

Visipaque Criteria &
Review of Contrast Dye Nephropathy
8/2003

Recommendation:

- Visipaque (iodixanol) is recommended for formulary inclusion with restricted use.
- Visipaque criteria for usage (same as NEJM study)
 - Diabetics treated with insulin or oral antidiabetic agents with a serum creatinine ≥ 1.3 mg/dl.
 - Non Diabetes with serum creatinine > 1.5 mg/dl
- A standardized hydration protocol is recommended for all patients receiving contrast medium: 0.9% sodium chloride at 1 ml/kg/hr starting the morning of angioplasty and continuing until the day following the procedure at 8 am. The rate of nephrotoxicity was reduced from 2% to 0.7% in a large prospective, randomized, controlled clinical trial, using normal saline versus half-normal saline.
- Oral acetylcysteine prophylaxis is recommended to prevent contrast dye induced renal failure, 600 mg bid the day before and day of the procedure as nephrotoxicity is reduced by 50%.

Findings:

- Iodixanol in a nonionic dimeric contrast medium and is iso-osmolar.
- Iodixanol is less painful when injected into small-caliber arteries.
- Viscosity of contrast media is linearly dependent on the iodine concentration of the contrast.
- Nonionic agents include: iohexol, iopamidol, ioversol, iodixanol, and metrizamide.
- Low osmolar contrast dyes have a lower risk of nephrotoxicity than high-osmolar contrast dyes
- *Iodixanol does not show any advantages in non-diabetics patients with normal renal function over low osmolar contrast medium.*
- The most common definition of contrast induced nephropathy is an increase in serum creatinine of 0.5 mg/dl or 25% (which ever is greater).
- Estimated mortality for RCIN (radio contrast induced nephropathy) is as high as 35%. The in-hospital mortality rate in patients developing renal insufficiency is directly related to the magnitude of the increase in serum creatinine, 3.8% with an increase in creatinine from 0.5 to 0.9 mg/dl and 64% with an increase of > 3 mg/dl.
- The incidence of nephropathy induced by low osmolar contrast media is low in the general population and has been calculated to be less than 2%.
- Infusion of contrast agents is the third leading cause of hospital-acquired acute renal failure.
- Serum creatinine usually peaks 2-3 days post contrast media exposure and returns to baseline in 10-14 days.
- RCIN that requires dialysis after percutaneous coronary interventions has an in-hospital mortality of 25% and 1 year mortality of 55%.
- Contrast induced nephropathy has been related to: Contrast media dose, Female, DM, Chronic Renal Insufficiency (women serum creatinine > 1.2 , men > 1.5 mg/dl), volume depletion, multiple myeloma, CHF NYHA Class III or IV, age > 70 years, cirrhosis
- The European Society of Urogenital Radiology guideline on administering contrast media recommends the following to avoid contrast induced nephrotoxicity :
 - Make sure the patient is well hydrated; use IV normal saline 4 hours before to 24 hours after contrast.
 - Stop nephrotoxic drugs for at least 24 hours
 - Do not administer mannitol and diuretics, in particular loop diuretics.
 - Do not perform multiple studies with contrast within a short period
 - Do not administer large doses of contrast
- Summary of finding for acetylcysteine use to prevent nephrotoxicity
 - Nine studies compared the rate of nephrotoxicity (serum creatinine increasing ≥ 0.5 mg/dl or 25%) for patients receiving contrast media given acetylcysteine with half-normal or normal saline (1 ml/kg/hour) versus patients given normal or half-normal saline (1 ml/kg/hour) for 12 hours pre and 12 hours post procedure. One thousand twenty four patients were studied.
 - Eight studies were of patients receiving contrast for cardiac catheterization and one was for a CT study.
 - Acetylcysteine 600 mg bid for 2 days (day before and day of procedure) was used in six studies, in one study 1200 mg was given before and after the procedure, and one study use 150 mg/kg IV given over 30 minutes preprocedure followed by 50 mg/kg CIV over 4 hours.
 - Inclusion criteria included baseline serum creatinine ≥ 1.2 mg/dl in four studies, > 1.36 mg/dl one study, > 1.4 mg/dl one study, > 1.6 mg/dl one study, > 1.7 mg/dl one study, > 2 to < 6 mg/dl one study. Patients included in the studies had a creatinine clearance greater than 8 ml/min and up to 60 ml/min.
 - 89% (8/9) were prospective randomized placebo control trials
 - Patients were hydrated with half normal saline or normal saline at 1 ml/kg/hour for 12 preprocedure and 12 hours postprocedure.
 - Nephrotoxicity, serum creatinine increasing ≥ 0.5 mg/dl or 25%, occurred in 17.4% (95/547) of the placebo group and 8.7% (45/519) of the acetylcysteine group.

