Nefropatie da mezzo di contrasto: prevenzione

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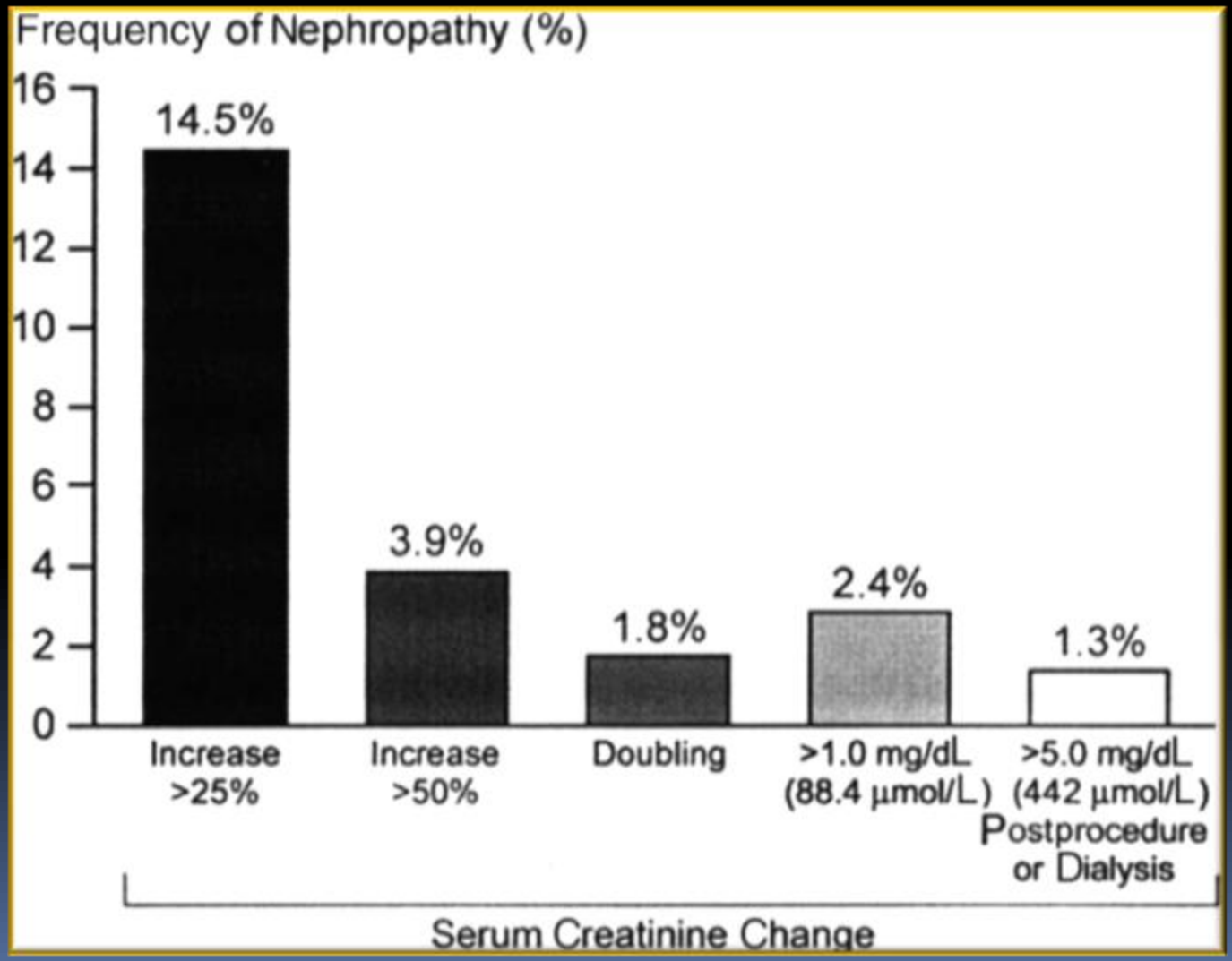
Definition

- An increase in serum creatinine generally occuring within 24hrs, peaking up to 5 days after, and returning to baseline within 3 weeks.

- Definition varies, increase in Cr of >25-50% from baseline and/or >0.5-1.0 mg/dL after 48-72 hrs.

Definition and frequency of CIN



Incidence

- CIN has decreased over the past decade from ~15% to ~7%

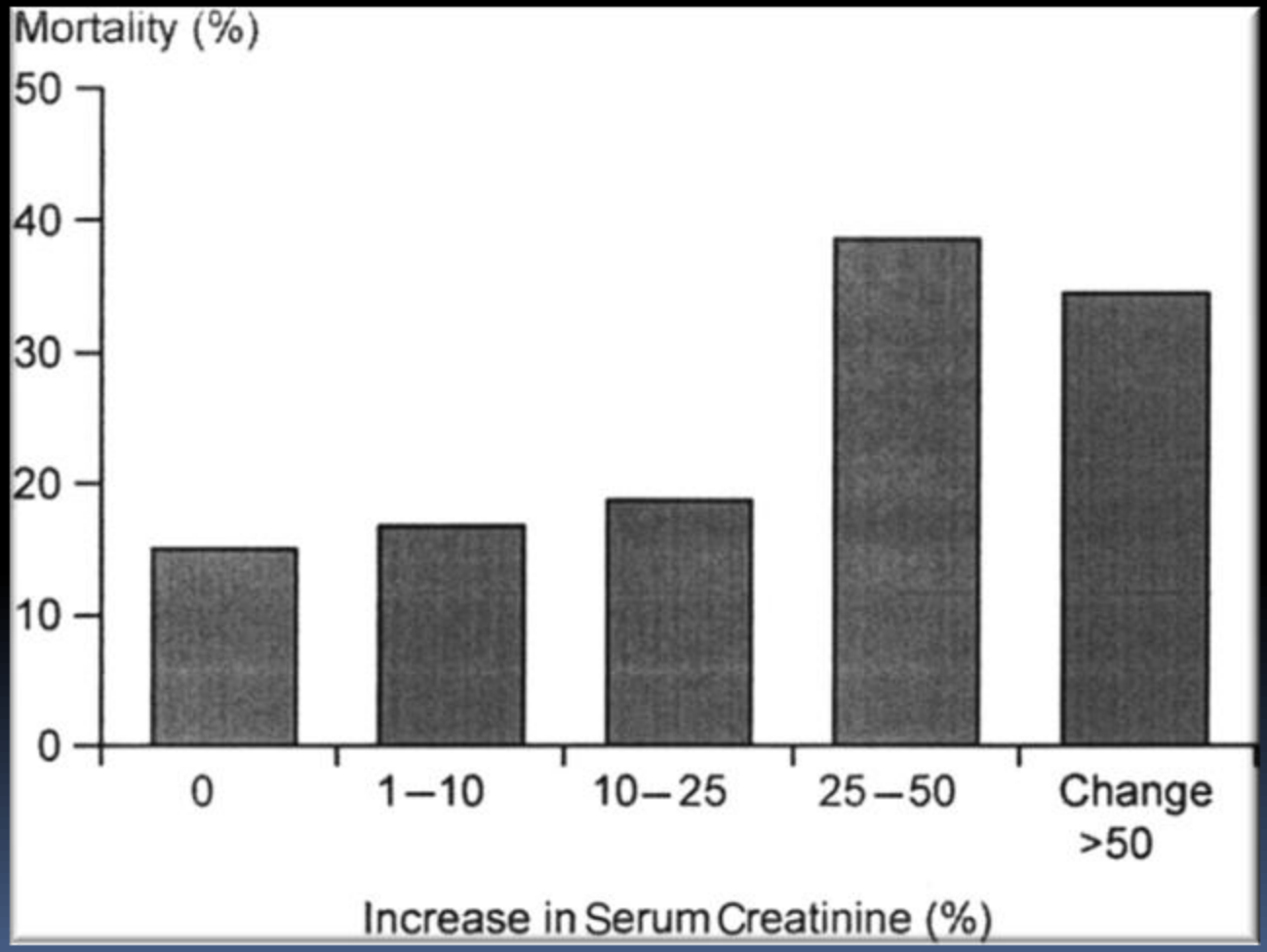
  (Nash et al. 4622 patients)

- Total number of cases did not decline due to increasing number of procedures requiring contrast

