Acute Kidney Injury

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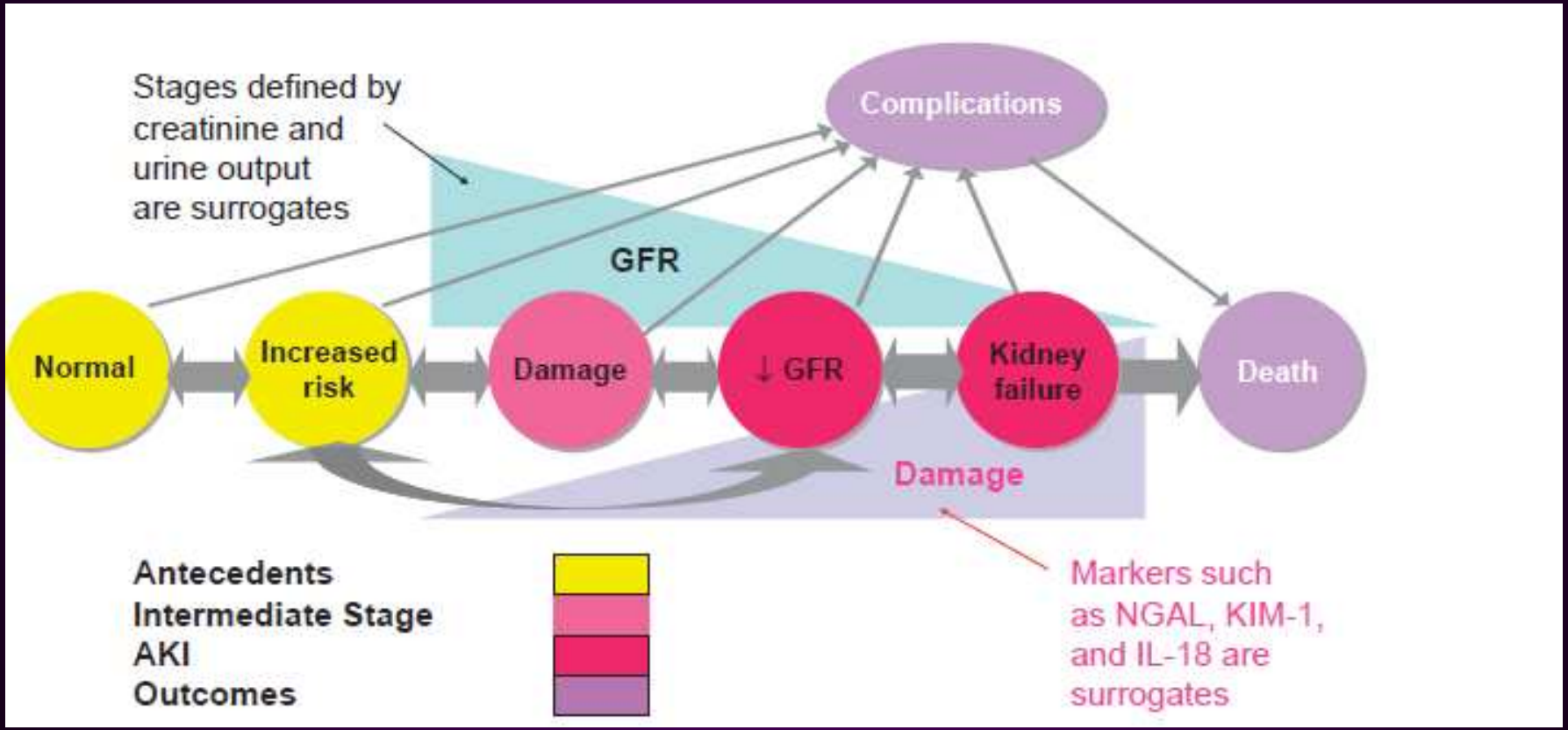
Acute Kidney Injury AKI

Acute Renal Failure ARF

Conceptual model of AKI



Outlines

- Diagnosis of AKI
- GFR measurement
- Epidemiology of AKI
- Prevention and treatment of AKI
- Prognosis after AKI

Definition of AKI

AKI is defined as any of the following (Not Graded):

- Increase in SCr by ≥0.3 mg/dl within 48 hours; or
- Increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume < 0.5 ml/kg/h for 6 hours.

KDIGO Clinical Practice Guideline for Acute Kidney Injury

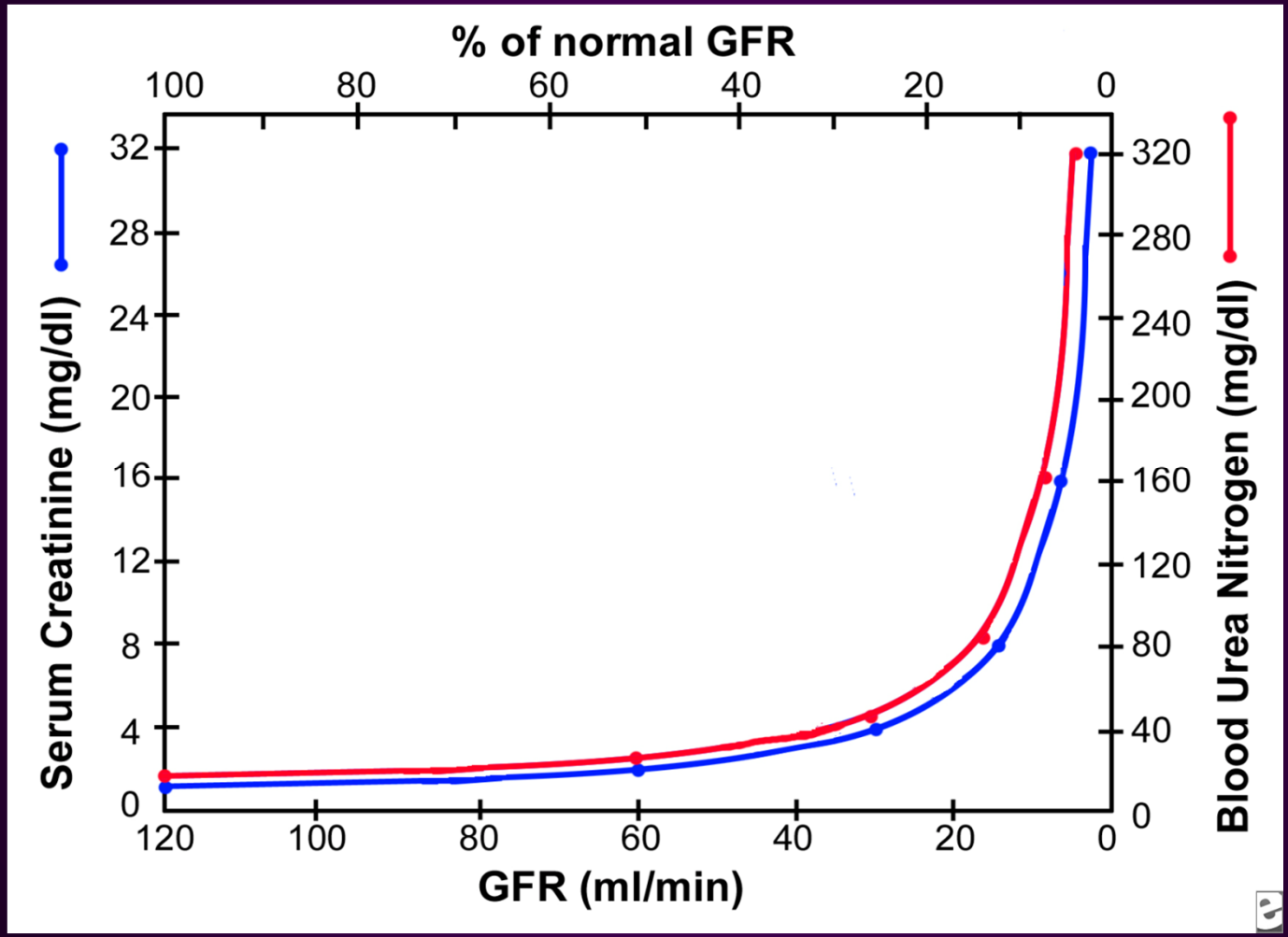
Kidney International 2012

Staging of AKI

Stage	Cr Criteria	Urine output Criteria
1	Cr↑by 1.5-1.9x baseline or Cr↑by 0.3 mg/dl	< 0.5 ml/kg/hr for 6-12 hr
2	Cr↑by 2-2.9x	< 0.5 ml/kg/hr for ≥12hr
3	Cr↑by more than 3x or Cr↑ to ≥4mg/dl or Initiation of RRT	< 0.3 ml/kg/hr for ≥ 24hr Or anuria for ≥ 12h

GFR measurement

Limitations of SCr



Dennen P, Douglas I, Anderson R,: Acute Kidney Injury in the Intensive Care Unit: An update and primer for the Intensivist. *Critical Care Medicine* 2010; 38:261-275.

How to assess GFR?

- Measured GFR
- Estimating GFR

GFR Measurement

Gold standard

- Inulin

Alternative

- Iothalamate
- Iohexol
- DTPA
- EDTA

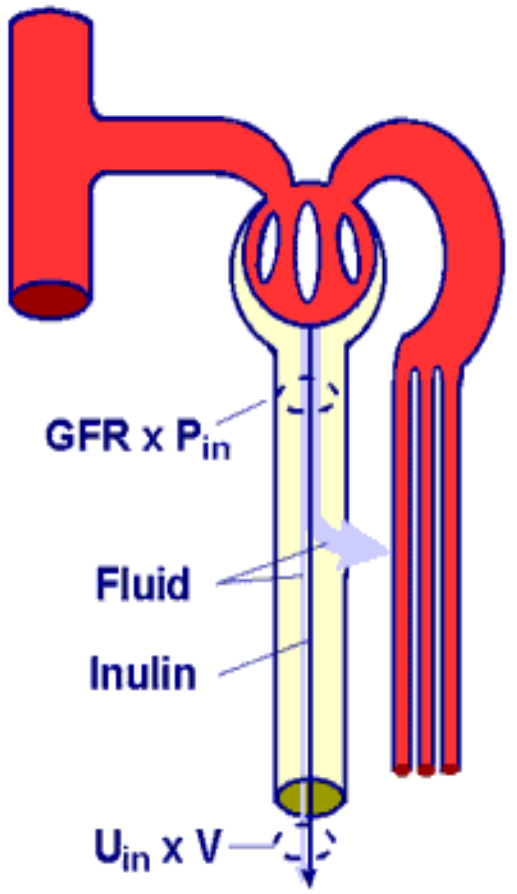
MEASUREMENT OF FILTRATION RATE

Amount entering = Amount leaving

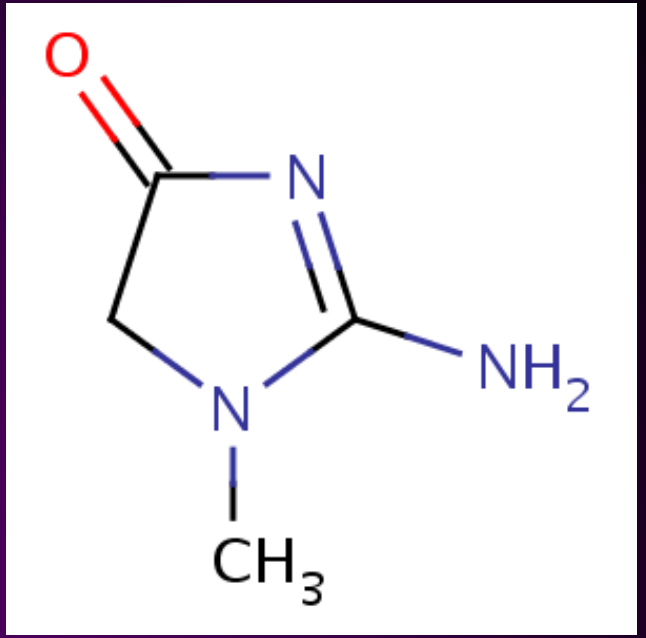
$GFR \times P_{in} = U_{in} \times V$ Eq. 3

$GFR = U_{in}V / P_{in}$ Eq. 4

Units are ml/min



Creatinine clearance



- Derived from the metabolism of creatine in skeletal muscle and from dietary meat intake .
- It is released into the circulation at a relatively **constant rate**.
- Creatinine is **freely filtered** across the glomerulus and is **neither reabsorbed nor metabolized** by the kidney.
- Approximately 10 to 40% of urinary creatinine is derived from **tubular secretion**.

