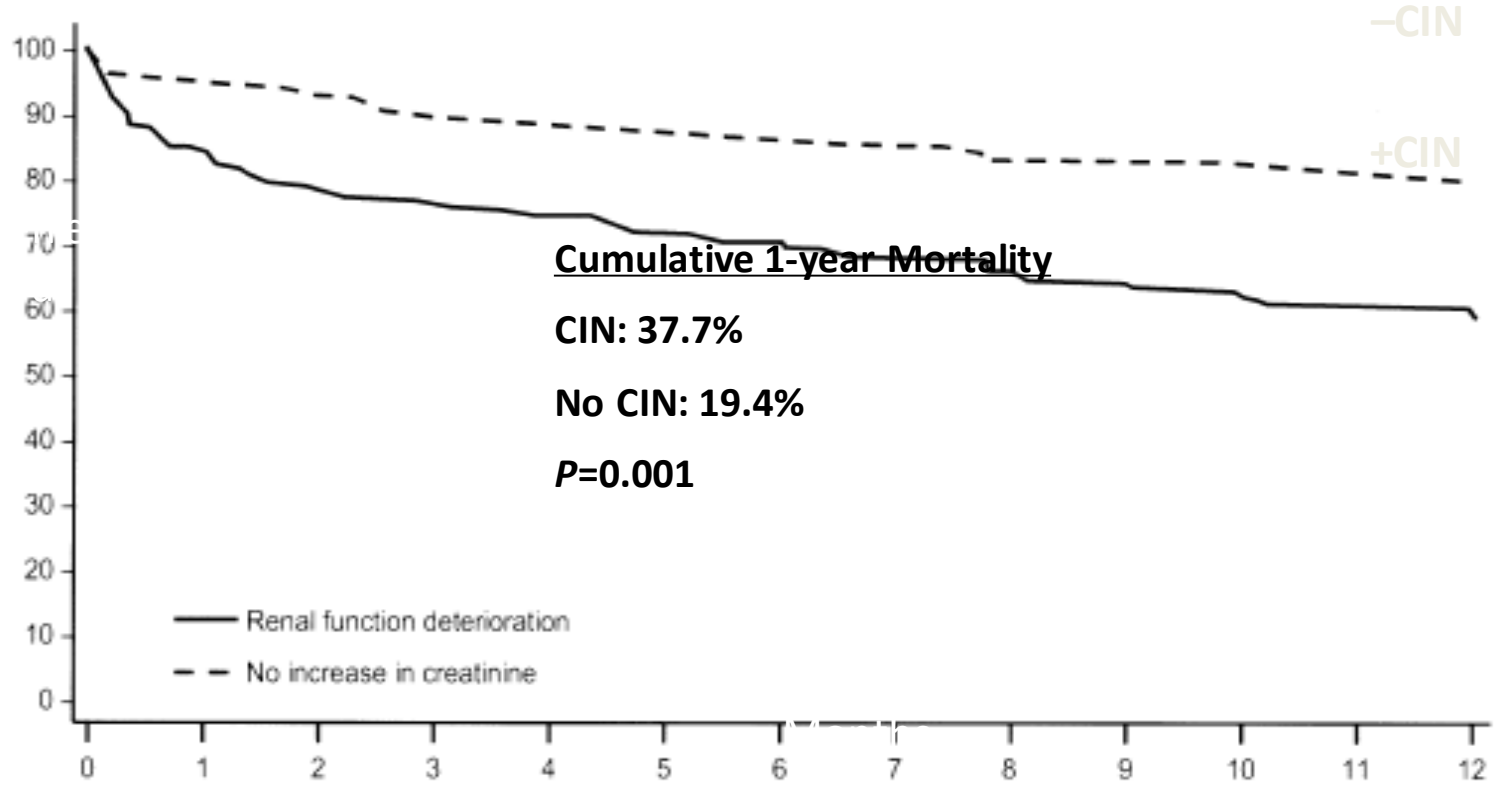
How do we handle CIN in the emergency situation

