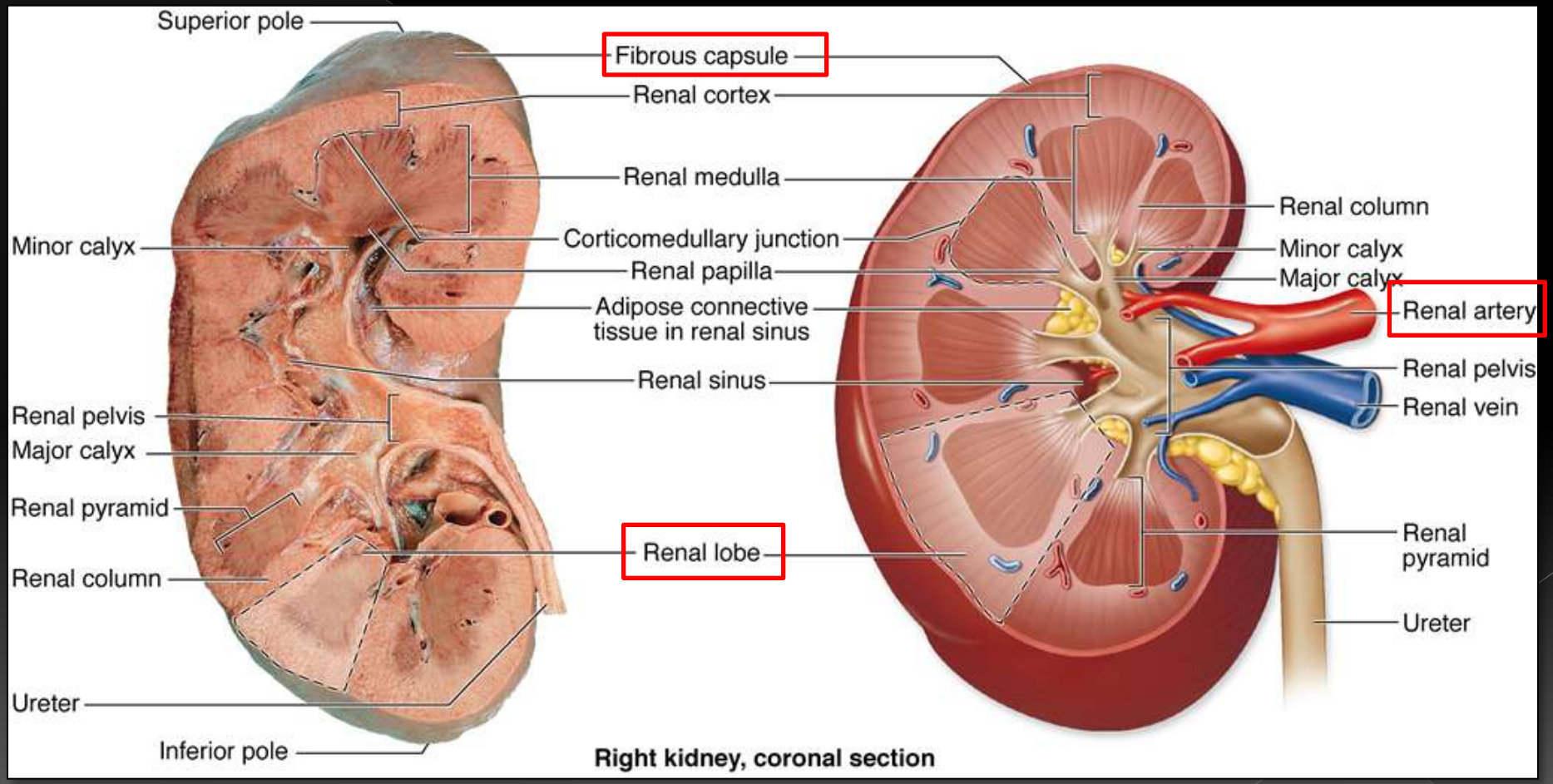
CATH LAB SYMPOSIUM 2010

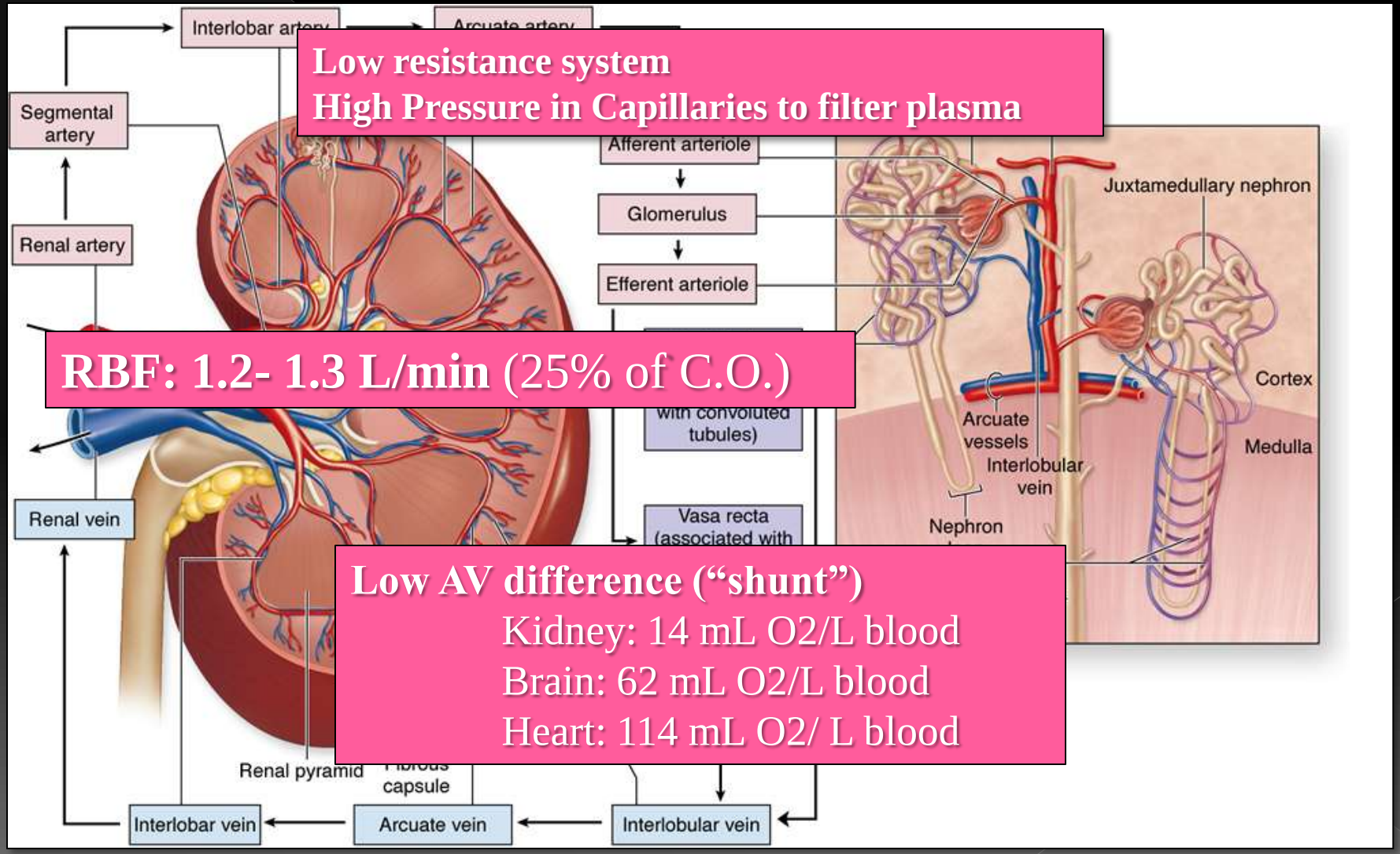
Kidneys and Contrast: Cath Lab Perspective

Luis F. Tami, MD
Cath Lab Director
Memorial Regional Hospital

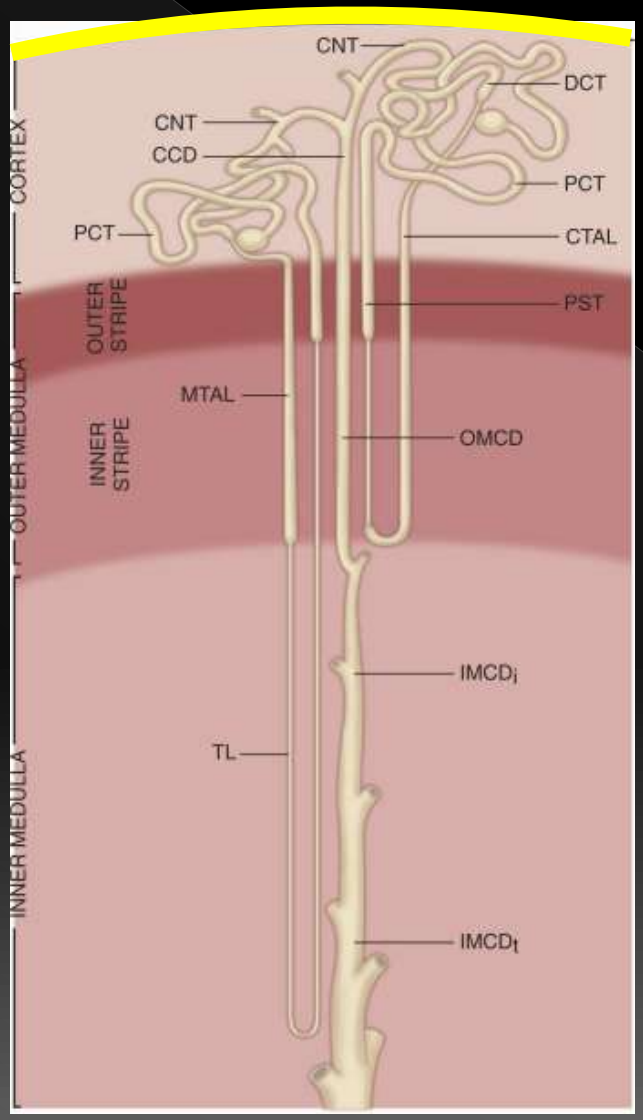
KIDNEYS ANATOMY



Renal Vasculature



Measurement of kidney Function: GFR



DEF: GFR is the sum of the individual filtration rates of all functional nephrons

RBF: 1.2- 1.3 L/min (25% of C.O.)