Impact

- CIN is the third most common cause of hospital acquired renal failure (after decreased renal perfusion and nephrotoxic medications), accounting for 11% of cases
- In-hospital mortality rate of CIN as high as 14%
- In patients with multiple risk factors, incidence of CIN can rise to 50% or greater

Creatinine rise and 1-year mortality

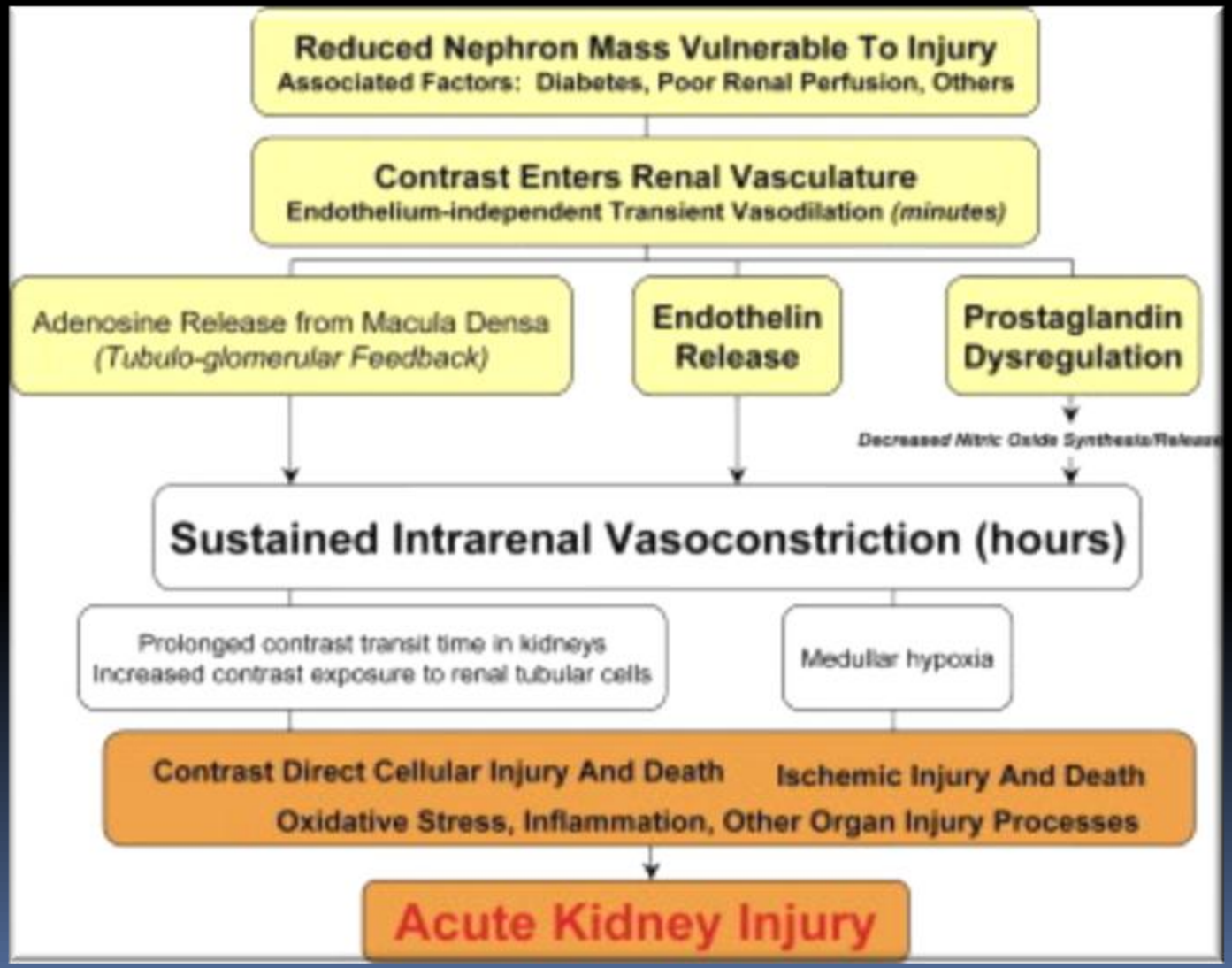


Clinical course and outcome

- CIN is associated with late cardiovascular events
  - AMI 24% vs. 11.6% (Lindsay et al. 2003);
  - TVR at 1 year 28.8% vs. 20.3%
  - CIN + CKMB rise $\longrightarrow$ 26% 1 year risk for death or MI (Lindsay et al. 2004)

- Higher incidence of in-hospital events with CIN
  - CABG
  - Bleeding requiring transfusion
  - Vascular complications
  - Longer hospital stay

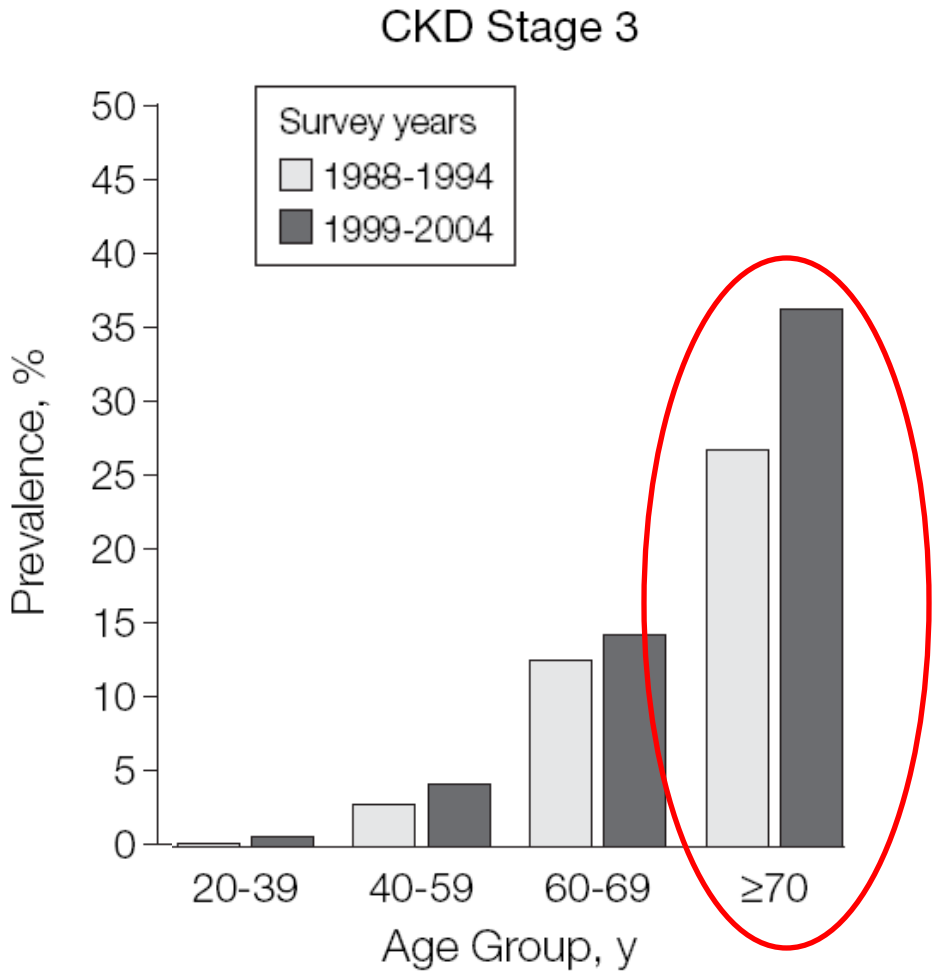
Postulated Pathophysiology of CIN



Effects of Aging on the Kidney

- Decreased kidney size
- Decreased renal blood flow
- Decreased number of functional nephrons
- Decreased tubular secretion
- Result: ⇓ glomerular filtration rate (GFR)