Measured creatinine clearance

If the effect of secretion is ignored.

All of the filtered creatinine = All of the excreted creatinine

$$GFR \times SCr = UCr \times V$$

$$GFR = [UCr \times V]/SCr$$

Limitation of creatinine clearance

- Incomplete urine collection
- Increasing creatinine secretion
  - The rise in the SCr is partially opposed by enhanced creatinine secretion.
  - In CKD, creatinine excretion is much greater than the filtered load, resulting in a potentially large overestimation of the GFR.

Estimating GFR (eGFR)

Cockcroft-Gault equation

eGFR = [(140 – age) x weight (kg)]/SCr x 72
x [0.85 if female]
and adjusted for BSA of 1.73 m^2

IDMS-traceable MDRD

175 x SCr (exp[-1.154]) x Age (exp[-0.203]) x
(0.742 if female) x (1.21 if black)

Creatinine based eGFR

CKD-EPI

$GFR = 141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa,1)^{-1.209} \times 0.993^{Age}$
$\times 1.018$ [if female] $\times 1.159$ [if black]

κ is 0.7 for females and 0.9 for males, α is –0.329 for females and –0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1

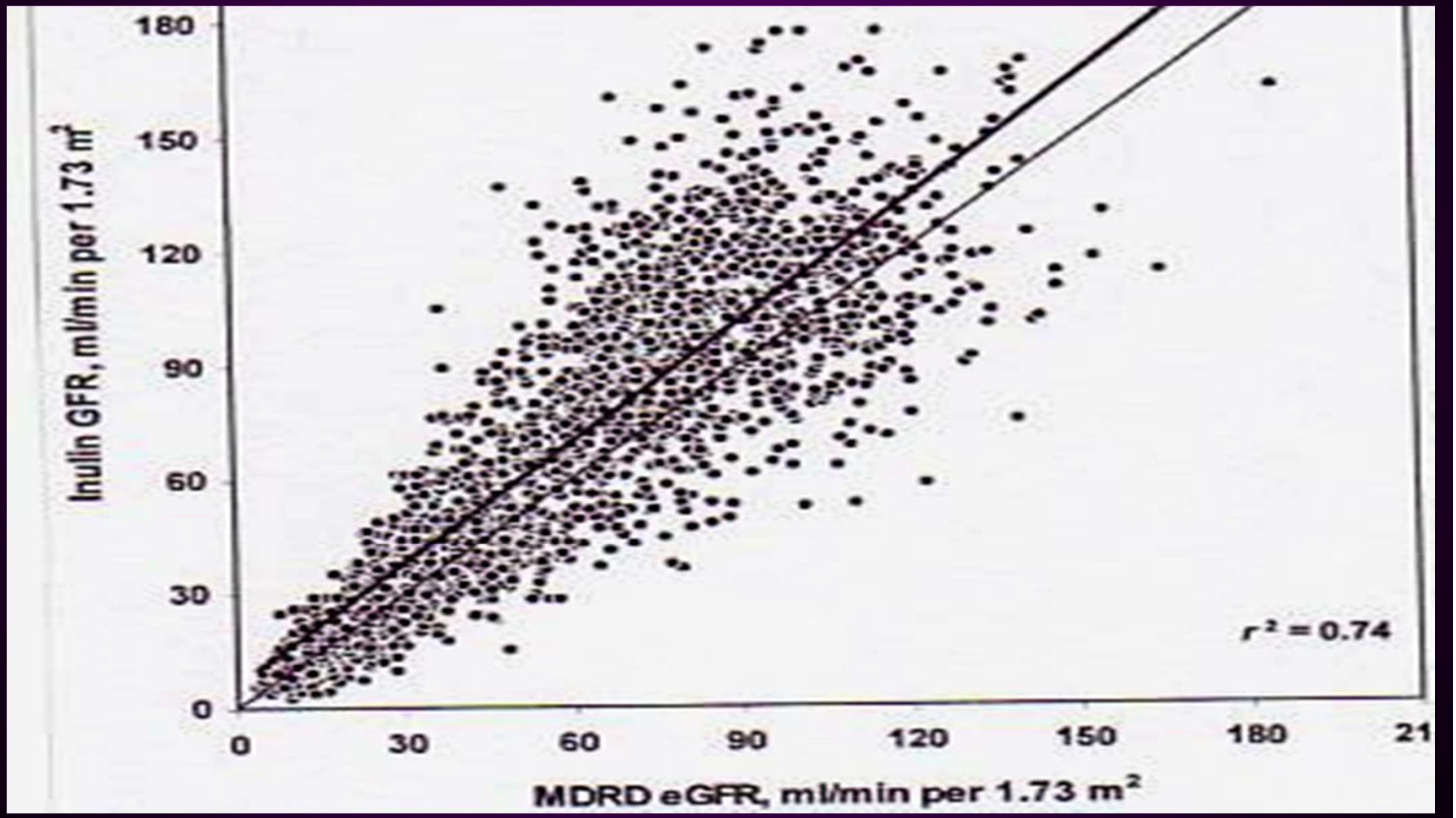
Thai eGFR

The reexpressed MDRD with Thai racial factor correction

$175 \times Cr_{Enz}^{(-1.154)} \times Age^{(-0.203)} \times 0.742$ (if female)
$\times 1.129$ (if Thai)

eGFR (MDRD) vs mGFR (Cin)

(Botev, et al, CJASN, 2009)



Serum creatinine measurement

- Alkaline picrate method: Modified Jaffe reaction
    - Colorimetric method
    - Interfere by Glucose, acetoacetate, proteins
- Enzymatic method:
    - Reagent for the enzymatic determination of creatinine with automated chemistry analyzers (creatinase)
- High-performance liquid chromatography (HPLC)
- MS-based procedure:
    - Gas chromatrography/isotope dilution mass spectrometry (GS/IDMS)

How to assess GFR?

Estimated GFR does not reflect measured GFR in AKI as accurately as in CKD.

Epidemiology of AKI

Epidemiology

AKI occurs in

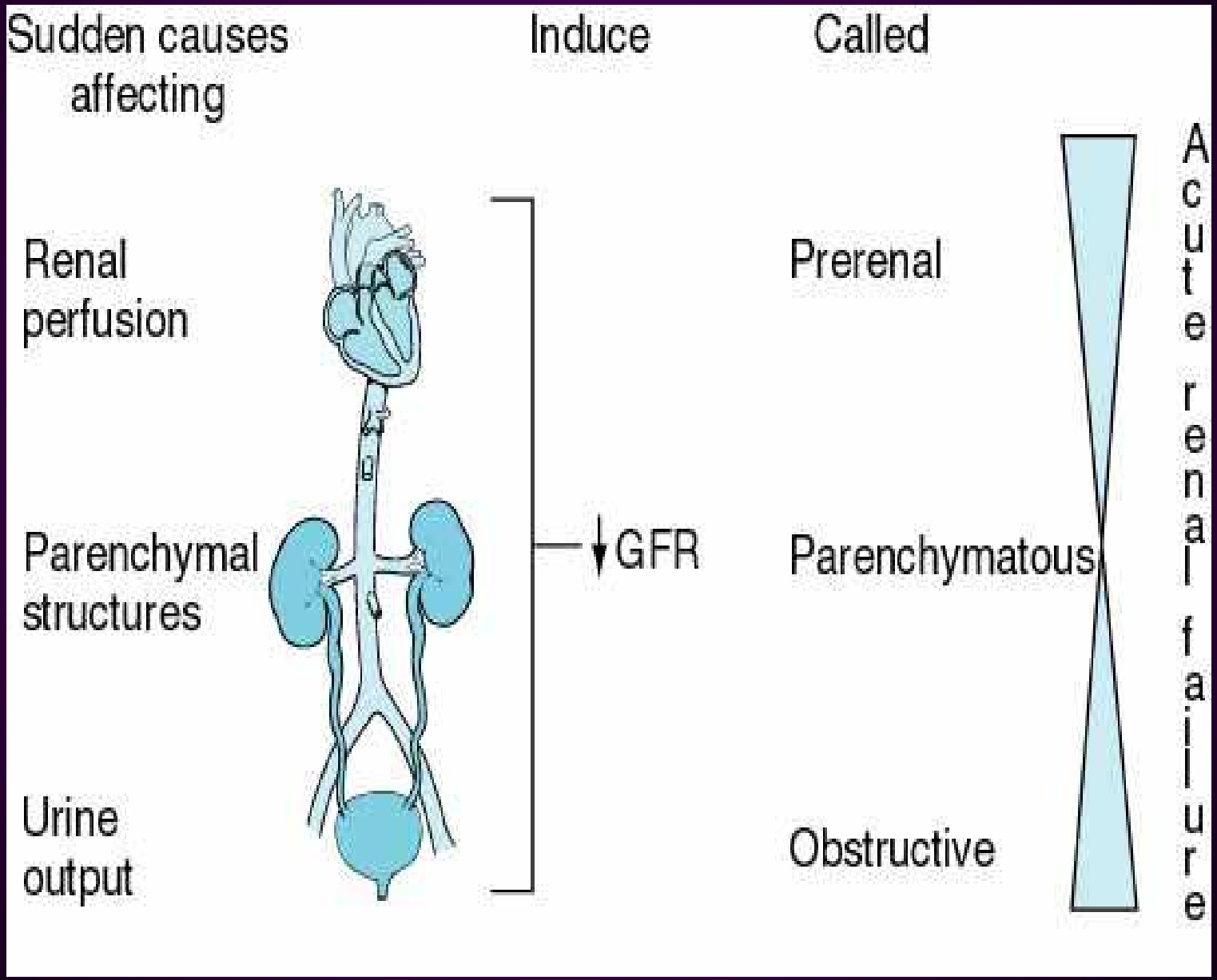
- ≈ 7% of hospitalized patients.
- 36 – 67% of critically ill patients (depending on the definition).
- 5-6% of ICU patients with AKI require RRT.

