

Contrast Induced Nephropathy

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- Definitions
- How do contrast agents cause nephropathy?
- What are the risk factors for contrast induced nephropathy
- Does contrast nephropathy increase mortality?
- Recommendations for prevention?

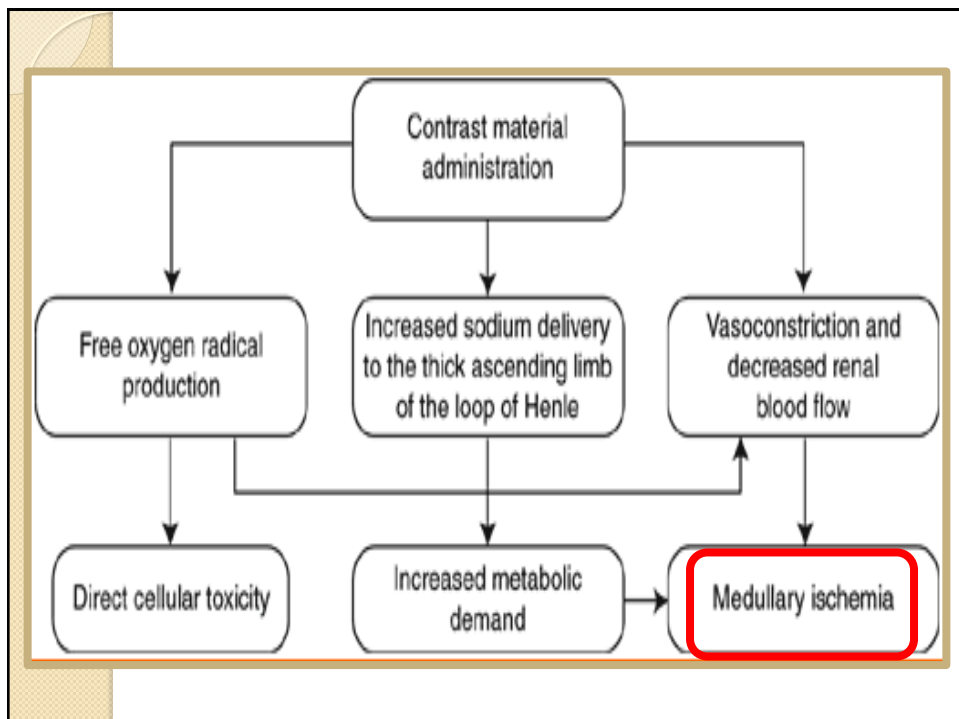
Definition

- Contrast-induced nephropathy (CIN) is defined as the impairment of renal function—measured as either a **25% increase in serum creatinine** from baseline or a **0.5 mg/dL increase in absolute SCr value**—within 48-72 hours after intravenous contrast administration.
- For renal insufficiency to be attributable to contrast administration, it should be acute, usually occurring within **2-3 days** (although it has been suggested that renal insufficiency developing up to **7 days** post-contrast administration be considered CIN).

Table 7 Summary of definitions of acute kidney injury

Urine output (common to all)	KDIGO stage ^{19,199} Serum creatinine	AKIN stage Serum creatinine	RIFLE class Serum creatinine or GFR
<0.5 mL/kg/h for 6 h	Stage 1 Increase of 1.5–1.9 times baseline or $\geq 27 \mu\text{mol/L}$ ($\geq 0.3 \text{ mg/dL}$) increase	Stage 1 Increase to >150–200% (1.5–2-fold) from baseline or $\geq 27 \mu\text{mol/L}$ ($\geq 0.3 \text{ mg/dL}$) increase	Risk Increase in serum creatinine $\times 1.5$ or GFR decrease >25%
<0.5 mL/kg/h for 12 h	Stage 2 Increase of 2–2.9 times baseline	Stage 2 Increase to >200–300% (>2–3-fold) from baseline	Injury Increase in serum creatinine $\times 2$ or GFR decreased >50%
<0.3 mL/kg/h for 24 h or anuria for 12h	Stage 3 Increase of >3 times baseline or increase in serum creatinine to $\geq 354 \mu\text{mol/L}$ ($\geq 4 \text{ mg/dL}$) or initiation of RRT	Stage 3 Increase to >300% (>3-fold) from baseline or $\geq 354 \mu\text{mol/L}$ ($\geq 4 \text{ mg/dL}$) with an acute increase of $>44 \mu\text{mol/L}$ ($>0.5 \text{ mg/dL}$) or initiation of RRT	Failure Increase in serum creatinine $\times 3$ or serum creatinine $\geq 354 \mu\text{mol/L}$ ($>4 \text{ mg/dL}$) with an acute rise $\geq 44 \mu\text{mol/L}$ ($>0.5 \text{ mg/dL}$) or GFR decreased >75%
			ESRD ESRD >3 months

HOW DO CONTRAST AGENTS CAUSE NEPHROPATHY?