Studies:

N Engl J Med. 2003 Feb 6;348(6):491-9.

Nephrotoxic effects in high-risk patients undergoing angiography.

Aspelin P, Aubry P, Fransson SG, Strasser R, Willenbrock R, Berg KJ; Nephrotoxicity in High-Risk Patients Study of Iso-Osmolar and Low-Osmolar Non-Ionic Contrast Media Study Investigators. Department of Radiology, Huddinge University Hospital, Stockholm, Sweden. peter.aspelin@cfs.ki.se

BACKGROUND: The use of iodinated contrast medium can result in nephropathy. Whether iso-osmolar contrast medium is less nephrotoxic than low-osmolar contrast medium in high-risk patients is uncertain. **METHODS:** *We conducted a randomized, double-blind, prospective, multicenter study comparing the nephrotoxic effects of an iso-osmolar, dimeric, nonionic contrast medium, iodixanol, with those of a low-osmolar, nonionic, monomeric contrast medium, iohexol.* The study involved 129 patients with diabetes with serum creatinine concentrations of 1.5 to 3.5 mg per deciliter who underwent coronary or aortofemoral angiography. The primary end point was the peak increase from base line in the creatinine concentration during the three days after angiography. Other end points were an increase in the creatinine concentration of 0.5 mg per deciliter or more, an increase of 1.0 mg per deciliter or more, and a change in the creatinine concentration from day 0 to day 7. **Inclusion criteria:** *Type 1 or 2 diabetes mellitus that was being treated with insulin or oral antidiabetic drugs and had either a stable serum 1.5-3.5 mg % for men and 1.3-3.5 mg % for women or calculated creatinine clearance ≤ 60 ml/min. A mandatory hydration protocol was not enforced. Hydration given was 40-50% of other studies.* **RESULTS:** The creatinine concentration increased significantly less in patients who received iodixanol. From day 0 to day 3, the mean peak increase in creatinine was 0.13 mg per deciliter in the iodixanol group and 0.55 mg per deciliter in the iohexol group (P=0.001; the increase with iodixanol minus the increase with iohexol, -0.42 mg per deciliter [95 percent confidence interval, -0.73 to -0.22]). Two of the 64 patients in the iodixanol group (3 percent) had an increase in the creatinine concentration of 0.5 mg per deciliter or more, as compared with 17 of the 65 patients in the iohexol group (26 percent) (P=0.002; odds ratio for such an increase in the iodixanol group, 0.09 [95 percent confidence interval, 0.02 to 0.41]). No patient receiving iodixanol had an increase of 1.0 mg per deciliter or more, but 10 patients in the iohexol group (15 percent) did. The mean change in the creatinine concentration from day 0 to day 7 was 0.07 mg per deciliter in the iodixanol group and 0.24 mg per deciliter in the iohexol group (P=0.003; value in the iodixanol group minus the value in the iohexol group, -0.17 mg per deciliter [95 percent confidence interval, -0.34 to -0.07]). **CONCLUSIONS:** *Nephropathy induced by contrast medium may be less likely to develop in high-risk patients when iodixanol is used rather than a low-osmolar, nonionic contrast medium.*