Prevalence of Chronic Kidney Disease in the U.S

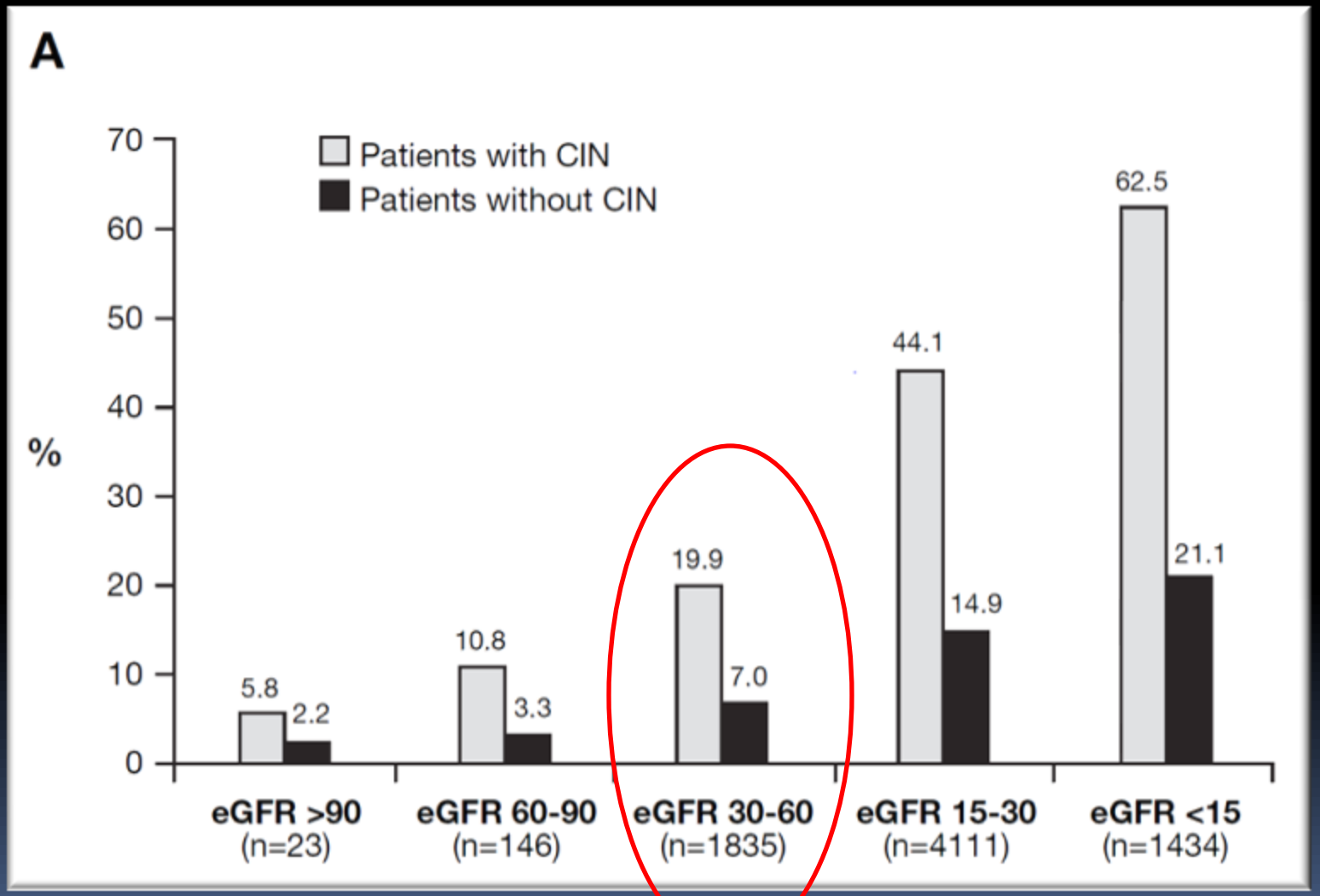


Stage 3:

GFR of 30 to 59 mL/min/1.73m2

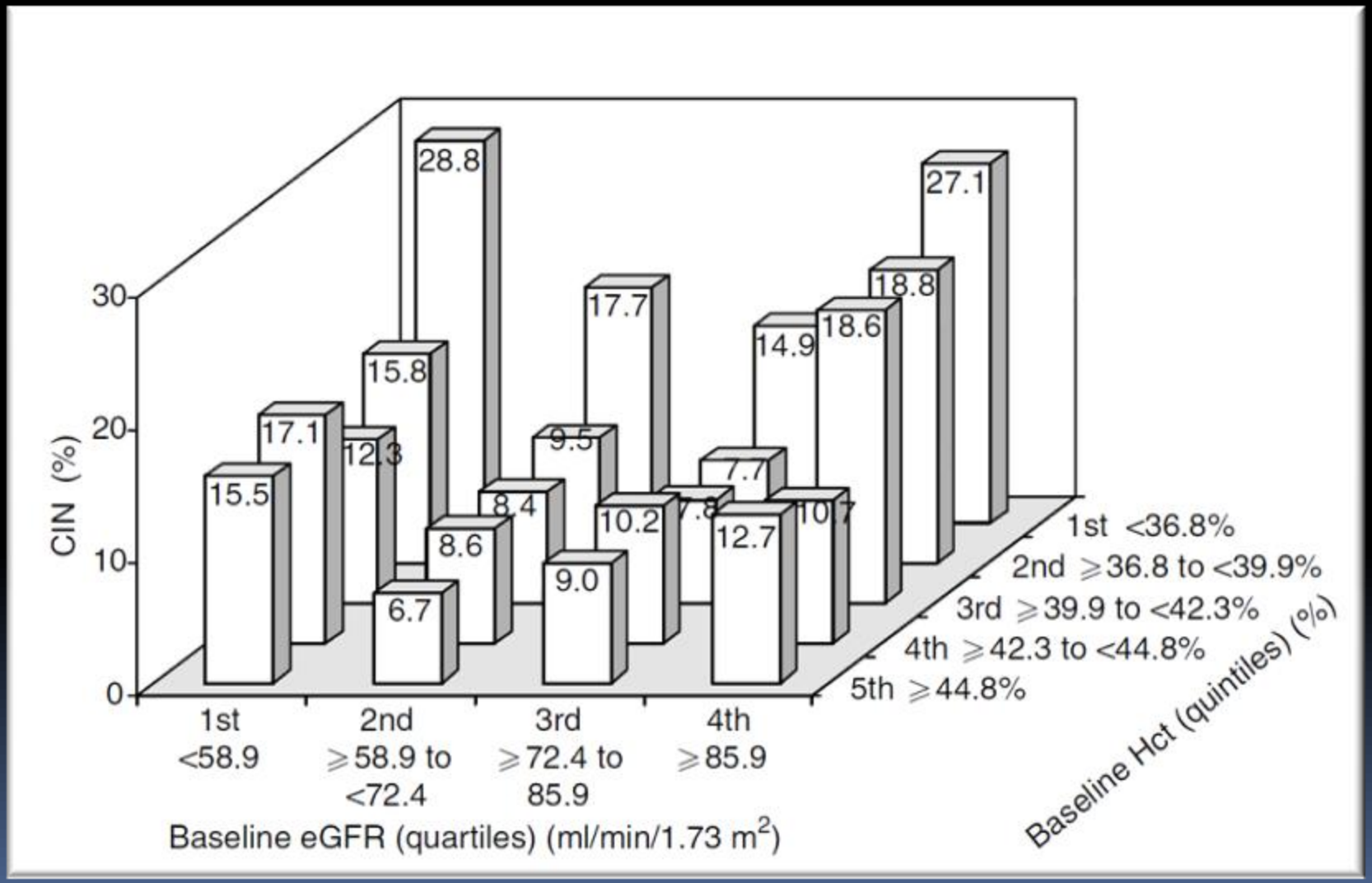
JAMA 2007, vol 298, No.17

One-year mortality stratified by baseline estimated GFR in pts with or without CIN.



