# Ischemisch postconditioneren als nieuwe methode om de uitkomst van non-heart beating niertransplantatie te verbeteren.

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Ischemic postconditioning leads to a quicker recovery of kidney function by decreasing ischemia-reperfusion injury of the graft.

| | |
|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON20707

**Bron**
NTR

**Verkorte titel**
PINK-trial

**Aandoening**

Kidney transplantation
Non-heart beating kidneys
Delayed graft function
Ischemia reperfusion injury

### Ondersteuning

**Primaire sponsor:** Erasmus MC, University Medical Center
**Overige ondersteuning:** Erasmus MC, University Medical Center

### Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Duration delayed graft function
measured through the (duration of) need for dialysis.

# Toelichting onderzoek

### Achtergrond van het onderzoek

With the ageing population and the successful treatment of many diseases like diabetes and hypertension, the incidence of chronic renal failure is rising. Kidney transplantation is the preferred treatment for end-stage kidney disease. With the increasing donor organ shortage, there has been an alarming shift from heart-beating (HB) organ donation after brain death, to organ donation after cardiac death (non heart-beating; NHB), now contributing to more than 40% of all deceased kidney transplantations performed. Transplantation with NHB donor kidneys results in inferior outcome, because of increased post-operative kidney cell damage. The main reason for this poor outcome is warm ischemia, occurring in the period between cardiac death and cold storage of the organ, inherent to the NHB procedure. Besides more delayed graft function (DGF), there is more acute rejection and possibly more chronic rejection in this subgroup. DGF, the delay in recovery of normal renal function post-transplantation, caused most commonly by acute tubular necrosis, leads to the need for dialysis for some days, sometimes weeks, postoperatively. It is associated with a prolonged hospitalization course, increased transplantation costs, and decreased graft survival.13 Finding new strategies to prevent DGF has become one of the major issues in kidney transplantation. Ischemia-reperfusion injuries are the best recognized lesions associated with DGF, resulting in acute tubular necrosis and inflammation. DGF is seen following 23–33% of transplants from HB donors, but is substantially more common following transplantation from NHB donors, no doubt because of the inevitable period of warm ischemia which these kidneys undergo. Transplanted kidneys with DGF have a 5 year survival of 60%, whereas kidney grafts without DGF are reported to have a 5 year survival of 82%. Furthermore, in NHB kidney transplantation up to 10% of transplants never function, which is so-called primary non-function. Since this does not appear to depend on recipient factors (it is extremely uncommon in HB kidney transplants), it must presumably be a result of damage to the transplanted organ prior to implantation.
An area of increasing interest is the possibility of rendering an organ resistant to subsequent injury by a prior ischemic insult, i.e. a preconditioning maneuver. Ischemic preconditioning of an organ confers protection against a subsequent ischemic attack. Nevertheless, the protective potential of ischemic preconditioning has not been realized in clinical practice because it necessitates an intervention applied before the onset of ischemia, which is often difficult to predict in non-surgical situations. A more amenable approach is to intervene at the onset of reperfusion, the timing of which is under the control of the operator. It has recently been shown that short, repeated sequences of ischemia and reperfusion after a prolonged

ischemic episode, called ischemic postconditioning, reduce infarct size by about 40% after an ischemic myocardial injury in animals as well as in humans. Modulation of acute kidney injury from ischemia-reperfusion injury holds the potential to reduce the incidence of early graft dysfunction, which allows safe expansion of the donor pool with kidneys that have suffered prolonged ischemic injury before organ recovery. Attempts to reduce the incidence of DGF in clinical kidney transplantation have mostly focused on improving hypothermic organ preservation and on reducing the nephrotoxic effects of immunosuppressive drugs. Ischemic postconditioning could thus be added as a non-invasive measure to this therapeutic arsenal. In animal studies, ischemic postconditioning has already demonstrated its clinical potential since it reduces renal ischemia-reperfusion injury.

### Doel van het onderzoek

Ischemic postconditioning leads to a quicker recovery of kidney function by decreasing ischemia-reperfusion injury of the graft.

### Onderzoeksopzet

Day 1, 4 and 7 and week 1, 2, 4 and 12.

### Onderzoeksproduct en/of interventie

Standard kidney transplantation will be performed. After the vascular anastomoses have been completed, arterial blood supply will be restored during 1 minute (reperfusion) after which the artery will be clamped (ischemia). This procedure will be performed for a total of 3 times.

The control group will not receive an intervention and will undergo standard kidney transplantation.

## Contactpersonen

### Publiek

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Recipient non-heart beating kidney transplantation.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients younger than 18 years;

2. Need for therapeutical oral anticoagulant drugs.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Open / niet geblindeerd |
| Controle: | Geneesmiddel |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 01-11-2011 |

| | |
|---|---|
| Aantal proefpersonen: | 20 |
| Type: | Werkelijke startdatum |

# Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 20-10-2011 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 36716
Bron: ToetsingOnline
Titel:

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL2970 |
| NTR-old | NTR3117 |
| CCMO | NL34987.078.11 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |
| OMON | NL-OMON36716 |

# Resultaten

**Samenvatting resultaten**
N/A