Nash K, Hafeez A, Hou S: Hospital-acquired renal insufficiency. *American Journal of Kidney Diseases* 2002; 39:930-936.

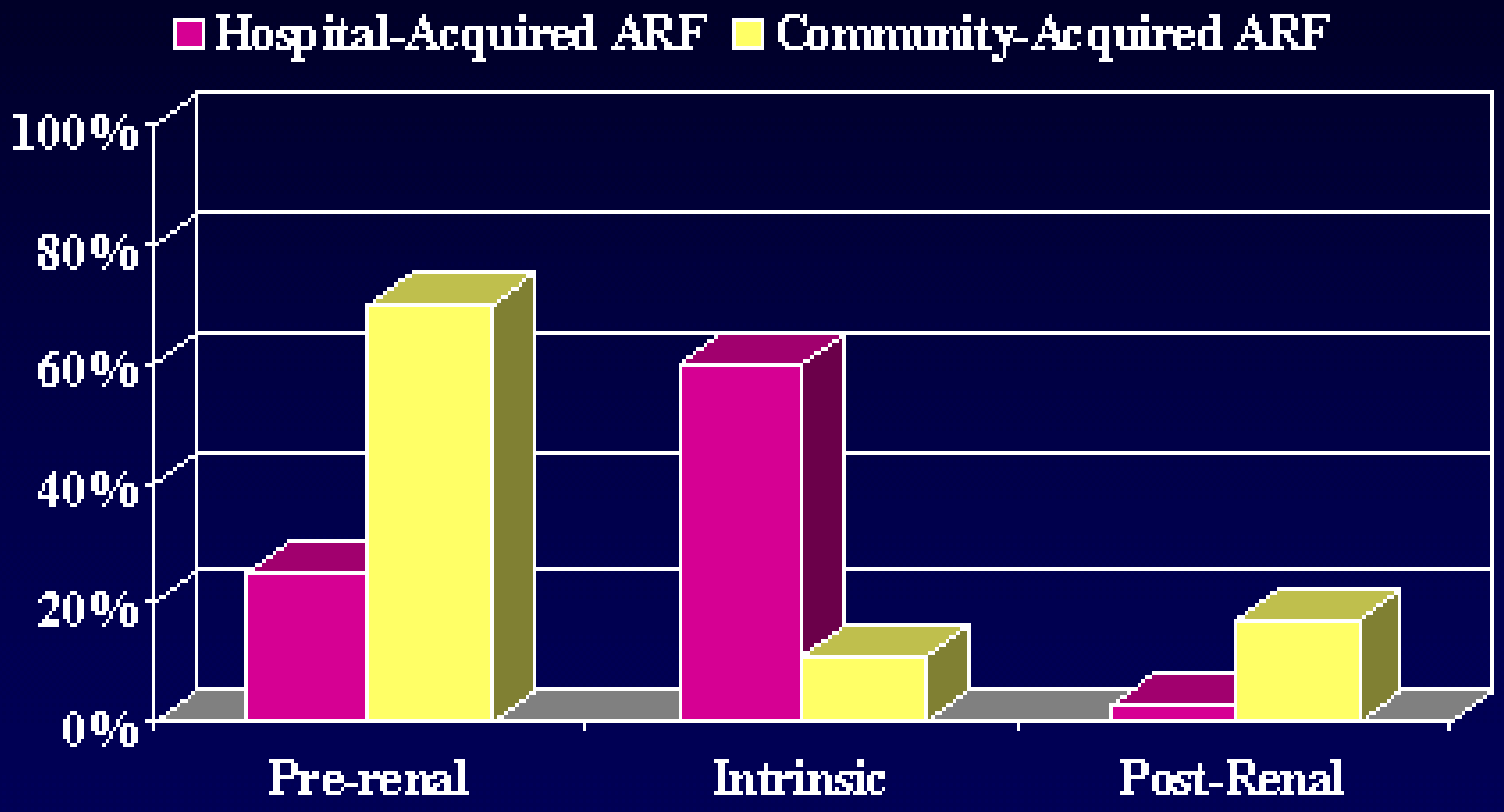
Hoste E, Clermont G, Kersten A, et al.: RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: A cohort analysis. *Critical Care* 2006; 10:R73.

Osterman M, Chang R: Acute Kidney Injury in the Intensive Care Unit according to RIFLE. *Critical Care Medicine* 2007; 35:1837-1843.

Cause of AKI

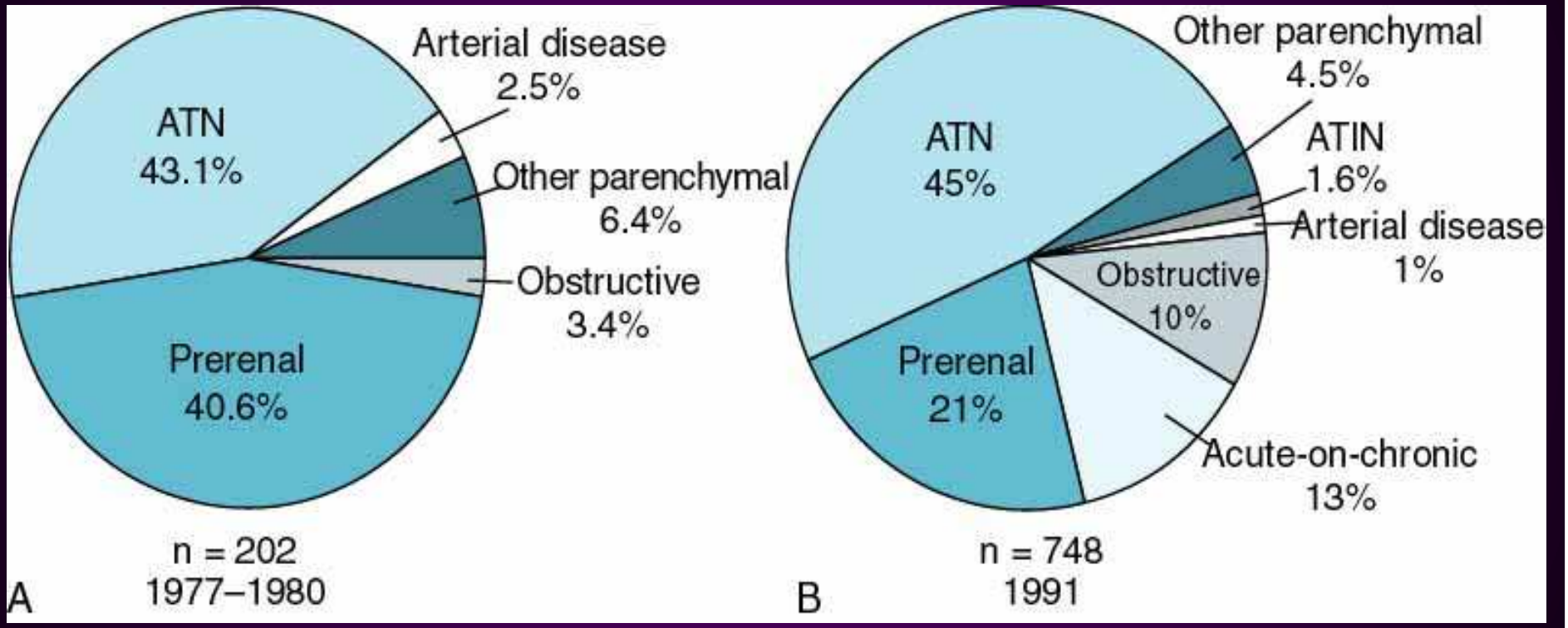

Sudden causes affecting
Induce
Called
Renal perfusion
Parenchymal structures
Urine output
GFR
Prerenal
Parenchymatous
Obstructive
Acute renal failure

Epidemiology of ARF



Hou SH, et al. Am J Med 1983; 74:243-248
Kaufman J, et al. Am J Kidney Dis 1991; 17:191-198