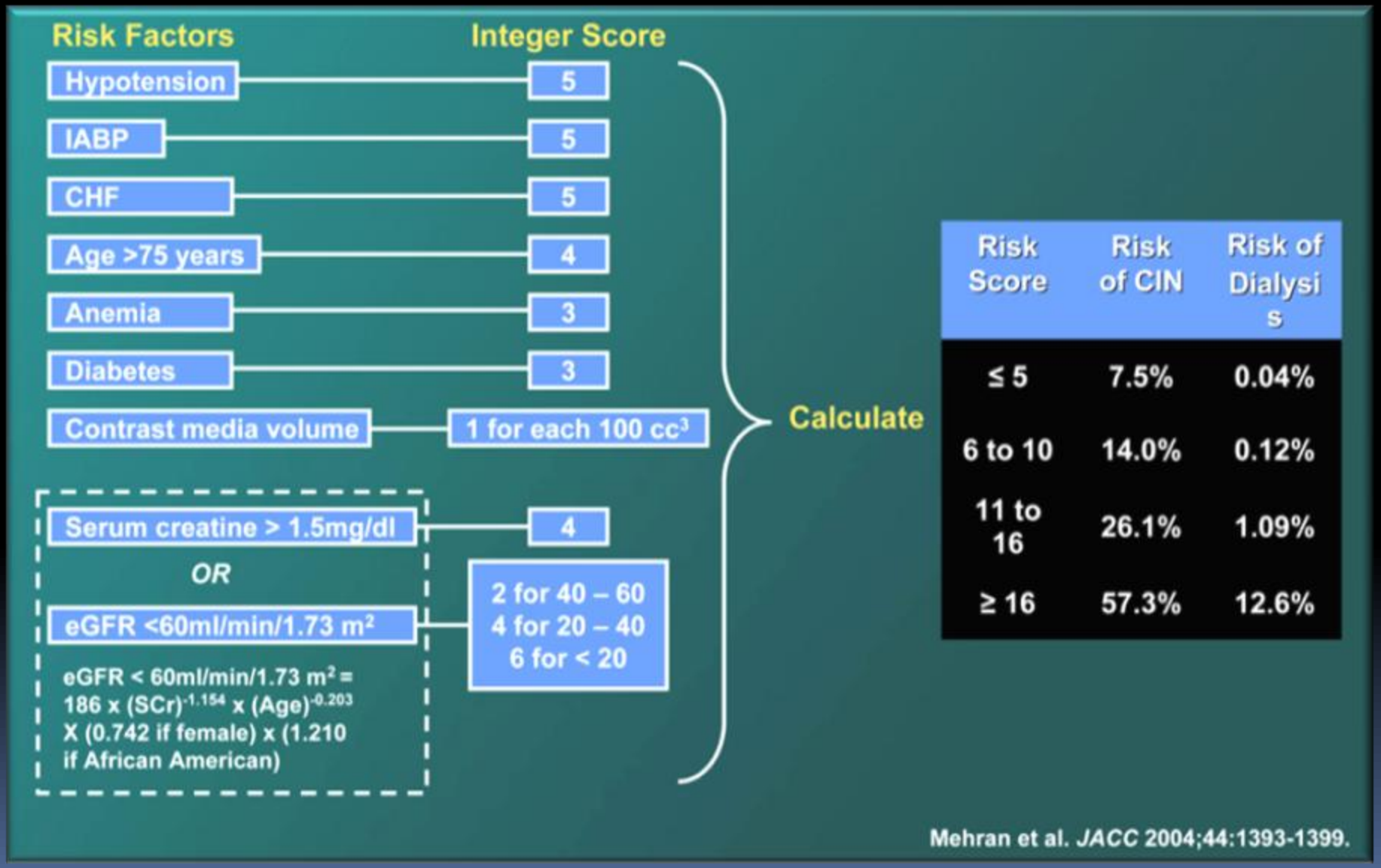
Rudnick M, *Clin J Am Soc Nephrol 2008*

Risk of CIN in relation to baseline hematocrit and eGFR

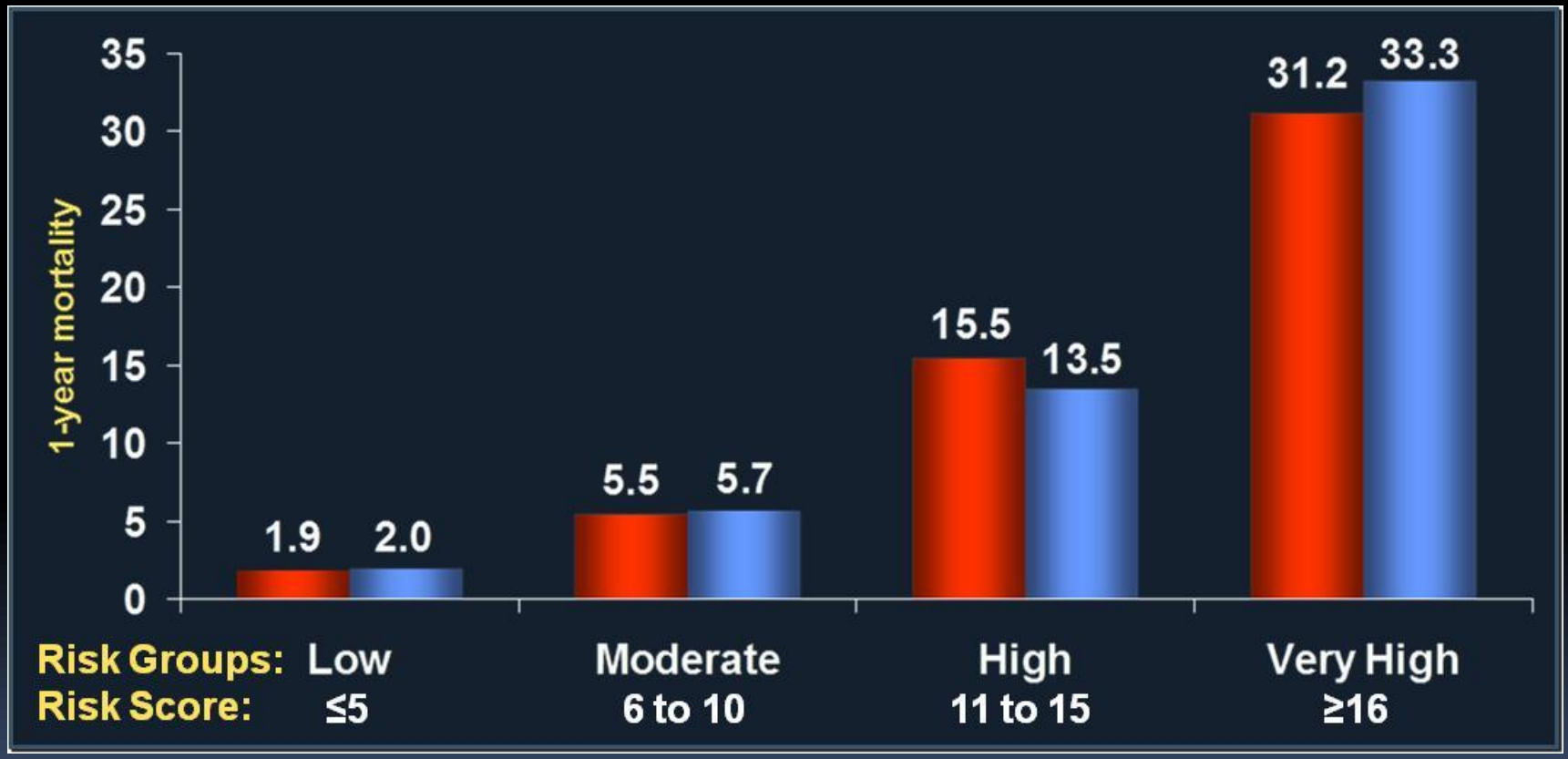


Mehran et al. Kidney International 2006

CIN Mehran Risk Score



CIN Risk Score & 1-year Mortality



Mehran et al. *JACC* 2004

Risk reduction strategies

- Contrast
- IVF
- $NaHCO_3$
- N-Acetylcysteine
- Ascorbic acid
- Statin
- ACEi
- Theophyllin/aminophylline
- Diuresis
- Dopamine/Fenoldopam
- Prostaglandin/prostacyclin
- ANP
- Mechanical (HD, hemofiltration, RenalGuard)

