

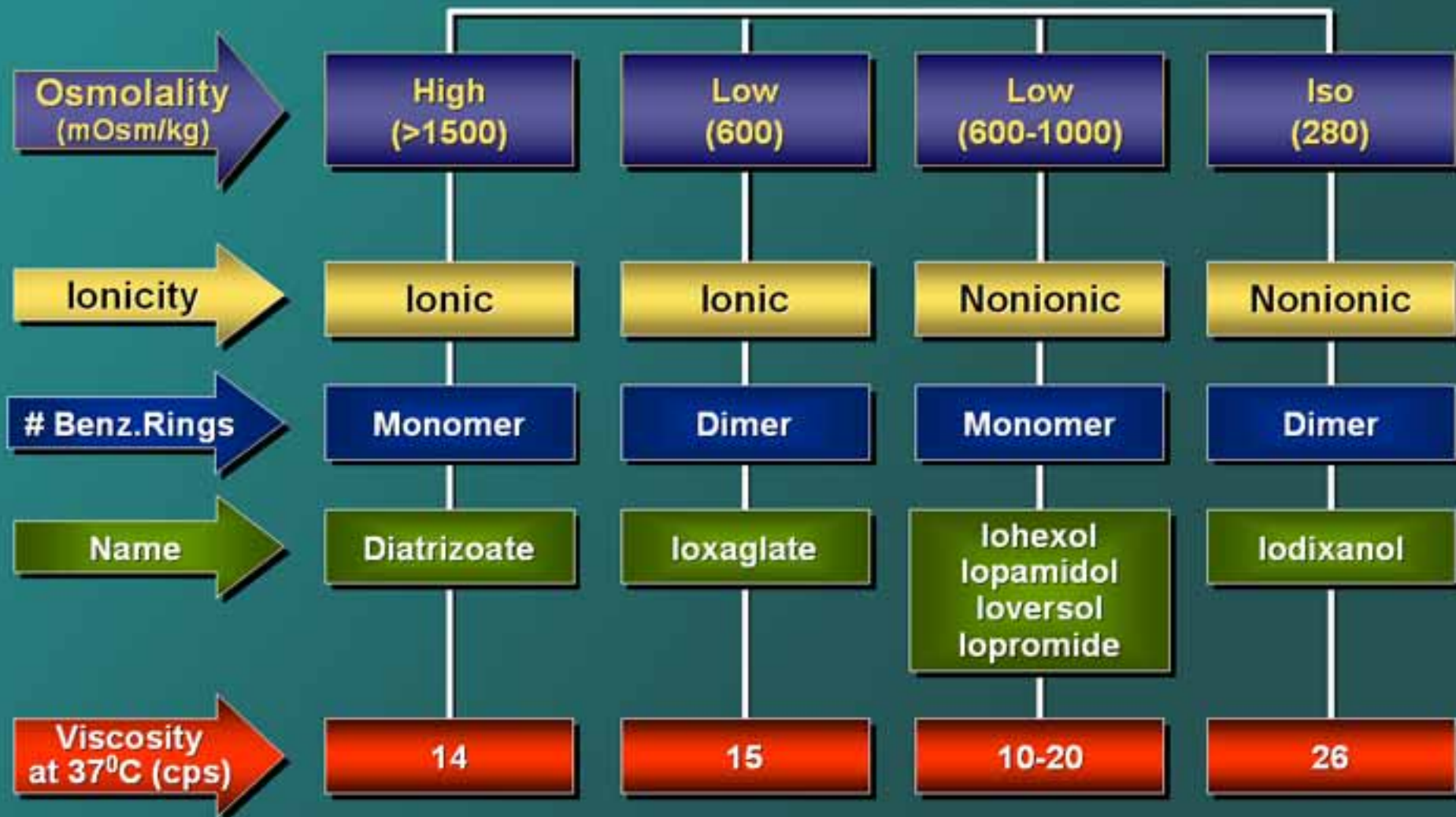
# **Complications Related to the Use of Radiocontrast Agents**