Types of acute renal failure



Western Europe

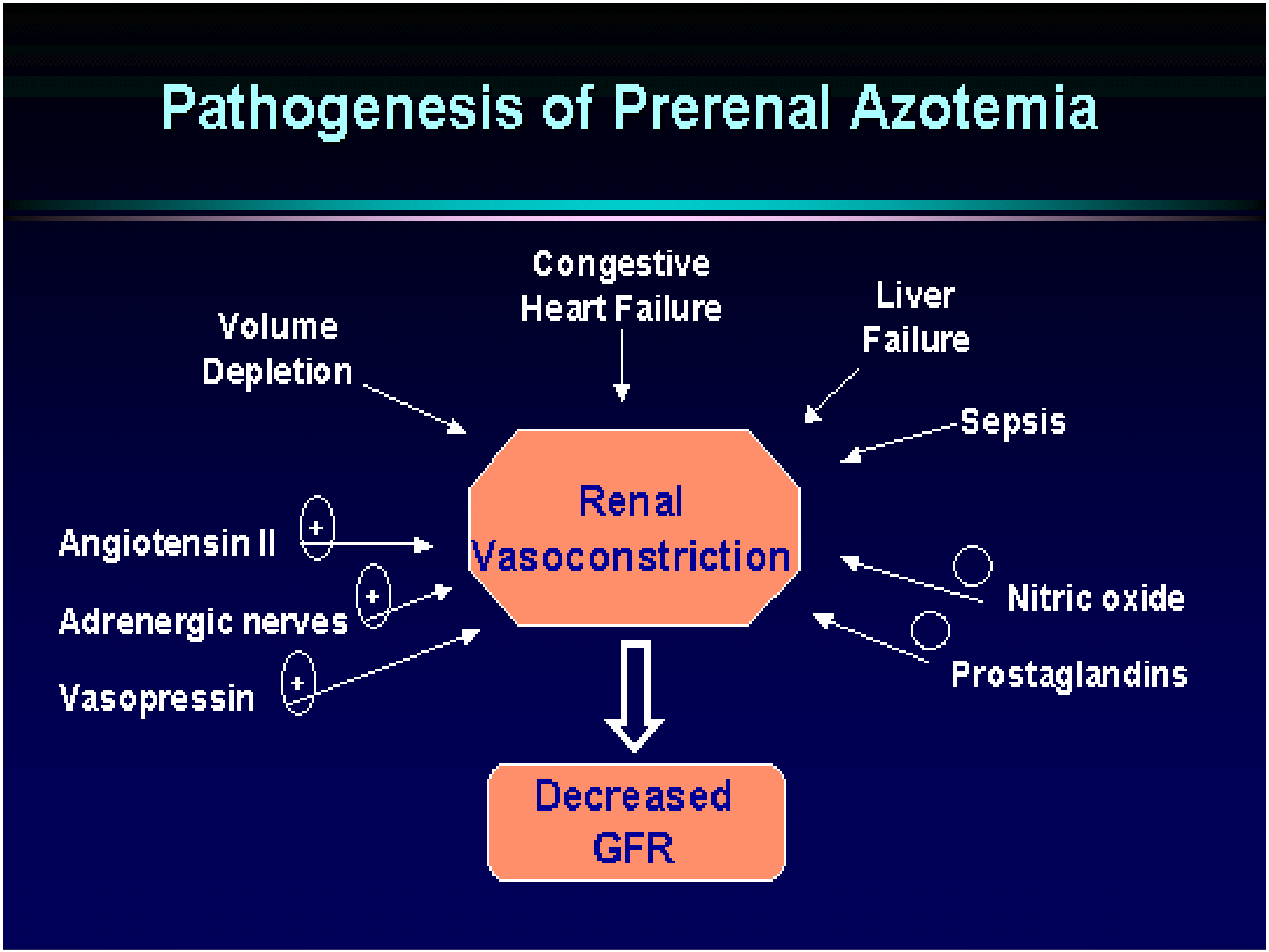
Madrid ARF study

Prerenal AKI

Cause of prerenal AKI

Hypovolemia	Peripheral vasodilation	Effective circulating volume depletion	Renal vascular occlusion
- **External loss** - Renal loss - GI loss - Dermal loss **- Internal loss or redistribution** - Pancreatitis - Traumatized tissue - Peritonitis - Gut obstruction - Burns	-Septic shock - Liver failure	-Congestive heart failure - Nephrotic syndrome - Cirrhosis - Severe hypoalbuminuria	-Dissecting aneurysm of aorta - Atherosclerosis or emboli - Hemodynamic - NSAIDs -ACEIs - ARBs

Pathogenesis of Prerenal Azotemia

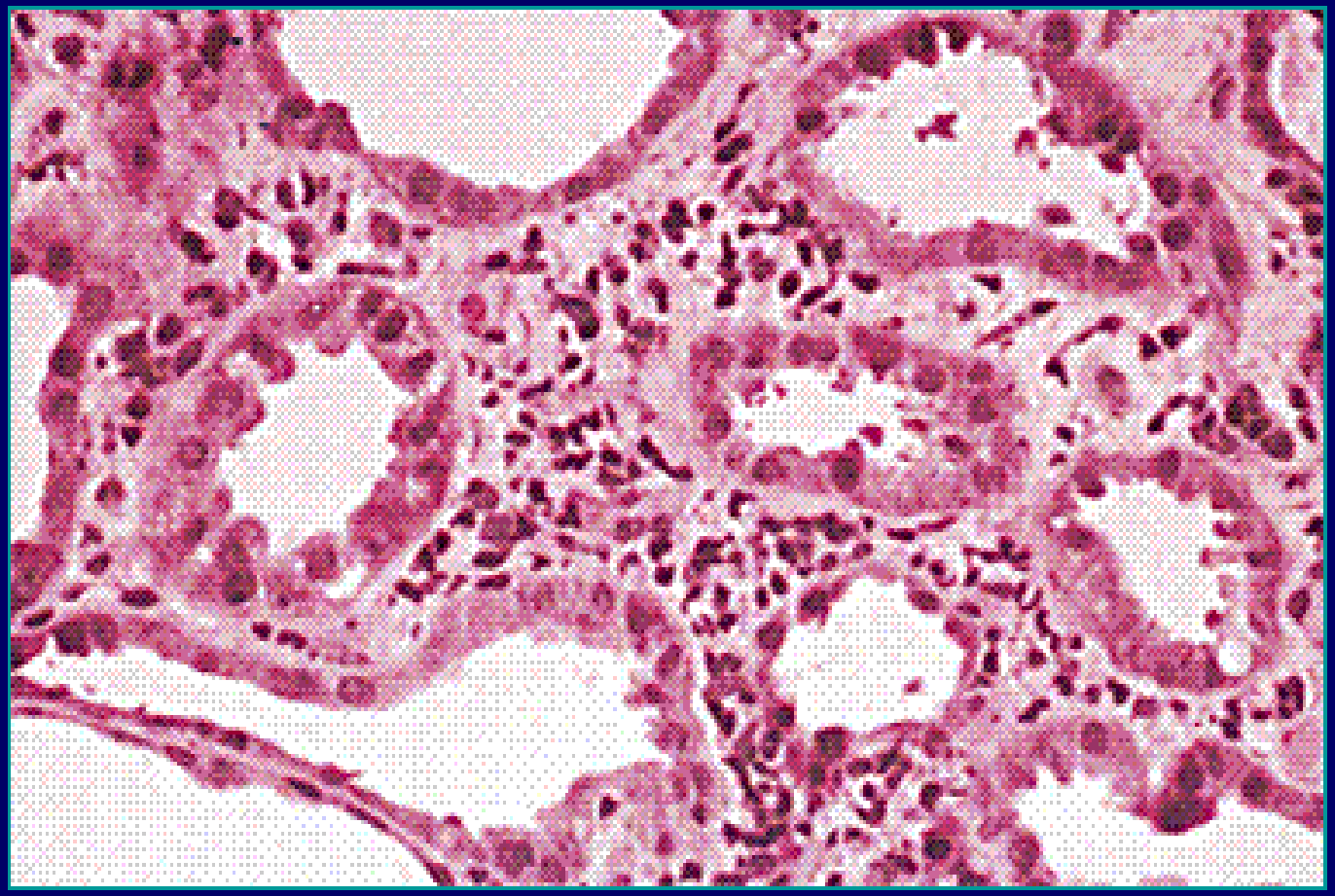


Intrinsic renal cause AKI

Intrinsic Acute Renal Failure

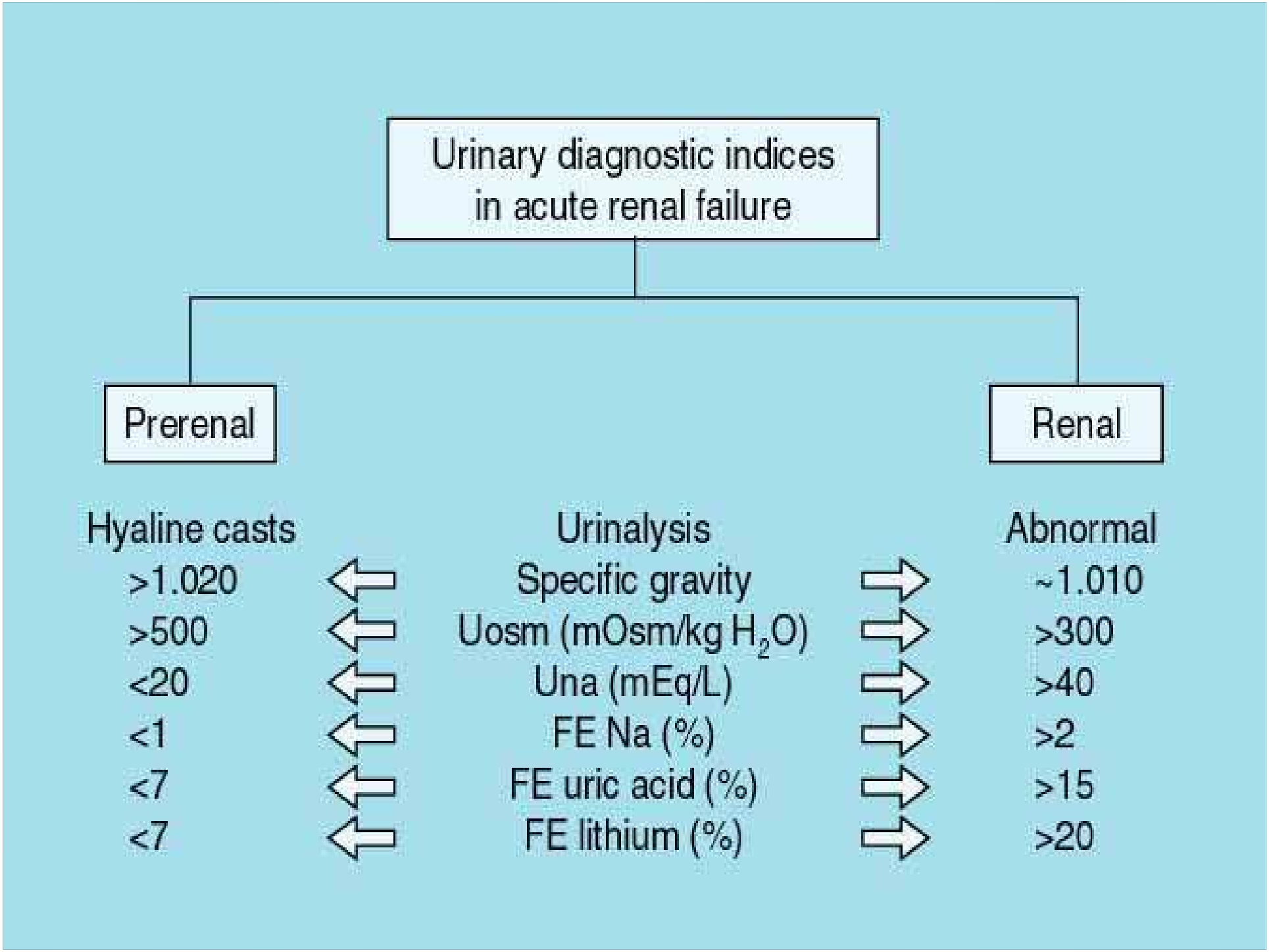
- Acute tubular necrosis (ATN)
- Acute interstitial nephritis (AIN)
- Acute glomerulonephritis (AGN)
- Acute vascular syndromes
- Intratubular obstruction