What are the risk factors for CIN?

Risk Factors for CIN

Patient-related Risk Factors

- Renal insufficiency
- Diabetes mellitus with renal insufficiency
- Age > 70 years
- Volume depletion
- Hypotension
- Low cardiac output
- Class IV CHF
- Other nephrotoxins
- Renal transplant
- Hypoalbuminemia (<35 g/l)

Procedure-related Risk Factors

- Multiple contrast media injection within 72 hrs
- Intra-arterial injection site
- High volume of contrast media
- High osmolality of contrast media

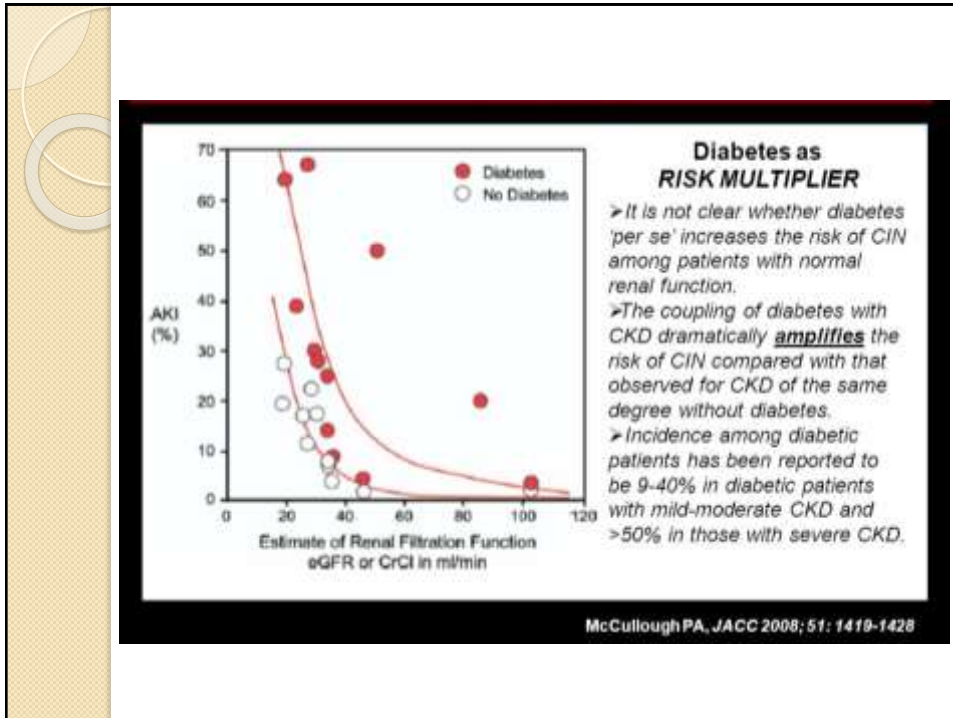
Lameire N et al. Am J Cardiol 2006;98:21K-26K.

Preexisting renal insufficiency

- is the **single greatest risk factor**.
- In one comprehensive review, an estimated **60%** of patients with contrast-induced nephropathy had preexisting renal insufficiency.
- The more severe the baseline renal insufficiency, the greater the risk.
- Although the risk of contrast-induced nephropathy for a given serum creatinine value can vary widely, one can **roughly estimate the percent risk by multiplying the serum creatinine concentration in milligrams per deciliter by 10**.

Diabetes mellitus

- Is often cited as a risk factor for contrast-induced nephropathy, but the risk ascribed to it is probably due to coexisting renal insufficiency, usually diabetic nephropathy, rather than to the diabetes per se.