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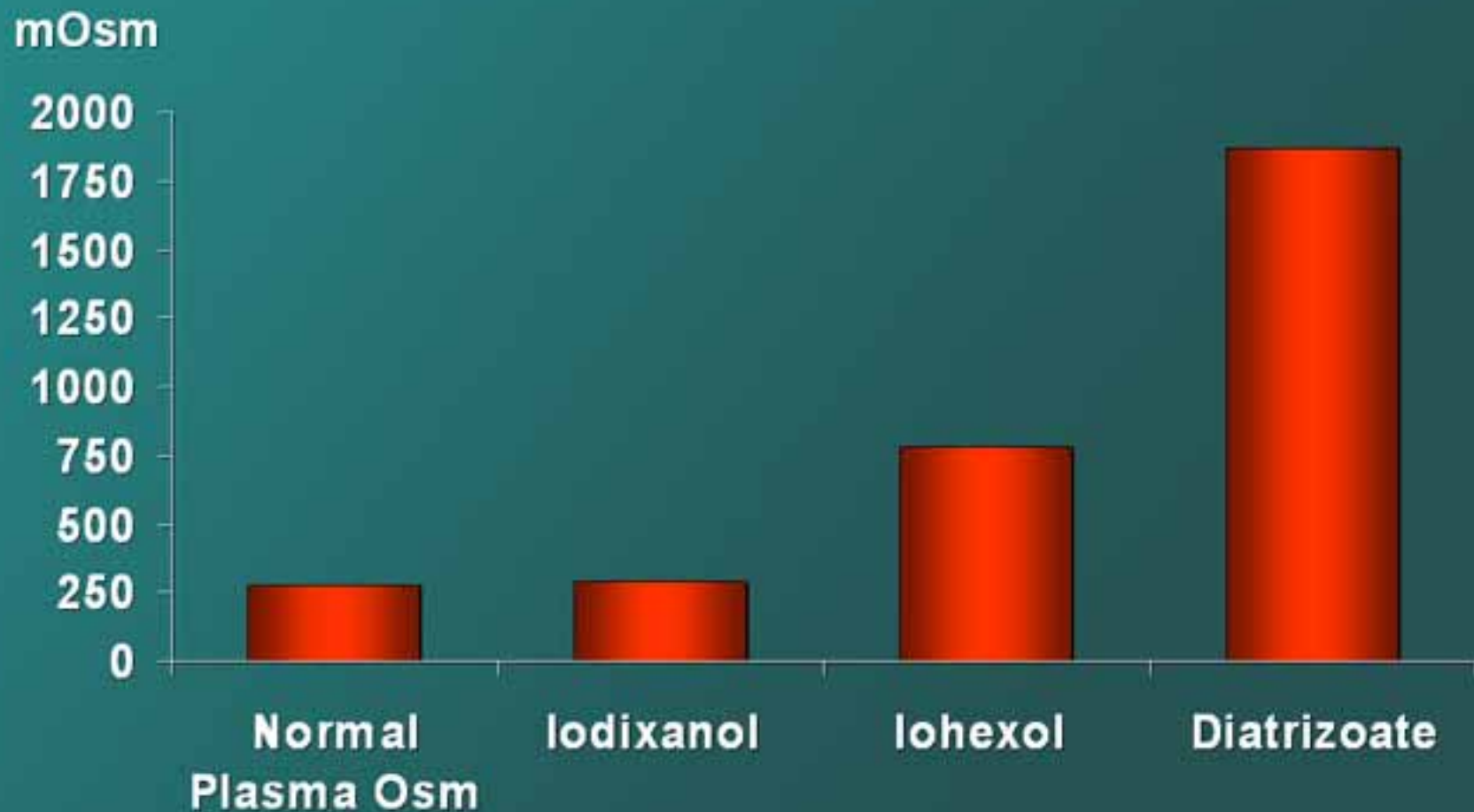
*The Cardiovascular Research Foundation and  
Columbia University Medical Center, New York, NY*



