Species specific differences in the sensitivity of the *-ketoglutarate dehydrogenase to ischemia/reperfusion injury.

Published: 22-07-2019
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The aim of this study is to evaluate whether there are species specific differences in the sensitivity of the *-KGDH complex and to identify the sensitive positions in the enzyme complex.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON55593

Source
ToetsingOnline

Brief title
Sensitivity of *-KGDH to ischemia/reperfusion injury.

Condition

- Other condition

Synonym
ischemia-reperfusion injury / delayed graft function

Health condition

niertransplantaties

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Interspecies differences, Ischemia/reperfusion injury, □-ketoglutarate dehydrogenase, Kidney transplantation

Outcome measures

Primary outcome

The activity of *-KGDH enzyme will be studied in an enzyme-assay.

Secondary outcome

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Study description

Background summary

Ischemia-reperfusion injury (I/R injury) is the paradoxical development of tissue damage after reperfusion of previously ischemic tissue and can cause organ dysfunction. I/R injury occurs in numerous settings such as transplantation, myocardial infarction and ischemic stroke. The pathophysiology of I/R injury is complex and not well understood. This is partly due to the fundamental differences between animals and humans, interfering with translation of preclinical findings to the human context.

Our group has been studying the mechanisms of clinical I/R injury in the context of renal transplantation. The data of these studies show that clinical I/R injury relates to critical metabolic deficiencies due to mitochondrial failure. 1-3 Post-reperfusion release of *-ketoglutarate in kidneys with I/R injury implies that impaired oxidative phosphorylation involves an almost instantaneous and persistent post-reperfusion defect at the level of the *-ketoglutarate dehydrogenase complex (*-KGDH). This observation is contrast to the observations in rodents4, and points to clear species specific differences in the susceptibility of the *-KGDH complex, with an almost instantaneous inactivation of the *-KGDH complex in humans. As such, the question arises

whether there are species specific differences in the sensitivity of the *-KGDH complex, and to identify the sensitive positions in the enzyme complex on basis of species differences in protein structure.
Recently we performed a pilot study with porcine kidney tissues and data showed that the *-KGDH complex is very sensitive to warm ischemia. Therefore, non-ischemic human kidney tissue is desired to study the dynamics of the *-KGDH complex and to identify the sensitive positions in the enzyme complex.

Study objective

The aim of this study is to evaluate whether there are species specific differences in the sensitivity of the *-KGDH complex and to identify the sensitive positions in the enzyme complex.

Study design

Exploratory patient study.

Study burden and risks

The study has no personal benefit for the patients themselves, but the risks associated with participation and the burden can be considered minimal. Follow-up is according to standard medical care.

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

Age *18 years old
Written informed consent obtained prior to the (partial or radical) nephrectomy procedure
Patients admitted in the LUMC for nephrectomy

Exclusion criteria

Any condition in which the procedure could jeopardize the patient or the graft
Mentally incompetent
Pregnancy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-06-2020
Enrollment:	10

Type:	Actual

Ethics review

Approved WMO Date:	22-07-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-06-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL69040.058.19