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# Patients at risk for contrast-induced nephropathy and mid-term effects after contrast administration: a prospective cohort study

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## ABSTRACT

Objectives: Determine the incidence of patients at risk for contrast-induced nephropathy (CIN), the incidence of CIN and mid-term effects (renal replacement therapy/death < one month) to measure the impact of CIN in a general patient population undergoing intravenous contrast-enhanced computed tomography (CECT).

Methods: We conducted a prospective study in consecutive patients undergoing intravenous CECT from October 2012 to May 2013. Data were obtained through scripted interviews and the electronic patient records. Presence of risk factors and kidney function before and after CECT and the follow-up for one month were evaluated.

Results: We included 998 patients (mean age: 60 years). Estimated GFR was ≥ 60 ml/mg/1.72 $m^2$ in 886 (88.8%) patients, 30-59 ml/mg/1.72 $m^2$ in 108 (10.8%) patients and < 30 ml/min/1.73 $m^2$ in 4 (0.4%) patients. We found diabetes mellitus in 137 (13.7%), anaemia in 70 (7.0%), congestive heart failure in 92 (9.2%), peripheral arterial disease in 34 (3.4%), age > 75 years in 126 (12.6%) patients and 301 (30.2%) used nephrotoxic medication. Fifty-eight (5.8%) patients were at risk for CIN; 35 (60.3%) risk patients received intravenous prophylactic hydration. Of the hydrated patients, 11 underwent follow-up within one week; of the non-hydrated patients seven underwent follow-up within one week. Two (2/58: 3.4%) patients developed CIN (increased serum creatinine ≥ 44 μmol/l or ≥ 25%); there was no difference between hydrated and non-hydrated patients (1/35:1/23). The incidence of renal replacement therapy and death within one month was zero for both.

Conclusion: The number of patients at risk is low. CIN incidence is low, even in patients not receiving prophylactic hydration. No patients received renal replacement therapy or died. The impact of CIN is low. Extensive CIN prevention guidelines seem superfluous.

## KEYWORDS

Acute kidney injury, computed tomography, contrast medium, prevention, risk factors

## INTRODUCTION

Contrast-induced nephropathy (CIN) is considered to be the most serious complication following intravascular contrast medium administration. It is defined by an increase in serum creatinine of ≥ 44 μmol/l or ≥ 25% within 24-72 hours after contrast medium administration.[1-3] CIN is associated with increased morbidity (usually defined as the need for renal replacement therapy) and mortality.[4]

To reduce CIN incidence, national CIN prevention guidelines have been introduced.[5,6] These state that patients with chronic kidney disease indicated by an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 $m^2$ in combination with other risk factors are at risk for CIN.[5,6] To enable prevention all patients receiving intravascular iodinated contrast medium should be screened to find those at risk.[5,6] Prevention measures for patients at risk entail discontinuation of diuretics and nephrotoxic medication in addition to prophylactic intravenous hydration before and after contrast-enhanced procedures. See *table 1* for more details on patients at risk.

**Table 1.** *Patients at risk for CIN according to CIN prevention guidelines*

| | |
|---|---|
| **Patients at risk for CIN** | |
| 1. | Multiple myeloma or Waldenström's disease with light chain proteinuria |
| 2. | eGFR 30-44 ml/min/1.73 m² |
| 3. | eGFR 45-59 ml/min/1.73 m² and diabetes mellitus |
| 4. | eGFR 45-59 ml/min/1.73 m² and ≥ 2 other risk factors (not diabetes mellitus) |
| **Other risk factors** | |
| 1. | Anaemia (haematocrit male: 0.39 l/l and female: 0.36 l/l) |
| 2. | Congestive heart failure |
| 3. | Peripheral vascular disease |
| 4. | Age > 75 years |
| 5. | Use of nephrotoxic medication/ diuretics (e.g. NSAIDs) |
| 6. | Dehydration |
| 7. | Symptomatic hypertension |
| 8. | Contrast administration within < 24 hours |

Most iodinated contrast medium administration takes place during intravenous contrast-enhanced computed tomography (CECT).[7] This patient population differs from the patient population undergoing cardiac intervention from which data for CIN prevention guidelines were obtained.[5,6] In CIN prevention guidelines a CIN incidence up to 35% is mentioned.[5,6] In addition, an incidence of up to 45% of renal replacement therapy and death following contrast-enhanced procedures in patients who developed CIN is mentioned in these guidelines.[5,6] In contrast to this patient population, the incidence of CIN following intravenous CECT, as established in two meta-analyses analyses, is low: 4.96% (95% CI: 3.79-6.47) and 6.4% (95% CI: 5.0-8.1) respectively.[8,9] The incidence of mid-term effects following intravenous CECT is suggested to be low to non-existent.[10]