# Contrast Media Classification



# Comparison of Osmotic Load of Commonly Used Radiocontrast Media

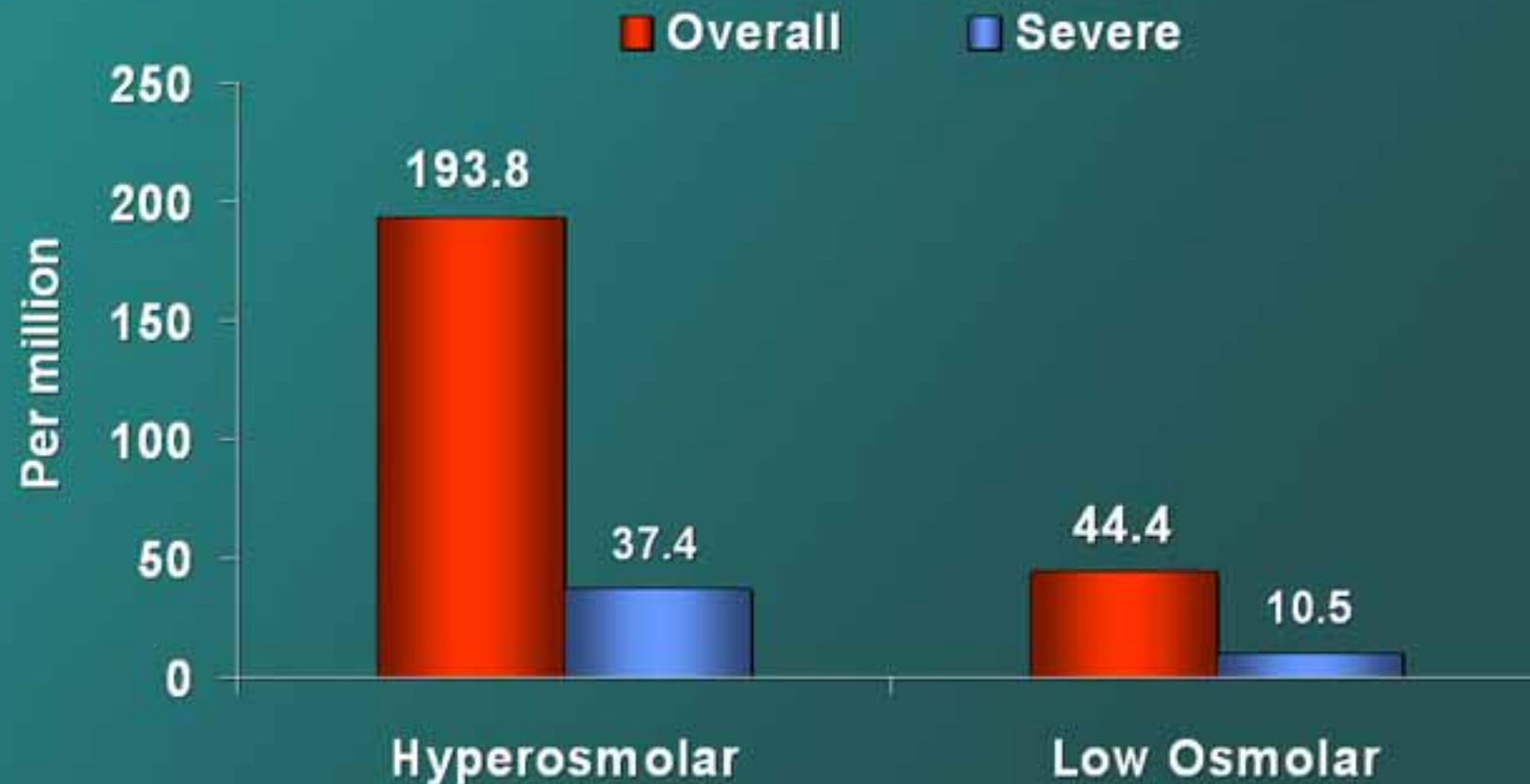


Aspelin, P et.al for the NEPHRIC Study Investigators *N Engl J Med* 2003; 348:491-499





# Contrast Media Reactions: Analysis of FDA Reports



Lasser EC *Radiology* 1997;203:605



# Side Effects of Contrast Media

- Hypersensitivity reactions
  - Mild: nausea & vomiting
  - Moderate: urticaria
  - Severe: anaphylaxis
- Other Side Effects
  - Pulmonary edema secondary to osmotic load
  - Arrhythmia



# Basic Principles Cont'd

- All contrasts are capable of producing adverse effects
- Alternative radio-dense contrasts (e.g., Gadolinium chelates) may have potential niches but are not practical substitutes for iodinated agents





# Characterizing Contrast

- Ionicity
- Osmolality
- Viscosity
- Additives
- Cation (for ionic agents)
- Organic compound

# Toxicity of Contrast

- Allergy And Allergy-like
- Cardiovascular
  - A. Electrophysiologic
  - B. Hemodynamic
- Nephrotoxicity
- Discomfort
- Hyperthyroidism





# Extent of Toxicity

- Toxicity Of Intra-venous Administration Usually Expressed As Hypersensitivity Or Nephrotoxicity
- Toxicity Of Coronary Administration Includes Hypotension And Arrhythmia
- Scai Registry: 0.23% Contrast Reaction But 0.47% Arrhythmia And 0.10% Death Both May Have Contrast Etiology

# Non-ionic vs Ionic LOM

## Adverse Reactions of Low Osmolality Contrast Media During Cardiac Angiography: A Prospective Randomized Multicenter Study

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*San Francisco, California*

A multicenter study was performed to determine the incidence of adverse reactions to two contrast media with similar low osmolality during cardiac angiography. The study was of a randomized double-blind design comparing ioxaglate (an ionic diuretic) and iopamidol (a nonionic compound) and included 500 patients; 250 patients received ioxaglate and 250 iopamidol. There were 58 adverse reactions attributed to the contrast media in the ioxaglate group and 29 in the iopamidol group ( $p < 0.001$ ). Chest pain occurred in 11 patients in the ioxaglate group compared with 5 in the iopamidol group ( $p = 0.123$ ). Nausea or vomiting was present in 20 and 2 patients, respectively ( $p < 0.0003$ ).