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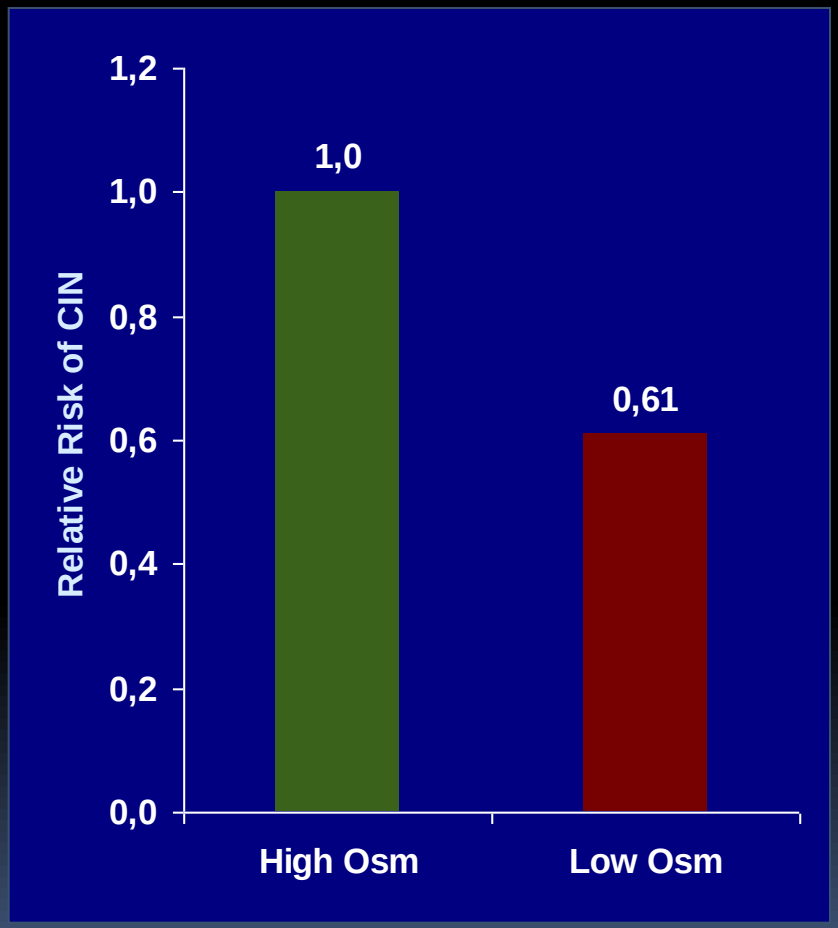
Meta-analysis: High vs Low Osm Contrast Media

- 39 Trials - 5146 patients
- CIN > 0.5 mg/dl
- CIN in 7% of all patients
- CIN in 30% of CRI patients
- For CRI, NNT=8 (treat 8 to prevent 1 CIN case)
- Low osmolal group included Ioxaglate (Hexabrix); Iodixanol (Visipaque) not studied