Peter Aspelin
Professor of Radiology
Karolinska Institutet

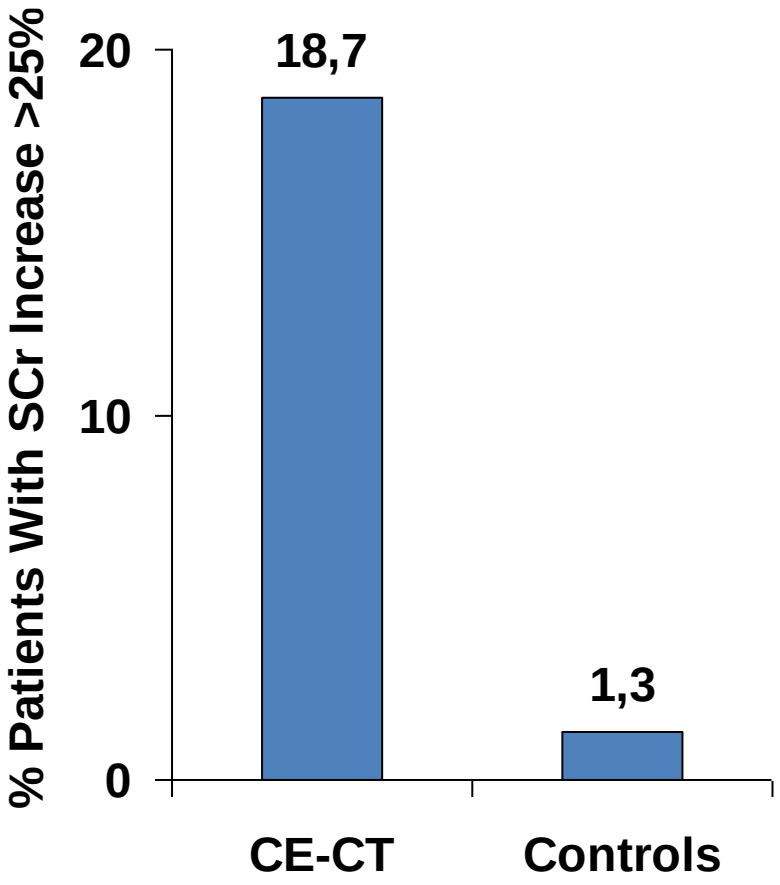
5th Nordic Course in Emergency Radiology, Oslo 2015

Is CIN dangerous?

Kaplan Meier 1-year Survival Rates Following CIN



CIN in CT: Intensive Care Unit Patients



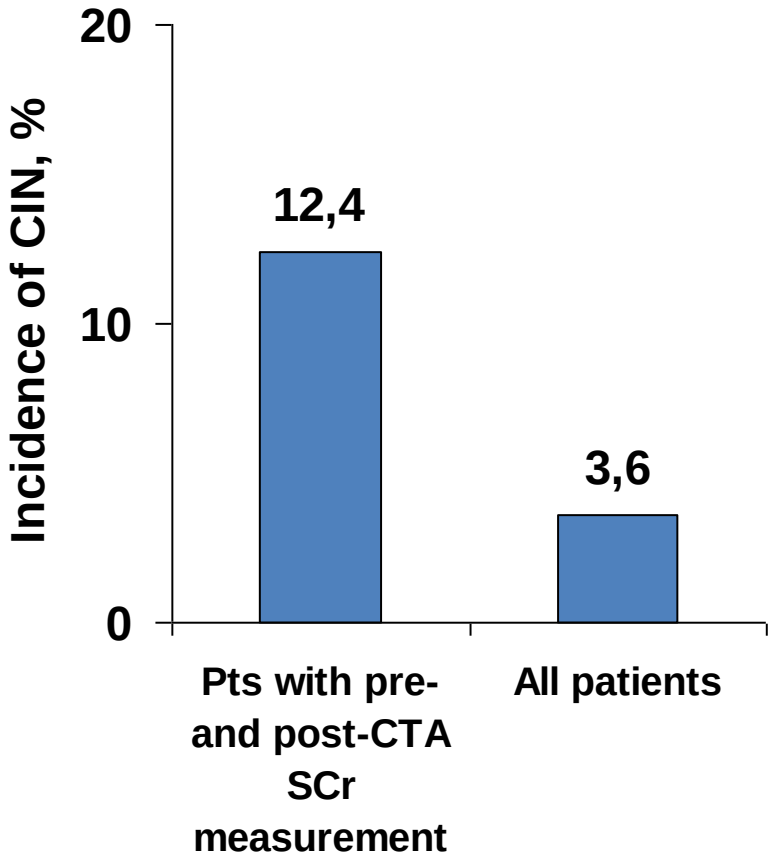
Parameter	CE-CT	Controls*
n	75	75
Age, y	64.5	66.1
Diabetes	34%	32%
Hypertension	60%	57%
CHF	18%	23%
CAD/PVD	57%	54%
SCr <1.5	88%	85%
SCr 1.5–2.0	12%	15%

*Controls are critically ill patients not given CM while in the ICU

CE-CT agent: iopamidol

Polena S et al. *Proc West Pharmacol Soc.* 2005;48:134-135.