Allergic adverse reactions, such as bronchospasm, urticaria and itching, occurred in 15 of the ioxaglate group and only 1 of the patients receiving iopamidol ( $p < 0.0007$ ). Fifty-two patients in

the ioxaglate group had a known allergic history (not to contrast medium) or asthma, whereas 77 receiving iopamidol had a similar history. Seven of the 52 ioxaglate-treated patients developed an allergic adverse reaction compared with none of the 77 in the iopamidol group ( $p = 0.001$ ). Of 41 patients receiving ioxaglate who were premedicated with diphenhydramine, 4 had an allergic adverse event. In the iopamidol group 45 patients received similar premedication and none had an allergic adverse reaction ( $p < 0.03$ ).

Thus, this multicenter study shows that adverse reactions occur more often with ioxaglate than with iopamidol and that patients with an allergic history have a greater risk with ioxaglate therapy compared with iopamidol.

*(J Am Coll Cardiol 1992;19:899-906)*





# Randomized Trial Designed to Evaluate Non-ionic and Ionic LOM in High Risk Patients

## A Randomized Trial of Low Osmolar Ionic Versus Nonionic Contrast Media in Patients With Myocardial Infarction or Unstable Angina Undergoing Percutaneous Transluminal Coronary Angioplasty

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Royal Oak, Michigan

**Objectives.** The purpose of this study was to determine prospectively whether the differences in anticoagulant and antiplatelet effects of ionic and nonionic contrast media alter angiographic or clinical outcomes in patients with unstable ischemic syndromes undergoing percutaneous transluminal coronary angioplasty.

**Background.** The interaction of platelets and thrombin with the endothelium of injured vessels contributes to thrombosis and restenosis after coronary angioplasty. Case reports and retrospective observations have reported an increased risk of thrombosis with the use of nonionic contrast media.

**Methods.** A total of 211 patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty were randomized to receive nonionic or ionic low osmolar contrast media. Coronary angiograms were assessed by a technician blinded to the study contrast media, and clinical events were monitored by an independent nurse for 1 month.

**Results.** Patients receiving the ionic media were significantly less likely to experience decreased blood flow during the procedure (8.1% vs. 17.8%,  $p = 0.04$ ). After the angioplasty, residual

stenosis, vessel patency, the incidence of moderate to large thrombi and use of adjunctive thrombolytic therapy were similar between the two groups. However, patients receiving ionic media had fewer recurrent ischemic events requiring repeat catheterization (3.0% vs. 11.4%,  $p = 0.02$ ) and repeat angioplasty during the initial hospital stay (1.0% vs. 5.8%,  $p = 0.06$ ). One month after angioplasty, patients receiving ionic contrast media reported significantly fewer symptoms of any angina (8.5 vs. 20.0%,  $p = 0.04$ ) or of angina at rest (1.4% vs. 11.8%,  $p = 0.01$ ) and a reduced need for subsequent bypass surgery (0% vs. 5.9%,  $p = 0.04$ ), compared with patients receiving the nonionic media.

**Conclusions.** These findings demonstrate that in patients with unstable ischemic syndromes undergoing coronary angioplasty, the use of ionic low osmolar contrast media reduces the risk of ischemic complications acutely and at 1 month after the procedure. Therefore, low osmolar ionic contrast media should be strongly considered when performing interventions in patients with unstable angina or myocardial infarction.