Acute Tubular Necrosis

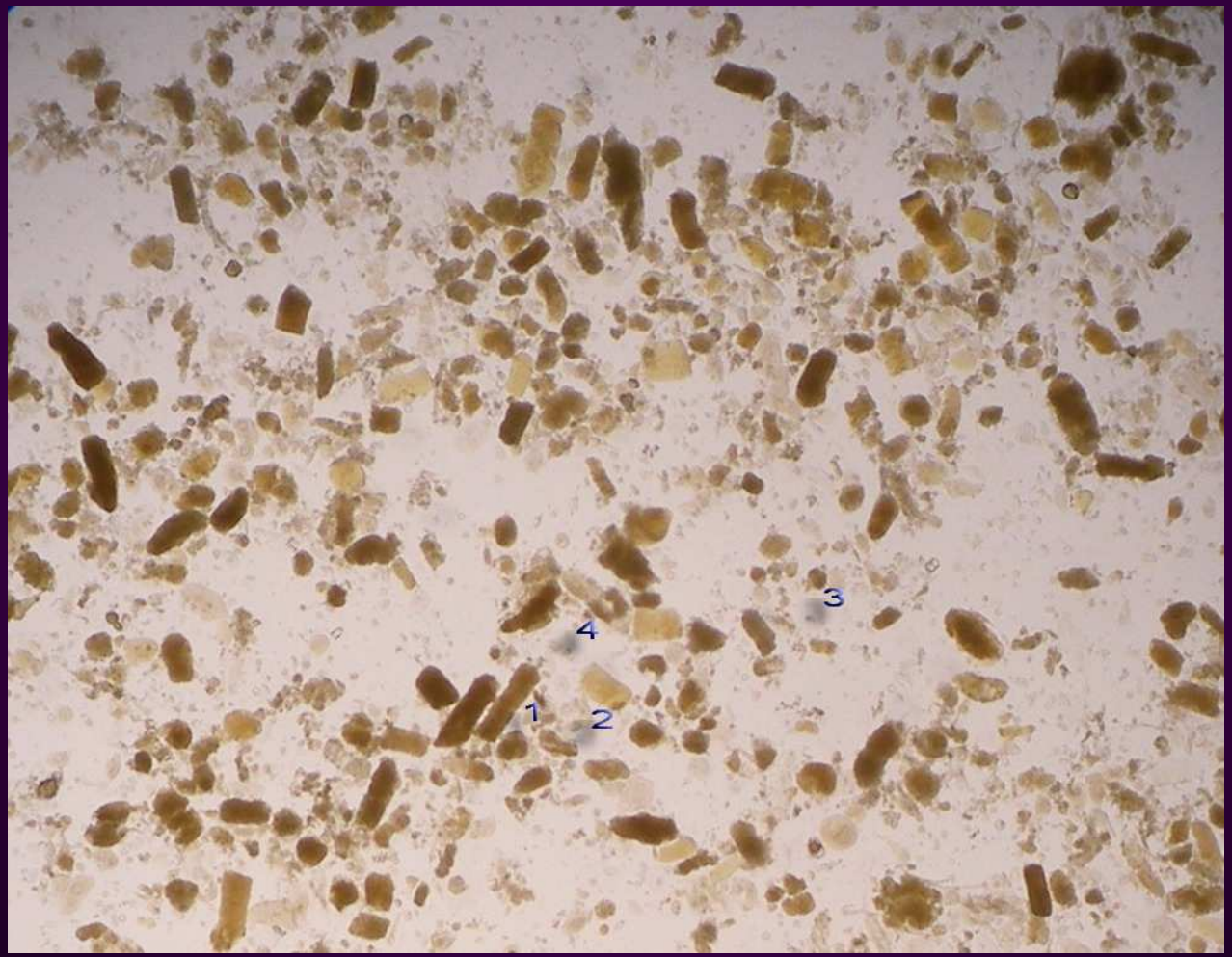


Acute Tubular Necrosis

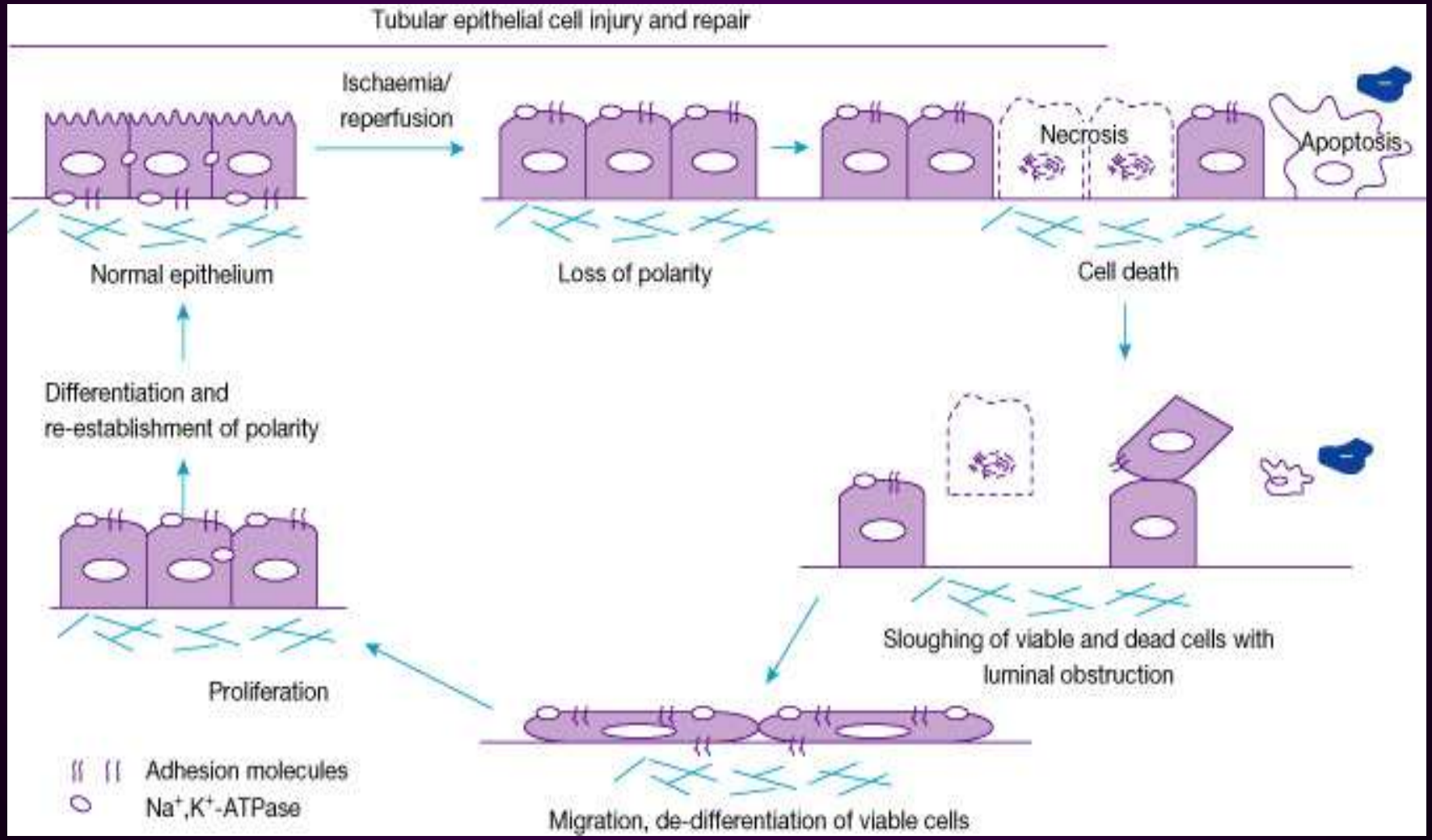
- Ischemic
  - prolonged prerenal azotemia
  - hypotension
  - hypovolemic shock
  - cardiopulmonary arrest
  - cardiopulmonary bypass
- Sepsis
- Nephrotoxic
  - drug-induced
    - radiocontrast agents
    - aminoglycosides
    - amphotericin B
    - cisplatinum
    - acetaminophen
  - pigment nephropathy
    - hemoglobin
    - myoglobin


Urinary diagnostic indices in acute renal failure
Prerenal
Renal
Hyaline casts
Urinalysis
Abnormal
>1.020
Specific gravity
~1.010
>500
Uosm (mOsm/kg H2O)
>300
<20
Una (mEq/L)
>40
<1
FE Na (%)
>2
<7
FE uric acid (%)
>15
<7
FE lithium (%)
>20

