Correlation between oxidative stress and microvascular perfusion defects in renal ischemia/reperfusion injury during kidney transplantation: an observational study.

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First, to determine the extent to which oxidative stress and microcirculatory perfusion defects occur during clinical kidney transplantation. Second, to study the relationship between these events and kidney function, inflammation and renal cellular...

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

Summary

ID

NL-OMON30630

Source
ToetsingOnline

Brief title
Oxidative stress and microvascular perfusion during kidney transplantation.

Condition

- Nephropathies
- Vascular therapeutic procedures

Synonym
ischemia/reperfusion injury, Kidney transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Kidney transplantation, Microcirculation, Oxidative stress, Reperfusion injury

Outcome measures

Primary outcome

Oxidative stress:

1. Renal arterio-venous difference in plasma F2-isoprostanes concentration.

2. Tissue F2-isoprostanes concentration.

3. Urine F2-isoprostanes concentration.

4. Advanced glycation end products (AGE*s) measured by skin autofluorescence.

Renal perfusion:

1. Renal artery flow measured by Laser-Doppler flow probe.

2. Microcirculatory perfusion measured by OPS imaging (parameters: volumetric

blood flow, functional capillary density).

Secondary outcome

Kidney function:

1. Dialysis dependency after transplantation.

2. Area under the curve for serum creatinine concentration over time (14 days).

3. Fractional excretion of sodium (14 days).

Inflammation: Serum cytokine concentrations (IFN-γ, TNF-α, IL-6, IL-10, IL-17,

IL-23).

Renal cellular injury: Urine NGAL and NAG concentrations.

Anti-oxidants: vitamin C, vitamin E, GSH/GSSG ratio, total anti-oxidant capacity.

Endothelial glycocalyx:

1. Thickness measured by OPS imaging

2. Renal arterio-venous differences in syndecan-1, heparin sulphate and hyaluronan concentrations.

Study description

Background summary

In animal models, oxidative stress and microcirculatory perfusion defects have been shown to cause renal ischemia/reperfusion injury. The discovery of F2-isoprostanes as markers of lipid peroxidation and orthogonal polarization spectral (OPS) imaging of the human microcirculation allow accurately study of these phenomena in clinical settings. This may lead to rational selection of interventional strategies for ischemic acute renal failure and may provide surrogate outcome measures for clinical trials.

Study objective

First, to determine the extent to which oxidative stress and microcirculatory perfusion defects occur during clinical kidney transplantation. Second, to study the relationship between these events and kidney function, inflammation and renal cellular injury. Third, to study the depletion of anti-oxidants to guide selection of interventions for future clinical trials. Fourth, to study the breakdown of the endothelial glycocalyx during renal ischemia/reperfusion injury.

Study design

Observational study.

Study burden and risks

During surgery, 6 blood samples of 10.5 mL will be taken from an arterial line and 4 blood samples of 10.5 mL from the renal vein (already exposed). Furthermore, 4 needle biopsies will be taken from the kidney. Taking these samples may be associated with bleeding from the puncture site that can be controlled during surgery. OPS imaging of the renal microcirculation and measurement of renal artery flow do not expose the patient to additional risks. Surgery will take approximately 15 minutes longer to allow these measurements to take place. During and after surgery, AGE*s are measured non-invasively with skin autofluorescence. This takes approximately 5 minutes and does not expose the patient to any risks. After surgery, 4 venous blood samples of 5 mL will be taken from a peripheral venous catheter (already present). Urine will be collected from the urinary catheter during the first 4 post-operative days (already present). All measurements will be done while the patient is admitted to the hospital. Physical and psychological discomfort from participating in study should be minimal. The patient will not benefit directly from the study; however, this study paves the way for interventional studies from which benefit for the patient is expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Kidney transplant recipient (living donor [and their donors] / deceased heart-beating donor / deceased non-heart-beating donor).
Partial nephrectomy with clamping of the renal vascular pedicle.

Exclusion criteria

Age < 18 years
Smoking
Donor > 60 years

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	10-12-2007
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	13-06-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-12-2007
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL15732.068.07