RPF: 650-700 mL/min

Normal GFR: 125 mL/minute (10% lower in women).
or 7.5 L/hr or 180 L/day

Urine output: 1 L/day

Therefore, 99% of filtrate is reabsorbed

Chronic Kidney Disease

Stages are based on GFR

ANGIOMAX: <30

LOVENOX: <50

INTEGRELIN: <60

CKD STAGE	DESCRIPTION	GFR (mL/min/1.73 m2)
1	Kidney damage with normal or increased GFR	> 90
2	Mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney Failure (Dialysis stage)	< 15

How to Calculate GFR ?

- **Abbreviated Modification of Diet in Renal Disease (MDRD) equation:**

eGFR, ml/min/1.73 m^2 =186 x (S Creatinine [mg/dL]) -1.154 x (Age-0.203 x (0.742 if female) x (1.210 if African American)

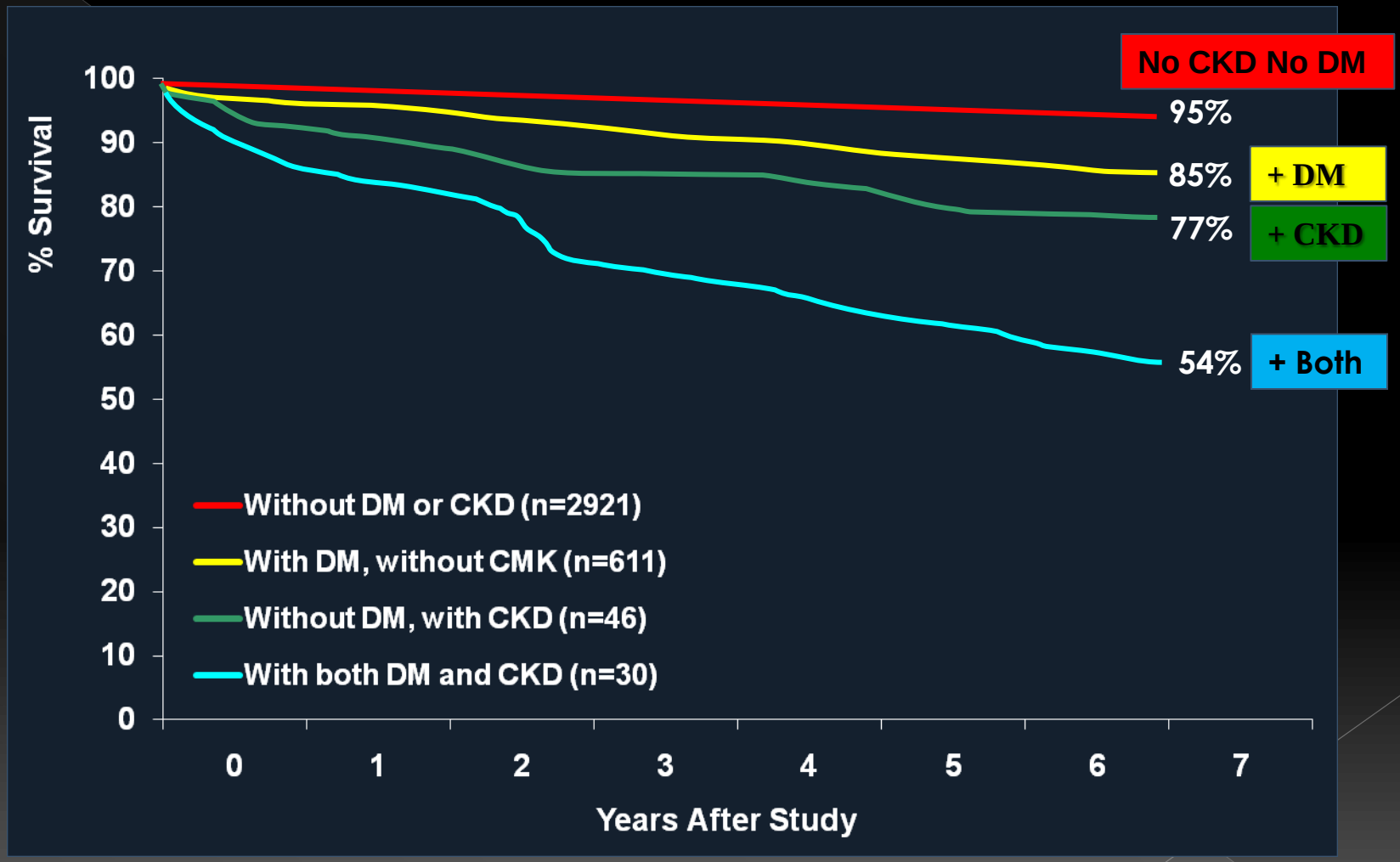
- **Cockcroft-Gault equation:**

$$\text{Creatinine Clearance, ml/min} = \frac{(140 - \text{age}) \times \text{Body Weight [kg]}^*}{\text{Serum Creatinine [mg/dL]} \times 72}$$

*** Multiple by 0.8 in female**

www.mdrd.com

Survival of CAD Patients in relation with CKD* and Diabetes (DM) BARI Trial + Registry

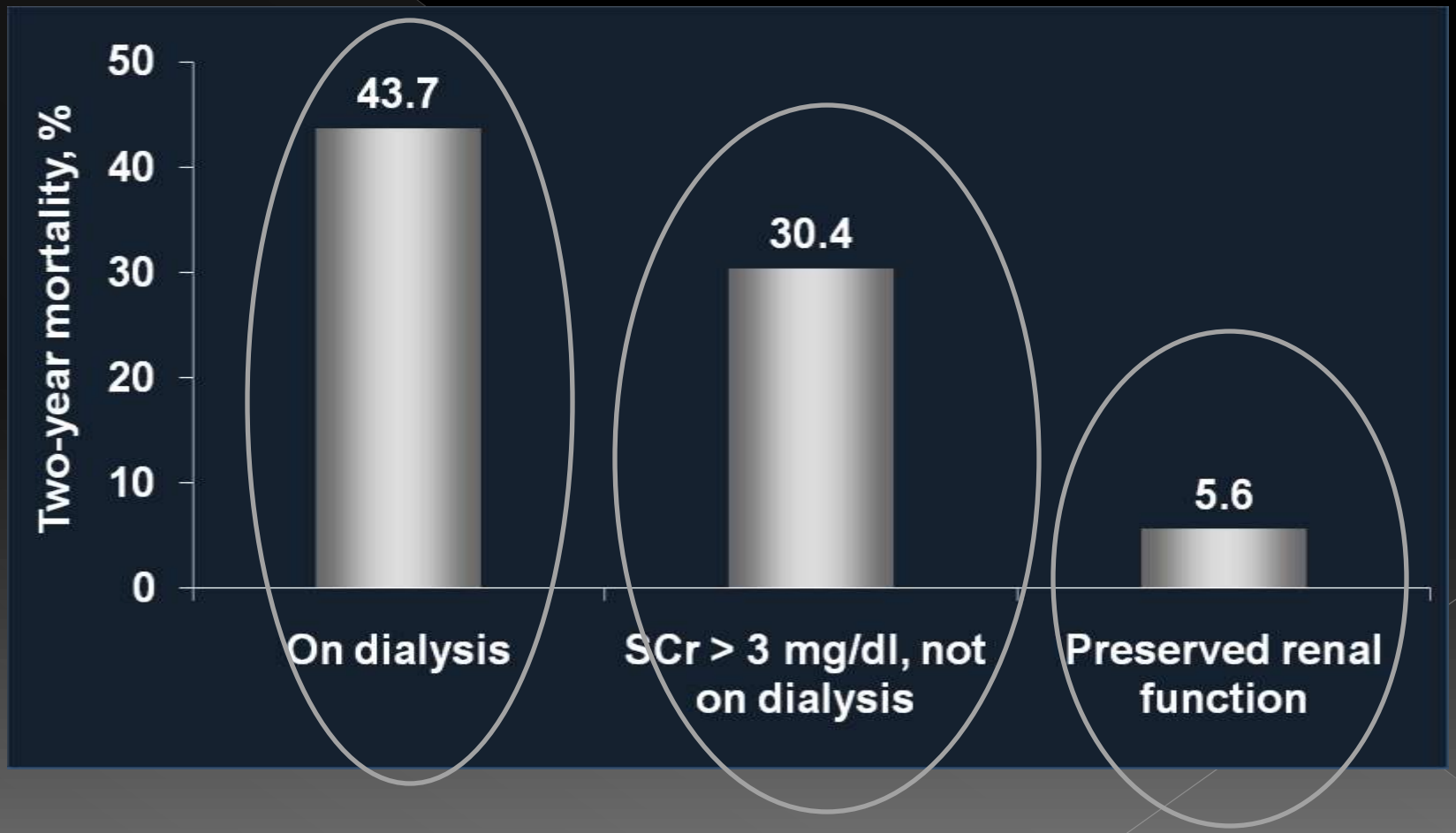


* CKD defined as baseline Cr > 1.5 mg/dl

Szczech L. et al., Circulation 2002; 105:2253-8.