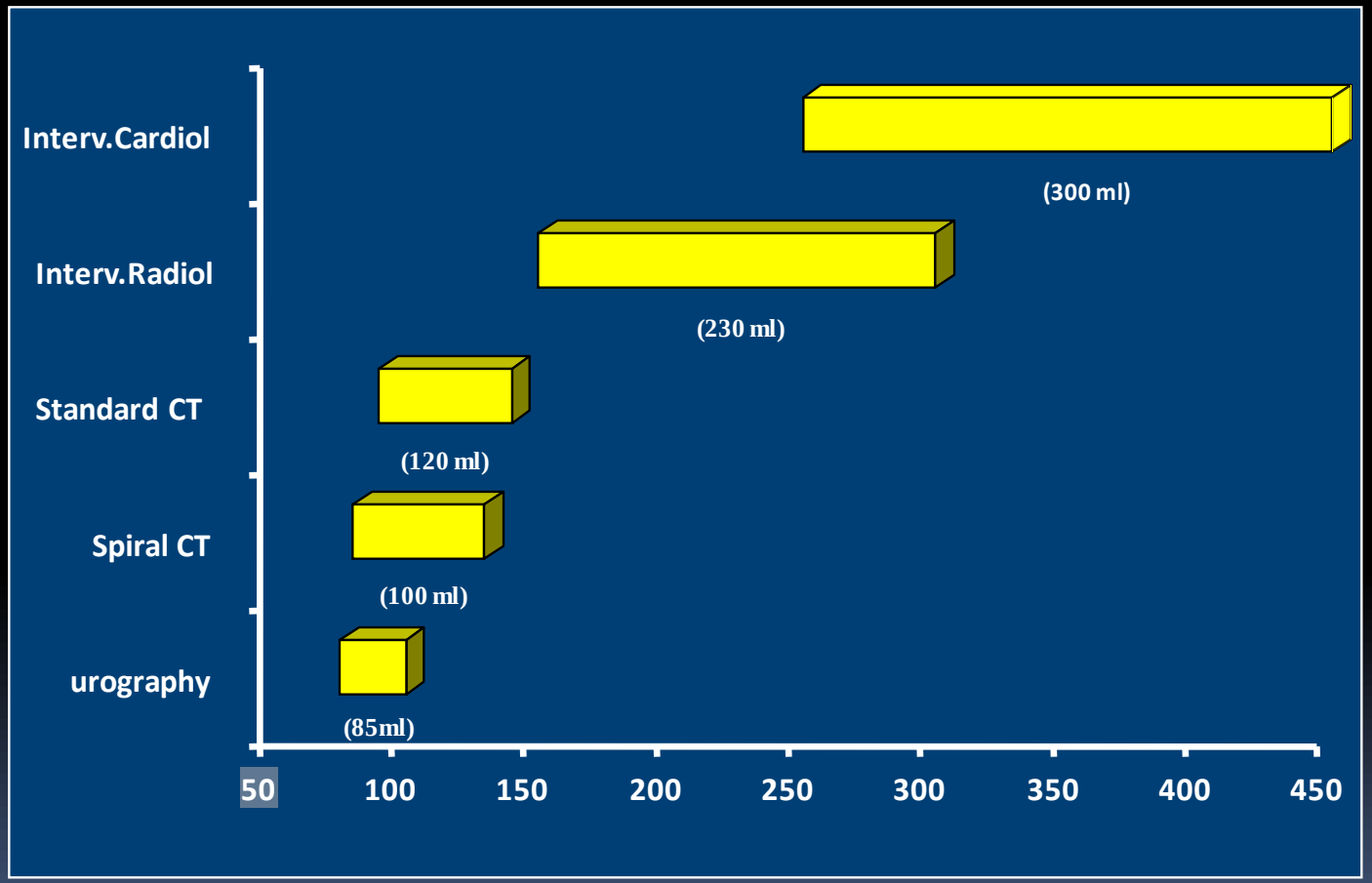


Barrett and Carlisle J Am Soc Nephrol 1992

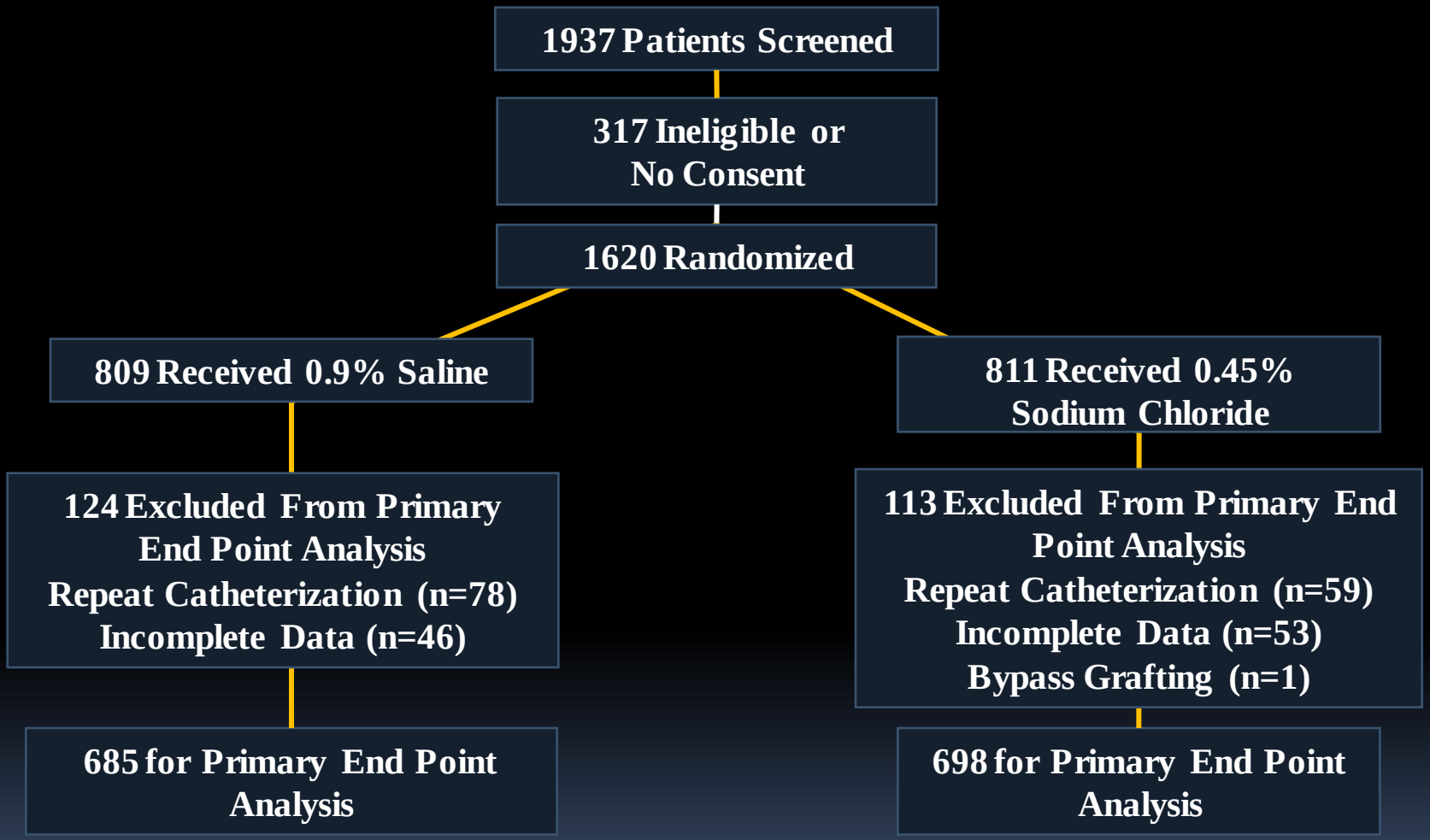
Contrast

- LOCM vs. IOCM- meta-analysis of 16 studies with 2763 patients: no difference when IOCM compared to LOCM collectively
- Contrast volume is independent predictor for CIN.
- CIN consensus panel: >100 ml of contrast is associated with higher incidence of CIN, but there is no threshold amount
- Intra-arterial administration is associated with higher rate of CIN

Contrast Volume in Different Diagnostic and Interventional Procedures



Optimal Hydration Regimen



Mueller et al Arch Intern Med 2002

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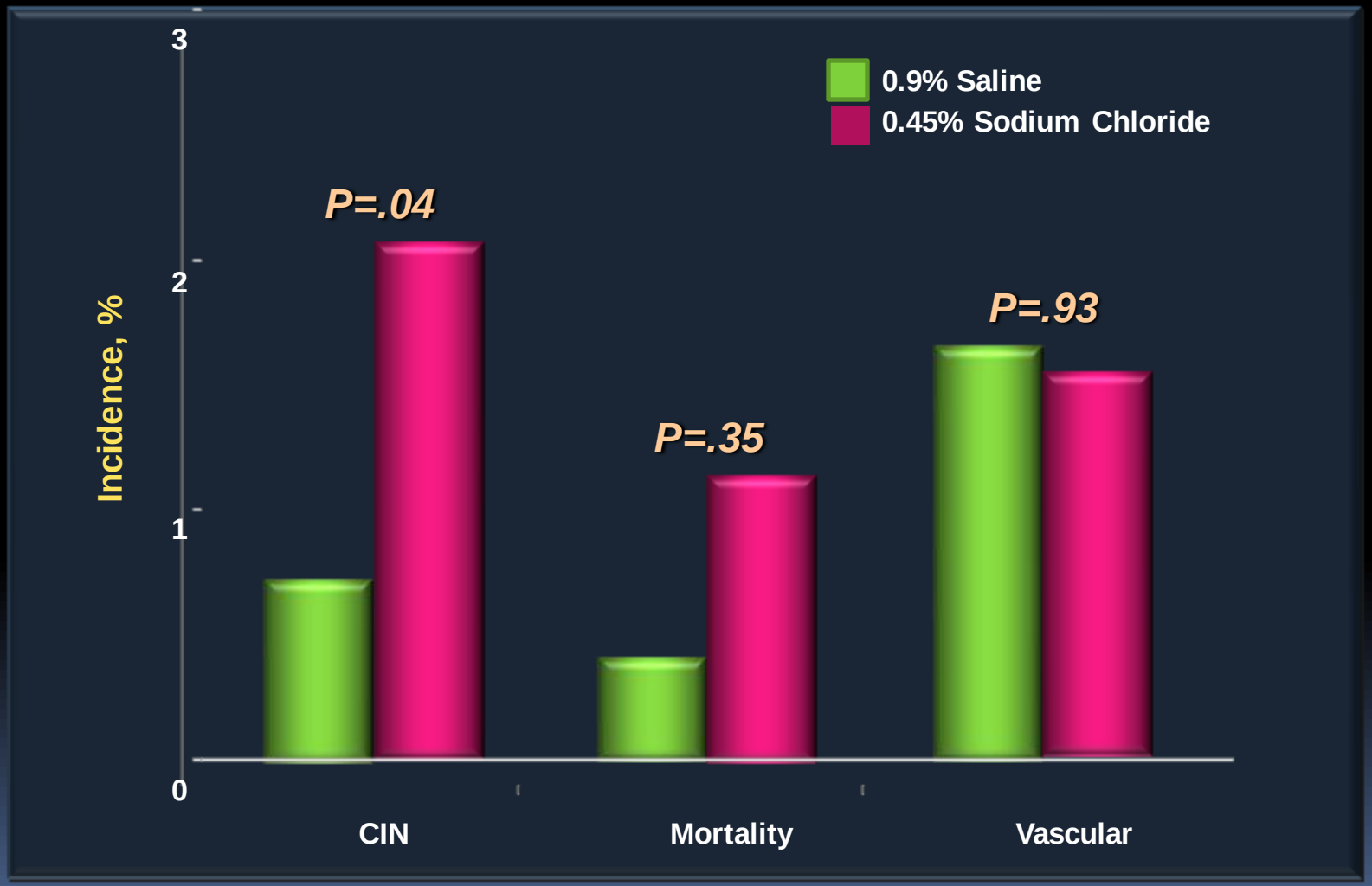


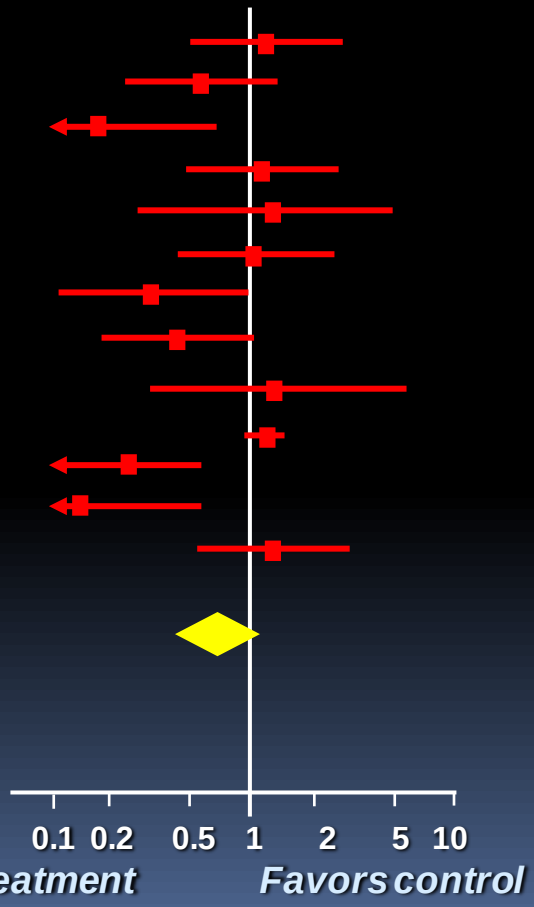
Mueller et al Arch Intern Med 2002

Sodium Bicarbonate

Study	N (Saline, Bicarb)	Procedure	Baseline Function (mL/min/1.73m2)	Fluid protocol	CIN rate (%)	p
RANDOMIZED						
Brar	353 (175, 178)	Cardiac	48 48	Saline Bicarbonate	13.6 13.5	0.97
Briguori	219 (108, 111)	Cardiac Peripheral	32 35	Saline Bicarbonate	9.9 1.9	0.02
Merten	119 (59, 60)	Cardiac Peripheral	45 41	Saline Bicarbonate	13.7 1.7	0.02
Masuda*	59 (29, 30)	Emergency cardiac	39 40	Saline Bicarbonate	35 7	0.01
NON-RANDOMIZED						
CARE	414 (246, 168)	Cardiac	50 50	Bicarbonate (-NAC) Bicarbonate (+NAC)	10.6 11.9	NS