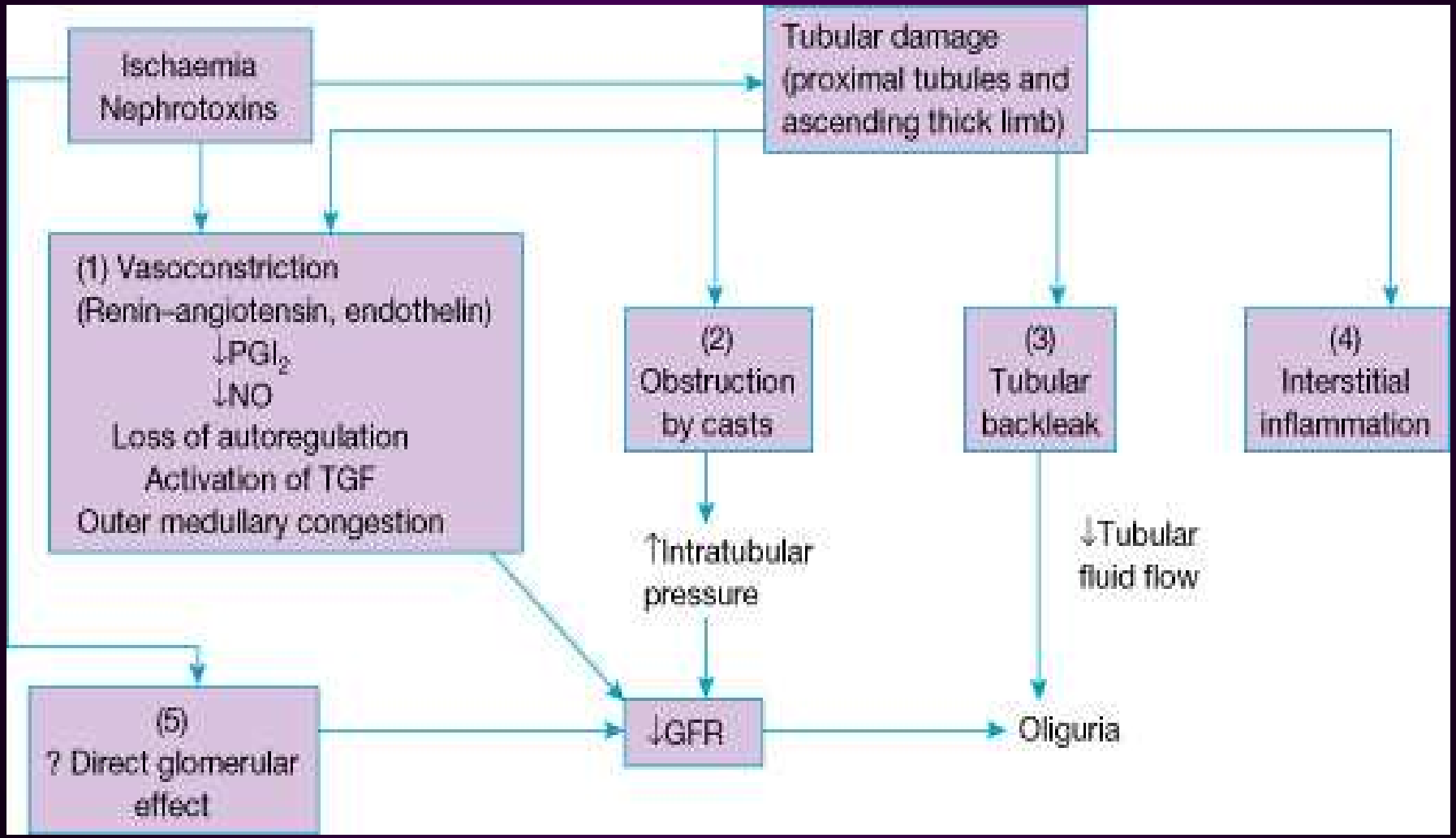
Muddy brown casts



Tubular epithelial cell injury & Repair of renal injury



Interplay of factors explaining the acute decrease in GFR

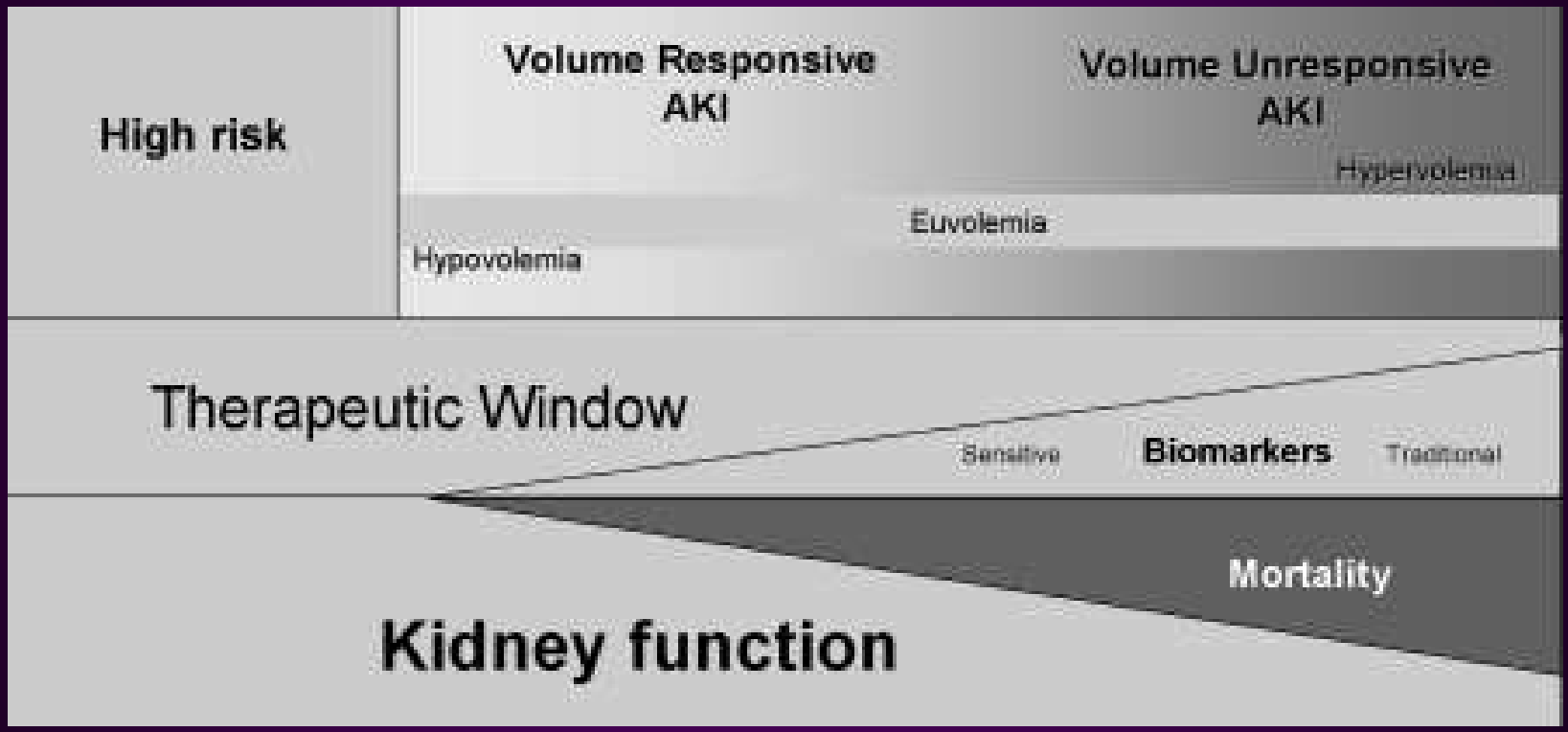


Prevention and treatment of AKI

Evaluation and initial management of patients with AKI

1) Assessment of the contributing **causes** of the kidney injury
2) Assessment of the clinical course including **comorbidities**
3) Assessment of **volume status**
4) Appropriate therapeutic measures designed to **reverse** or **prevent** worsening of functional or structural kidney abnormalities

Conceptual model for development and clinical course of AKI



Clin J Am Soc Nephrol. 2008 July; 3(4): 962–967.

Fluid management

3.1.1: In the absence of hemorrhagic shock, we suggest using **isotonic crystalloids** rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients at risk for AKI or with AKI. (2B)

VASOPRESSORS

3.1.2: We recommend the use of vasopressors in **conjunction** with fluids in patients with vasomotor shock with, or at risk for, AKI.

(1C)

GLYCEMIC CONTROL

3.3.1: In critically ill patients, we suggest insulin therapy targeting plasma glucose **110–149 mg/dl**. (2C)

Nutritional support

3.3.2: We suggest achieving a total energy intake of 20–30 kcal/kg/d in patients with any stage of AKI. (2C)

3.3.3: We suggest to **avoid restriction** of protein intake with the aim of preventing or delaying initiation of RRT. (2D)

Suggesting protein intake

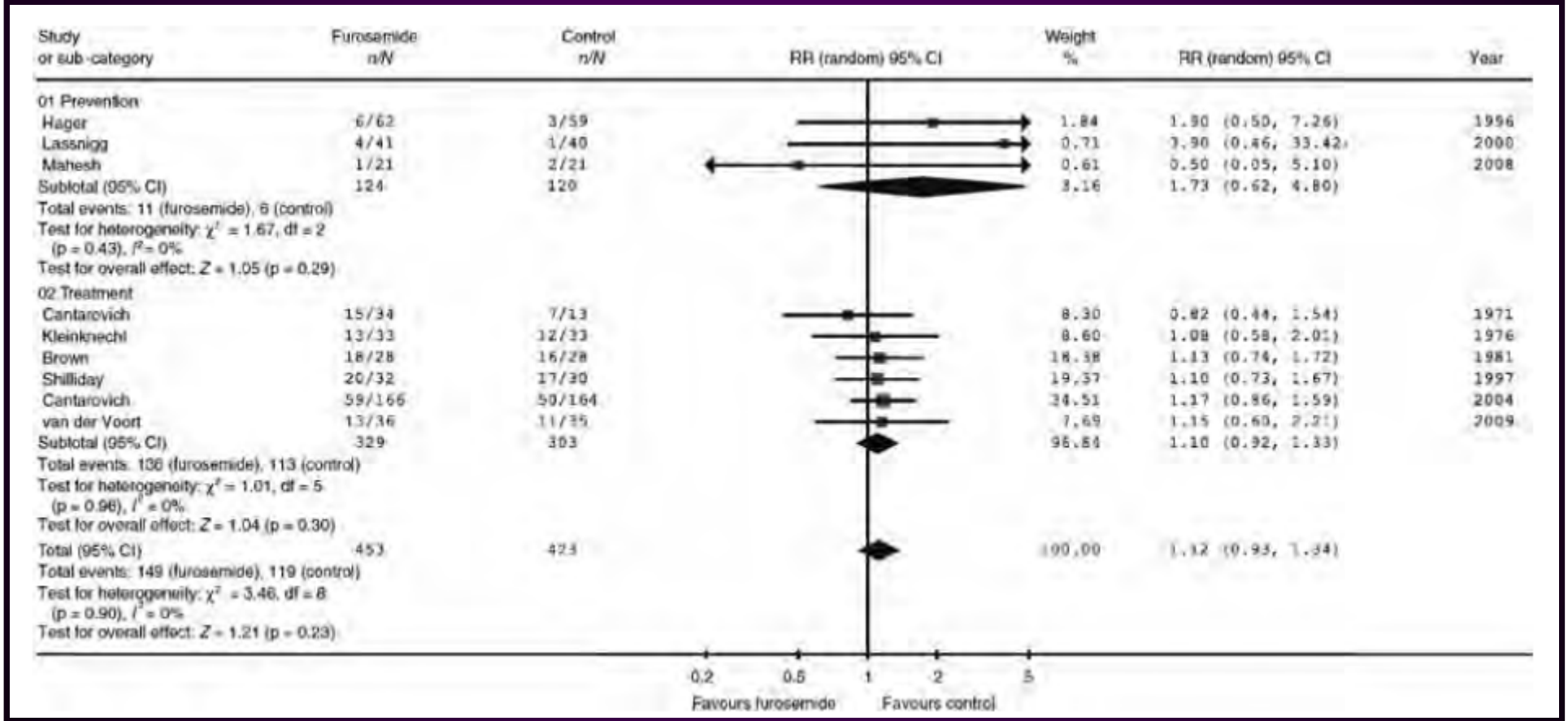
Type of patients	Protein requirement
Noncatabolic patients without RRT	0.8–1.0 g/kg/d
AKI on RRT	1.0–1.5 g/kg/d
Continuous renal replacement therapy (CRRT)	up to 1.7 g/kg/d
Hypercatabolic patients	up to 1.7 g/kg/d

Diuretic use

3.4.1: We recommend **not using** diuretics to prevent AKI. (1B)

