Time to Excretion of Contrast, a Maastricht Prospective Observational Study

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational invasive

Summary

ID

NL-OMON50819

Source
ToetsingOnline

Brief title
TEMPOS

Condition

- Renal disorders (excl nephropathies)

Synonym
post-contrast acute kidney injury; post-contrast acute increase in serum creatinine

Research involving
Human

Sponsors and support

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

Intervention

Keyword: acute kidney injury, delayed contrast elimination, intravascular iodinated contrast contrast-induced acute kidney injury, post-contrast acute kidney injury iodinated contrast elimination time contrast retention, renal insuficiency

Outcome measures

Primary outcome

The primary outcome is time to contrast-free urine, i.e., time to the first contrast-free urine sample from the time of intravascular iodinated contrast administration.

Secondary outcome

A secondary outcome is the percentage of contrast eliminated, i.e., percentage of total contrast administered excreted in urine within 5 days.

Relevant characteristics of patients and procedures will be recorded to identify patients at increased risk of delayed contrast elimination. In the context of post-contrast acute kidney injury, change in serum creatinine is the gold standard recommended in all (inter)national guidelines on safe use of iodinated contrast material. To evaluate the relationship between elimination time and adverse post-contrast outcomes therefore, post-contrast incidences of classic and KDIGO definitions of acute kidney injury will be determined.

The following definitions for acute kidney injury will be used, based on baseline serum creatinine values (visit 1.0) and peak serum creatinine changes from baseline (visits 1.1-1.5; see Table 1):

- an increase in serum creatinine greater than 44umol/l or 25% from baseline

(classic)

- an increase in serum creatinine greater than 26.5 umol/L from baseline or

more than 1.5 times the baseline value (KDIGO)

In addition, post-contrast changes in eGFR within 5 days from baseline; 1-month post-contrast change in eGFR; and 1-month post-contrast incidences of eGFR decline >=5 mL/min/1.73m2, dialysis and mortality will be recorded. Time to peak change in serum creatinine within 5 days post-contrast will also be determined. Finally, samples will be stored in order to determine serum contrast (patients with retention or <100% excretion of contrast in urine) and/or serum/urine renal damage markers (such as KIM-1, NGAL and IL-18).

Study description

Background summary

Intravascular iodinated contrast administration has become crucial to modern medicine. Currently it is estimated that over 250 million injections are given each year worldwide during medical scans and interventions. Risk of contrast-induced kidney injury is expected to be strongly correlated with exposure time. Studies on the excretion of iodinated contrast material are few and have mostly been carried out in patients with normal renal function. It is therefore not known how long contrast is retained before excretion in patients with reduced renal function: some papers state most of the administered contrast is eliminated within 1 to 2 hours post-contrast, others include case wise reports of renograms persisting for many days post-contrast. Chronically reduced renal function is expected to be a factor in delayed contrast elimination, but it is not known which patients are most susceptible or to what extent.

Reduced renal function is expected to increase the delay in contrast elimination. Delayed contrast elimination is hypothesised in turn to increase contrast toxicity, which is expected to increase the risk of post-contrast adverse events. Patients with eGFR <30 mL/min/1.73m2 are most at risk of renal

injury after intravascular iodinated contrast material injection; patients with eGFR 30-59 mL/min/1.73m2 are considered at moderate to ow risk, and patients with eGFR >=60 mL/min/1.73m2 are considered to be at low to no risk. Whereas such contrast administration appears to be safe for the majority of patients even with eGFR <30 mL/min/1.73m2, reports of individuals with post-contrast adverse events persist. It may be that the distinguishing characteristic is contrast retention.

A second issue pertaining to iodinated contrast elimination is gaining more and more attention: contrast-pollution in water. Currently pilots are being carried out in which patients are asked to collect all urine during 24-hours and to subsequently dispose the urine containers as a waste product. Whether this 24-hour collection is necessary has not been determined.

Study objective

The aim of the current study is to determine contrast elimination time and % contrast eliminated within 5 days in three groups of patients, (with severely reduced, moderate, and mildly reduced to normal renal function). Secondary aims are to explore whether specific situations/characteristics result in higher probability of delayed elimination of contrast, and whether there is a link between elimination time and adverse post-contrast outcomes.