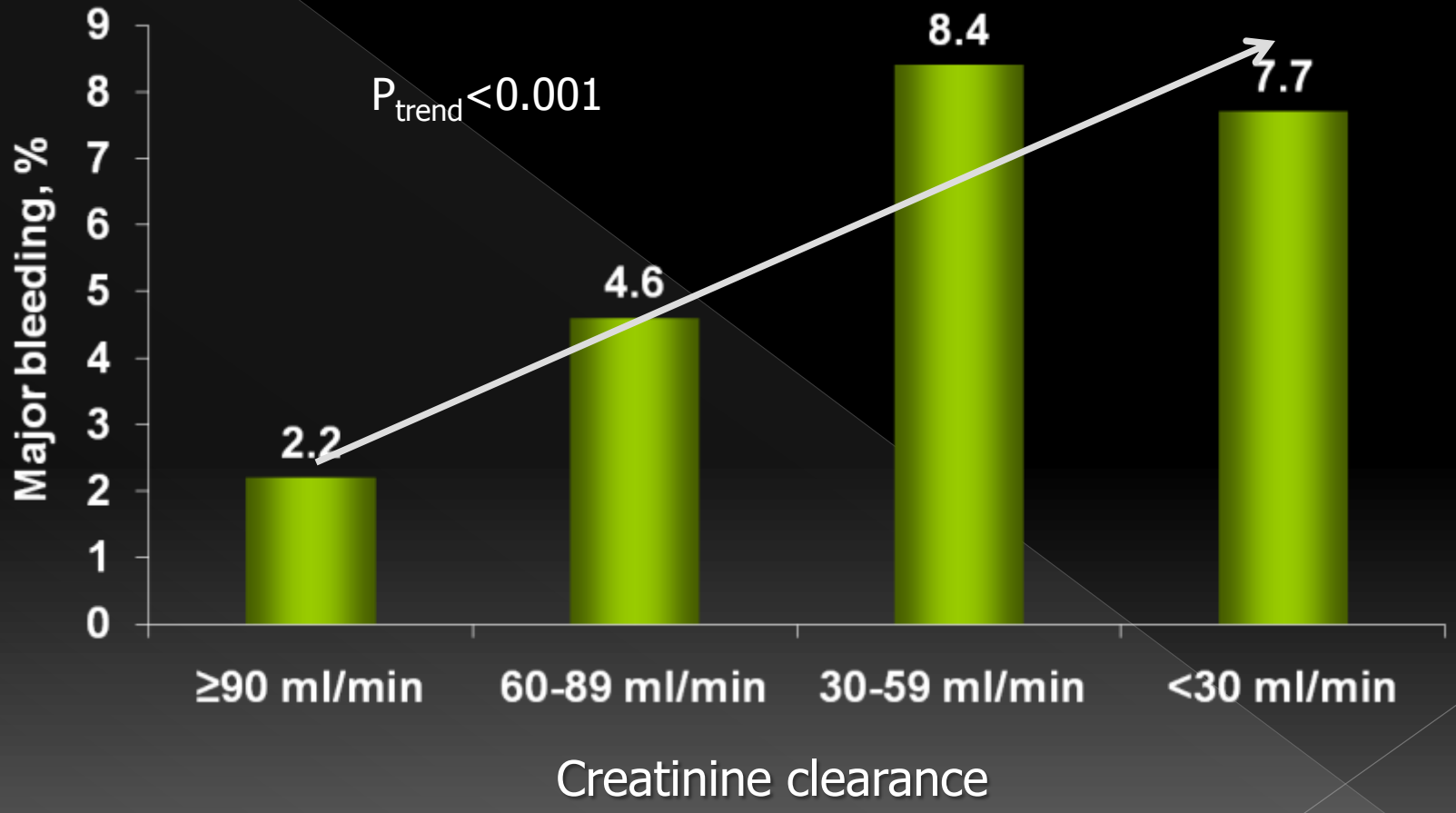
Mortality Post PCI in Relation to Renal Function

2650 consecutive patients from Mayo Clinic at 2 yrs



Major Bleeding in Relation to Renal Function:

Meta-Analysis of 3 Randomized Trials



Chew DP et al, Am J Cardiol. 2003;92:919-923

Predictors of Excessive Anticoagulation in ACS Patients: CRUSADE Registry

- Older age
- Female gender
- Lower weight
- **Chronic renal insufficiency**
- Diabetes mellitus
- Congestive heart failure

Alexander KP et al, JAMA 2005;294:3108-3116.

GFR (mL/min)

Integrelin: <60
Lovenox: <50
Angiomax:<30

60 years old person of
70 kg

CREATININE	Male	Female	
0.8	97	83	
1.0	78	66	
1.2	66	55	
1.5	56	44	80 yr old
1.8	43	37	→ 27
2.4	32	27	

Contrast-Induced Acute Kidney Injury (AKI) or Contrast-Induced Nephropathy (CIN)

Definition

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

increase by > 25%

or

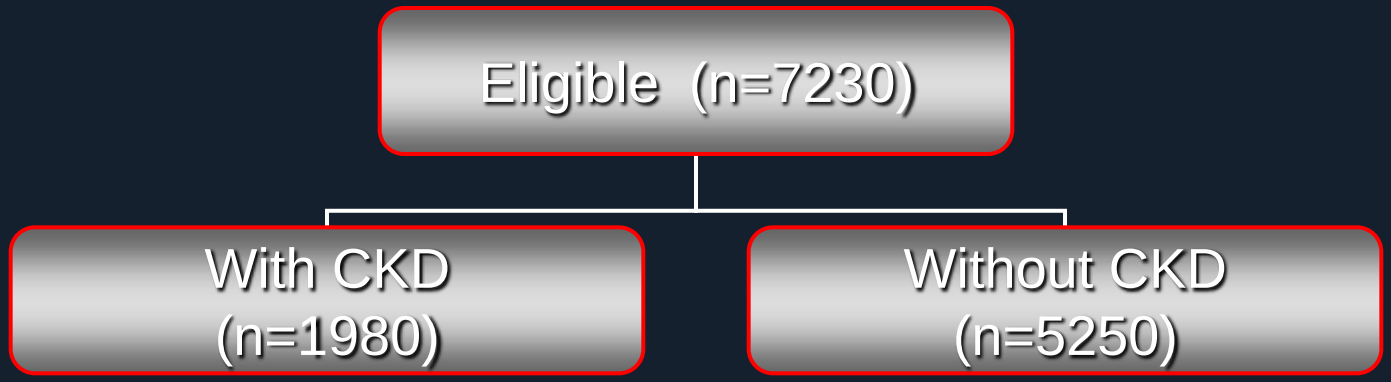
absolute ↑ of > 0.5 mg/dL

} from baseline serum creatinine within 24-48 hrs

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

Is CIN bad for our patients?

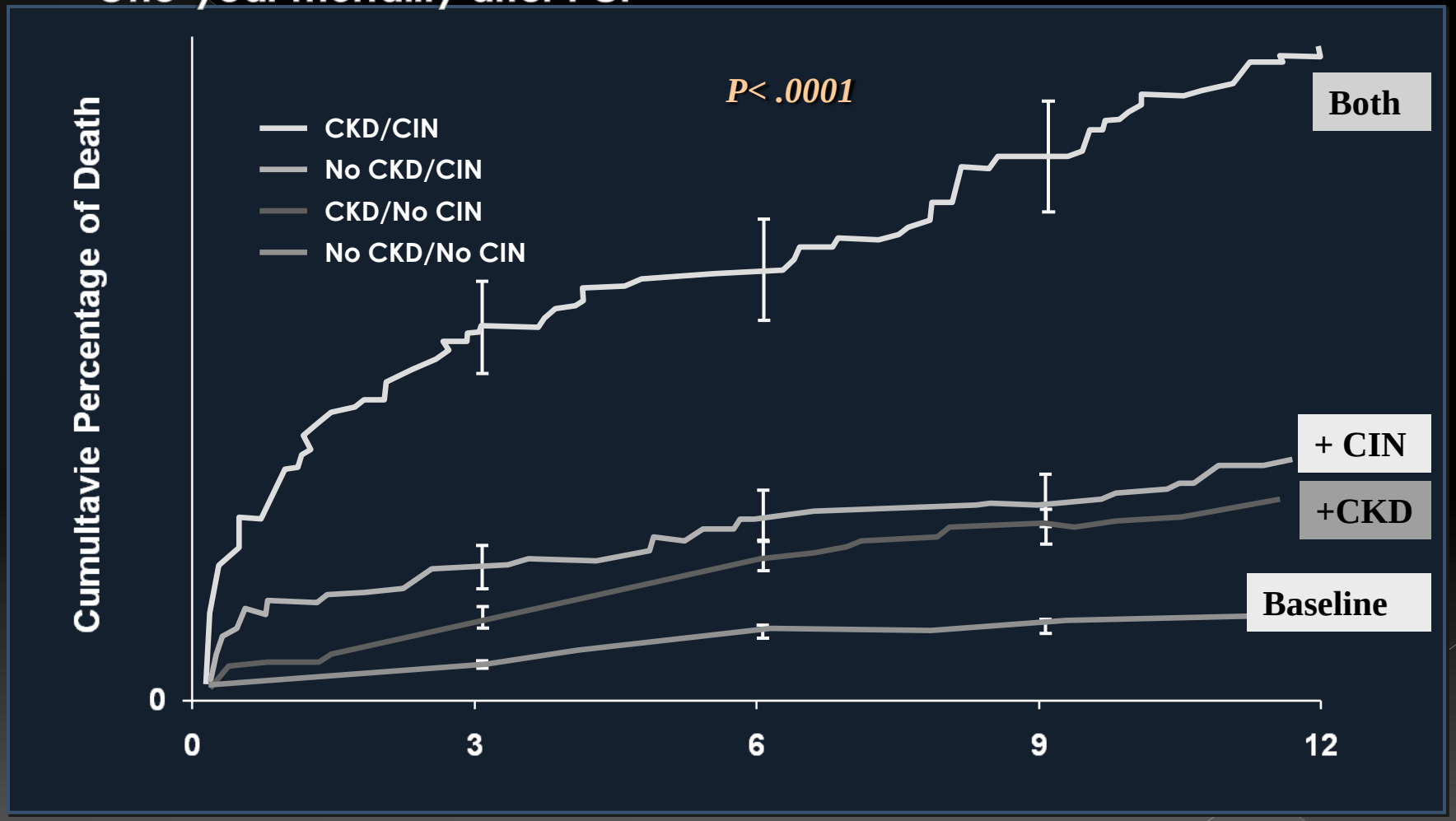
n = 7230 consecutive patients who underwent first PCI over a period of 5 years



- FACTORS FOR CIN: Peri-procedural hypotension, lower eGFR, older age, diabetes, greater amount of contrast medium and atherosclerosis
- CONCLUSION: CIN was related to higher mortality in both groups (with or without CKD).