CIN in CT: Chest CTA for Pulmonary Embolism in the Emergency Department



Parameter	Pts with pre + post CTA SCr	Pts with pre-CTA SCr only
N	354	870
Age, y	53	47
Diabetes	22%	12%
HTN	48%	36%
CHF	9%	6%
CAD*	14%	8%
SCr ≥1.2 mg/dL	25%	19%

*24% incidence of CIN in pts with history of CAD

CE-CT agent: iopamidol

Mitchell AM, Kline JA. *J Thromb Haemost*. 2007;5:50-54.

Can “pseudo CIN ”(raise in SCr) occur without contrast media?

“Pseudo CIN” without contrast medium

- 32.000 patients – serum creatinine measurements
- Same frequency of CIN with/without contrast media administration

Newhouse, AJR 2008

“Pseudo CIN” without contrast medium

- 11500 patients – serum creatinine measurements
- Same frequency of “AKI” without contrast media as after an IOCM (CT study)

Bruce AJR March 2009

How do we then know that CIN exists at all

We know that CM are nephrotoxic

Contrast-induced nephropathy (CIN)

Nils Alwall (Lund, Sweden)
1st clinical dialysis equipment

Alwall N, Johnsson S, Tornberg, A Werkö L.

Acute renal failure following angiography.

Acta Chir Scand

1955;109:11-19.

Frequency of Acute Kidney Injury Following Intravenous Contrast Medium Administration:

A Systematic Review and Meta-Analysis[1]

Jennifer S. McDonald, PhD
Robert J. McDonald, MD, PhD
Jules Comin, MD
Eric E. Williamson, MD
Richard W. Katzberg, MD
M. Hassan Murad, MD, MPH
David F. Kallmes, MD

[1]From the Department of Radiology (J.S.M., R.J.M., E.E.W., D.F.K.), Division of Preventive Medicine (M.H.M.), and Department of Neurosurgery (D.F.K.), **Mayo Clinic, 200 1st St SW, Rochester**, MN 55905; Department of Medical Imaging, **St Vincent's Hospital, Melbourne, Australia** (J.C.); and Department of Radiology, **University of California, Davis, Davis, Calif** (R.W.K.)

Radiology: Volume 267: Number 1—April 2013

Frequency of Acute Kidney Injury Following Intravenous Contrast Medium Administration: A Systematic Review and Meta-Analysis

- Systematic review and meta –analysis on patients that
- Received Iodin CM where Scr values were obtained before before and after CM injection with a control group, that NOT received any CM.
- 26.000 patients (13 studies).

.

Jennifer S. McDonald et al; Radiology, 2013; 267:119--128

Frequency of Acute Kidney Injury Following Intravenous Contrast Medium Administration:

- AKI after CM injection6,4%
- AKI in the NON CM group 6,5%

Jennifer S. McDonald et al; Radiology, 2013; 267:119--128

Frequency of Acute Kidney Injury Following Intravenous Contrast Medium Administration:

Sub-group analysis

- No differences whether the patients had renal insufficiency or diabetes
- No differences between CM (high-low or iso).

Jennifer S. McDonald et al; Radiology, 2013; 267:119--128

Two studies on incidence on CIN with propensity matching.

McDonald RJ, McDonald JS, Bida JP, Carter RE, Fleming CJ, Misra S, Williamson EE, Kallmes DF.

Intravenous contrast material-induced nephropathy: causal or coincident phenomenon?

Radiology. 2013 Apr;267(1):106-18

Davenport MS, Khalatbari S, Dillman JR, Cohan RH, Caoili EM, Ellis JH.

Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material.

Radiology. 2013 Apr;267(1):94-105

Contrast Material–induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material[1]

Matthew S. Davenport, MD
Shokoufeh Khalatbari, MS
Jonathan R. Dillman, MD
Richard H. Cohan, MD
Elaine M. Caoili, MS, MD
James H. Ellis, MD

1 From the Department of Radiology, **University of Michigan Health System**, 1500 E Medical Center Dr, B2-A209P, **Ann Arbor, MI 48103** (M.S.D., J.R.D., R.H.C., E.M.C., J.H.E.); and **Michigan Institute of Clinical and Health Research, University of Michigan, Ann Arbor, Michigan** (S.K.).