Nephrotoxic Effects in High-Risk Patients Undergoing Angiography (NEJM 2003;348:491-9)		
	Iodixanol (Visipaque) Nonionic iso-osmolar dimeric contrast	Iohexol (Omnipaque) Nonionic, low-osmolar, Monomeric contrast
	N=64	N=65
Age	71 ± 6	70.6 ± 8.6
Mean Increase in Serum Creatinine (range)	0.13 ± 0.22 (-0.21 to 0.84)	0.55 ± 0.98 (-0.24 to 5.42)
Creatinine Peak Increase ≥ 0.5 mg/dl (Days 0-3)	3% (2/64)	26% (17/65)
Creatinine Peak Increase ≥ 1 mg/dl (Days 0-3)	0% (0/64)	15% (10/65)
Volume of Contrast	163 ± 88 (2.1 ml/kg)	162 ± 82 (2.1 ml/kg)
Baseline Creatinine mg/dl	1.49 ± 0.53	1.6 ± 0.52
Baseline Creatinine Clearance	50.1 ± 12.8	47.3 ± 16.6
Baseline Creatinine mg/dl	1.49 ± 0.53	1.6 ± 0.52
Weight (kg)	76.5 ± 12.4	77.2 ± 14.4
Unbalanced Factors in Study		
Duration of Diabetes (years)	12.8 ± 9.8	18 ± 12
Number of Previous examinations with iodinated contrast medium	75	46
Coronary Angiography Performed	97% (62/64)	98.5% (64/65)
Number of diseased vessels identified (% of patients)		
1	14%	22%
> 1	72%	65%
Hydration given IV ml	977 ± 853 (12.8 ml/kg)	934 ± 596 (12.1 ml/kg)
% of Patients PTCA Performed	17%	25%

Eur Radiol. 1998;8(1):144-7

Effects of a dimeric vs a monomeric nonionic contrast medium on renal function in patients with mild to moderate renal insufficiency: a double-blind, randomized clinical trial.

Carraro M, Malalan F, Antonione R, Stacul F, Cova M, Petz S, Assante M, Grynne B, Haider T, Palma LD, Faccini L. Institute of Medicina Clinica, Ospedale di Cattinara, University of Trieste, Strada di Fiume 447, I-34 149 Trieste, Italy.

The efficacy and safety of nonionic dimeric contrast media in subjects with impaired renal function is largely unknown. The present study was aimed at determining the risk of tubular nephrotoxicity in patients with mild to moderate renal insufficiency who underwent intravenous urography (IVU) with the nonionic dimeric contrast agent iodixanol (Visipaque, Nycomed Imaging, Oslo, Norway). *In a double-blind protocol 64 patients (55 males; mean age 68.3 years) with serum creatinine between 135 (1.5 mg/dl) and 265 micromol/l (3 mg/dl) who were to undergo IVU were randomized to receive iodixanol (a nonionic dimer) or iopromide (a nonionic monomer), 600 mg I/kg b. w.* Renal function was evaluated before and 1 h, 6 h, 24 h, 48 h and 7 days after IVU with analysis of serum creatinine, urinary enzymes alanylaminopeptidase and N-acetyl-beta-glucosaminidase, and urinary microproteins alpha-1-microglobulin and albumin. Renal function remained stable in both contrast medium groups during the follow-up period. No statistically significant differences were observed between the monomer and the dimer in terms of urinary enzyme and microprotein excretion or serum creatinine. Transient radiocontrast-induced nephropathy developed in 1 patient who had received iodixanol. The administration of the nonionic dimeric contrast medium iodixanol, or of the nonionic monomer iopromide, entailed a low nephrotoxic potential in patients with mild to moderate renal insufficiency undergoing excretory urography.

	Iodixanol N=32	Iopromide N=32
Diabetes Mellitus	6.3% (2/32)	3.1% (1/32)
Contrast Dose	148 + 21.3	152.8 + 24.4
Baseline Creatinine	1.7 mg/dl	1.69 mg/dl
Contrast Induced Nephropathy	3.1% (1/32) (creatinine increased from 2.5 to 5.4 mg/dl in non-diabetic)	0/32

Acta Radiol Suppl. 1995;399:265-70. Related Articles, Links

Main results of the first comparative clinical studies on Visipaque.

Grynne BH, Nossen JO, Bolstad B, Borch KW.

