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NEPhrotoxicity In High-Risk Patients: Study of Nonionic Iso-osmolar Iodixanol and Low-osmolar Iohexol (NEPHRIC), an IA Trial

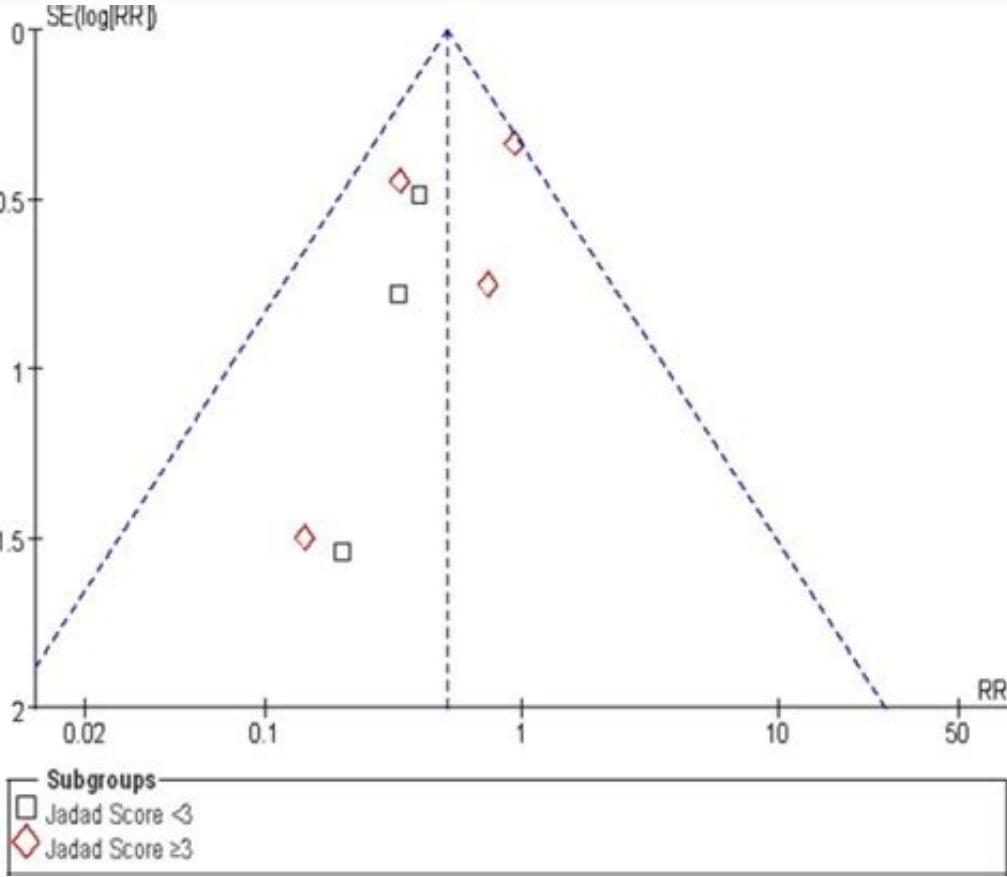
- Randomized, double-blind, prospective, multicenter trial
- 17 centers, 5 countries in Europe
- Enrollment: Jan 1999 – Sept 2001
- 135 pts undergoing coronary or aortofemoral angiography
- Randomized to iodixanol (n=64) or iohexol (n=65)
- Inclusion
 - DM (type 1 or 2 treated with insulin or oral antidiabetic drugs) + impaired renal function
 - SCr:
 - ≥1.5 mg/dL (133 μmol/L) (male)
 - ≥1.3 mg/dL (115 μmol/L) (female)
 - or a calculated CrCl ≤60 mL/min

Primary Endpoint
Mean peak $\uparrow$ in SCr on day 3

$P=0.001$

Iodixanol 320 n=64: 0.13 mg/dL
Iohexol 350 n=65: 0.55 mg/dL

Aspelin P et al. *N Engl J Med*. 2003;348:491-499.