Dangas et al, Am J Cardiol 2005; 95:13-19.

Mortality after PCI: Relation to CIN/CKD



Dangas et al, Am J Cardiol 2005; 95:13-19.

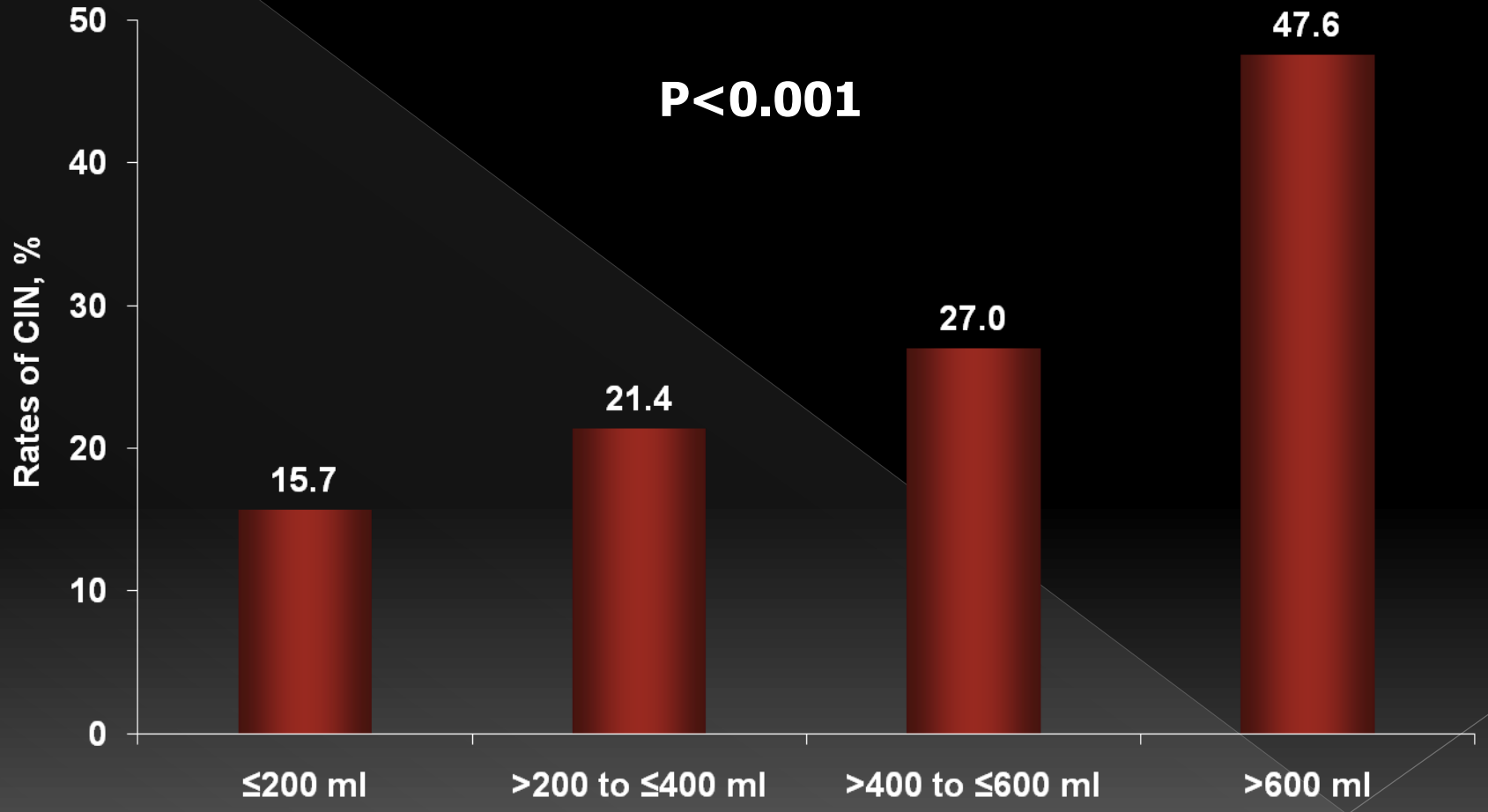
CKD and CIN: Poor prognosis

Risk Factors for CIN

Patient-related Risk Factors
• Chronic Kidney Disease
• Diabetes mellitus
• Older age
• Anemia
• Volume depletion
• Low cardiac output
• Advanced CHF
• Nephrotoxic drugs (NSADIs)
• Renal transplant

Procedure-related Risk Factors
• Contrast Volume
• Hypotension
• Blood loss
• Multiple procedures within 72 hrs
• High-Osmolar Contrast

Rates of CIN as a Function of Contrast Medium Volume in Diabetic Cohort



Nikolsky E et al. AJC 2004;94:300-305.

Prevention of CIN

Treatment	Effect
Hydration	+
Hemofiltration	+
Prostaglandin E_1	+/–
Sodium bicarbonate	+/–
N-acetyl-l-cysteine	+/–
Dopamine	+/–
Fenoldopam	+/–
Theophylline	+/–
Calcium channel blockers	+/–
Hemodialysis	+/–
Atrial natriuretic peptide	+/–
Statins	+/–

+ positive effect; – no effect; +/– conflicting data or not enough data

Hydration

Avoid CHF:

Assess patient's LV Systolic and diastolic function

Right heart catheterization may help in some patients

Hydration

Patient at Risk (GFR < 60 mL/min/1.73m^2)

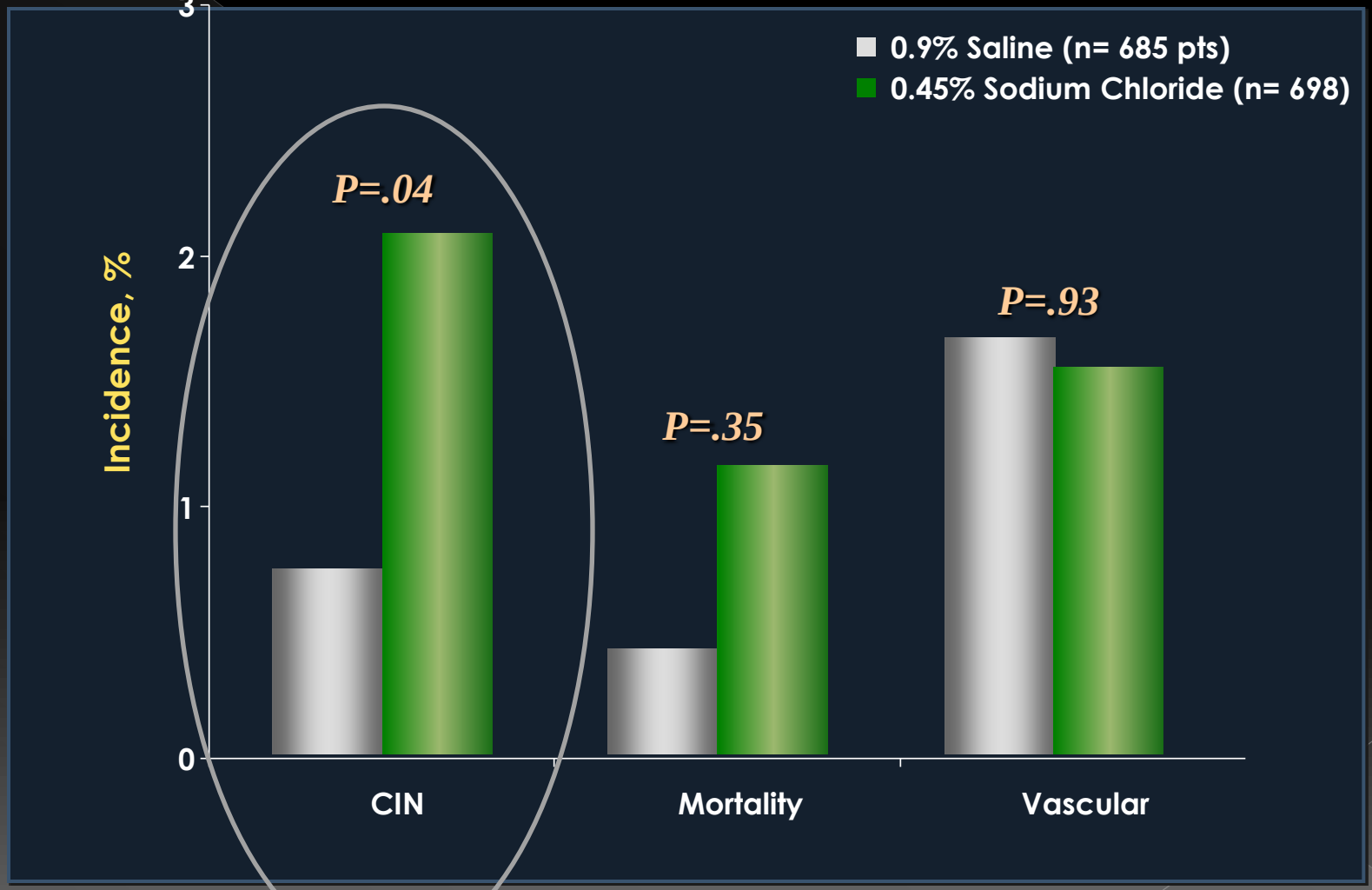
0.9 NS at 1-1.5 mL/Kg/h for 12 hrs before and 12 hrs after procedure