Clinical Research & Development, Nycomed Imaging AS, Oslo, Norway.

The results are reviewed from 18 European clinical vascular studies in 1950 patients where iodixanol (Visipaque) - a new isotonic, dimeric, nonionic contrast medium (CM) - is compared to other CM. *Visipaque gave better patient comfort, i.e., less pain and heat sensation after vascular injections than the comparative CM.* Adverse events reported after Visipaque were otherwise similar to nonionic CM but lower than after ioxaglate (Hexabrix) and other ionic CM. Human renal safety of *Visipaque has been extensively studied. Only small changes in glomerular filtration rate and serum creatinine were measured with the monomeric nonionic CM as well as with Visipaque.* The excretion of marker enzymes for renal tubular cell function was generally lowest for Visipaque. Thus Visipaque was highly tolerable in the kidneys. To study cardiac safety, electrophysiological and hemodynamic changes were recorded. Visipaque had generally no electrophysiological or hemodynamic effects, or less pronounced effects compared to the other CM. Radiograms revealed that Visipaque 320 mg I/ml yielded the same attenuation as 350 to 370 mg I/ml of the other CM and, similarly, 270 mg I/ml of Visipaque gave as good visualization as 300 mg I/ml of comparative CM.

Nephron Clin Pract. 2003 Jan;93(1):C29-34

A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity.

Trivedi HS, Moore H, Nasr S, Aggarwal K, Agrawal A, Goel P, Hewett J.

Nephrology Section, Harry S. Truman Memorial Veterans' Hospital and Division of Nephrology, Department of Internal Medicine, University of Missouri-Columbia, Columbia, Mo 65201-5297, USA. trivedi8@hotmail.com

Though simple and attractive, the role of hydration for the prophylaxis of contrast nephrotoxicity has not been definitively established. We prospectively evaluated the role of deliberate saline hydration in patients undergoing nonemergency cardiac catheterization.

Patients (n = 53) were randomized on the day prior to scheduled catheterization to one of two groups - group 1 (n = 27) received normal saline for 24 h (at a rate of 1 ml/kg/h) beginning 12 h prior to scheduled catheterization, and group 2 (n = 26) were allowed unrestricted oral fluids. Exclusion criteria: calculated creatinine clearance less than 20 ml/min, clinically decompensated heart failure, and states of decreased effective arterial volume (such as nephrotic syndrome, cirrhosis of liver). Serum creatinine measured 24 and 48 h postcardiac catheterization was compared to the pre-randomization baseline value. The mean baseline calculated creatinine clearance was 79.6 +/- 31.9 ml/min and the mean baseline creatinine was 106 +/- 28 micromol/l (1.2 +/- 0.32 mg%). An increase in serum creatinine by at least 44.2 micromol/l (0.5 mg/dl), within 48 h of contrast exposure, was considered to represent clinically significant acute renal insufficiency. Ten subjects (18.9%) developed acute renal insufficiency. The incidence of acute renal insufficiency was significantly lower in group 1 (1 out of 27) as compared to group 2 (9 out of 26; p = 0.005 for comparison between groups; relative risk 0.11, 95% confidence interval 0.015 to 0.79). Twenty-four hours after contrast exposure, the mean increase in creatinine was less in group 1 vs. group 2 (8 +/- 11 vs. 20 +/- 21 micromol/l, p = 0.02). The increase in creatinine was not significantly different in group 1 vs. group 2 48 h after contrast exposure (12 +/- 21 vs. 29 +/- 40 micromol/l, p = 0.17). *Deliberate saline hydration decreases the incidence of contrast-related acute renal failure and the severity of contrast-induced renal dysfunction in patients undergoing non-emergency cardiac catheterization.*