Volume and type of contrast media

Cigarroa et al reported an empiric formula for calculating the maximal acceptable contrast dose (MACD):

5 ml x body weight (kilograms)/serum creatinine (milligrams per deciliter)

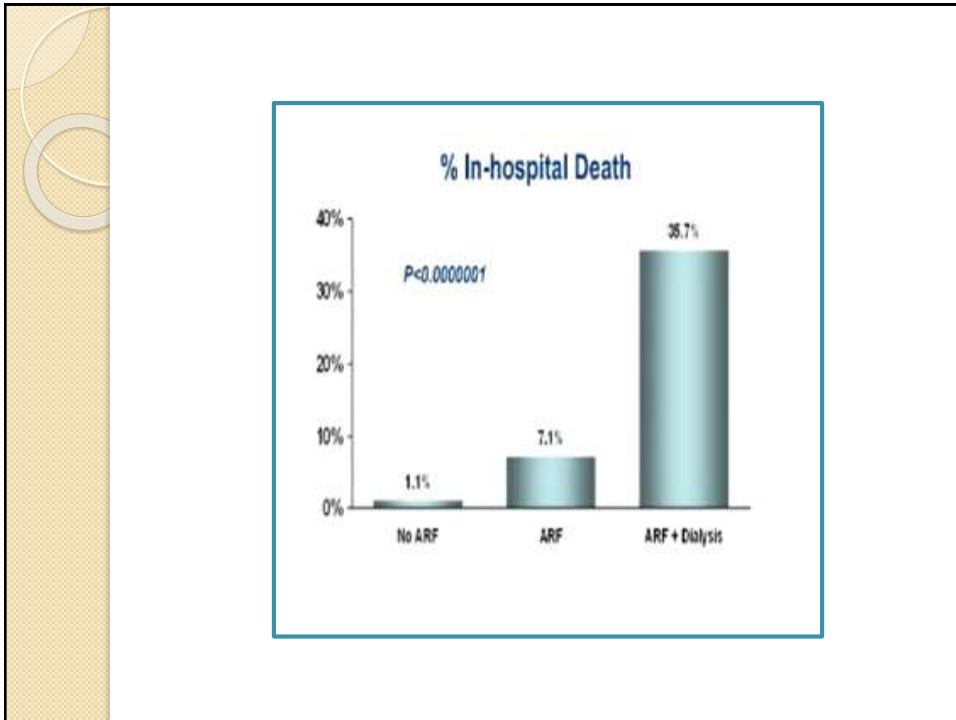
The use of contrast beyond the MACD was later correlated to an increased risk of CI-AKI

Table 2: Contrast-Induced Nephropathy Risk Assessment Tool

Risk Factor	Points	
Systolic BP <80mm Hg	5	
Intra-aortic balloon pump	5	
Chronic CHF	5	
Age >75 years	4	
Anemia (Hct <39 men, <36 women)	3	
Diabetes	3	
Contrast media volume	1 point per 100 cc ³ of contrast used	
Serum creatinine >1.5 mg/dL	4	
or Est GFR 40-59 mL/min	2	
or Est GFR 20-39 mL/min	4	
or Est GFR <20 mL/min	6	
Total Points	CIN Risk	Dialysis Risk
less than 5	7.50%	0.04%
6 to 10	14.00%	0.12%
11 to 16	26.10%	1.09%
more than 16	57.30%	12.60%

SOURCE: Adapted from Mehran R, et al.

**DOES CONTRAST
NEPHROPATHY
INCREASE
MORTALITY?**



Hydration is indicated, but what kind, how much?

