# Iohexol for measuring renal function.

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Primary objective: To determine the prevalence of AKI in critically ill children based on clearance of iohexol.Secondary objectives:1. To determine the prevalence of AKI in critically ill children using serum creatinine, creatinine clearance,...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Renal disorders (excl nephropathies) |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON49710

**Source**
ToetsingOnline

**Brief title**
HERO-study

### Condition

- Renal disorders (excl nephropathies)

**Synonym**
Kidney failure, loss of renal function

**Research involving**
Human

### Sponsors and support

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

### Intervention

**Keyword:** Acute Kidney Injury (AKI), Critically ill children, GFR, Iohexol

## Outcome measures

### Primary outcome

Prevalence of AKI based on iohexol plasma clearance.

### Secondary outcome

Secundary study parameters are:

1. Prevalence of AKI in critically ill children using serum creatinine, creatinine clearance, urinary iohexol, serum cystatin C, serum PENK and/or blood urea nitrogen based eGFR equations.

2. Serum PENK levels, in relation to iohexol based GFR-measurements in critically ill children.

3. Difference in prevalence of SCr-AKI, AKI based on creatinine clearance, cysC-AKI, Schwartz-AKI, PENK-AKI and AKI based on urinary iohexol clearances compared with the prevalence of iohexol-AKI and to assess agreement between those methods

4. Risk factors for the development of AKI when based on iohexol clearance.

Exploratory studyparameters are:

1. SNPs related to the development of AKI.

2. Performance of GFR1p formula as determined by the developed pop PK model defined by the percentage of GFR determinations that lie within 10% of the reference value (P10).

3. Relation between the clearance of iohexol and GFR determined using endogenous markers in children direct post kidney transplantation as well as in

children receiving extra corporeal membrane oxygenation (ECMO).

# Study description

### Background summary

Approximately 25% of all children admitted to the PICU will develop AKI during the first seven days after admission. AKI is associated with a worse outcome, including an increased risk of mortality compared to patients without AKI. However, this AKI prevalence estimation is based on serum creatinine based GFR (eGFR), which is known to be inaccurate.

We postulate that measured GFR (mGFR) based on iohexol clearance in critically ill children will detect a higher prevalence of AKI than currently used methods based on endogenous markers. Furthermore, we hope to get a better understanding of the value of a new biomarker to estimate GFR. If an underestimation of the prevalence of AKI is indeed demonstrated by our study, we aim to identify certain patient groups that are especially prone to underdiagnosis by the currently used methods. In the future, this could lead to earlier adjustment of therapy and treatment in AKI patients. All gained information will lead to better mechanistic insight in the relative contribution of GFR and renal tubular transporter function to renal function in this critically ill population, including knowledge on the maturation of transporter function and the interplay with critical illness.

### Study objective

Primary objective: To determine the prevalence of AKI in critically ill children based on clearance of iohexol.

Secondary objectives:
1. To determine the prevalence of AKI in critically ill children using serum creatinine, creatinine clearance, cystatin C and/or blood urea nitrogen based eGFR equations as well as urinary iohexol clearances.
2. To determine serum PENK levels in critically ill children.
3. To compare the prevalence of AKI when diagnosis is based on plasma iohexol clearances with the prevalence of AKI based on serum creatinine, creatinine clearance, serum cystatin C, PENK and/or BUN based eGFR and to assess agreement between those methods.
4. To determine risk factors for the development of AKI when based on iohexol clearance.

Exploratory endpoints:
1. To explore the relationship of genetic variation with the development of AKI.

2. To assess whether calculation of single point GFR leads to accurate GFR determination in critically ill children and neonates when using a population PK model and Bayesian feedback in comparison with the gold standard.
3. To explore the relation between the clearance of iohexol and GFR determined using endogenous markers in children direct post kidney transplantation as well as in children receiving extra corporeal membrane oxygenation (ECMO).

**Study design**

Observational study with minimal invasive procedures. Diagnostic study.

**Study burden and risks**

Risks:
In the context of this study, iohexol will be administered as a diagnostic marker. Iohexol is used in pediatric standard care in several European countries (including the Netherlands; Amsterdam UMC) in children of all ages with chronic kidney disease.
As the rate of adverse events related to the use of iohexol is only 0.0066% in 15,000 routine GFR measurements in Italian adults, the risks and burdens associated with this study are negligible. Blood samples are only taken from an indwelling catheter (already in place for clinical purposes) or concomitantly with regular blood work. The urine sample will be collected by using a urine catheter (if already placed for clinical purposes).

Benefits:
Individual patients will not benefit from the iohexol clearance measurements as those are not part of clinical care routines and will not be evaluated on the same date. However, potential benefits of participating patients will be an ongoing extensive assessment with reference to their kidney function by determining creatinine as well as cystatin C and blood urea nitrogen concentrations, both two to four times a day. This may enable earlier interventions in patients at risk by the treating physician.

Group relatedness:
This research is group-related as data from healthy adults or healthy children cannot be extrapolated to critically ill children as GFR differs significantly between those groups. It is known that GFR changes with age, however, the impact of critical illness on GFR in those children is still unknown. This study will help to identify critically ill children with AKI. eGFR-calculations based on endogenous markers can be improved for critically ill children when gold standard GFR measurements are available. In the future, this will decrease the risk of toxicity in patients with AKI.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

## Inclusion criteria

0-18 years of postnatal age
>37 weeks of gestational age (for infants < one year postnatal age)
Bodyweight >2500g
Patients admitted to pediatric or neonatal intensive care unit
PELOD-II (pediatric logistic organ dysfunction score) of 1 or higher (<= at least one failing organ)
Indwelling central line or arterial line in place for clinical purposes, or scheduled regular blood work for clinical reasons (at least once a day)
Informed written consent

### Exclusion criteria

Known medical history of allergic reaction to injection of iodinated contrast material
Receiving renal replacement therapy
Language or cognitive inability (of parents/caregivers) to understand written and oral informed consent.

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 17-05-2019 |
| Enrollment: | 125 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 10-04-2019 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 15-09-2020 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 | NL68547.091.18 |