A randomized Prospective trial to Assess the Role of Saline Hydration on the Development of Contrast Nephrotoxicity Nephron Clin Pract 2003;93:c29-c34		
	Saline N=27	Control N=26
Age	68.5 ± 8	67.2 ± 11.2
Weight (kg)	83.3 ± 14.8	83.8 ± 14.8
Serum Creatinine	1.1 ± 0.24	1.3 ± 0.37
Creatinine Clearance	76 ± 23	83 ± 39
0.9% NS @ 1 ml/kg for 24 hours, starting 12 hours prior to procedure	Yes (24 ml/kg)	No (Unrestricted oral fluids)
Creatinine Peak Increase ≥ 0.5 mg/dl	3.7% (1/27)	34.6% (9/26) p=0.005
Change in Serum creatinine 24 hour after angiography mg/dl	0.09 ± 0.12	0.226 ± 0.24 p=0.02
Change in Serum creatinine 48 hour after angiography mg/dl	0.135 ± 0.24	0.328 ± 0.45
Volume of Contrast	201 ± 92 (2.4 ml/kg)	187.3 ± 88 (2.2 ml/kg)
Contrast Type	Ionic Low Osmolality	Ionic Low Osmolality
Baseline Creatinine	1.1 mg/dl ± 0.24	1.27 ± 0.37 NS

Arch Intern Med. 2002 Feb 11;162(3):329-36.

Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty.

Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H. Herz-Zentrum, Bad Krozingen, Germany. chmueller@uhbs.ch

BACKGROUND: The administration of radiographic contrast agents remains an important cause of acute renal failure. The optimal infusion for hydration has not been evaluated. **OBJECTIVE:** To compare the incidence of contrast media-associated nephrotoxicity with isotonic or half-isotonic hydration. **DESIGN:** Prospective, randomized, controlled, open-label study. **METHODS:** *Patients scheduled for elective or emergency coronary angioplasty were randomly assigned to receive isotonic (0.9% saline) or half-isotonic (0.45% sodium chloride plus 5% glucose) hydration at 1 ml/kg/hr beginning the morning of the procedure for elective interventions and immediately before emergency interventions. This was continued until 8 am the following morning. The rate during angioplasty was adjusted to clinical conditions.* Note: ACS patients received a 500 ml of Ringers solution preadmission (147 meq/l sodium). An increase in serum creatinine of at least 0.5 mg/dL (44 micromol/L) within 48 hours was defined as contrast media-associated nephrotoxicity. Secondary end points were cardiac and peripheral vascular complications. Exclusion criteria: ESRD with regular hemodialysis, cardiogenic shock, and mechanical ventilation **RESULTS:** A total of 1620 patients were assigned to receive isotonic (n = 809) or half-isotonic (n = 811) hydration. Primary end point analysis was possible in 1383 patients. Baseline characteristics were well matched. Contrast media-associated nephropathy was significantly reduced with isotonic (0.7%, 95% confidence interval, 0.1%-1.4%) vs half-isotonic (2.0%, 95% confidence interval, 1.0%-3.1%) hydration (P =.04). *Three predefined subgroups benefited in particular from isotonic hydration: women, persons with diabetes, and patients receiving 250 mL or more of contrast.* The incidence of cardiac (isotonic, 5.3% vs half-isotonic, 6.4%; P =.59) and peripheral vascular (isotonic, 1.6% vs half-isotonic, 1.5%, P =.93) complications was similar between the 2 hydration groups. **CONCLUSION:** *Isotonic hydration is superior to half-isotonic hydration in the prevention of contrast media-associated nephropathy.*

Prevention of contrast media-associated nephropathy (Arch Intern Med. 2002 Feb 11;162(3):329-36)		
	Normal Saline N=685	Half Normal Saline plus Dextrose 5% N=698
Baseline Clinical Characteristics		
Age, average	64 (63-65)	64 (63-65)
Chronic Renal Insufficiency	20% (138/685)	21% (148/698)
Diabetes Mellitus	16% (107/685)	16% (110/698)
Baseline Creatinine mg/dl	0.92 (0.9-0.94)	0.93 (0.9-0.95)
Baseline Creatinine Clearance	84	84
Contrast Type	Low Osmolar Nonionic (Ultravist)	Low Osmolar Nonionic (Ultravist)
Contrast Volume (ml)	232 (226-238)	236 (229-243)
Non ionic low-osmolar (Ultravist 370)		
Hydration		
Total Hydration (1ml/kg/hr)	2022 (approximately 24 ml/kg)	2028 (approximately 24 ml/kg)
Pre Procedure (ml)	443	428
During Procedure (ml)	362	369
Post Procedure (ml)	1217	1229
Outcome Variables		