Table 3

Contrast-Induced Nephropathy Hydration^a Strategies²³

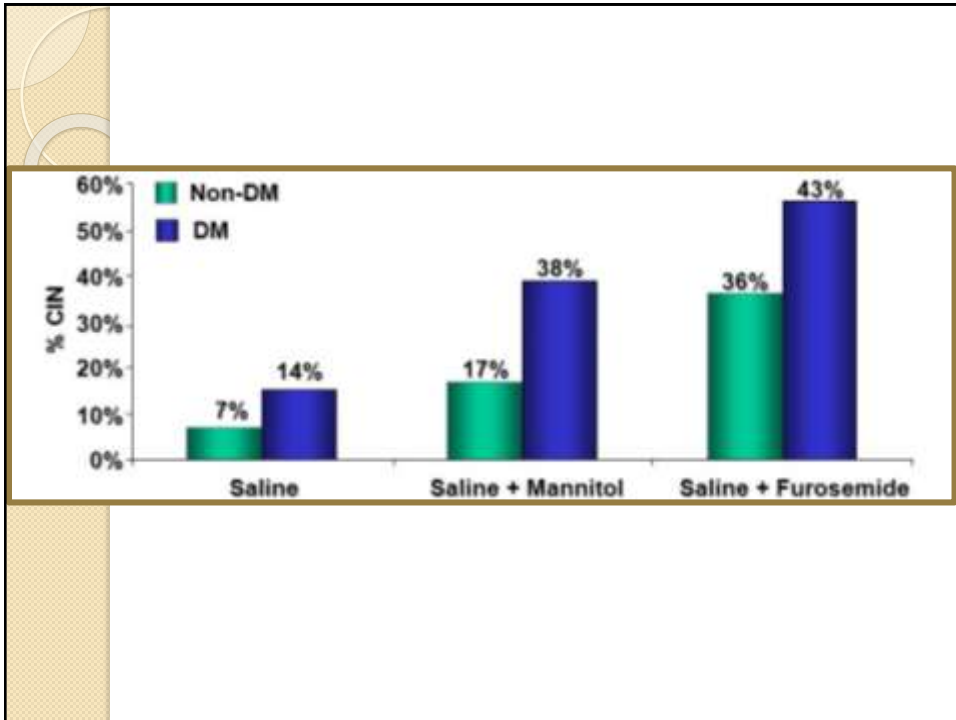
Fluid	Timing of Administration	Recommendation
Normal saline	12 hours before procedure	1 mL/kg per hour for 12 hours before and after contrast administration
Isotonic saline or sodium bicarbonate solution	1-3 hours before procedure	3 mL/kg per hour for 1-3 hours before and 6 hours after contrast administration
150 mEq sodium bicarbonate in dextrose 5% in water	1 hour before procedure	3 mL/kg per hour for 1 hour before and 1 mL/kg per hour for 6 hours after administration

^aAt a minimum, 300-500 mL of intravenous fluids should be administered before contrast.

HOW HYDRATION PREVENTS CONTRAST INDUCED NEPHROPATHY?

The theoretical rationale for hydration is that it should decrease the activity of the renin-angiotensin system, reduce the levels of other vasoconstrictive hormones thus increasing renal blood flow and **avoiding renal ischemia.**

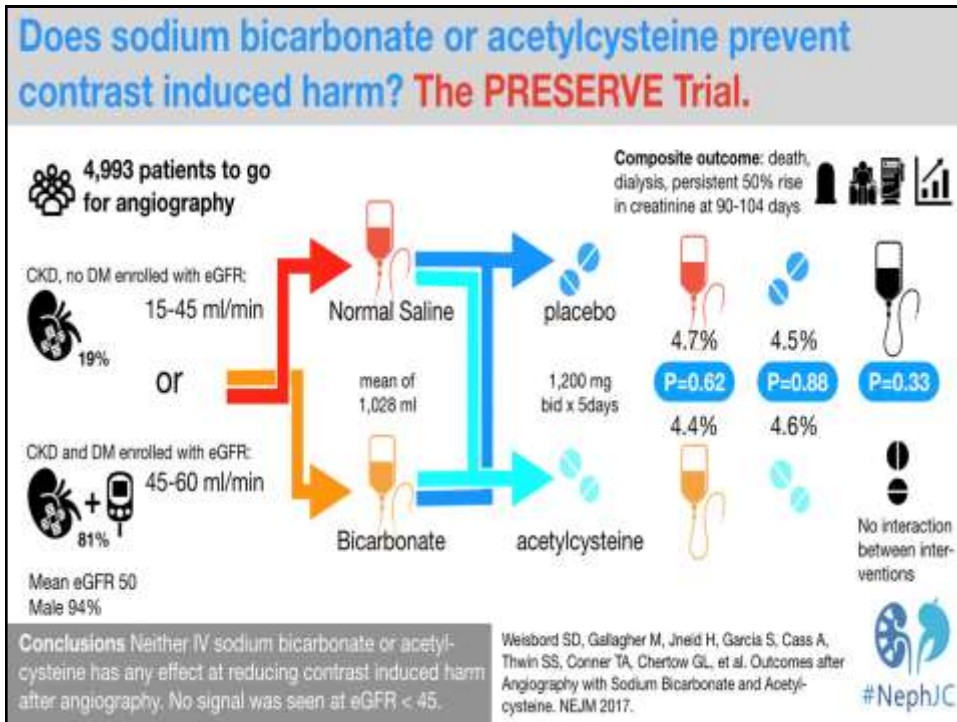
SALINE ALONE
... VS ...
SALINE PLUS
DIURESIS ?