N- acetylcysteine (NAC) and Contrast-induced Nephropathy: a Meta-analysis of 13 Randomized Placebo Controlled Trials

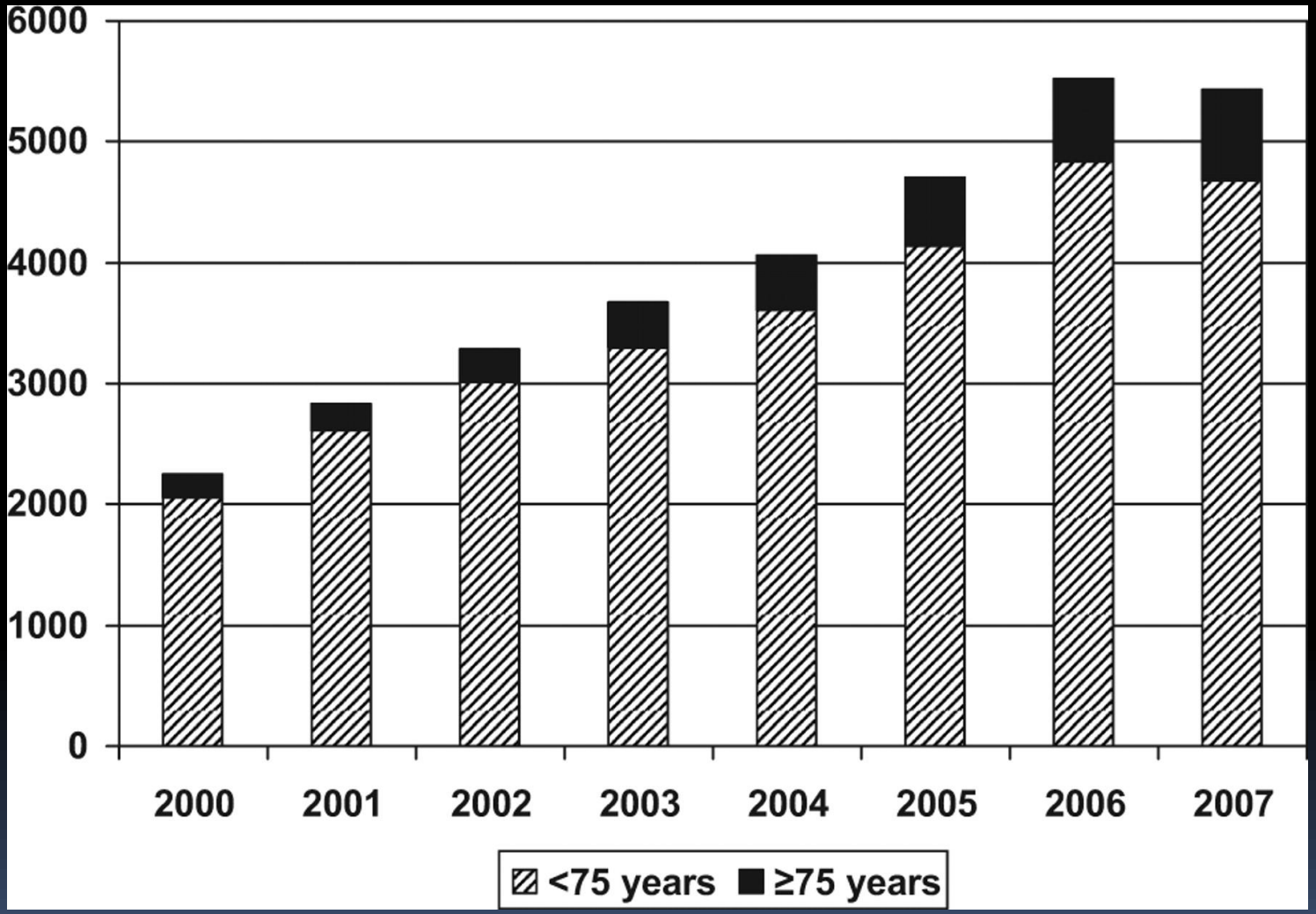
Study or substudy	NAC n/N	Control n/N	RR (Random) 95% CI	Risk Ratio (Random) 95% CI
Allaqaband et al	8/45	6/40		1.19 (0.45, 3.12)
Briguori et al	6/92	10/91		0.59 (0.23, 1.57)
Diaz-Sandoval et al	2/25	13/29		0.18 (0.04, 0.72)
Durham et al	10/38	9/41		1.20 (0.55, 2.63)
Goldenberg et al	4/41	3/39		1.27 (0.30, 5.31)
Gomes et al	8/78	8/78		1.00 (0.40, 2.53)
Kay et al	4/102	12/98		0.32 (0.11, 0.96)
Nguyen-Ho et al	9/95	19/85		0.42 (0.20, 0.89)
Oldemeyer	4/49	3/47		1.28 (0.30, 5.41)
Pate et al	57/238	50/239		1.14 (0.82, 1.60)
RAPIDO	2/41	8/39		0.24 (0.05, 1.05)
Shyu	2/60	15/61		0.14 (0.03, 0.57)
Fung et al	8/46	6/45		1.30 (0.49, 3.46)
Total: (95% CI)	950	932		0.68 (0.46, 1.02)



Total events: 124 (NAC), 162 (Control)
Test for heterogenety: Ch=27.54 (P0.005), I^2=56.4%
Test for overall effect: Z=1.88 (*P=0.05*)

Waiting for a more appropriate prevention strategy in the real world of an ageing population

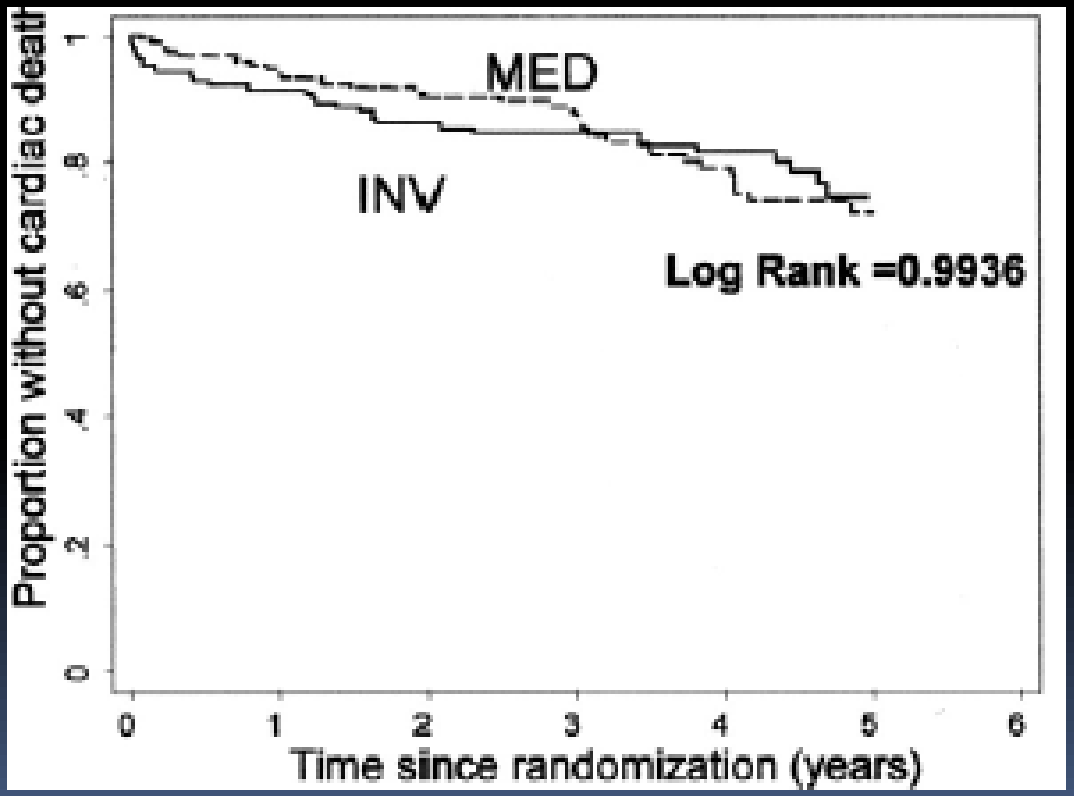
Numbers of nonemergency PCIs per annum by age group.