Contrast Nephropathy (≥ 0.5 mg/dl increase)	0.7% (5/685)	2% (14/698) P=0.04
Dialysis	0% (0/685)	0.1% (1/698) NS
Contrast Nephropathy: Subgroup Analysis		
Without Diabetes	0.9% (5/578)	1.4% (8/588)
Diabetes	0% (0/107)	5.5% (6/110) P=0.01
Normal Renal Function	0.4% (2/547)	1.5% (8/550)
Prior Renal Insufficiency (≥ 1.3 mg/dl)	2.2% (3/138)	4.1% (6/148) NS
Baseline Creatinine > 1.6 mg/dl	14.3% (2/14)	11.8% (2/17) NS
Diabetes and Chronic Renal Insufficiency Clcr < 60 ml/min (Personal correspondence)	0% (0/16)	17.4%(4/23)

N Engl J Med. 1989 Jan 19;320(3):143-9

Contrast material-induced renal failure in patients with diabetes mellitus (for greater than 5 years), renal insufficiency (scr ≥ 1.7 mg/dl), or both. A prospective controlled study.

Parfrey PS, Griffiths SM, Barrett BJ, Paul MD, Genge M, Withers J, Farid N, McManamon PJ.

Division of Nephrology, Health Sciences Centre, Memorial University, St. John's, Canada.

To determine the risk of nephrotoxicity induced by the infusion of radiographic contrast material, we undertook a prospective study of consecutive patients undergoing radiographic procedures with intravascular contrast material. There were three study groups: patients with diabetes mellitus and normal renal function ($n = 85$), patients with preexisting renal insufficiency (serum creatinine level, greater than or equal to 150 μmol per liter (1.7 mg/dl)) without diabetes ($n = 101$), and patients with both diabetes and renal insufficiency ($n = 34$). *The control group consisted of patients undergoing CT scanning or abdominal imaging procedures without the infusion of contrast material who had diabetes mellitus ($n = 59$), preexisting renal insufficiency ($n = 145$), or both ($n = 64$). Physicians were advised to prescribe 0.45 % saline for 2 days after the procedure at a rate equal to urine flow. No other prophylactic measures were used.* Patients in both groups who had acute renal failure were assessed by a blinded nephrologist to determine whether definite predisposing factors for acute renal failure (other than contrast) were present. Clinically important acute renal failure (defined as an increase of greater than 50 percent in the serum creatinine level within 2-3 days after imaging) attributable to the contrast material did not occur in nondiabetic patients with preexisting renal insufficiency or in diabetics with normal renal function. The incidence of clinically important contrast-induced renal failure among the diabetic patients with preexisting renal insufficiency was 8.8 percent (95 percent confidence interval, 1.9 to 23.7 percent), as compared with 1.6 percent for the controls. The incidence of acute renal insufficiency, more broadly defined as an increase of greater than 25 percent in the serum creatinine level after the infusion of contrast material, was 11.8 percent among all patients with preexisting renal insufficiency. After the exclusion of patients whose acute renal insufficiency could be attributed to other causes, the incidence was 7.0 percent (95 percent confidence interval, 3.2 to 12.8 percent), as compared with 1.5 percent in the control group. The risk of acute renal insufficiency attributable to the contrast material was therefore 5.5 percent, and the relative risk associated with the infusion of contrast material was 4.7. These rates were similar whether the osmolarity of the contrast material was high or low. *We conclude that there is little risk of clinically important nephrotoxicity attributable to contrast material for patients with diabetes and normal renal function or for nondiabetic patients with preexisting renal insufficiency.* The risk for those with both diabetes and pre-existing renal insufficiency is about 9 percent, which is lower than previously reported. Note: 75% of patients received high-osmolarity contrast material.