OR

0.9 NS 3 mL/kg, 1 hour prior to procedure and 1.5mL/Kg/h for 4-6 hrs after procedure

May use sodium bicarbonate 3 amps (150 mEq) in 1 L D5W instead of NS

Optimal Hydration: 0.9 NS vs 0.45 NS

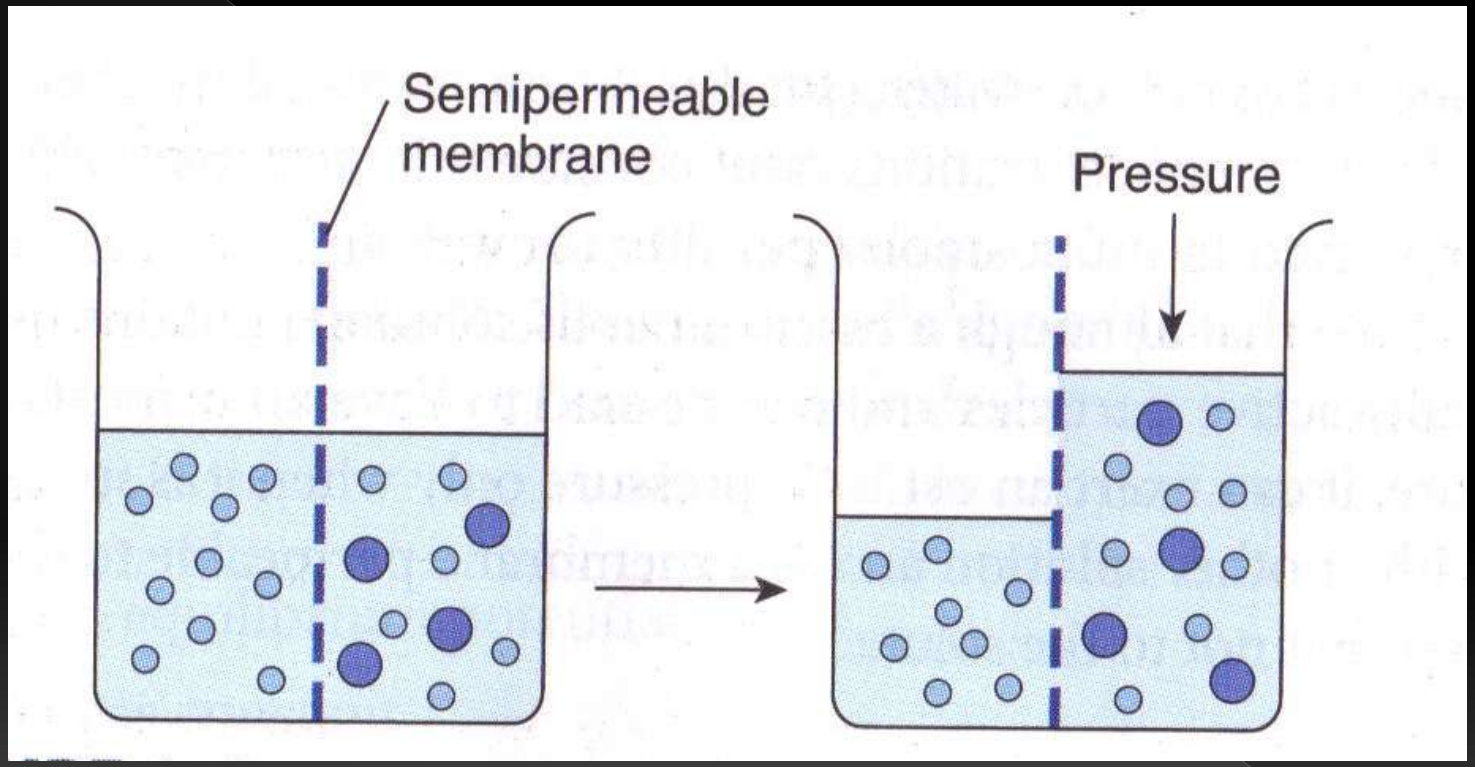


Mueller et al *Arch Intern Med* 2002

Contrast Media

- Iodine: Provides radio-opacity, relatively non-toxic
- Osmolality: In relation to plasma (290 mOsm/Kg)
- Viscosity: Friction between molecules (injector pressure)
- Ionic vs Non-ionic
- Platelet activation/clot formation
- Cost

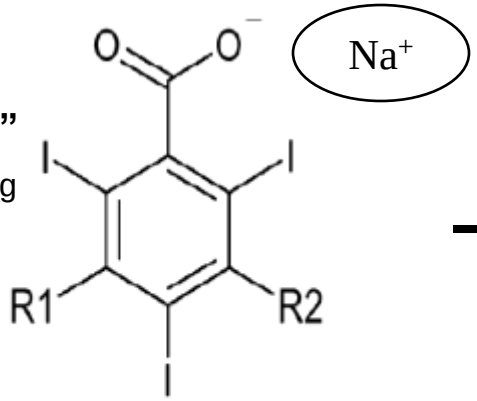
Osmosis and Osmolality



•Osmolality is related to the number of particles per unit of water: Plasma is 290 mOsm/L.
•Isotonic fluids have same osmolality than plasma (e.g. normal saline)

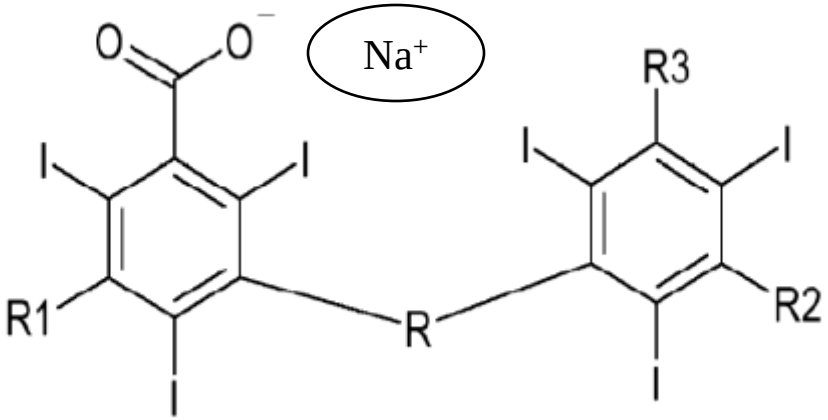
Contrast Media: Prototypic Structures

Ditrizoate
"High Osmolar"
>1500 mOsm/kg



Ionic Monomer

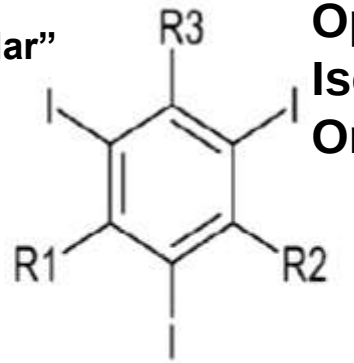
Hexabrix
700 mOsm/Kg



Ionic Dimer

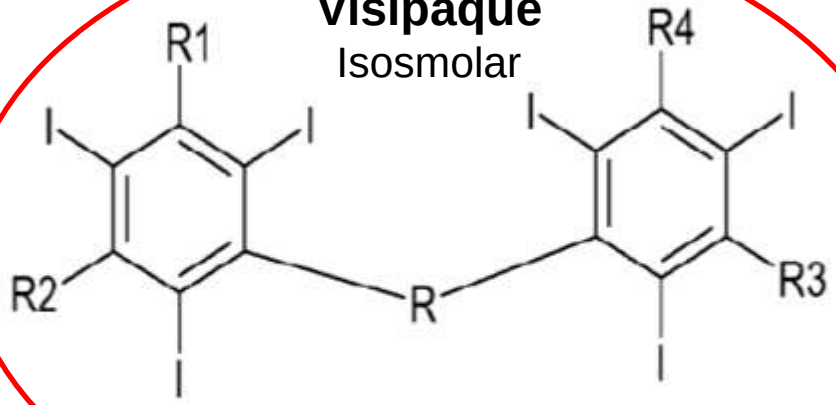
"Low Osmolar"
700 mOsm/kg

Optiray
Isovue
Omnipaque



Nonionic Monomer

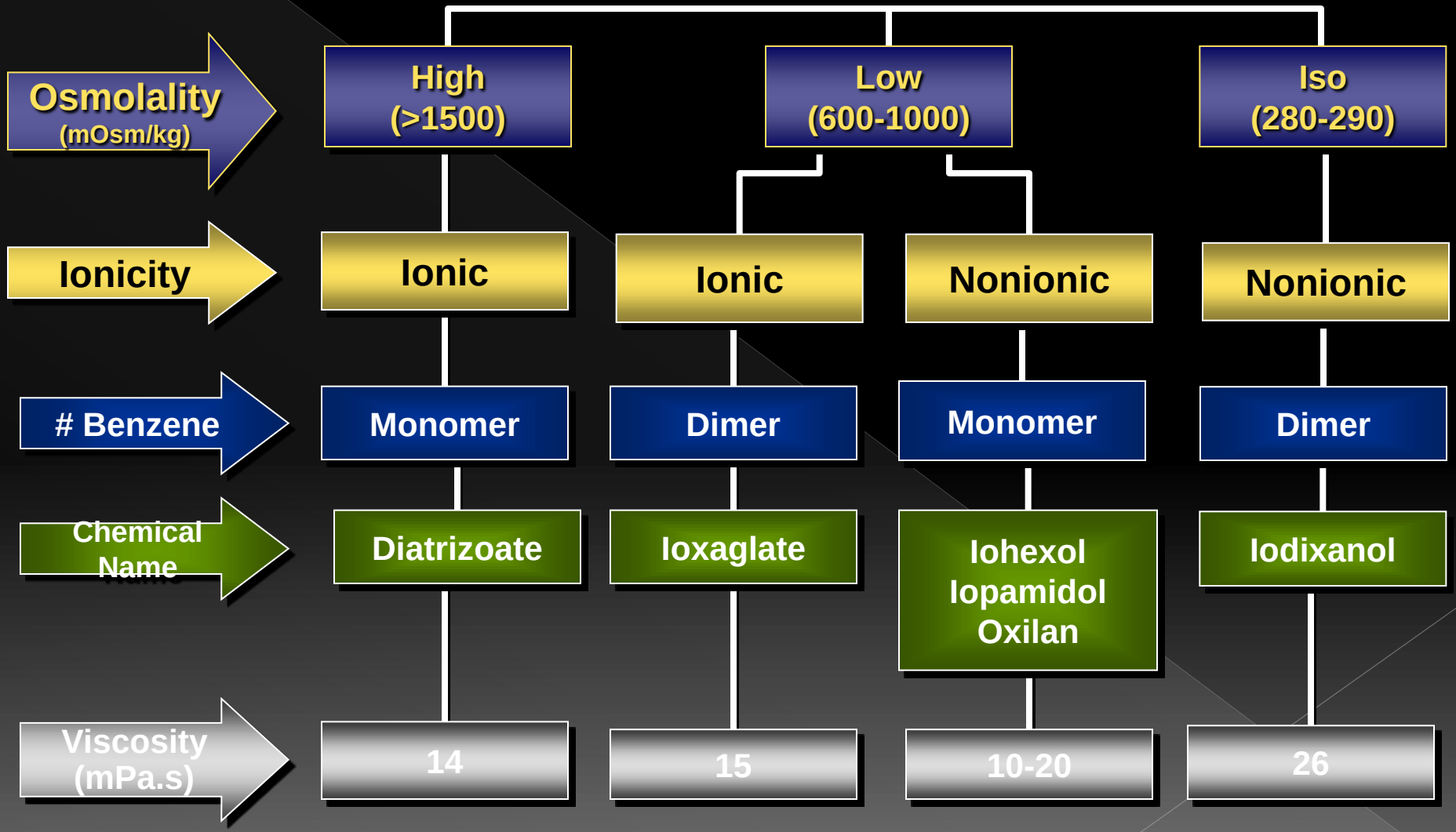
Visipaque
Isosmolar



Nonionic Dimer

Voeltz MD, Nelson MA, McDaniel MC, Manoukian SV. J Invasive Cardiol 2007;19(Suppl A):1A-9A.