Radiology: Volume 267: Number 1—April 2013

Contrast Material Induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material:

Propensity scoring

- A method to control for different variables that increases the probability that the patient will get a condition (CIN)

Matthew S. Davenport et al; Radiology, 2013; 267:94-105

Contrast Material Induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material:

Propensity scoring

- The drawback is that you can only adjust for known and correctly measured variables

Matthew S. Davenport et al; Radiology, 2013; 267:94-105

Contrast Material Induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material:

- To determine the frequency of CIN after intravenous injection of CMAtt bestämma frekvensen av CIN vid intravenös kontrastmedelsinjektion

- 430.000 CT-investigations of which 20.000 patients received CM and 20.000 that had NO CM injection
- With the same ”propensity score”

Matthew S. Davenport et al; Radiology, 2013; 267:94-105

Contrast Material Induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material:

Resultat

- Patients with normal or <1.5 mg/dl (132.6 μmol/L) in SCr no increased risk
- Patienter with SCr >136 μmol/L and (154 mg/dl) had an INCREASED risk

- And was DOUBLED at SCr >180 μmol/L (2.0 mg/dl)

Matthew S. Davenport et al; Radiology, 2013; 267:94-105

Intravenous Contrast Material-induced Nephropathy: Causal or Coincident Phenomenon?

Robert J. McDonald(2)
Jennifer S. McDonald
John P. Bida
Rickey E. Carter
Chad J. Fleming
Eric E. Williamson
David F. Kallmes

Robert J. McDonald et al; Radiology, 2013; 267:106-118

Intravenous Contrast Material-induced Nephropathy: Causal or Coincident Phenomenon?

- Retrospective study to see if there was a difference between patients that had a Contrast CT and non-enhaced CT

Robert J. McDonald et al; Radiology, 2013; 267:106-118

Intravenous Contrast Material-induced Nephropathy: Causal or Coincident Phenomenon?

- 53.000 patients with 1.5 milj SCr values

Robert J. McDonald et al; Radiology, 2013; 267:106-118

Intravenous Contrast Material-induced Nephropathy: Causal or Coincident Phenomenon?

Result

- No difference between those who received CM and those who did not independent of SCr.
- No difference in subgroups divided on level of SCR (3 levels, below 1.5 mg/ml; 1.5-2 mg/dl and >2.0 mg/dl).

Conclusion

- The authors question the relationship between CM and CIN, AT ALL

Robert J. McDonald et al; Radiology, 2013; 267:106-118

How do we then know that CIN exists at all

If CIN exist after intraarterial CM injections. Why would intravenous be less dangerous?

Contrast-induced acute kidney injury and clinical outcomes after intra-arterial and intravenous contrast administration: Risk comparison adjusted for patient characteristics by design

Judith Kooiman, MSc,[a,b] Pum A. Le Haen, MD,[c] Gülçin Gezgin, BSc,[a] Jean-Paul P. de Vries, MD, PhD,[d] Doeke Boersma, MD,[d] Harald F. Brulez, MD, PhD,[e] Yvo W. Sijpkens, MD, PhD,[f] Aart J. van der Molen, MD,[g] Suzanne C. Cannegieter, MD, PhD,[h] Jaap F. Hamming, MD,[i] and Menno V. Huisman, MD, PhD[a] *Leiden, The Hague, Nieuwegein, and Amsterdam, The Netherlands*

From the [a]Department of Thrombosis and Haemostasis, **Leiden University Medical Center (LUMC), Leiden**, The Netherlands, [b]Department of Nephrology, **LUMC, Leiden**, The Netherlands, [c]Department of Radiology, **Haga Ziekenhuis, The Hague**, The Netherlands, [d]Department of Vascular Surgery, **St. Antonius Hospital, Nieuwegein**, The Netherlands, [e]Department of Nephrology, **St. Lucas Andreas Hospital, Amsterdam**, The Netherlands, [f]Department of Nephrology, **Bronovo Hospital, The Hague**, The Netherlands, [g]Department of Radiology, **LUMC, Leiden**, The Netherlands, [h]Department of Clinical Epidemiology, **LUMC, Leiden**, The Netherlands, and [i]Department of Vascular Surgery, **LUMC, Leiden**, The Netherlands.