	Creatinine increased $> 50\%$	Mean Initial creatinine (mg/dl)	Mean % Change in creatinine	Intravenous 0.45% Saline after imaging %	Volume of Contrast (ml)
Diabetic with no renal insufficiency					
Contrast group N=85	0*	1	+ 6.1 \pm 2.7%	35%	140 \pm 76
Control group N=59	1.7% (1/59)*	1.1	-0.1 \pm 2.3%	29%	
Diabetic with renal insufficiency Creatinine 1.7 mg/dl					
Contrast group N=34	8.8% (3/34)	3	+ 2.4 \pm 5 %	38%	95 \pm 43
Control group N=64	1.6% (1/64)	3.1	-0.1 \pm 2 %	22%	
Non Diabetic with mild					

renal insufficiency Creatinine 1.7-2.8 mg/dl					
Contrast group N=57	3.5% (2/57)	2.2	+ 4 ± 3.8 %	41%	116 ± 95
Control group N=60	6.7% (4/60)	2.2	-0.9 ± 3.4 %	30%	
Nondiabetic with severe renal insufficiency Creatinine > 2.8 mg/dl					
Contrast group N=44	4.5% (2/44)	4.1	5.8 ± 3.6 %	41%	116 ± 95
Control group N=85	2.3% (2/85)	5	-2.8 ± 2.6 %	30%	

* Also, required serum creatinine on day to rise above 1.4 mg/dl

	Nephrotoxicity**	
	Contrast group	Control Group
Diabetic with no Renal Insufficiency	2.4% (2/85)	3.5% (2/59)
Diabetic and nondiabetic with renal insufficiency Creatinine > 1.7 mg/dl	7% (9/128)	1.5% (3/197)
Diabetic with renal insufficiency Creatinine > 1.7 mg/dl	8.8% (3/34)	1.6% (1/61)
Non diabetic with renal insufficiency Creatinine > 1.7 mg/dl	6.4% (6/94)	1.5% (2/136)

**Creatinine increase > 25% and to a level above 1.4 mg/dl on day 2.

**Patients with definite predisposing factors for acute renal failure as determined by a blinded nephrologist were excluded from this analysis.

Kidney Int. 1995 Jan;47(1):254-61.

Nephrotoxicity of ionic (diatrizoate-Renografin 76) and nonionic (iohexol-Omnipaque 350) contrast media in 1196 patients: a randomized trial. The Iohexol Cooperative Study.

Rudnick MR, Goldfarb S, Wexler L, Ludbrook PA, Murphy MJ, Halpern EF, Hill JA, Winniford M, Cohen MB, VanFossen DB. Division of Nephrology, Graduate Hospital, University of Pennsylvania School of Medicine, Philadelphia, USA.

The incidence of nephrotoxicity occurring with the nonionic contrast agent, iohexol, and the ionic contrast agent, meglumine/sodium diatrizoate, was compared in 1196 patients undergoing *cardiac angiography in a prospective, randomized, double-blind multicenter trial*. Patients were stratified into four groups: renal insufficiency (RI), diabetes mellitus (DM) both absent (N = 364); RI absent, DM present (N = 318); RI present, DM absent (N = 298); and RI and DM both present (N = 216). Serum creatinine levels were measured at -18 to 24, 0, and 24, 48, and 72 hours following contrast administration. *Prophylactic hydration, D5-1/2NS or equivalent at 100 ml/hr was started 4 hours prior to and continued 24 hours post procedure unless clinically contraindicated*. Acute nephrotoxicity (increase in serum creatinine of ≥ 1 mg/dl 48 to 72 hours post-contrast) was observed in 42 (7%) patients receiving diatrizoate compared to 19 (3%) patients receiving iohexol, $P < 0.002$. *Differences in nephrotoxicity between the two contrast groups were confined to patients with RI alone or combined with DM*. In a multivariate analysis, baseline serum creatinine, male gender, DM, volume of contrast agent, and RI were independently related to the risk of nephrotoxicity. Patients with RI receiving diatrizoate were 3.3 times as likely to develop acute nephrotoxicity compared to those receiving iohexol. Clinically severe adverse renal events were uncommon (N = 15) and did not differ in incidence between contrast groups (iohexol N = 6; diatrizoate N = 9). In conclusion, in patients undergoing cardiac angiography, only those with pre-existing RI alone or combined with DM are at higher risk for acute contrast nephrotoxicity. (ABSTRACT TRUNCATED AT 250 WORDS)