(*J Am Coll Cardiol* 1996;27:1381-6)





# Ideal Contrast

- Excellent absorption of x-ray
- No cardiac toxicity
- No nephrotoxicity
- No limitation to dose
- Non-allergenic
- Quickly eliminated; multiple paths
- Low viscosity
- Iso-osmolal
- Customized



# Contrast-Induced Nephropathy

## Definition

- New onset or exacerbation of renal dysfunction after contrast administration in the absence of other causes:

increase by > 25%

or

absolute  $\uparrow$  of > 0.5 mg/dL

from baseline  
serum creatinine

Occurs 24 to 48 hrs post-contrast exposure, with creatinine peaking 5 to 7 days later and normalizing within 7 to 10 days in most cases





# Contrast-Induced Nephropathy:

## Incidence

- 3rd most common cause of hospital acquired renal failure
- Occurs in less than 1% of general population
- Occurs in "only" 5.5% of patients with renal insufficiency
- But, occurs in 50% of patients with both renal insufficiency and diabetes mellitus

Parfrey PS, et al, *NEJM* 1989; 320:143-149





# Contrast-induced Nephropathy: Incidence, Risk Factors

**1,826 consecutive pts undergoing PCI:**

**ARF w/o dialysis = 144.6/1,000 or 14.5%**

**ARF with dialysis = 7.7/1,000 or 0.7%**

Predictors of ARF +D	OR	CI	P
Cr Clearance	0.83	0.77-0.89	<0.001
Diabetes	5.47	1.41-21.32	0.01
CONTRAST dose	1.008	1.002-1.013	0.01

McCullough et al. *Am J Med* 1997; 103-375

# Risk Factors for CIN

## Patient-related Risk Factors

- Renal insufficiency
- Diabetes mellitus with renal insufficiency
- Age
- 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