The effort and costs that have to be made to detect patients at risk for CIN and subsequently apply prevention measures seems to be disproportional considering the low CIN incidence and the probability that there are no mid-term effects following CIN.[10-12] These facts have led to discussion about the need for such extensive prevention programs in terms of feasibility, patient benefit and costs.[13-17]

To our knowledge there are no studies evaluating the incidence of patients at risk for CIN, the incidence of CIN, need for renal replacement therapy and death in a sizable number of consecutive patients undergoing intravenous CECT. If we have this overview of the real impact and consequences (mid-term effects) of CIN on a general patient population undergoing intravenous CECT, we could provide some clarity in the discussion on the necessity and extensiveness of the current CIN prevention guidelines in these patients. Therefore, we describe the following findings in a general patient population undergoing intravenous CECT:

1. The incidence of patients at risk for CIN.
2. The incidence of CIN defined as an increase in serum creatinine of ≥ 44 μmol/l or ≥ 25% within seven days after intravenous CECT.
3. The incidence of renal replacement therapy or death within one month after intravenous CECT.

## MATERIALS AND METHODS

### Study design and setting

We conducted a prospective cohort study at the Academic Medical Center, University of Amsterdam from October 2012 to May 2013. The data obtained from this patient population were published previously in an article regarding screening strategies in the context of CIN prevention and another article concerning costs related to screening strategies was recently accepted for publication.[11,12] Informed consent was waived by the hospital's medical ethics committee because the study was non-invasive and patient burden during participation in this study was considered to be negligible.

### Study population

We included consecutive patients scheduled to undergo intravenous CECT. Exclusion criteria were: patients aged < 18 years and patients who were admitted to the emergency department or the intensive care unit because most CIN prevention guidelines describe separate prevention strategies for these patients.[5,6] Patients were also excluded if they did not wish to participate; they did not speak Dutch or English and came without a translator; were not approachable due to logistical reasons or their data were incompletely entered in the database.

Patients received either Iopromide (Ultravist 300, Bayer, Leverkusen, Germany), or Iomeprol (Iomeron 400, Bracco, Milan, Italy) during the intravenous CECT. Both are low-osmolar and non-ionic contrast media.

### Data collection and measurements

Data were collected by scripted interviews using a questionnaire and from the hospital's electronic patient record. The patients were interviewed on the day of the intravenous CECT. The interviews were conducted by four researchers, three medical students and one research fellow (SM, GN, RW, DV), all instructed to conduct the interview in an uniform manner according to the questionnaire.

*Baseline characteristics:* Demographic data (age, sex, length, weight, Afro-European) and type and indication

for intravenous CECT were collected. Body mass index (BMI) was calculated based on height and weight (kg/m$^2$).

*Kidney function:* From the electronic patient records we collected information on kidney function (i.e. eGFR, serum creatinine) before the intravenous CECT. The eGFR was calculated according to the Modification of Diet in Renal Disease (MDRD) formula. We corrected the eGFR for the Afro-Europeans (black people) by multiplying the outcome by 1.20, in accordance with the MDRD formula. eGFR was known in all patients as indicated by the national guideline used in our hospital.[5] This means that in general this was measured < 12 months prior to the intravenous CECT. However, in case of known kidney disease or a clinically relevant event (e.g. cardiovascular event, use of nephrotoxic medication) which could have influenced kidney function and took place in the past 12 months, kidney function was measured after the event. We also registered the time interval between baseline eGFR measurement and intravenous CECT.

*Risk factors:* We assessed the presence of risk factors for CIN. During the interview patients were asked whether or not they suffered from diabetes mellitus and (congestive) heart failure. We checked the electronic patient record to verify the presence of the above-mentioned risk factors. In addition, we checked the electronic patient record to see if patients had anaemia, peripheral arterial disease, if patients used diuretics/ nephrotoxic drugs (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), aminoglycosides) and if patients were diagnosed with either multiple myeloma or Waldenström's disease with light chain proteinuria.
Patients were considered to be anaemic if they had a haematocrit < 0.39 l/l (males) or < 0.36 l/l (females) in accordance with the World Health Organisation definition of anaemia and in accordance with national CIN prevention guidelines.[5,6] We considered medication to be nephrotoxic if this was mentioned in the national database containing information on all (human) registered drugs in the Netherlands and Europe.[18]
Other risk factors such as dehydration, symptomatic hypotension and contrast administration within < 24 hours are mentioned in the guidelines, but were not assessed as we were not able to objectively determine dehydration and symptomatic hypotension during the interview or in the electronic patient record. Another risk factor described in the CIN prevention guideline is contrast administration within < 24 hours before intravenous CECT. This was not applicable as these patients underwent elective intravenous CECT.