	Iohexol (non ionic)	Diatrizoate (Ionic)
Mean dose of contrast ml/kg	1.78	1.78
Mean total volume of IV hydration ml	2393 ± 1362 (29 ml/kg)	2434 ± 1426 (30 ml/kg)
Mean Age (years)	63.8 ± 10.5	63.7 ± 10.3
Weight (kg)	82.1 ± 15.9	81.9 ± 16.9
	Iohexol	Diatrizoate
	Nephrotoxicity (Increase in serum creatinine ≥ 0.5 mg/dl)	

All Patients	13.4% (79/591)	21.1% (125/592) p < 0.002
No Diabetes or Renal Insufficiency	8.5% (16/188)	8.2% (14/171)
Diabetes Mellitus	7.2% (11/153)	11.1% (18/162)
Renal Insufficiency (scr \geq 1.5 mg/dl)	12.2% (18/148)	27% (40/148)
Renal Insufficiency & Diabetes Mellitus	33.3% (34/102)	47.7% (53/111)

Radiology. 1993 Jul;188(1):171-8. Related Articles, Links

Metaanalysis of the relative nephrotoxicity of high- and low-osmolality iodinated contrast media.

Barrett BJ, Carlisle EJ. Division of Nephrology, Health Sciences Centre, St John's Newfoundland, Canada.

To determine whether low-osmolality contrast media (LOCM) are less nephrotoxic than high-osmolality contrast media (HOCM), the authors searched MEDLINE and EMBASE databases and other sources to find randomized trials with data collected on changes in glomerular filtration rate or serum creatinine (SCr) level with LOCM and HOCM. Forty-five trials were found. Data were unavailable from 14 trials. When the P values from the other 31 trials were pooled, an overall P value of 0.02 was found. Among 24 trials with available data, the mean change in SCr was 0.2-6.2 μ mol/L less with LOCM than HOCM. Among 25 trials with available data, the pooled odds of a rise in SCr level of more than 44 μ mol/L with LOCM was 0.61 (95% confidence interval [CI], 0.48-0.77) times that after HOCM. For patients with existing renal failure, this odds ratio was 0.5 (CI, 0.36-0.68), while it was 0.75 (CI, 0.52-1.1) in patients without prior renal failure. Greater changes in SCr level occurred only in those with existing renal failure and were less common with LOCM (odds ratio, 0.44; CI, 0.26-0.73). Use of LOCM may be beneficial in patients with existing renal failure.

Agent	Indications for Adults	Osmolality (mOsmo/kg)	Viscosity at Body Temperature
	Non-Ionic Agents		
Isovue-M 200 (Iopamidol 200 mg/ml 41%)	Myelography, CT, cisternography, ventriculography	413	2
Isovue-M 300 (Iopamidol 300 mg/ml 61%)		616	4.7
Optiray-(Ioversol 240 mg/ml 51%)		502	3
Optiray 320 (Ioversol 320 mg/ml 68%)	Angiography, arteriography, venography, aortography, ventriculography, CT, urography	702	5.8
Optiray-350 (Ioversol 350 mg/ml 74%)	Arteriography, ventriculography, CT, urography, angiography, venography,	792	9
Visipaque 270 (Iodixanol ?? mg/ml)	Intra-arterially: angiography, angiocardiology, ventriculography, arteriography IV: Urography, CT, venography	290	6.3
Visipaque 320 (Iodixanol 320 mg/ml)	Intra-arterially: angiocardiology, ventriculography, arteriography IV: Urography, CT	290	11.8
	Ionic Low Osmolar		
Hexabrix (Ioxaglate meglumine 39.3% and Ioxaglate Sodium 19.6%)	Arteriography, ventriculography, aortography, angiography, venography, phlebography, urography, CT, arthrography, hysterosalpingography	600	7.5