**ORAL
OR
IV HYDRATION ?**

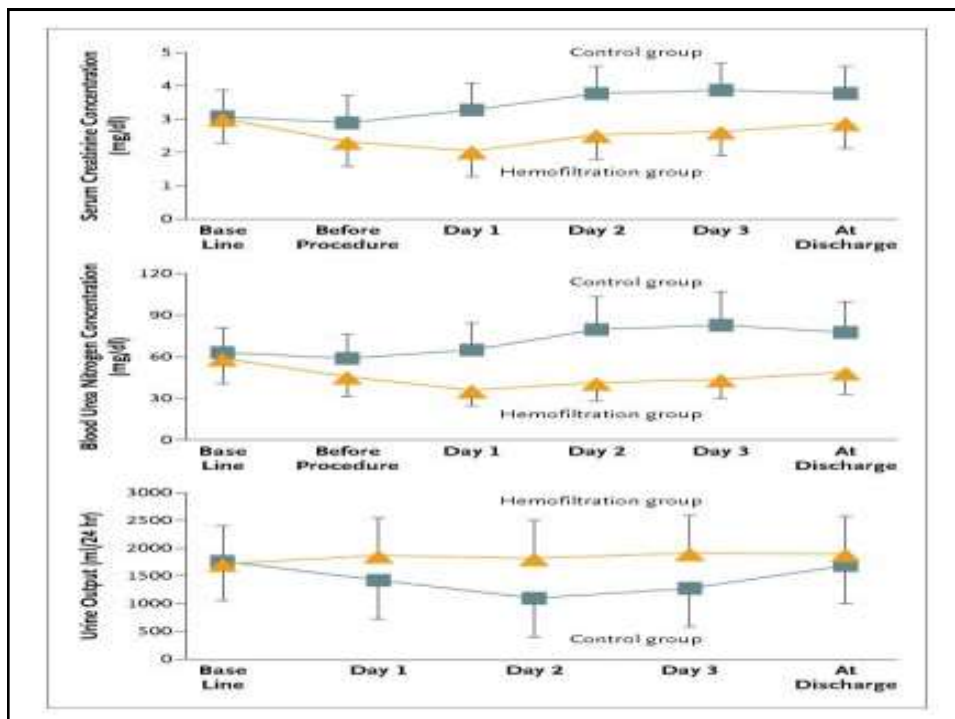
The Preparation for Angiography in Renal Dysfunction (**PREPARED**) trial showed that, in patients with chronic kidney disease undergoing coronary angiography, **hydration on an outpatient basis before catheterization, coupled with a brief period of intravenous hydration, was equivalent to overnight intravenous hydration.**

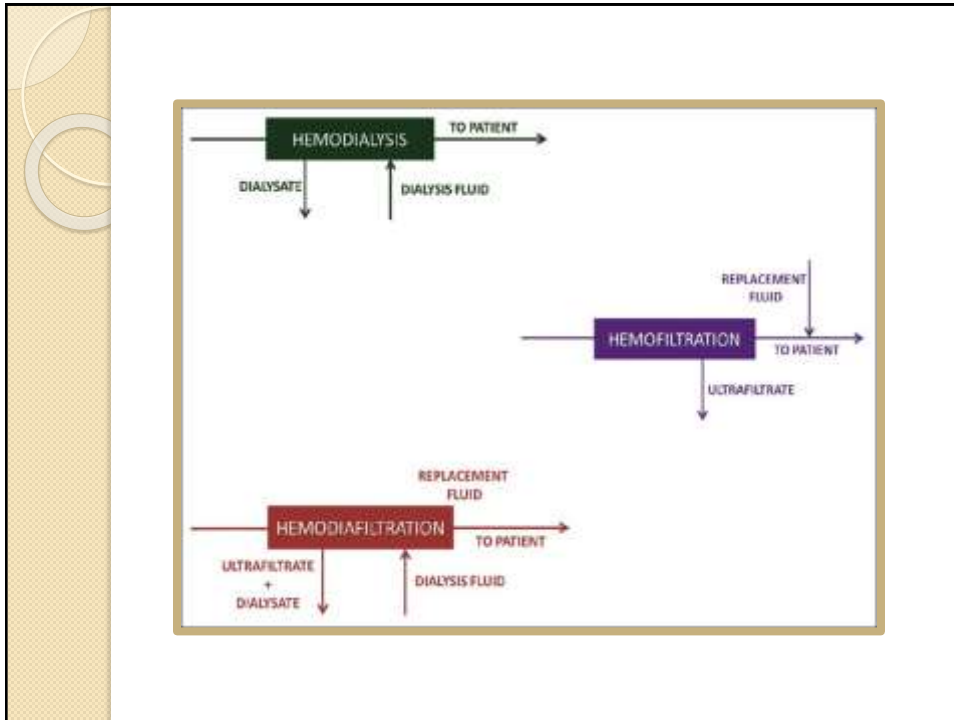
**What about NAC
and Sodium
bicarbonate ?**