(Am Heart J 2013;0:1-7.e1.)

Contrast-induced acute kidney injury and clinical outcomes after intra-arterial and intravenous contrast administration: Risk comparison adjusted for patient characteristics by design

- Comparative study between patients that received both intra -arteriell and intravenous injection of CM within one year.

Kooiman J. et al; Am Heart J, 2013; 165:793-799

Contrast-induced acute kidney injury and clinical outcomes after intra-arterial and intravenous contrast administration: Risk comparison adjusted for patient characteristics by design

Result

- 14% CIN following intra-arteriel CM injection
- 11,7% following intravenous CM injection
- NO statistical difference
- *Conclusion*
- CI-AKI is the same after intra- arteriel as intravenous injection

Kooiman J. et al; Am Heart J, 2013; 165:793-799

Safety first

- As there are no good RCT studies comparing the risk between i.v. and i.a injections, we better assume the risk is the same.

- The recommendation is therefore to regard all patiens as having the same risk

How do we then know that CIN exists at all

First: We know that CM are nephrotoxic
Second: CIN is an arbitrary binomal value

Radiology 1966;86:835-838

Complications of "No Arteriography"[1]

STANLEY BAUM, M.D., GEORGE N. STEIN, M.D., and KOSON K. KURODA, M.D.

"A striking similarity was noted in the incidence and character of untoward reactions occuring within 48h prior to angiography and those within 48h afterwards"

CIN with contrast medium

- Differences in randomized controlled studies must be due to ”true CIN”,
  but the frequency may be overestimated, especially in not ”high-risk patients”.

- Occur in experimental animal studies.

RCT

- Statistical difference is superior to no difference

- "No difference" does not automatically imply equality
  "Abscence of evidenc not equal to evidence of absence "

Limitations

- Number of and level of risk-patients, sample size,
  time for measuring Scr and timing and number of postdose
  SCR measures etc

Levels of Evidence

Highest

Level A

- High-quality randomized controlled trial (RCT)
- High-quality meta-analysis

Level B

- Well-designed, nonrandomized clinical trial
- Nonquantitative systematic review
- Lower quality RCTs
- Clinical cohort studies
- Case-controlled studies
- High-quality, historical, uncontrolled studies
- Well-designed epidemiological studies

Level C

- Consensus viewpoint
- Expert opinion

Lowest

American Academy of Family Physicians. http://www.aafp.org/x17444.xml. Accessed 8/8/06.

Why is it difficult to prove the existense of CIN?

Because allt the studies hav used, both prevention strategies according to the ACR recomendations and sometimes also used Visipaque(iso-osmolar CM in high risk patiens

CIN is NOT an ” statistical-group” problem, but an Individual personalized medicin problem. How do we prevent the individual patient from getting nephrones killed?

All injections of CM is a risk benefit equation.
If the benefit is greater than the risk- then do it!

How to avoid …….

”Luck favours a prepared mind”

Louis Pasteur

CIN- prevention

We know the risk factors

How to handle CIN in emergency radiology

Identify the risk patient

Plan the investigation-calculate the contrast media dose needed

Find out (in OMNIVIS) if the dose correlates to the renal function

Hydrate (plasma expansion) the patient

Measures that can be taken at CT in order to reduce the risk of CIN

- Hydrate (before and after)
- Reduce the CM dose. Keep it below (dose in g Iodine) 50% of the eGFR.
- Dose in relation to body weight
- Reduce the dose by reducing the KV (when possible)
- Optimize injection timing
- Flush the catheter

EVERY contrast medium injection must contain

A consideration- is it necessary for the diagnosisis

What is the risk/benefite analysis

A well considered risk = OK

Ignorance = NO

Give the patient the required dos needed to get the correct diagnosis

How to handle CIN in emergency radiology

A MAN HAS TO DO WHAT A MAN HAS TO DO

John Wayne

Conclusion

- 1. CIN (CM-AKI) exists
- 2. The risk may have been overexaggerated.
- 3. With adequate preventive actions you may reduce the risk and use the least nephroroxic CM.
- 4. The average group of patients may have a low risk but the individual patients may have a large risk of CIN
- 5. Know the risk and do what you can to prevent CIN- Safety first
- 6. THEN DO IT