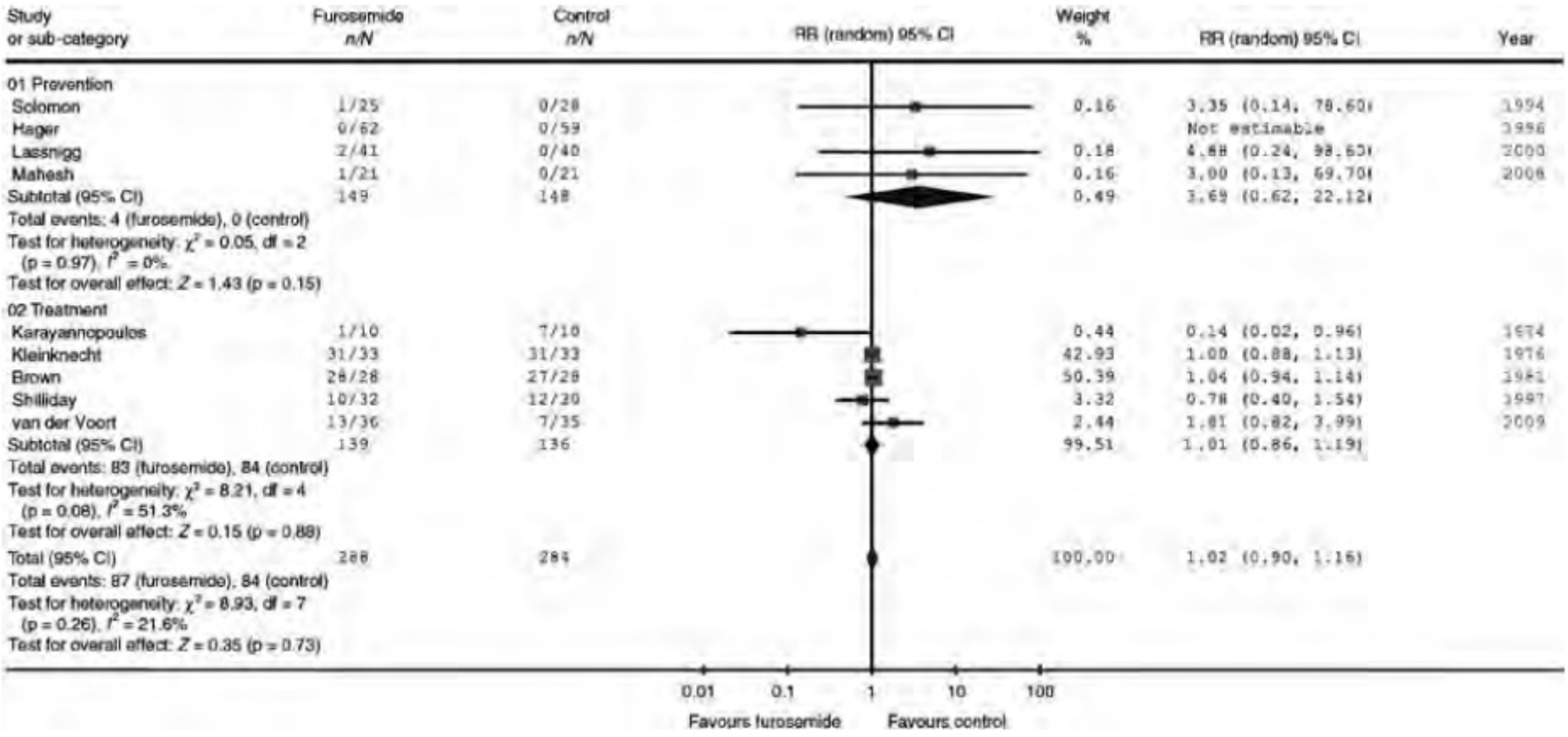
3.4.2: We suggest **not using** diuretics to treat AKI, except in the management of volume overload. (2C)

Effect of furosemide vs. control on all-cause mortality



Anaesthesia 2010; 65: 283–293

Effect of furosemide vs. control on need for RRT



Anaesthesia 2010; 65: 283–293

Vasodilator therapy

3.5.1: We recommend **not using** low-dose dopamine to prevent or treat AKI. (1A)

3.5.2: We suggest **not using** fenoldopam (pure dopamine type-1 receptor agonist) to prevent or treat AKI. (2C)

3.5.3: We suggest **not using** atrial natriuretic peptide (ANP) to prevent (2C) or treat (2B) AKI.

Contrast-induced AKI

4.1.1: In individuals who develop changes in kidney function after administration of intravascular contrast media, evaluate for CI-AKI as well as for **other possible causes** of AKI. (Not Graded)

4.2.1: **Assess the risk** for CI-AKI and, in particular, screen for pre-existing impairment of kidney function in all patients who are considered for a procedure that requires intravascular (i.v. or i.a.) administration of iodinated contrast medium. (Not Graded)

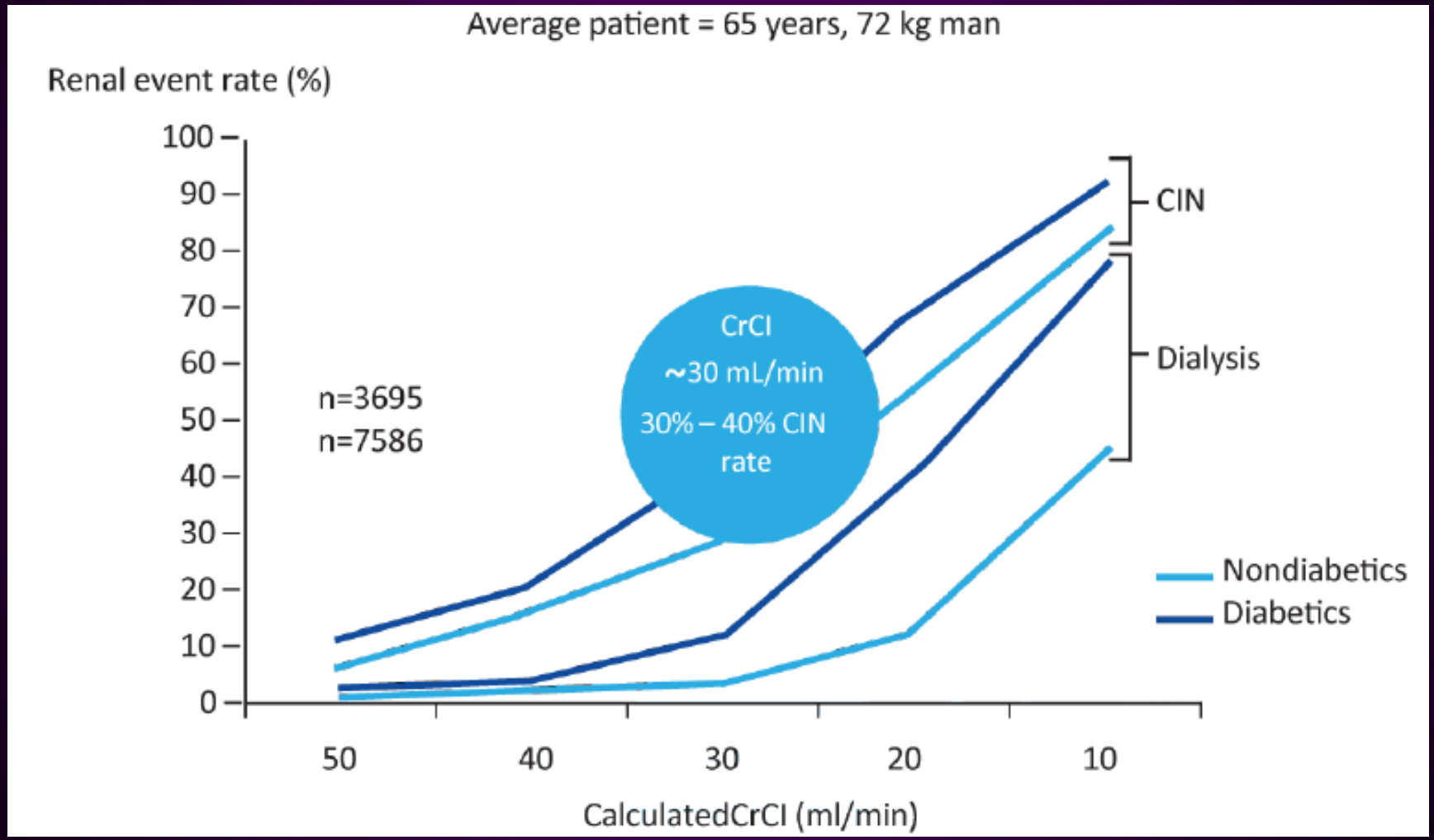
CI-AKI risk-scoring moderate for percutaneous coronary intervention

Risk factors	Integer score (calculate)
Hypotension	5
IABP	5
CHF	5
Age >75 years	4
Anemia	3
Diabetes	3
Contrast-media volume	1 per 100 ml
SCr >1.5 mg/dl (>132.6 μmol/l) *or* eGFR <60 ml/min per 1.73 m^2	4 2 for 40–60 4 for 20–39 6 for <20

Score < 5 → Low risk
Score 6-16 → Moderate risk
Score > 16 → High risk

J Am Coll Cardiol 2004; 44: 1393–1399

Validated risk of CIN and dialysis after diagnostic angiography



CI-AKI prevention (1)

4.2.2: Consider **alternative** imaging methods in patients at increased risk for CI-AKI.

(Not Graded)

4.3.1: Use the **lowest** possible dose of contrast medium in patients at risk for CI-AKI. (Not Graded)

4.3.2: We recommend using either **iso-osmolar** or **low osmolar** iodinated contrast media, rather than high-osmolar iodinated contrast media in patients at increased risk of CI-AKI. (1B)

CI-AKI prevention (2)

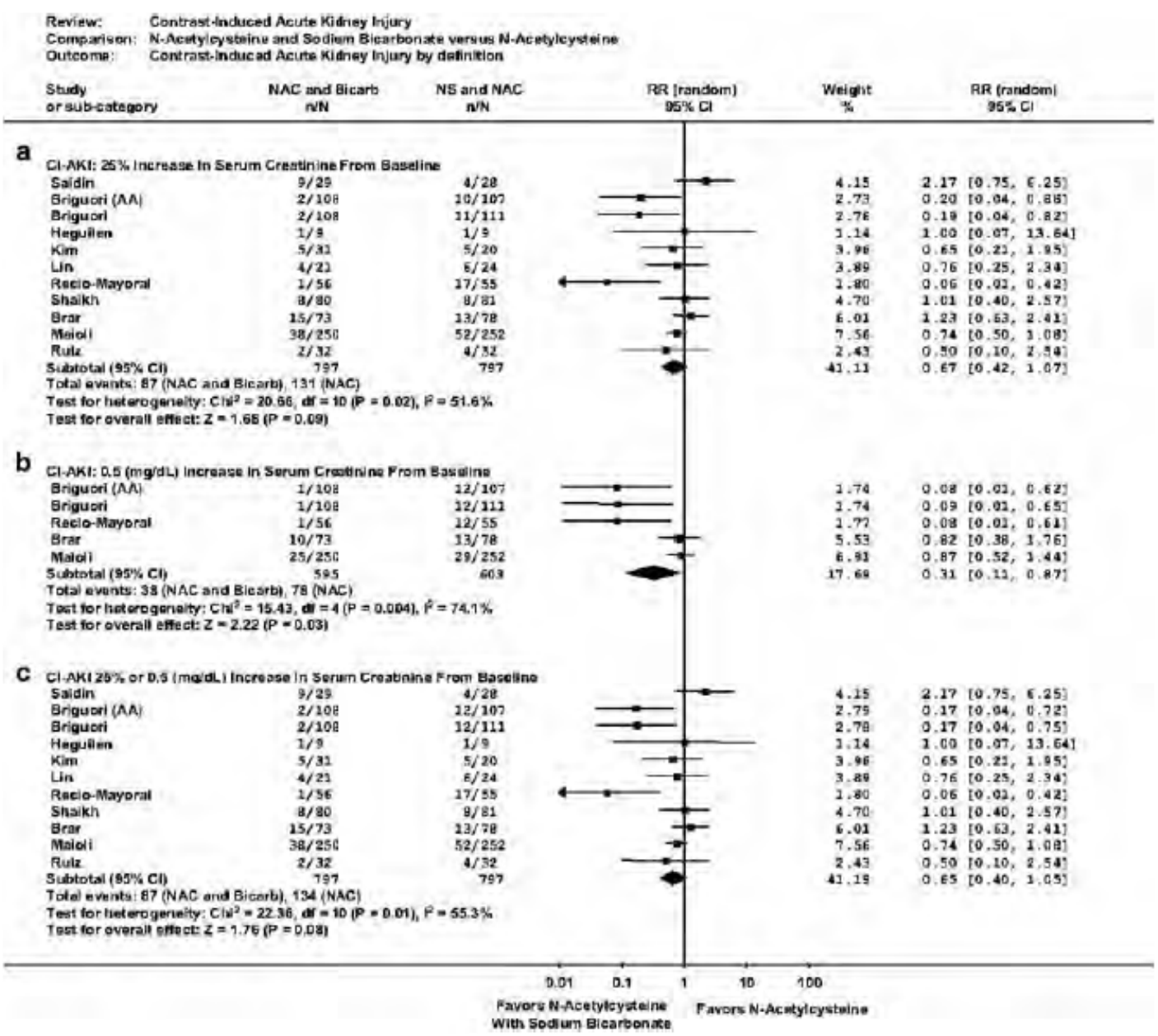
4.4.1: We recommend i.v. volume expansion with either **isotonic sodium chloride** or **sodium bicarbonate solutions**, rather than no i.v. volume expansion, in patients at increased risk for CI-AKI. (1A)