Contrast Media Classification



Abdominal Angio with 5F, Visipaque: Settings at 900 psi ……

Achieved values

VISIPAQUE: Isosmolar and well tolerated BUT viscous contrast

CIN and Contrast Type

Prospective Randomized Trials

Low-osmolar	Iso-osmolar	Condition	Statistical result
Iohexol (844)	Iodixanol	Coronary, CKD (SCr* 3.1), 35% DM	No difference[1] (Omnipaque)
Iohexol (844)	Iodixanol	Coronary, CKD (SCr 1.5), 100% DM	Iodixanol superior to iohexol (NEPHRIC)[2]
Ioversol (792)	Iodixanol	Coronary, CKD (SCr 2.0), 52% DM	No difference (optiray)[3]
Iopamidol (796)	Iodixanol	MDCT, CKD (SCr 1.6)	No difference[4]
Iopamidol (796)	Iodixanol	Coronary, CKD (SCr 1.45), 41% DM	No difference (isovue) (CARE)[5]
Ioxaglate (600)	Iodixanol	Coronary, CKD (SCr 1.34, 48% DM	Iodixanol superior to ioxaglate (RECOVER)[6]
Ioxaglate (600)	Iodixanol	Coronary, CKD, contrast>150	No difference (ICON)[7]

[1]*Chalmer and Jackson, BJR 1999*

[2]*Aspelin et al (NEPHRIC), NEJM 2003*

[3]*Rudnick et al, (VALOR), ASN 2005*

[4]*Barrett et al (IMPACT), Invest Rad 2006*

[5]*Solomon et al (CARE), Circ 2007*

[6]*Jo et al (RECOVER), JACC 2006*

[7]*Mehran (ICON), TCT 2006*

CONTRAST TYPE: Conclusion

- Low Osmolar better than High Osmolar Contrast.

- Isosmolar Contrast (Iodixanol, Visipaque™):
  - For CIN prevention: Not conclusively better than low-osmolar BUT 3.5 times more expensive per cc
  - Provides less osmotic load than low-osmolar agents (Advantage in CHF, acute MI or dialysis patients)
  - Most adequate than other agents for PERIHERAL angiography due to consistently LESS PAINFUL INJECTIONS.

CONTRAST Trial:

IV Fenoldopam for the Prevention of CIN

Design

- **DESIGN:** Prospective, placebo-controlled, double-blind, multicenter randomized trial
- **OBJECTIVE:** Examine the efficacy of IV fenoldopam in preventing CIN after invasive cardiovascular procedures.

A total of **315** pts with GFR<60mL/min at 28 centers in the US from 2001 to 2002

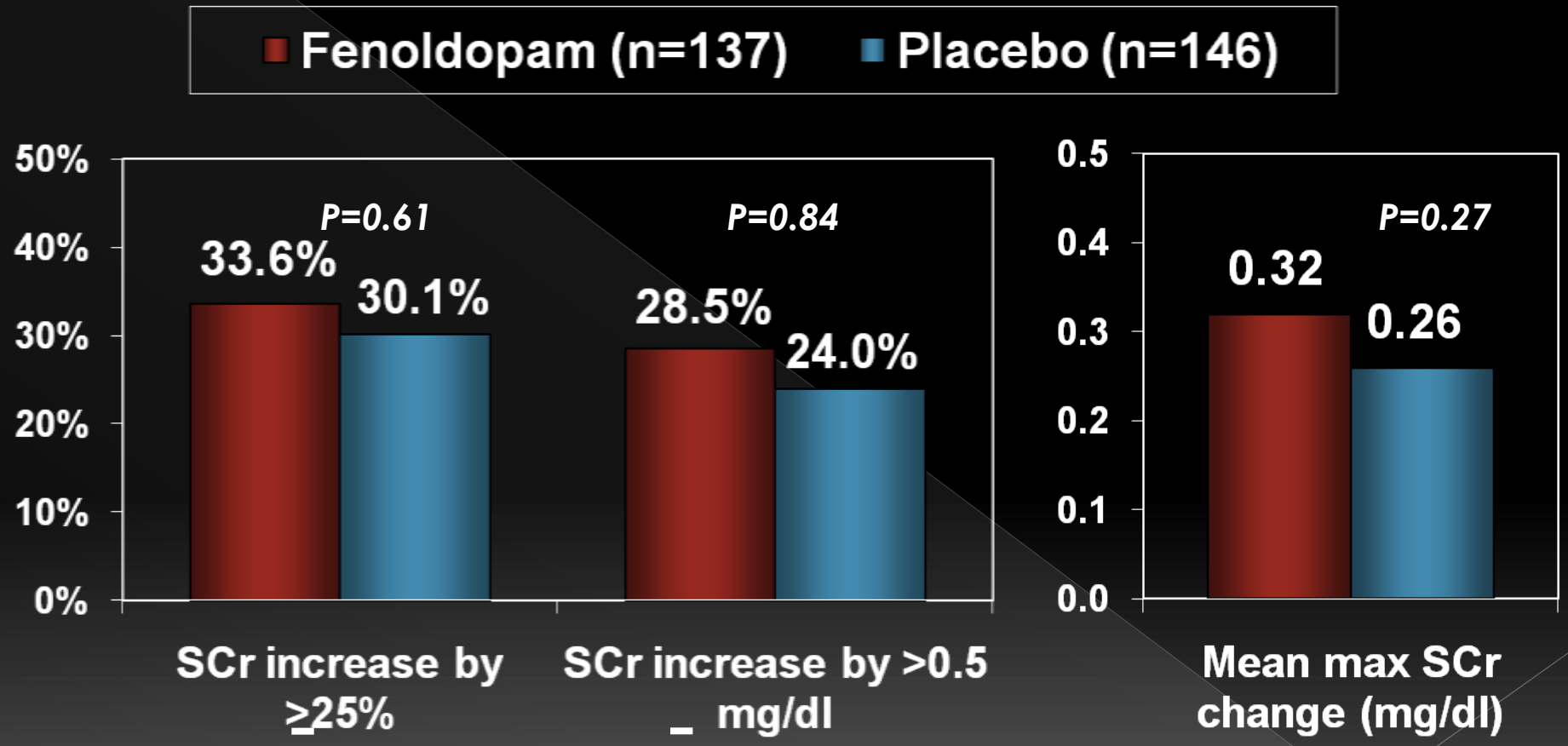
Randomization

IV fenoldopam (0.05 ugr/kg/min titrated to 0.10 ugr/kg/min) 1 hr pre- to 12 hrs post procedure	IV placebo 1 hr pre- to 12 hrs post procedure
N=157	N=158

Primary endpoint: **CIN** (increase of ≥25% in SCr level within 96 hours post-procedure).