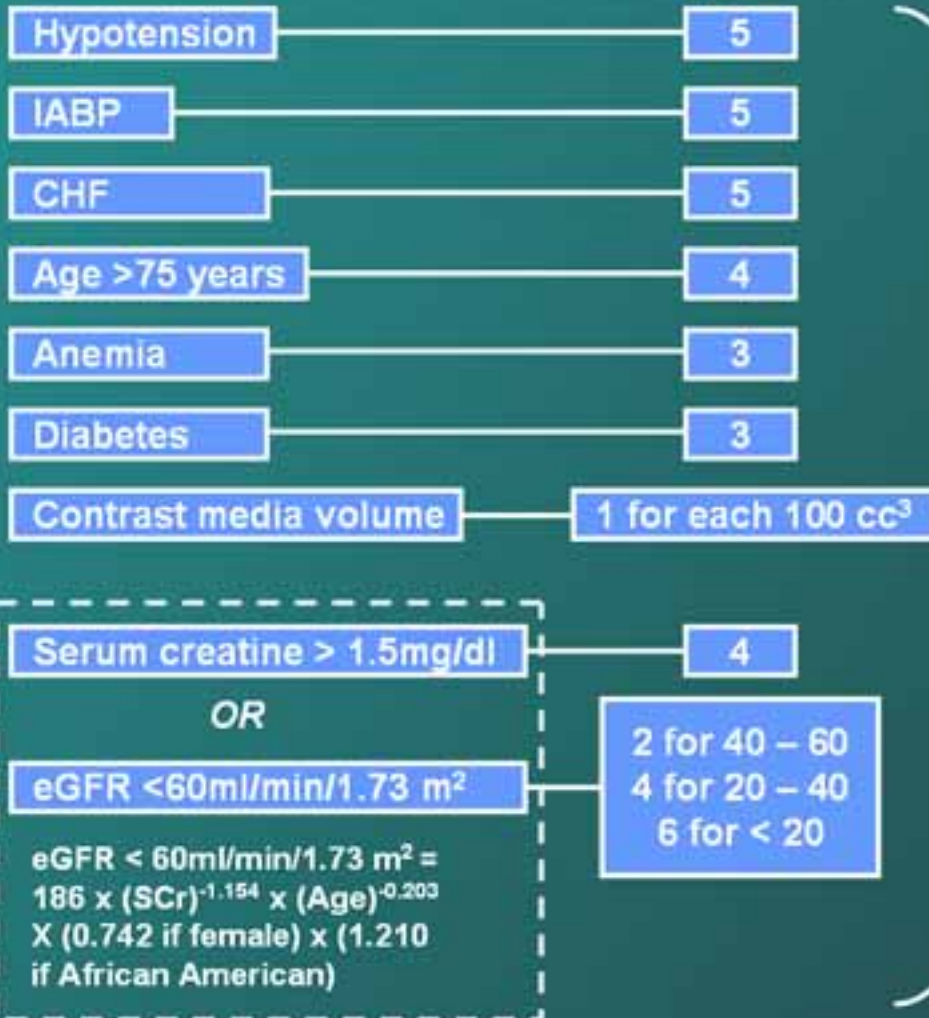




# Scheme to define CIN risk score

## Risk Factors

## Integer Score



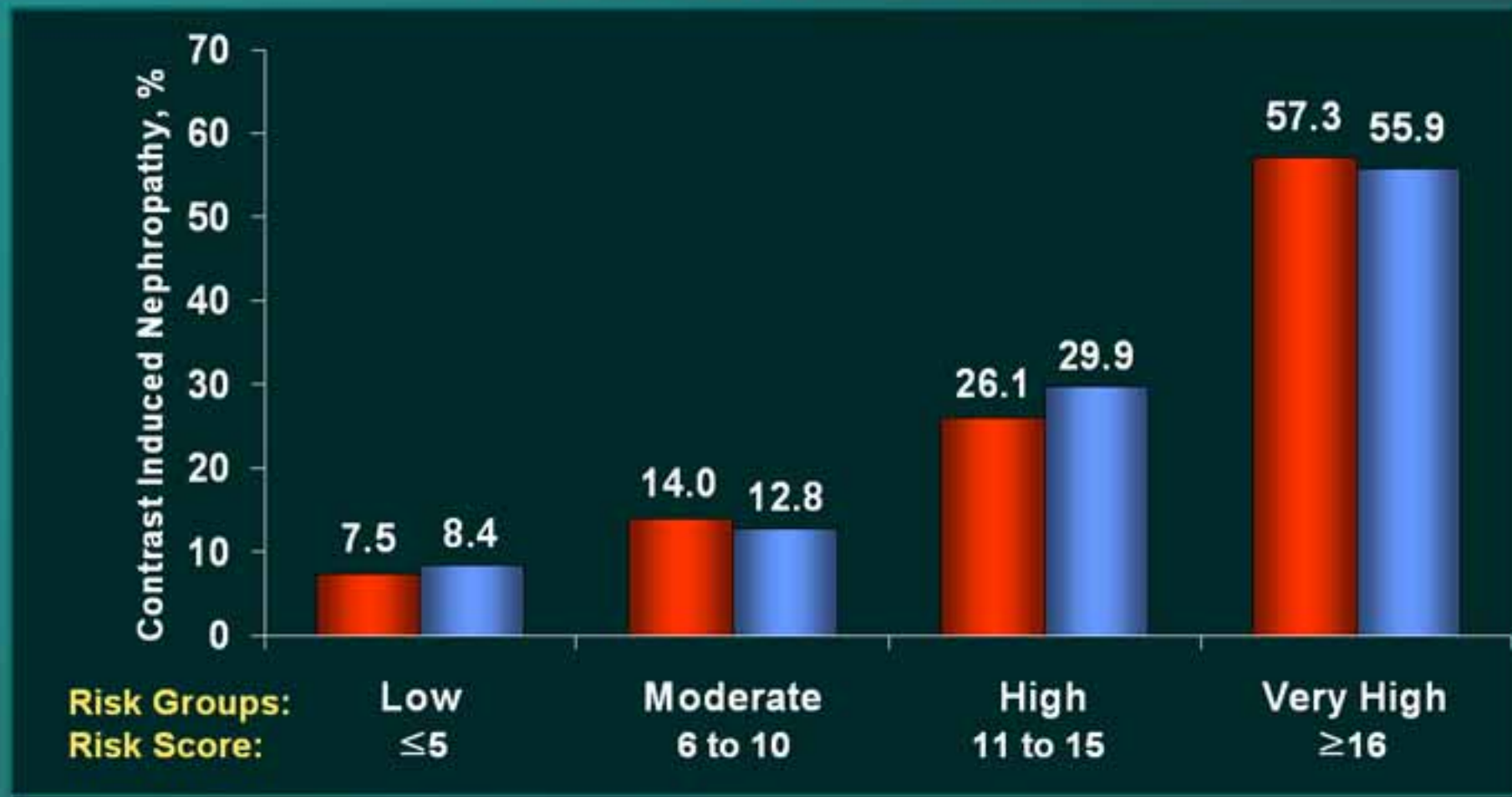
**Calculate**

Risk Score	Risk of CIN	Risk of Dialysis
≤ 5	7.5%	0.04%
6 to 10	14.0%	0.12%
11 to 16	26.1%	1.09%
≥ 16	57.3%	12.6%

Mehran et al. *JACC* 2004;44:1393-1399.



# CIN risk score



*CIN risk score derived from the development dataset predicted this complication in the validation set. (Red bars = development dataset; blue bars = validation dataset.)*

Mehran et al. *JACC* 2004;44:1393-1399.