Intravenous fluid administration

Type	Procedure	
	Before	After
0.9% NaCl	1 mL/kg/hr for 12 hrs	1 mL/kg/hr for 12 hours
7.5% $NaHCO_3$ 150 ml + 5%D/W 850 ml	3 mL/kg/hr for 1 hr	1 mL/kg/hr for 6 hours

ROLE OF NAC IN THE PREVENTION OF CI-AKI

4.4.3: We suggest using oral NAC, together with i.v. isotonic crystalloids, in patients at increased risk of CI-AKI. (2D)



JACC Cardiovasc Interv 2009; 2: 1116–1124

CI-AKI prevention (3)

- Metformin should be **discontinued** on the day of the proposed CM administration, withheld for the subsequent 48 hours and recommenced after renal function has been re-evaluated and found to have returned to baseline.

Consensus Guidelines for the Prevention of Contrast Induced Nephropathy 2011

Canadian Association of Radiologists

GENERAL GUIDELINE FOR ALL PATIENTS WITH EGFR <60 mL/min:

- Avoid Dehydration
- Consider alternate Imaging studies not requiring iodinated contrast medium
- Minimize contrast medium volume
- Avoid repeat iodinated contrast studies within especially within 48 hours
- Use low- or iso-osmolar non-ionic contrast medium

- eGFR < 45 mL/min AND
- Intravenous Contrast Administration

MILD-MODERATE RISK OF CIN

- IV hydration
- Avoid dehydration (Oral fluids if IV hydration impractical)
- f/u SCr and eGFR in 48 – 72 hrs.

- eGFR < 60 mL/min AND
- Intra-arterial Contrast Administration
- OR any eGFR w/ acute illness, unstable renal function or inpatients

MODERATE-HIGH RISK OF CIN

- Hold nephrotoxic drugs (esp. NSAIDs and diuretics),
- Hydrate with IV NACl or $NaHCO_3$
- Consider NAC
- f/u SCr and eGFR in 48 – 72 hrs.

Dialysis Interventions

5.1.1: Initiate RRT emergently when **life-threatening** changes in fluid, electrolyte, and acid-base balance exist. (Not Graded)

5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (Not Graded)

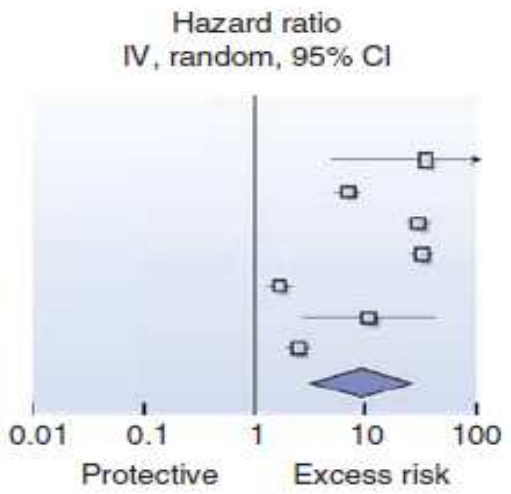
Prognosis

Meta-analysis of CKD and ESRD associated with AKI

a

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Weiss *et al.* (13)	10.0	32.79 (4.30–249.77)
Amdur *et al.* (22)	15.5	6.64 (5.05–8.74)
Lo *et al.* (11)	15.5	28.08 (21.01–37.53)
James *et al.* (16)	15.6	29.99 (24.32–36.99)
James *et al.* (15,23)	15.5	1.60 (1.20–2.14)
Ando *et al.* (19)	12.4	9.91 (2.48–39.63)
Ishani *et al.* (21)	15.6	2.33 (1.83–2.96)
Total (95% CI)	100.0	8.82 (3.05–25.48)

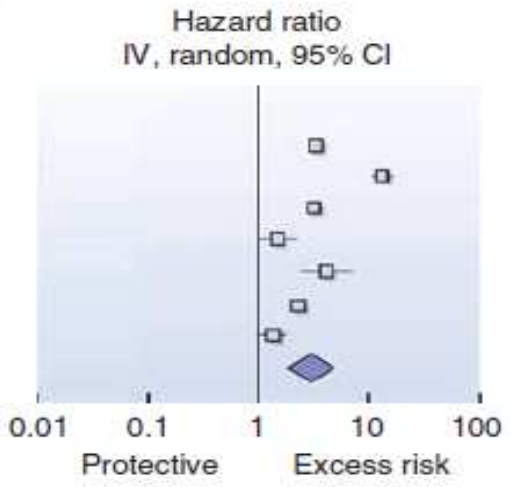
Heterogeneity: $\tau^2 = 1.87$; $\chi^2 = 446.89$, d.f. = 6 ($P < 0.00001$); $I^2 = 99\%$. Test for overall effect: $Z = 4.02$ ($P < 0.0001$)



b

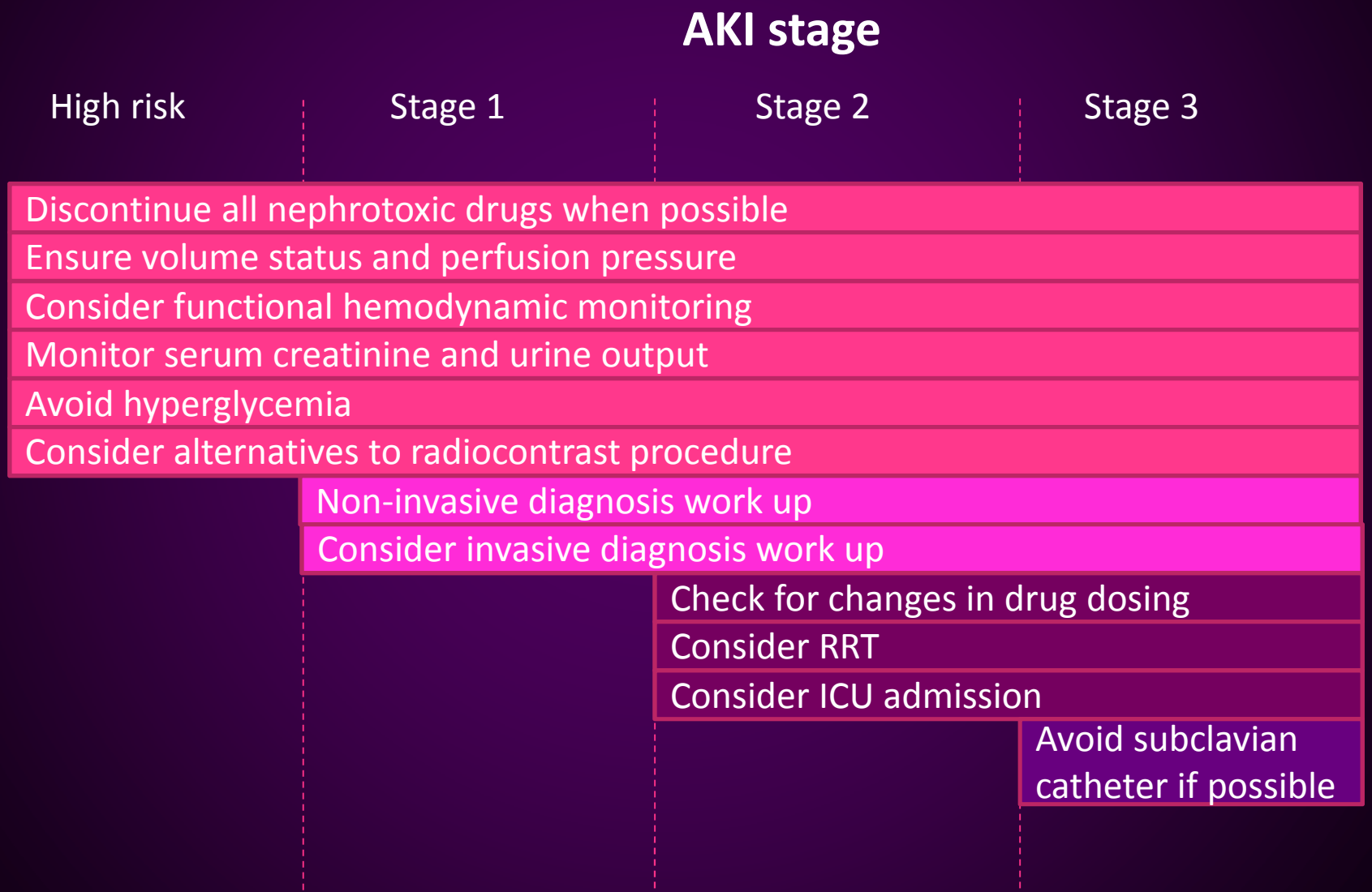
Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Newsome *et al.* (14)	15.0	3.26 (2.87–3.70)
Ishani *et al.* (20)	14.8	12.99 (10.57–15.96)
Wald *et al.* (17)	14.9	3.22 (2.70–3.85)
Hsu *et al.* (10)	13.5	1.47 (0.95–2.28)
James *et al.* (15,23)	12.5	4.15 (2.32–7.41)
Lafrance *et al.* (18)	15.0	2.33 (2.08–2.61)
Choi *et al.* (12)	14.4	1.37 (1.02–1.84)
Total (95% CI)	100.0	3.10 (1.91–5.03)

Heterogeneity: $\tau^2 = 0.40$; $\chi^2 = 252.85$, d.f. = 6 ($P < 0.00001$); $I^2 = 98\%$. Test for overall effect: $Z = 4.58$ ($P < 0.00001$)



Kidney International (2012) **81**, 442–448

Stage-based management of AKI



Summary

- Definitions for AKI
- Surveillance of high risk patients for AKI is an essential component of patient management.
- Pre-renal and ischemic ATN are the same spectrum of disease
- Lack of established pharmacotherapy for AKI.
- RRT should start based on clinical context.

Thank you for your atttention