*CIN prophylaxis:* We also used the questionnaire to assess whether or not patients were instructed to increase oral fluid intake, discontinue potential nephrotoxic medication/ metformin or received prophylactic intravenous hydration in accordance with the hospital CIN prevention protocol. That protocol indicates that patients who need prophylactic intravenous hydration should receive 0.9% sodium chloride (NaCl), 3-4 ml/kg/h for four hours before and after intravenous CECT. In patients with severe kidney disease or congestive heart failure administration of 1 ml/kg/h for 12 hours is recommended before and after intravenous CECT. The final decision to actually apply prevention measures in patients at risk was left to the discretion of the treating physician.

**Incidence of patients at risk for CIN**

From the above-mentioned data we were able to assess how many patients fit the profile of patients at risk for CIN. We considered the following patients to be at risk for CIN: 1) Patients with multiple myeloma or Waldenström's disease with light chain proteinuria; 2) Patients with an eGFR 30-44 ml/min/1.73 m$^2$; 3) Patients with an eGFR 45-59 ml/min/1.73 m$^2$ and diabetes mellitus; 4) Patients with an eGFR 45-59 ml/min/1.73 m$^2$ and ≥ two other risk factors (anaemia; congestive heart failure; peripheral vascular disease; age > 75 years; use of nephrotoxic medication (e.g. NSAIDs) and diuretics. See also *table 1* for an overview of patients at risk for CIN. We calculated the incidence of patients at risk for CIN by dividing the number of at-risk patients by the total number of patients included in the cohort study.

**Follow-up for CIN incidence and mid-term effects**

CIN incidence: Serum creatinine levels were checked before and after intravenous CECT. By comparing the levels of serum creatinine before and after administration of intravenous CECT, we determined whether CIN occurred. We defined CIN as an increase of serum creatinine ≥ 44 µmol/l or ≥ 25% within seven days. We considered this time interval to be acceptable to determine CIN, as the time interval for CIN determination of 24-72 hours, mentioned in the literature, is not feasible in daily clinical practice due to weekends and holidays.
Mid-term effects: For the mid-term events we assessed the outcomes death and need for renal replacement therapy within one month in patients at risk for CIN.

*Statistical analysis*

Normally distributed variables were reported as means ± standard deviation (SD) and categorical variables as numbers and percentages. Data were statistically analysed using SPSS 20® (SPSS20 Inc., Chicago, IL, USA). Differences between groups were assessed by $\chi^2$ test or Fisher's exact test. A two-sided p-value of < 0.05 was used as an indicator for statistical significant differences.

We used Excel and Access (Microsoft Office® 2003 for Windows XP) to organise the obtained data.

## RESULTS

### Patient population

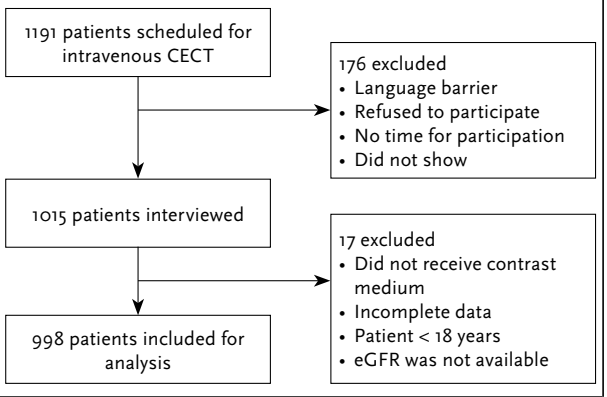
Between October 2012 and May 2013 there were 1191 eligible patients. Of these patients, 176 could not be interviewed due to a language barrier, or the patients did not want to participate, there was no time to interview the patient or the patient did not show up for the examination. We finally interviewed 1015 patients. Seven patients did not receive intravenous iodinated contrast medium during their computed tomography; for another six patients the data could not be used for analysis due to incomplete data, one patient was < 18 years and in three of these patients the eGFR was missing. We finally included 998 patients for analysis. See *figure 1* for more information on eligible, interviewed and included patients.

### Patient characteristics

We included 545 (54.6%) males and 453 (45.4%) females with a mean age of 59.94 years ± 13.56 (SD), 57 patients (5.7%) with Afro-European ethnicity, a mean height of 173 cm ± 10 (SD), a mean weight of 76 kg ± 16 (SD) and a mean BMI of 25 kg/m² ± 5 (SD).

We included 886 (88.8%) patients with an eGFR ≥ 60 ml/mg/1.72 m². There were 108 (10.8%) patients with an eGFR between 30-59 ml/mg/1.72 m² (chronic kidney disease stages 3A and 3B) and 4 (0.4%) with an eGFR < 30 ml/min/1.73 m² (stage 4). Most intravenous CECT examinations were related to malignancy (n = 708, 70.9%), concerned intravenous CECT of the chest and abdomen (n = 387, 38.8%) and were performed in outpatients (n = 925, 92.7%). See details in *table 2*.

