk factor of DGF is ischemia injury sustained during organ preservation. Optimizing the preservation of grafts during the preservation phase is essential to reduce this ischemic injury. In those older and more marginal donor kidneys, an optimized preservation is therefore of even greater importance.

Study objective

Objective of this study is to compare 1-year garft survival after hypothemic machine perfusion with oxygentaed perfusion solution versus static cold storage of extended criteria kidneys from DBD donors.

Study design

The study will be conducted as a prospective, randomized, parallel group, single blinded, controlled, multi-centre, non-paired superiority trial; allocation will be on a 1:1 basis and an intention-to-treat method will be used to analyze the results.
After accepting the potential ECD organ for donation, kidneys will be allocated following the standard Eurotransplant/ UK-transplant allocation rules.
In a non-paired-design, each ECD kidney that has been accepted for transplantation by one of the participating centres will be randomly assigned to SCS or to SCS followed by reconditioning by end-ischemic oxygenated HMP (HRMP+O2). Randomizing kidneys after they have been accepted for transplantation avoids a potential bias that acceptance of the kidney is being influenced by the preservation modality.
If two kidneys are accepted for transplantation by the same centre the surgeon

will decide which kidney to transplant first according to their local protocol. It is not essential for both kidneys from a donor to enter the trial. If only one of the kidneys is deemed transplantable, it can still be included in the trial analysis.
Exceptionally anatomical situations may not allow connection of a kidney to the perfusion circuit. In this situation the kidney should be preserved by cold storage alone even though it was randomized to HRMP+O2.

Intervention

Intervention is oxygenated hypothermic machine perfusion while the controlgroup excists of kidney that have been preserved by static cold storage.

Study burden and risks

Since the intervention occurs prior to kidney transplantation, there are no study specific changes to the standard follo-up care. Also, there are no additional strategies, outside general measures to ensure regular recipient follow-up, for monitoring and improving adherence necessary. For the recipient, no changes will be made considering standard care, with the exception of taking additional bloodsamples during transplantation. A minimal burden and risk for the participants included in this study. The risk associated with participation is that the oxygenation at the time of machine perfusion could have an harmfull effect on the future function of the graft. During a large animaltrial on pigs the later function of the graft was better after oxygenated machine perfusion. There is a minimal burden an a small risk for the participants included in this study.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For the donor and the donated kidney:
- All kidneys from DBD donors (Donation after BrainDeath) fulfilling the UNOS-ECD criteria; donors aged 60 years or older, or donors aged 50 years or older with two of the following riskfactors: hypertension. terminal creatinin >1,5mg/dL or a cerebral vascular cause of death.;For the recipient of the donated kidney:
- Aged 18 years or older
- Listed for renal transplantation due to end stage renal disease on the ET or NHSBT renal waiting list within one of the participating centers.
- Participant is willing to participate in the study and has provided written informed consent.
- This transplantation is the participant's first or re-transplantation.

Exclusion criteria

For the donor and the donated kidney:
- Kidneys used for a multi-organ transplant procedure.
- Kidneys from standard criteria donors (SCD).
- Kidneys procured from a DCD donor (Donation after Circulatory Death).
- Kidneys used for a double kidney transplant within the same recipient.
- Kidneys procured from donors older than 85 years.;For the recipient:
- Simultaneous participation in another perfusion trial.
- Scheduled to undergo multi-organ transplantation.
- Planned dual-kidney transplantation.
- Is unable or unwilling to provide informed consent.
- If the kidney is judged to be not transplantable.
- Simultaneous participation in another perfusion trial.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2014
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Machine perfusion system (Kidney Assist)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	29-10-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ISRCTN	ISRCTN63852508
CCMO	NL49912.042.14