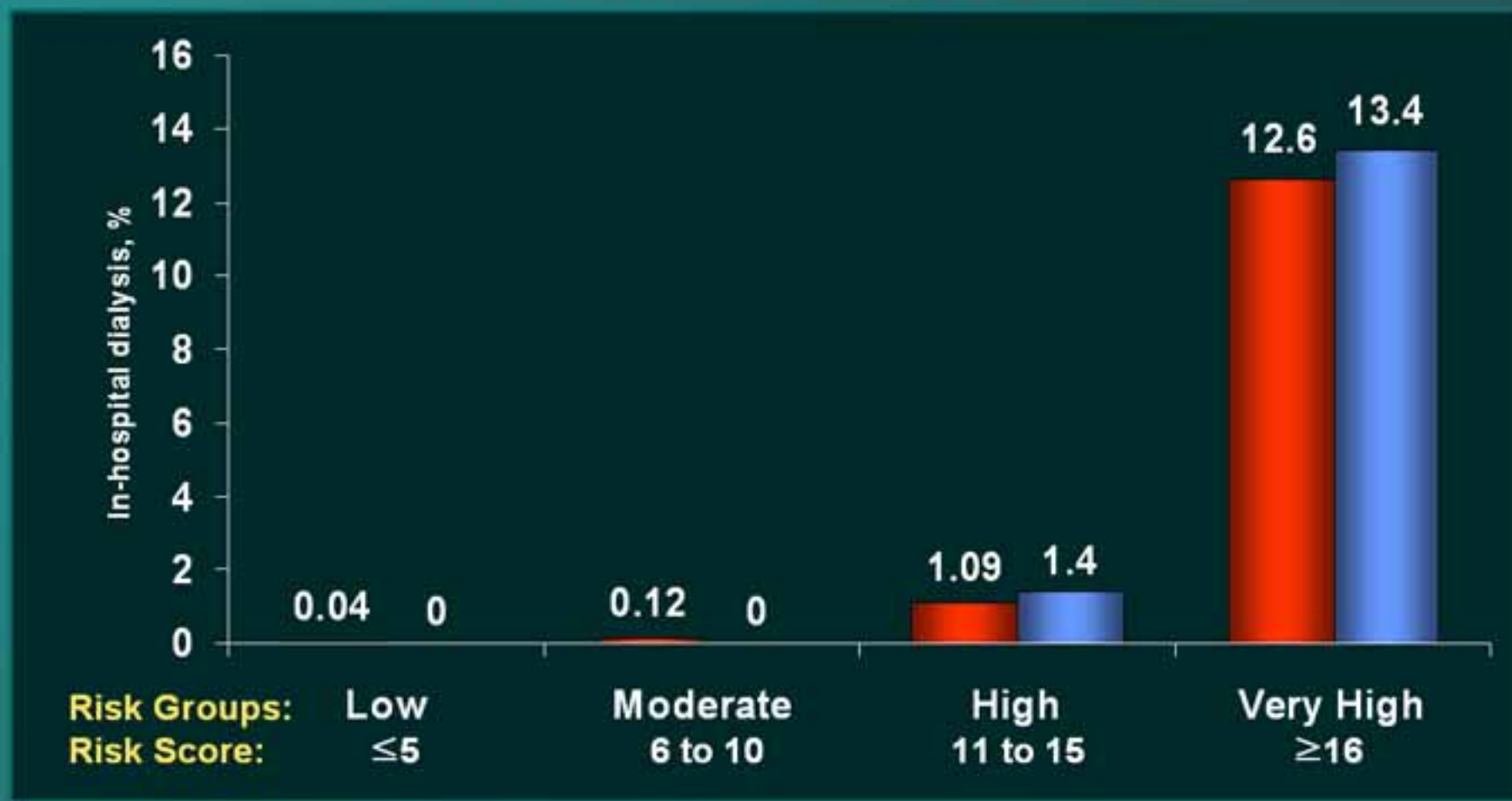


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# CIN risk-score & HD

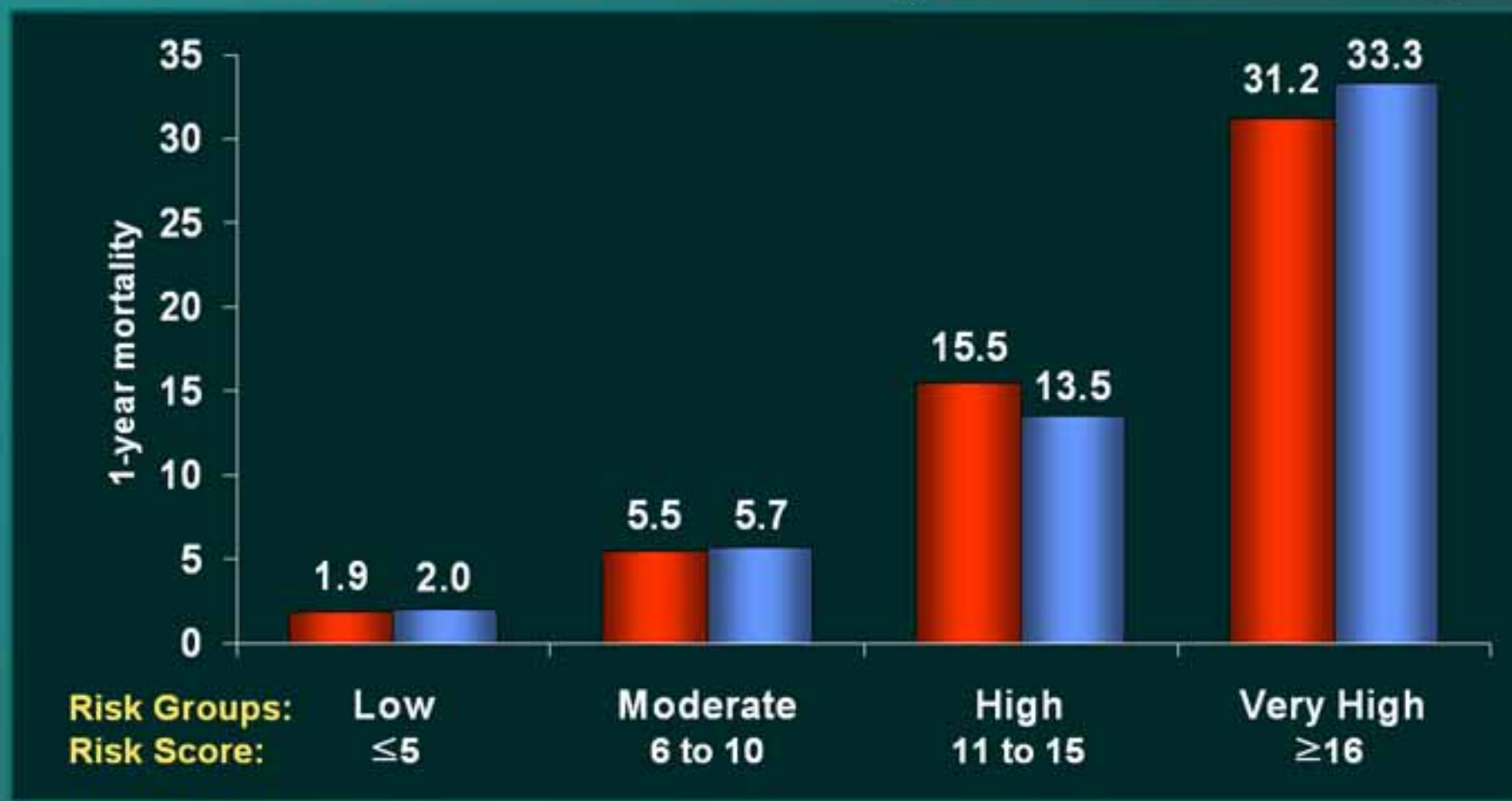


*In-hospital hemodialysis can be predicted by a high or very high risk score value similarly in the development and validation datasets. (Red bars = development dataset; blue bars = validation dataset.)*

Mehran et al. *JACC* 2004;44:1393-1399.



# CIN Risk Score & 1-year mortality



*Prognostic significance of the proposed risk score for CIN extended to prediction of 1-year mortality. (Red bars = development dataset; blue bars = validation dataset.)*

Mehran et al. *JACC* 2004;44:1393-1399.





# Risk of Contrast-induced Nephropathy in Relation to Baseline Hematocrit



Nikolsky, Mehran, et al. KI 2005



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# Conclusions

- Ionicity, osmolality and viscosity are 3 distinct properties of the iodinated radiocontrast agents
- Potentially important differences may exist among them (i.e. ionic less thrombogenic, low osmolar less nephrotoxic, ?role of viscosity)
- Knowledge of Rx of their side-effects is warranted
- CIN is an important complication that can be predicted using a simple risk model
- Appropriate preventive measures should be taken to avoid CIN
  - Hydration pre-PCI (12 hours recommended)
  - D/C nephrotoxic drugs (NSAIDS, abx etc)
  - n-acetylcysteine (? effect w/ large contrast volume)
  - Limit contrast agent volume
  - Low Osmolar better than High Osmolar
  - Bicarbonate based hydration role not well defined