**Figure 1.** *Patient inclusion flowchart*




**CECT = contrast-enhanced computed tomography; eGFR = estimated glomerular filtration rate.**

### Kidney function (estimated serum creatinine and glomerular filtration rate at baseline)

The mean baseline serum creatinine was 79 µmol/l ± 23 (SD) in all patients, 74 µmol/l ± 16 (SD) in the patients with an eGFR ≥ 60 ml/mg/1.73 m², 115 µmol/l ± 23 (SD) in patients with an eGFR between 30-59 ml/mg/1.73 m², and 225 µmol/l ± 49 (SD) in patients with eGFR < 30 ml/min/1.73 m².

The exact eGFR was only available in patients with eGFR < 60 ml/min/1.73 m² (mean: 49 ± 9 (SD)), as in patients with an eGFR ≥ 60 ml/min/1.73 m² the absolute value of eGFR is not registered in our electronic patient record/laboratory results. The mean eGFR was 50 ml/min/1.73 m² ± 8 (SD) in patients with an eGFR between 30-59 ml/mg/1.73 m² and 22 ml/min/1.73 m² ± 4 (SD) in the patients with an eGFR < 30 ml/mg/1.73 m². See *table 3* for details on baseline kidney function.

In the majority of the patients (646/998, 64.7%) eGFR was measured within one month before intravenous CECT. In 201 patients, eGFR was measured between 1-3 months before intravenous CECT, and in 146 patients this was between 3-12 months. In five patients the exact time between eGFR measurement and the intravenous CECT was unknown as patients were referred from other institutions. See *table 3* for more details.

### Risk factors and preventive measures

Diabetes mellitus was present in 137 (13.7%) patients. Seventy (7.0%) had anaemia at the time of the intravenous CECT, 92 (9.2%) suffered from congestive heart failure, 34 (3.4%) had peripheral arterial disease, 126 (12.6%) of the patients were older than 75 years and 301 (30.2%) of the patients used nephrotoxic medication or diuretics.

In total 145 (14.5%) patients indicated that they had received information to increase oral fluid intake on the day before and the day of the intravenous CECT and 132 (13.2%) actually increased their oral fluid intake as a result of this. Twenty-one patients indicated that they were advised to discontinue medication on the day before and the day of the intravenous CECT and 22 patients indicated that they stopped taking their medication. One patient had stopped all medication on his own initiative because he thought this would be beneficiary for the intravenous CECT. In total 60 patients received prophylactic intravenous hydration, including eight patients with an eGFR ≥ 60 ml/min/1.73 m². Data are presented in *table 3*.

### Patients at risk for CIN

Of the 108 patients with eGFR 30-59 ml/min/1.73 m², 56 patients were eventually identified as at risk for CIN: one patient with multiple myeloma or Waldenström's disease, 26 patients with an eGFR between 30-44 ml/min/1.73 m², 15 patients with an eGFR between 45-59 ml/min/1.73 m² + diabetes mellitus and 14 patients with eGFR between 45-59 ml/min/1.73 m² and two risk factors (comprising anaemia,