Johnman C et al. Circ Cardiovasc Interv 2010

A Randomized Trial of Invasive vs Medical Therapy in Elderly Pts with Chronic Symptomatic Coronary Artery Disease (TIME)

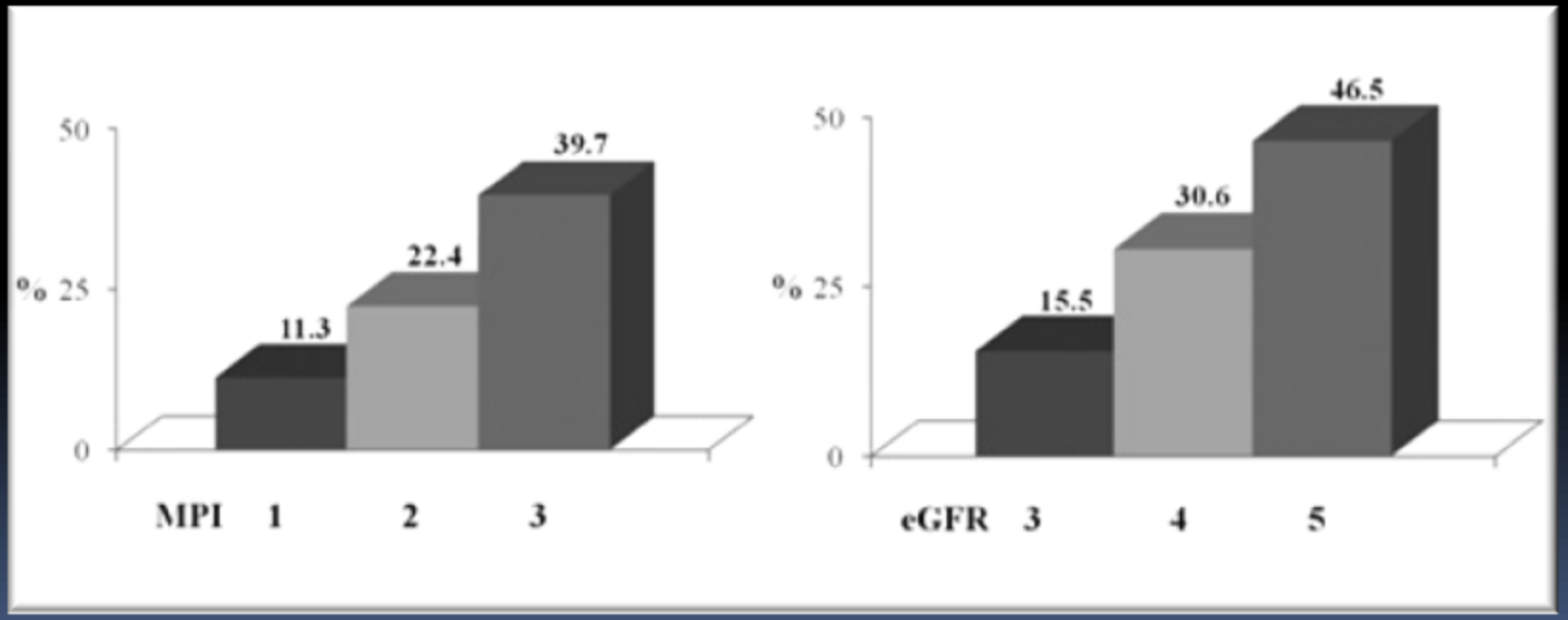
- N. 305 pts older than 75 yrs



Pfisterer et al. Circulation 2004

Multidimensional prognostic index (MPI) in the management of older patients with chronic kidney disease

Mortality incidence for 100 person-years in 1198 older CKD patients



Pilotto A, J Nephrol 2012

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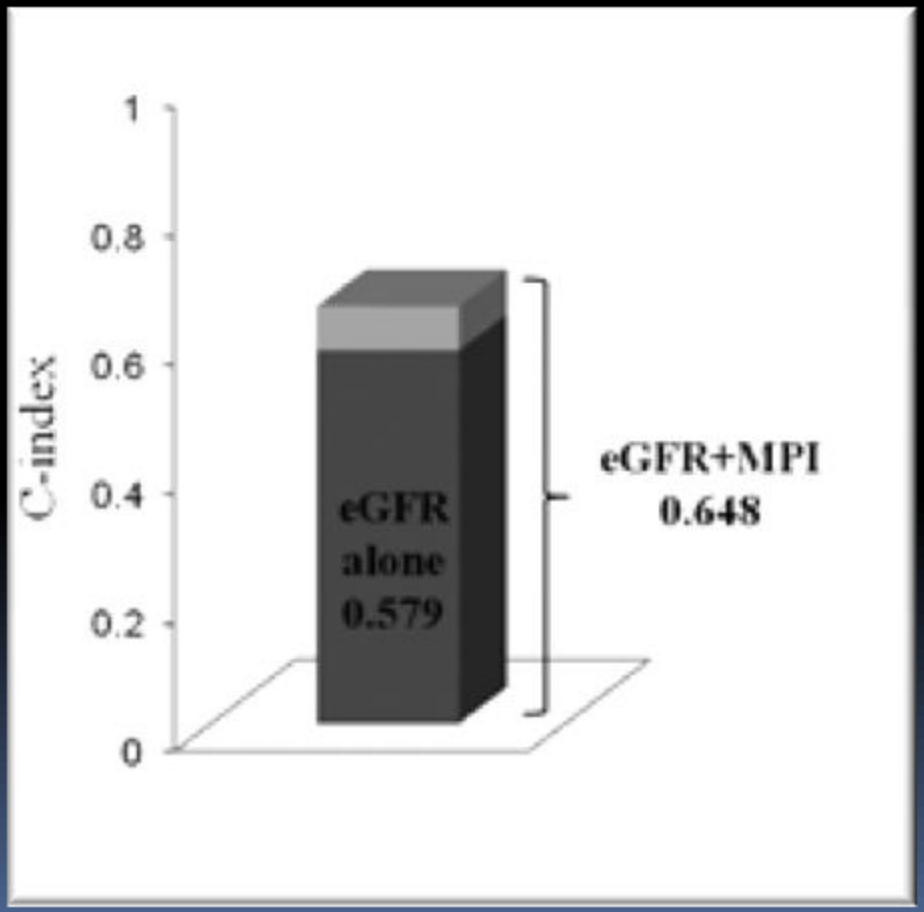

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Conclusions

- The discussion of the clinical importance of CIN invokes polarized opinions
- Some experts argue that CIN is a laboratory- defined outcome with minimal biologic significance
- Although there is no evidence of a causal relationship or that reducing CIN improves overall outcome, CIN is associated with worse outcomes in pts with CKD
- Elderly pts (over 75yrs) are at high risk of CIN even in the presence of low comorbidity

General Guidelines for all patients with GFR <= 40 mL/min:

- Consider alternative imaging studies
- Contrast volume is minimized per standard protocols.
- Avoid repeat contrast studies within 24 hours.

GFR < 30 mL/min
High risk for CIN
Consider alternative study

- IV 0.9% Saline
- FU GFR in 48 hours

GFR 30-40mL/min
Low to Moderate risk for CIN

- Inpatient - IV 0.9% Saline
- Outpatient-
  - IV 0.9% Saline or
  - Oral hydration

GFR > 40 mL/min
Very Low risk for CIN

- Proceed with examination

Peri-Procedural Fluid Administration Protocols

Intravenous:
IV 0.9% saline at 100 ml/hr 6 to 12 hours before and 4 to 12 hours after CM.

Oral hydration: Liberal fluids the day before and up to 2 hours before CM and immediately following CM.