Iodinated Contrast IS NOT Nephrotoxic

Clinical Evidence

AKI in 0.8–1.7% of those exposed to contrast¹

without contrast: AKI OR 1 (ref)
with contrast: AKI OR 1.00²

16,800 patients: CT

32,200 patients: no contrast

same incidence of AKI as in contrast nephropathy studies³

Basic Science

Pathophysiology Unknown

medullary O₂ supply/demand mismatch?

endothelial dysfunction?
reactive oxygen species
prostaglandin deficiency
nitric oxide deficiency
NF- κ B activation
WBC adhesion
apoptosis

proximal tubule cell damage?
loss of polarity, tight junctions
mitochondrial toxicity
(membrane potential, enzyme activity)
decreased proliferation
apoptosis

vascular smooth muscle constriction?

TGF: Mechanism Fail

loop diuretics → ↓ TGF BUT no ↑ GFR in contrast nephropathy

¹Liss P et al, *Kidney Int* 2000; ²Hinson JS et al, *Ann Emerg Med* 2017; ³Hewhouse JH et al, *Am J Roentgenol* 2008

@JamesNovakNeph

Proposed algorithm for prevention of contrast-induced acute kidney injury

All patients	eGFR <60 ml/min	eGFR <30ml/min
Pre-procedure	Mehran score MCAD	IV Hydration Avoid nephrotoxin
Intra-procedure	Iso osmolar contrast Limit contrast IVUS Tip injections Staging	D/W Nephrology Renal transplant IV Bicarbonate
Post procedure		Use Renal guard Serum creatinine F/U till 72 hours

MANAGEMENT OF PERIOPERATIVE ANAPHYLAXIS	
recognize and remove suspected drug/trigger	
Oxygen	ventilate with 100% oxygen
Epinephrine (adrenaline)	1 mg/10 ml used 1-2 times intramuscularly/venously repeat with increasing doses every 3-5 minutes as needed may need continuous infusion
Fluid bolus	20 ml/kg balanced salt solution repeat as necessary
Phenylephrine (Neo-Synephrine)	0.1 mg/kg IV bolus to effect if inadequate response to epinephrine
Hydrocortisone	2-3 mg/kg IV
Diphenhydramine	1-2 mg/kg IV
Ranitidine (Zantac)	1-5 mg/kg IV

Contrast-induced nephropathy guidelines 2019. Contrast induced nephropathy guidelines 2018. Contrast induced nephropathy guidelines.

1 Controplast-Inducted NephropatyMartin Gregory, MD, PhD Ogden Medical and Surgic Society May 17, 2018 2 2 Joint Controversial Netropathy Purely iatrogen Has well characterized the risk factors The timing of the precipitated event is widely foreseeable Carries serious consequences in the short and long term 3 Questions to be addressed How big is the problem of CI-AKI? Who is at risk? What are the most risky procedures? How to protect patients from CI-AKI? Is contrast a concern in AKI patients? Contrast is a concern in patients with terminal kidney disease (ESRD). You need to call an ESRD patient right after the contrast? Is the MRI with gadolinium safer? 4 The total incidence of CNS is not decreasing the total incidence of CNS n. From 15% to 7% in period 2105 to 1015 McCullough PA et al. Acute renal failure after coronary intervention: incidence, risk factors and relationship to mortality. Am J Med 1997; 103 (5): 5 Solomon R et al. N. Engl J Med 1994; 331:1416-1420. Serum creatinine concentrations Immediately prior to administration of radiocontrast agents (after twelve hours of hydration) and 48-hour thereafter in patients with chronic renal impairment. Figure one. Serum creatinine concentrations Immediately prior to administration of radiocontrast agents (after twelve hours of hydration) and 48-hour thereafter in patients with chronic renal impairment. The mean (axis) for each treatment group is indicated by heavy lines and circles. The increase in serum creatinine was significantly higher in the furosemide group compared to the salt group (P .30). Liver transplantation, liver syndrome even risk factors. The overall risk concerns approximately one million doses in the general population. The reported incidence of NSF in patients with impaired renal function is estimated between 0.1 and 1% for Magnevist. Very low risk with Group II agents, but avoid if GFR

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