**Table 2.** *Patient characteristics*

| | Total study population (n = 998) | eGFR ≥ 60 ml/min/1.73 m² (n = 886) | eGFR 30-59 ml/min/1.73 m² (n =108) | eGFR <30 ml/min/1.73 m² (n = 4) |
|---|---|---|---|---|
| *Baseline characteristics* | | | | |
| Male: female n (%) | 545 (54.6%):453 (45.4%) | 487 (55.5%):399 (45.5%) | 57 (52.8%):51 (47.2%) | 1 (25.0%):3 (75%) |
| Afro-European n (%) | 57 (5.7%) | 48 (5.4%) | 9 (8.3%) | 0 (0%) |
| Age (years) mean ± SD | 60 (14) | 59 (14) | 66 (12) | 63 (20) |
| Height (cm) mean ± SD[a] | 172 (10)[a] | 173 (10) | 17 (9) | 173 (13) |
| Weight (kg) mean ± SD | 76 (16) | 76 (16) | 80 (19) | 72 (8) |
| BMI (kg/m²) mean ± SD[a] | 25 (5)[a] | 25 (5) | 27 (5) | 24 (3) |
| *Type of CT scan* | | | | |
| Chest/ Abdomen n (%) | 387 (38.8%) | 339 (38.3%) | 48 (44.4%) | 0 |
| Abdomen n (%) | 146 (14.6%) | 131 (14.8%) | 14 (13.0%) | 1 (25.0%) |
| Kidney n (%) | 107 (10.7%) | 89 (10.0%) | 17 (15.7%) | 1 (25.0%) |
| Pancreas n (%) | 95 (9.5%) | 90 (10.2%) | 5 (4.6%) | 0 |
| Cardiac n (%) | 56 (5.6%) | 49 (5.5%) | 6 (5.6%) | 1 (25.0%) |
| Chest n (%) | 53 (5.3%) | 51 (5.8%) | 2 (1.9%) | 0 |
| Aorta n (%) | 45 (4.5%) | 39 (4.4%) | 5 (4.6%) | 1 (25.0%) |
| Liver n (%) | 39 (3.9%) | 33 (3.7%) | 6 (5.6%) | 0 |
| Cerebrum n (%) | 12 (1.2%) | 12 (1.4%) | 0 (0.0%) | 0 |
| Other n (%) | 58 (5.8%) | 53 (6.0%) | 5 (4.6%) | 0 |
| *Indication for CT scan* | | | | |
| Malignancy n (%) | 448 (44.9%) | 393 (44.4) | 55 (50.9%) | 0 |
| Suspected malignancy n (%) | 260 (26.1%) | 233 (26.3) | 27 (25.0%) | 0 |
| Vascular deformation n (%) | 79 (7.9%) | 70 (7.9) | 8 (7.4%) | 1 (25.0%) |
| Nephrological disease n (%) | 34 (3.4%) | 29 (3.3) | 5 (4.6%) | 0 |
| Infection n (%) | 51 (5.1%) | 51 (5.8) | 0 | 0 |
| Kidney donation n (%) | 15 (1.5%) | 15 (1.7) | 0 | 0 |
| Family history of cardiac disease n (%) | 13 (1.3%) | 12 (1.4) | 1 (0.9%) | 0 |
| Pulmonary embolism n (%) | 7 (0.7%) | 5 (0.6) | 2 (1.9%) | 0 |
| Macroscopic anaemia n (%) | 6 (0.6%) | 3 (0.3) | 2 (1.9%) | 1 (25.0%) |
| Cysts (liver, kidney, pancreas) n (%) | 7 (0.7%) | 7 (0.8) | 0 | 0 |
| Angina pectoris n (%) | 9 (0.9%) | 8 (0.9) | 1 (0.9%) | 0 |
| Other n (%) | 69 (6.9%) | 60 (6.8) | 7 (6.5%) | 2 (50.0%) |
| *Patient status* | | | | |
| Inpatient n (%) | 73 (7.3%) | 55 (6.2%) | 17 (15.7%) | 1 (25.0%) |
| Outpatient n (%) | 925 (92.7%) | 831 (93.8%) | 91 (84.3%) | 3 (75.0%) |

[a] **n = 997, one patient did not know his or her height.**

congestive heart failure, peripheral arterial disease, age > 75 years, use of nephrotoxic medication). The remaining 52 patients with an eGFR 45-59 ml/min/1.73 m² (19 with one risk factor and 33 with no risk factors) were not considered to be at risk for CIN, therefore no follow-up data were registered.

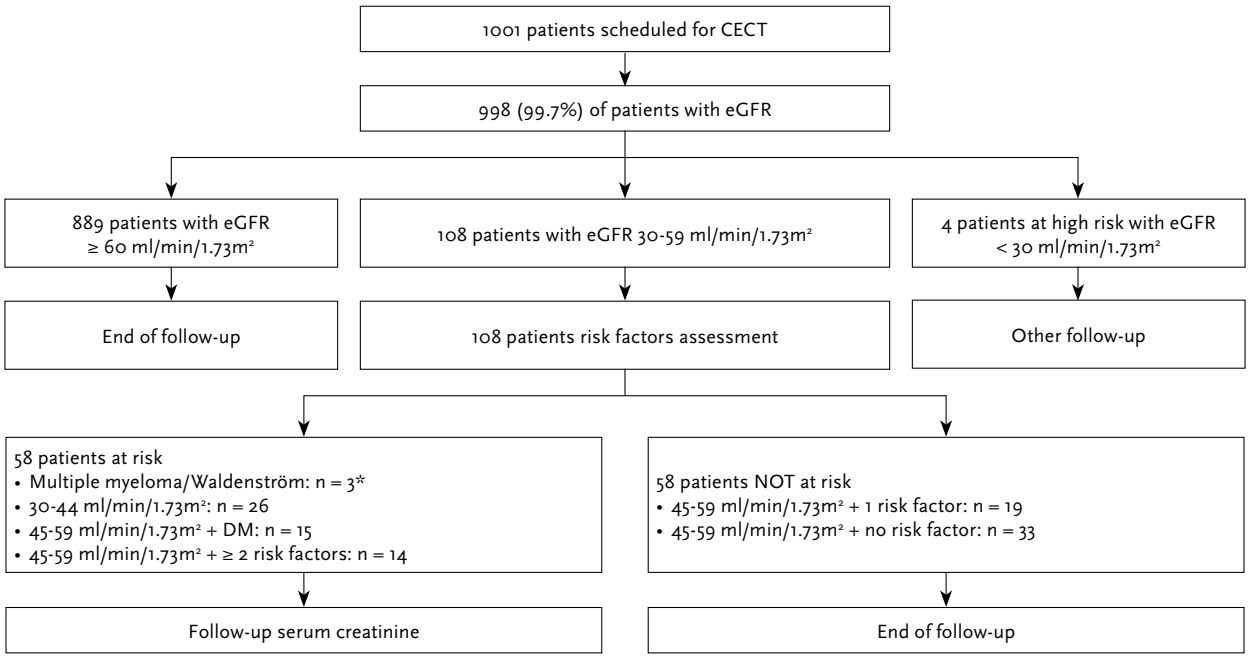
In the group of patients with eGFR ≥ 60 ml/min/1.73 m², two patients with multiple myeloma or Waldenström's disease were also considered to be at risk for CIN. The total number of patients at risk for CIN was 58 patients (5.8%). See details in *figure 2*.