Stone G. et al. JAMA. 2003 ;290:2284-2291

CONTRAST Trial

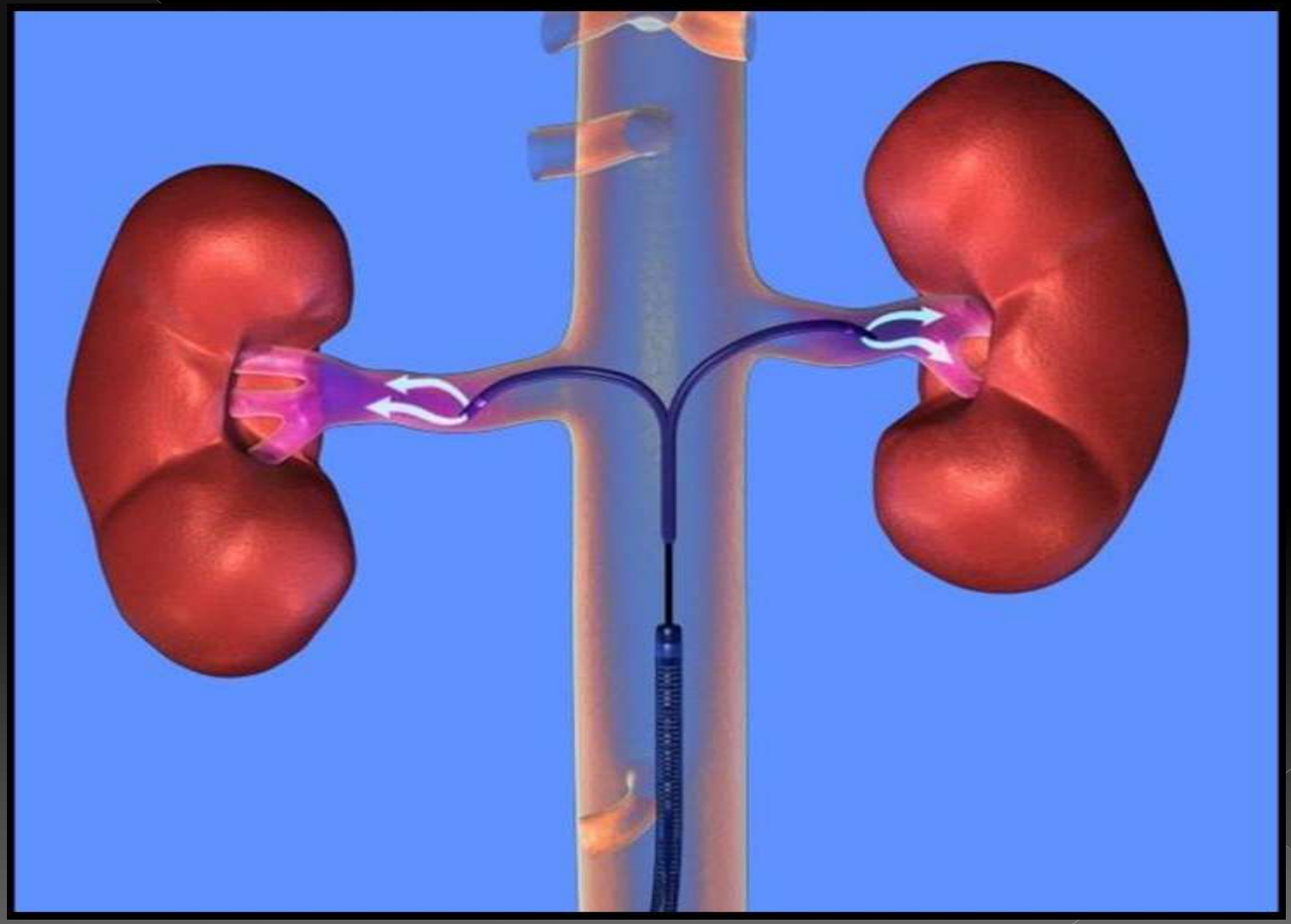


Stone G. et al. JAMA. 2003 ;290:2284-2291

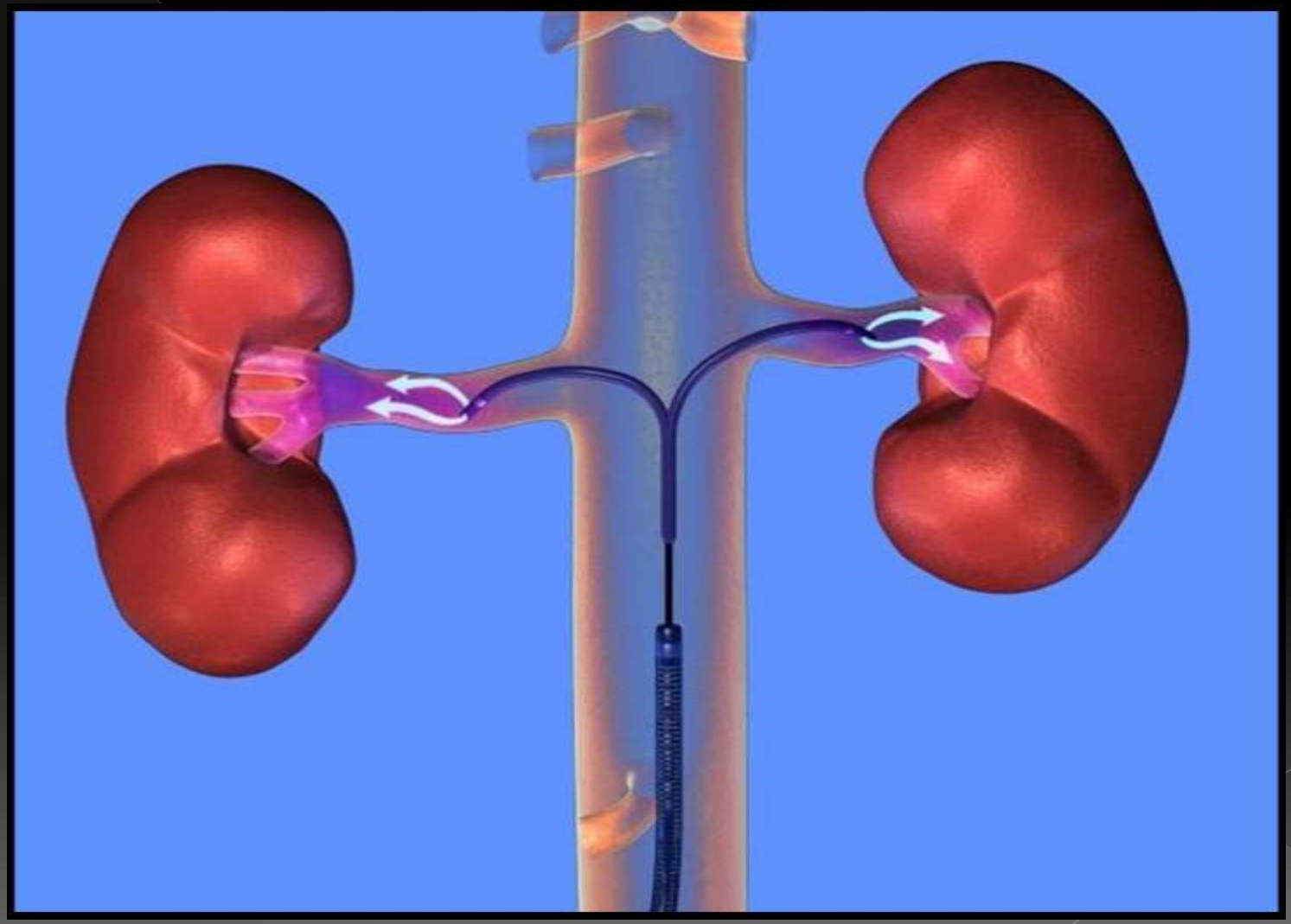
Fenoldopam

- Short acting Dopamine-1 agonist, vasodilator of BOTH renal cortical and medullary blood flow.
- NEGATIVE effect of IV fenoldopam in CIN prevention (CONTRAST trial)
  - Problems: First pass metabolism
  - Hypotension limits IV dose