HEMODIALYSIS AND HAEMOFILTRATION

- Removal of contrast media by **hemodialysis** after the procedure in patients with preexisting renal failure has been shown to have **no effect** on contrast-induced nephropathy and is unwarranted as a routine practice.
- Vogt et al. evaluated **prophylactic hemodialysis** to see if the contrast agent could be efficiently removed, thus reducing the concentration to which the kidneys were exposed, but this procedure showed **no beneficial effect** compared with using saline hydration alone.





- Although these results are extremely encouraging, the widespread use of hemofiltration is limited by its relatively high cost.
- It does, however, offer a very high-risk group of patients (those with serum creatinine levels > 4 mg/dL and undergoing multiple interventions requiring a larger volume of contrast agent than that used during simple diagnostic radiographic procedures) an effective preventive strategy,

Recommendations for prevention of contrast induced nephropathy:

Recommendations	Dose	Class ^a	Level ^b
Patients undergoing coronary angiography or MDCT			
Patients should be assessed for risk of contrast-induced AKI.		IIa	C
Patients with moderate-to-severe CKD			
Hydration with isotonic saline is recommended. ^d		I	A
Use of low-osmolar or iso-osmolar contrast media is recommended.	<350 mL or <4 mL/kg or total contrast volume/GFR <3.4.	I	A
Short-term, high-dose statin therapy should be considered.	Rosuvastatin 40/20 mg or atorvastatin 80 mg or simvastatin 80 mg.	IIa	A
Iso-osmolar contrast media should be considered over low-osmolar contrast media		IIa	A
Volume of contrast media should be minimized.		IIa	B

Furosemide with matched hydration may be considered over standard hydration in patients at very high risk for CIN or in cases where prophylactic hydration before the procedure cannot be accomplished.	Initial 250 mL intravenous bolus of normal saline over 30 min (reduced to ≤ 150 mL in case of LV dysfunction) followed by an i.v. bolus (0.25–0.5 mg/kg) of furosemide. Hydration infusion rate has to be adjusted to replace the patient's urine output. When the rate of urine output is > 300 mL/h, patients undergo the coronary procedure. Matched fluid replacement maintained during the procedure and for 4 hours post-treatment.	IIb	A
N-Acetylcysteine administration instead of standard hydration is not indicated.		III	A
Infusion of sodium bicarbonate 0.84% instead of standard hydration is not indicated.		III	A
Severe CKD			
Prophylactic haemofiltration 6 hours before complex PCI may be considered.	Fluid replacement rate 1000 mL/h without negative loss and saline hydration continued for 24 hours after the procedure.	IIb	B
Prophylactic renal replacement therapy is not recommended as a preventive measure.		III	B

Strategies for preventing contrast-induced nephropathy

Strategies that do not work

- Mannitol
- Furosemide
- Dopamine
- Atrial natriuretic factor
- Fenoldopam
- Hemodialysis
- NAC
- Sodium Bicarbonate

Still under study

Strategies that may work

- Calcium channel blockers
- Theophylline
- Iso-osmolar contrast media
- Hemofiltration
- Ascorbic acid
- Prostaglandins

Pearls

- The risk of contrast-induced nephropathy is directly proportional to the severity of preexisting renal insufficiency.
- Hydration with normal saline solution is the most widely accepted preventive intervention.
- N-acetylcysteine and Sodium bicarbonate has no effect in preventing CIN.
- Newer contrast agents that are nonionic and of lower osmolality than older agents are less nephrotoxic but can still cause nephropathy.
- Due to the logistical effort and high cost associated with hemofiltration, larger randomized trials should be performed before this technique can be recommended as standard prophylaxis against contrast-induced nephropathy in high-risk patients.