**Table 3.** *Kidney function and other risk factors*

| | Total study population (n = 998) | eGFR ≥ 60 ml/min/1.73 m² (n = 886) | eGFR 30-59 ml/min/1.73 m² (n =108) | eGFR < 30 ml/min/1.73 m² (n = 4) |
|---|---|---|---|---|
| *Kidney function* | | | | |
| Serum creatinine (µmol/l) mean ± SD[a] (number of patients in which data were available) | 80 ± 23 a | 74 ± 16 (n = 863) | 115 ± 23 (n = 106) | 225 ± 49 (n = 4) |
| eGFR (ml/min/1.73 m²) mean ± SD[b] | | - | 50 ± 8b | 22 ± 4 |
| *Risk factors associated with our guidelines[c]* | | | | |
| Diabetes mellitus n (%) | 137 (13.7%) | 112 (12.6%) | 25 (23.1%) | 0 |
| Anaemia n (%) | 70 (7.0%) | 56 (6.3%) | 13 912.0%) | 1 (25.0%) |
| Congestive heart failure n (%) | 92 (9.2%) | 76 (8.6%) | 16 (14.8%) | 0 |
| Peripheral vascular disease n (%) | 34 (3.4%) | 25 (2.8%) | 9 (8.3%) | 0 |
| Age > 75 years n (%) | 126 (12.6%) | 95 (10.7%) | 30 (27.8%) | 1 (25.0%) |
| Use of nephrotoxic medication n (%) | 301 (30.2) | 254 (28.7%) | 45 (41.7%) | 2 (50.0%) |
| Multiple myeloma or Waldenström's disease n (%) | 3 (0.3%) | 2 (0.2%) | 1 (0.1%) | |
| *Preventive measures* | | | | |
| Oral fluid intake advised n (%)/ followed advice n (%) | 145 (14.5%)/ 132 (13.2%) | 118 (13.3%)/107 (12.1%) | 26 (24.1%)/25 (23.1%) | 1 (25.0%)/0 (0.0%) |
| Discontinue medication advice n (%)/stopped medication n (%) | 21 (2.1%)/22 [d]92.2%) | 16 (1.8%)/ 16(1.8%) | 4 (3.7%)/ 5[d] (4.6) | 1 (25.0%)/ 1 (25.0%) |
| Prophylactic intravenous hydration n (%) | 60 (6.0%) | 8 (0.9%) | 50 (46.3%) | 2 (50.0%) |

**[a]Serum creatinine values were missing in 25 patients; [b]absolute eGFR was missing in 3 patients; [c]other three risk factors: hydration, symptomatic hypertension and contrast administration within < 24 hours were not assessed; [d] One patient had stopped all medication on own initiative thinking this would be beneficiary for the intravenous iodinated contrast enhanced examination.**

**Figure 2.** *Defining patients at risk*




*** Two of these patients had an eGFR ≥ 60 ml/min/1.73 m²; CECT = contrast-enhanced computed tomography; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate.**

**Prevention regimen in patients at risk**

Of the 58 patients at risk for CIN, 35 underwent prophylactic intravenous hydration and the remaining 23 patients did not receive prophylactic intravenous hydration. Patients with multiple myeloma or Waldenström's disease were equally distributed between patients who received prophylactic intravenous hydration and patients not receiving prophylactic intravenous hydration (1/35 vs 2/23; p = 0.556). The number of patients with an eGFR 30-44 ml/min/1.73 m² were also equally distributed (19/35 vs 7/23; p = 0.074) between patients who received prophylactic intravenous hydration and patients who did not. The same applies for patients with an eGFR between 45-59 ml/min/1.73 m² + diabetes mellitus (8/35 vs 7/23; p = 0.519) and for patients with an eGFR between 45-59 ml/min/1.73 m² + ≥ 2 risk factors: 7/35 vs 7/23; p = 0.364. See details in *figure 3*.