Renal Infusion Catheter

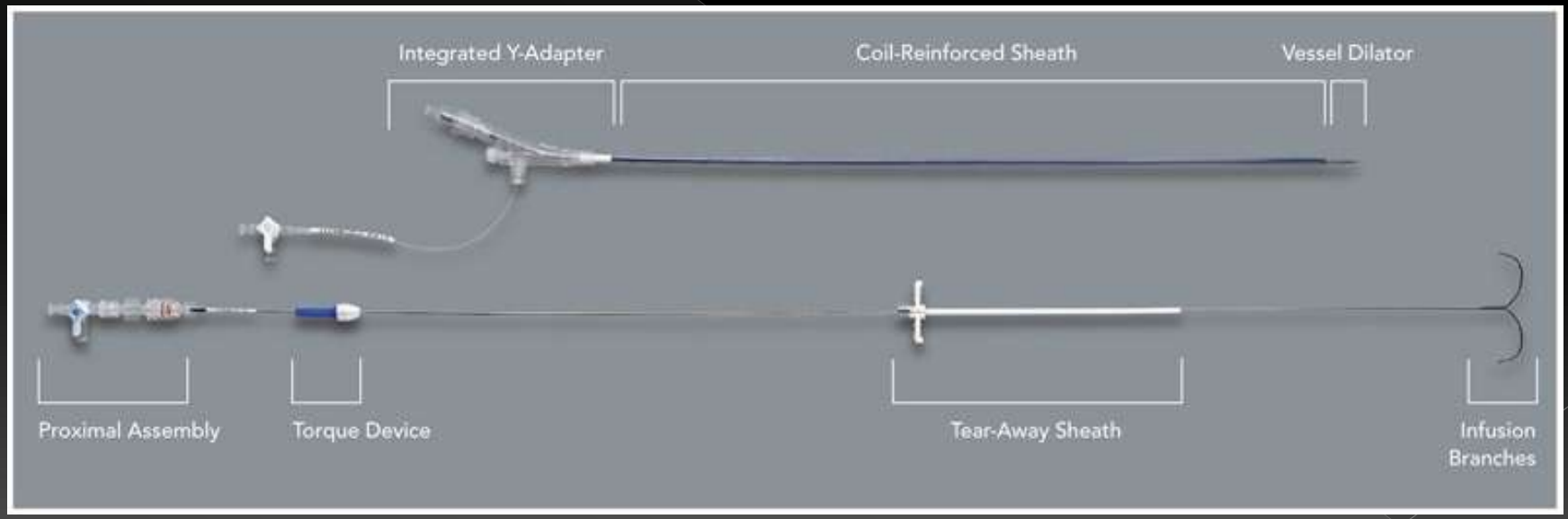


Renal Infusion Catheter



Targeted Renal Therapy

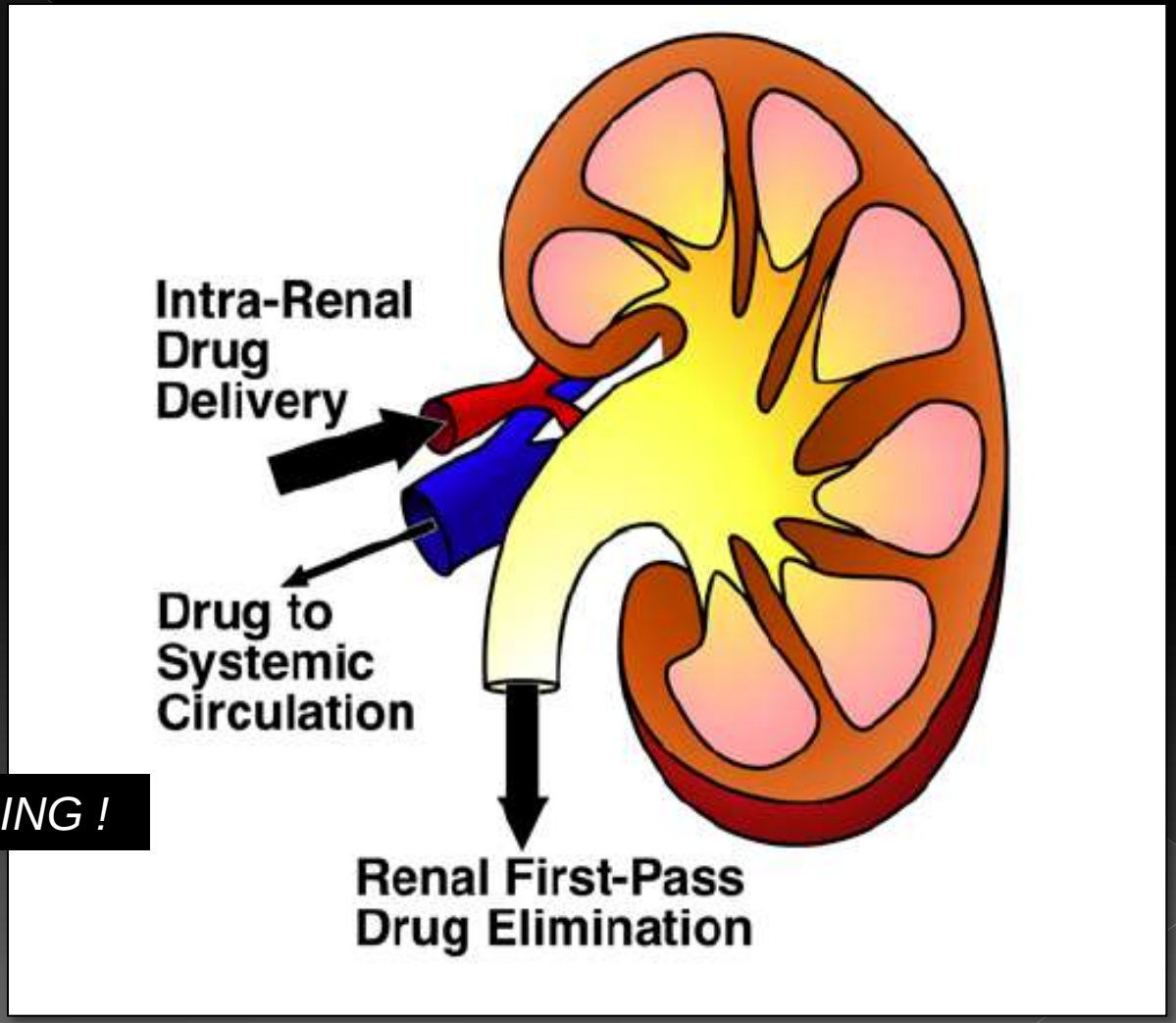
Benephit™ Infusion System (FlowMedica, Inc., Fremont, CA)



Intrarenal Fenoldopam

- Serum Fenoldopam levels are 30-50% lower by IR infusion.
- Less hypotension allows higher doses.
- GFR significantly increased by IR infusion and not by IV infusion (and persists few hrs. after IR infusion)

Targeted Renal Delivery



PROMISING !

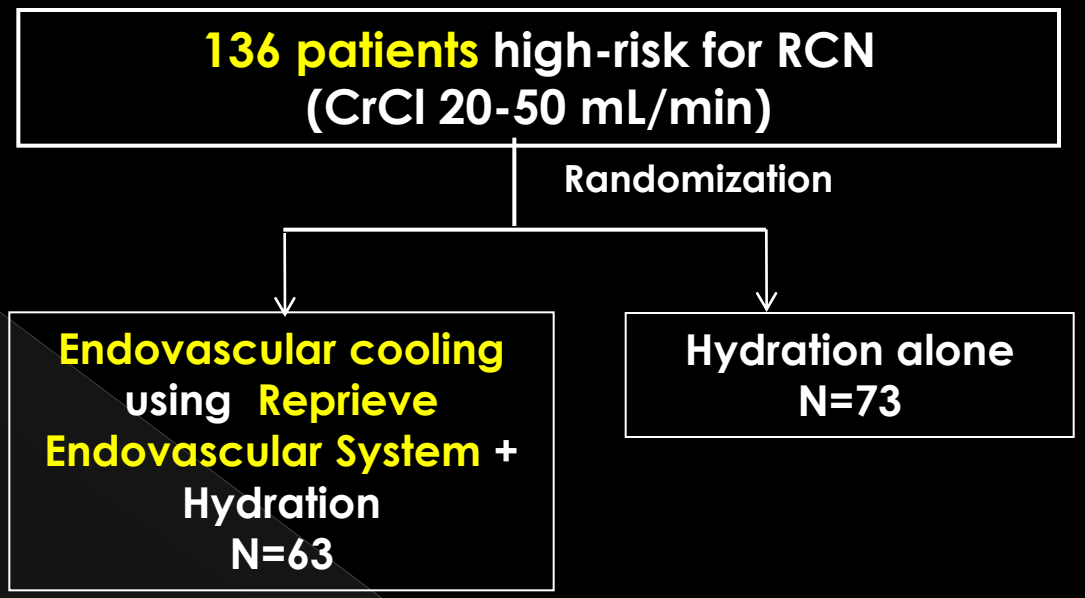
COOL-RCN:

Cooling to Prevent Radiocontrast Nephropathy

Design

Prospective, randomized, open label, active control, parallel assignment

OBJECTIVE: Evaluate whether endovascular cooling can reduce the incidence of CIN in high-risk patients undergoing diagnostic or interventional catheterization procedures

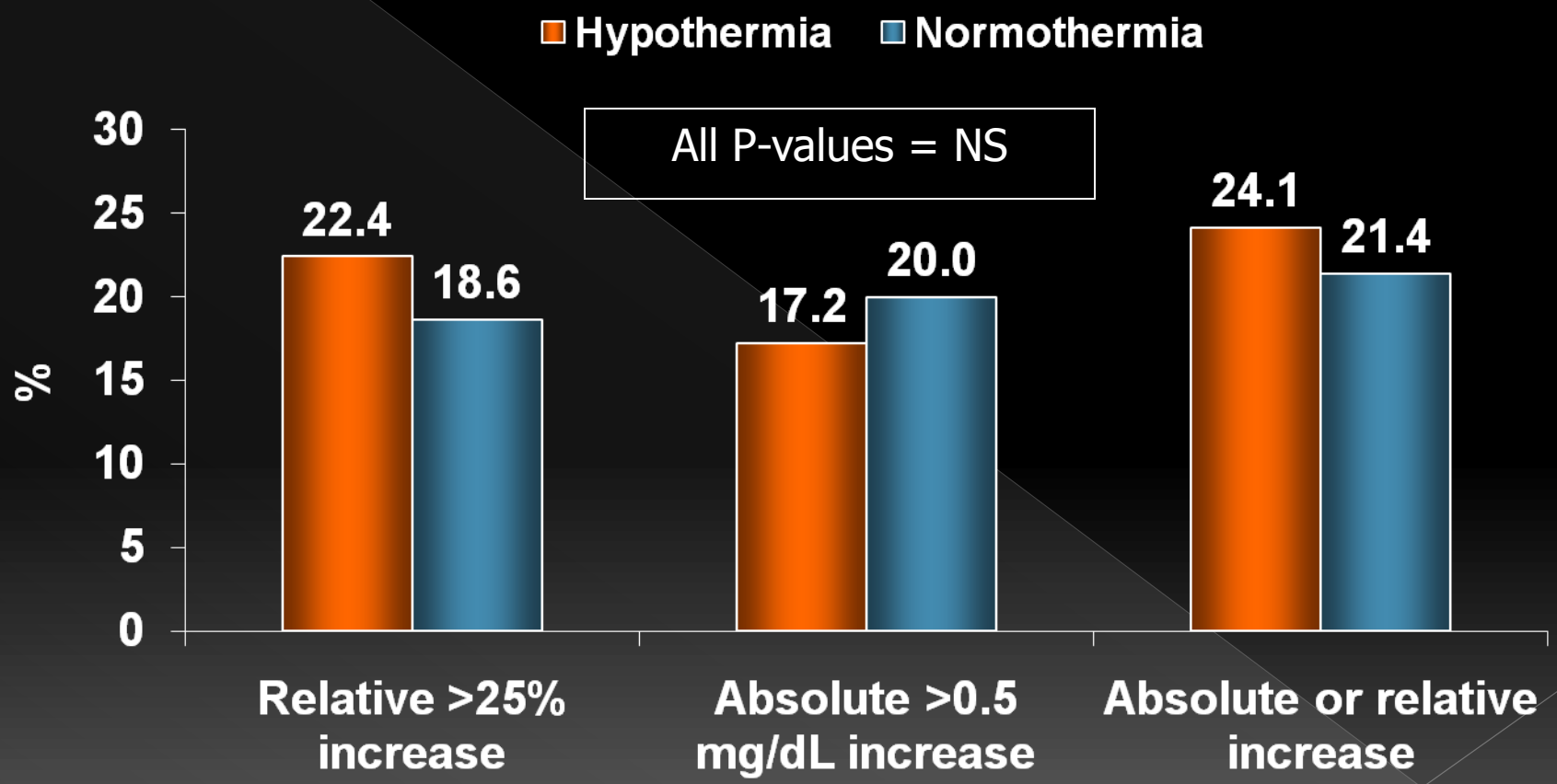


Primary endpoint: rates of CIN

Stone GW et al, TCT 2008

COOL-RCA: Results

Increase in SCr from baseline to 96 hours



Stone GW et al, TCT 2008

Conclusions (1)

- CKD is one of the most powerful predictors of poor outcome post PCI
- CIN remains a frequent source of acute renal failure and is associated with increased morbidity and mortality.
- Several patient and procedural factors predispose patients to CIN
- Preventive measures pre procedure, as well as careful post procedure management should be routine in all patients

Conclusions (2)

- Hydration 0.9 NS pre-cath (12 hours recommended).
- Hold nephrotoxic drugs (NSAIDS, antibiotics, etc)
- Role of N-acetylcysteine is disputable
- No role for IV Fenoldopam
- Sodium bicarbonate may be useful, but need more definitive data
- Limit contrast agent volume
- Low-osmolar agents are better than high-osmolar
- Within low or ISO osmolar, the data are contradictory
- Role of local drug delivery (e.g. Fenoldopam) for prevention of CIN requires further investigation
- No role of Cooling Therapy (COOL CIN Study)