Relevant characteristics of patients and procedures will be recorded to identify patients at increased risk of delayed contrast elimination (see section 3). To explore the clinical relevance of delayed contrast elimination, 1-month eGFR decline and incidences of dialysis and mortality will be compared amongst matched pairs between subgroups categorized according to elimination time.

Study design

TEMPOS is a single centre, observational, cohort study at Maastricht UMC+, amongst patients referred for an elective procedure with intravascular iodinated contrast.

Contrast elimination will be determined by assays of contrast content in urine samples. All urine will be collected during approximately 4 days: from first urination after intravascular iodinated contrast administration until the time of visit 2.5; a baseline urine sample will be collected before contrast-administration (see Table 1). Renal function will be monitored using venepuncture samples: serum creatinine will be measured before (baseline) and during 5 days post-contrast, as well as at 1-month post-contrast. Both urine and serum samples will be stored at the biobank Maastricht UMC+ for renal damage marker assays.

The study will include 72 patients with eGFR <30 mL/min/1.73m2 (derived from the MIRACLE study), 72 patients with eGFR 30-59 mL/min/1.73m2, and 72 patients with eGFR >=60 mL/min/1.73m2. The latter two groups will be matched by age, sex and contrast procedure type to the 72 eGFR <30 mL/min/1.73m2 patients. Each patient will be followed for approximately one month.

To explore the clinical relevance of delayed contrast elimination, 1-month eGFR decline and incidences of dialysis and mortality will be compared amongst patient subgroups categorized according to contrast elimination time. It is unknown what contrast elimination times will be. Contrast elimination will therefore be considered delayed if contrast elimination time exceeds the patient group median value, and vice versa. Furthermore, the following subgroups will also be evaluated: 1. Normal (contrast-free urine within <=24 hours); 2. Delayed (contrast-free urine within 24-48 hours); 3. Severely delayed (contrast-free urine >48 hours). Subgroup cut-off values may be added at a later stage (e.g., in the event of many or no patients with elimination >48 hours).

Study burden and risks

Patients with eGFR <30 mL/min/1.73m2 are most at risk of renal injury after intravascular iodinated contrast material injection; patients with eGFR 30-59 mL/min/1.73m2 are considered at moderate to ow risk, and patients with eGFR >=60 mL/min/1.73m2 are considered to be at low to no risk. Whereas such contrast administration appears to be safe for the majority of patients even with eGFR <30 mL/min/1.73m2, reports of individuals with post-contrast adverse events persist. It may be that the distinguishing characteristic is contrast retention.

In order to determine elimination time and identify which patients retain contrast, patients will be asked to collect urine every time they naturally urinate and to note time and date on the container provided. Urine will be collected for approximately 4 days: from first urination after intravascular iodinated contrast administration until the study visit on day 5 post-contrast (Table 1). Urine containers will be collected during study visits.

Longer elimination time of contrast will potentially increase renal toxicity. Therefore, renal function (serum creatinine in venepuncture blood sample) will be determined during 5 days and at 1-month post-contrast (Table 1). One baseline and one post-contrast venepuncture blood sample and serum creatinine measurement are standard care for all patients with eGFR <60 mL/min/1.73m2 (see Table 2). The risks of venepuncture and participation in this study are deemed negligible.

Patients are not expected to personally benefit from participating in this study, although their renal function will be monitored extra closely. Results of this study may help better determine the causal relationship between

contrast exposure and nephrotoxicity, identify which individual patients are at risk, and help to better determine safety of intravascular iodinated contrast administration in future.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria
- referred for an elective procedure with intravascular administration of iodinated contrast material at Maastricht UMC+
- age, sex and contrast procedure type match the age, sex and contrast procedure type of an eGFR <30 mL/min/1.73m2 patient (MIRACLE participants)

- with eGFR 30-59 mL/min/1.73m2 or >=60 mL/min/1.73m2

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: age <18 years; dialysis or pre-dialysis; intravascular contrast administration <30 days before the first baseline; emergency or intensive care status.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	144
Type:	Anticipated

Ethics review

Approved WMO

Date:	05-05-2021
Application type:	First submission
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
Other	ClinicaTrials.gov NCT04603261
CCMO	NL75628.068.20