**Incidence of CIN**

Of the 35 at-risk patients who received prophylactic intravenous hydration, 11 patients had a follow-up serum creatinine measurement within seven days. Of the 23 at-risk patients who did not receive prophylactic intravenous hydration, seven patients underwent serum creatinine follow-up within seven days. In total two patients had CIN (2/58 patients at risk for CIN: 3.4%, 2/18 11.1%). When taking into account the total number of screened patients, the incidence of CIN was 0.2% (2/998). Data on further serum creatinine follow-up were not available.

The distribution of the number of patients with CIN between patients who received prophylactic intravenous hydration and patients who did not receive prophylactic intravenous hydration was comparable (1/35 vs 1/23; p = 0.761). See *figure 3*.

**Mid-term follow-up of patients at risk**

None of the 58 patients at risk for CIN received renal replacement therapy or died within one month after intravenous CECT (see also *figure 3*).

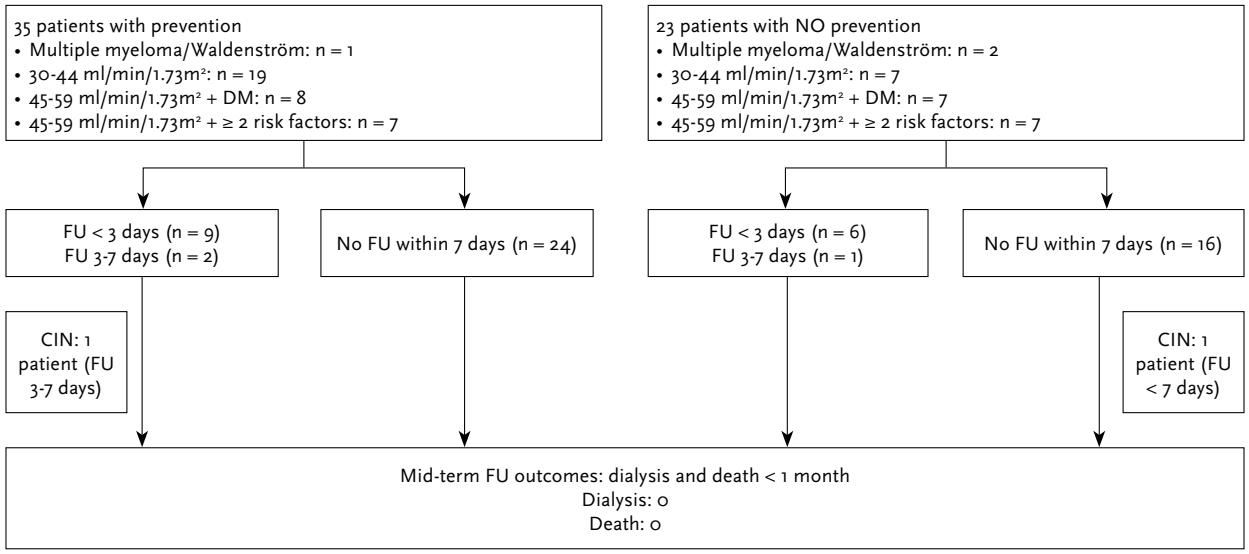
## SUMMARY AND CONCLUSIONS

**Summary**

Firstly, our study showed that the number of patients at risk for CIN in a general population undergoing intravenous CECT is low (5.8%), even in a population with a high prevalence of relevant risk factors (66.8%). Secondly, the CIN incidence was low to very low. In the group of patients at risk for CIN, the CIN incidence was 3.4% (2/58) and in the total group of screened patients this was 0.2% (2/998). Prophylactic intravenous hydration does not seem to influence CIN incidence. Thirdly, mid-term effects following intravenous CECT were non-existent.

When we consider the patients at risk for CIN we found that almost all patients defined as being at risk had eGFR 30-59 ml/min/1.73 m² (10.8% of the patient population (108/998)). In a study by Liu *et al.* a higher number (31/171, 18.2%) of patients were seen with an eGFR 30-59 ml/min/1.73 m², but the number of patients at risk for CIN was also low: 10 patients (5.8%) would be categorised as at risk, which is comparable to our patient population.[19] Recent updates of international CIN prevention guidelines

**Figure 3.** *Follow-up serum creatinine and mid-term follow-up of 58 patients at risk*




**DM = diabetes mellitus; FU = follow-up.**

indicate that prevention measures are only indicated in patients with an eGFR < 45 or 40 ml/min/1.73 m² in combination with risk factors for CIN.[20,21] In addition, a recent study by Davenport *et al.* comparing patients who did and did not undergo intravenous CECT showed no significant difference in CIN or acute nephropathy incidence in patients with an eGFR ≥ 30 ml/min/1.73 m² (odds ratio: 2.96 (95% CI: 1.22-7.17).[22] If we were only to consider patients with an eGFR < 45 or < 30 ml/min/1.73 m² this would decrease the incidence of patients at risk in our patient population to 3.0% or 0.4% (30 or 4/998), respectively.

The low CIN incidence in our patient population is in accordance with two meta-analyses performed on CIN incidence, which mostly contained patients at risk for CIN (overall pooled CIN incidences were 4.96% (95% CI: 3.79-6.47) and 6.4% (95% CI: 5.0-8.1)).[8,9] In our study not all patients at risk received prevention measures; this might be a reflection of the fact that clinicians do not always consider CIN to be clinically relevant because they seldom or never experience mid-term effects. In addition (inter)national surveys show that the majority of clinicians and radiologists do not know exactly which patients belong to the at risk category and what the appropriate steps would be in this case.[23,24] These factors could reduce compliance. The fact that the distribution of CIN incidence was equal between patients who did and did not receive prophylactic intravenous hydration before and after intravenous CECT could imply that this prevention measure is not as effective as has been assumed up to now. This is confirmed in studies were a high number of patients did not receive prophylactic intravenous hydration: 348/493 (70.6%) and 577/663 (87.0%).[4,25] Here there was no difference in CIN incidence between patients who did and did not receive prophylactic intravenous hydration (3.2 vs 1.4% calculated Fisher's exact test, p = 0.363).

Finally, this paper showed incidences of 0% for the need for renal replacement therapy and for death. Mid-term effects following intravenous CECT were also assessed in a systematic review and meta-analysis by McDonald *et al.*[26] They analysed the difference in need for renal replacement therapy and death following intravenous CECT comparing patients undergoing intravenous CECT with patients undergoing unenhanced procedures in an effort to see if there is causality between intravenous CECT and acute nephropathy and these mid-term effects.[26] The pooled RRs for need of renal replacement therapy and occurrence of death were 0.88 (95%: CI 0.23-3.43; p = 0.85) and 0.95 (95% CI: 0.55-1.67; p = 0.87), respectively, when comparing the two groups.[26] In the group of patients undergoing intravenous CECT, the number of patients needing renal replacement therapy was 24/7270 (0.33%) compared with 0% in our population and death was 178/7359 (2.0%) compared with 0% in our population.[26] However, the follow-up period for these outcomes in the studies included in the review by McDonald was defined as three months,[27] or as the duration of hospitalisation,[28,29] or was not defined at all.[30,31] This could have led to overestimation or underestimation of the incidence of these mid-term effects. Another limitation of their study is that they did not take into account the use of prophylactic intravenous hydration.

**Limitations**

This study was performed in an academic hospital and most of the intravenous CECT examinations were related to (suspected) malignancies (70.9%). However, this spectrum of patients is representative for patients undergoing intravenous CECT in daily clinical practice in many institutions.[19,32] Secondly, in this study, the standard follow-up within seven days was not accurately performed in 68.9% (40/58) of the patients at risk. Because we collected the data for this study by following daily clinical practice, we were not able to interfere with clinical practice in order to perform accurate follow-up of kidney function in all patients. As we were not able to complete serum creatinine follow-up for all patients, it is possible that we underestimated CIN incidence. However, we were able to complete follow-up for the need of renal replacement therapy and outcome of death for all patients at risk for CIN.

Furthermore, we did not include controls who did not undergo intravenous CECT to evaluate causality between intravenous CECT, CIN incidence and mid-term effects. However, since CIN incidence was low (0.2%) and mid-term effects did not occur, we think that we have substantial evidence that CIN incidence and incidence of mid-term effects are not as relevant as has been assumed up till recently and there is no causality between intravenous CECT and nephropathy, renal replacement therapy and death. The addition of controls would not change this conclusion.

We did not perform a power analysis and considering the incidence of need for renal replacement therapy and death our sample size is relatively small.

## CONCLUSIONS

The number of patients at risk for CIN and CIN incidence was low. In addition, there were no mid-term effects following intravenous CECT. Our results imply that only a small group of patients would benefit from CIN prevention guidelines. In addition, mid-term effects following intravenous CECT are absent, making extensive CIN prevention guidelines seem superfluous. We therefore propose that only patients with severe chronic kidney disease stage 4-5 (eGFR < 30 ml/min/1.73 m²) should be considered to be at risk for CIN. We think

that the screening strategies for patients at risk should be tailored and the present strategy in which all patients are considered to be at risk for CIN should be replaced. Whether these patients (eGFR < 30 ml/min/1.73 $m^2$) would benefit from prophylactic intravenous hydration is questionable.

Further evidence to support this proposal should be acquired in a randomised controlled trial comparing at-risk patients receiving CIN prophylaxis with at-risk patients not receiving CIN prophylaxis. Thereby, also taking into account cost, complications of CIN and intravenous prophylactic hydration and health-related quality of life aspects.

## DISCLOSURES

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