AKI : Risk Assessment & Prevention

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NHS Foundation Trust

Disclosures:

Research Funding : Astute Medical, SBRI/D4D's Renal Technologies
Commercial Trials: Roche
Honorarium/Travel Expenses: Fresenius/Astute Medical

"Before we begin this family meeting, how about we go around and say our names and a little something about ourselves."

In the Beginning….

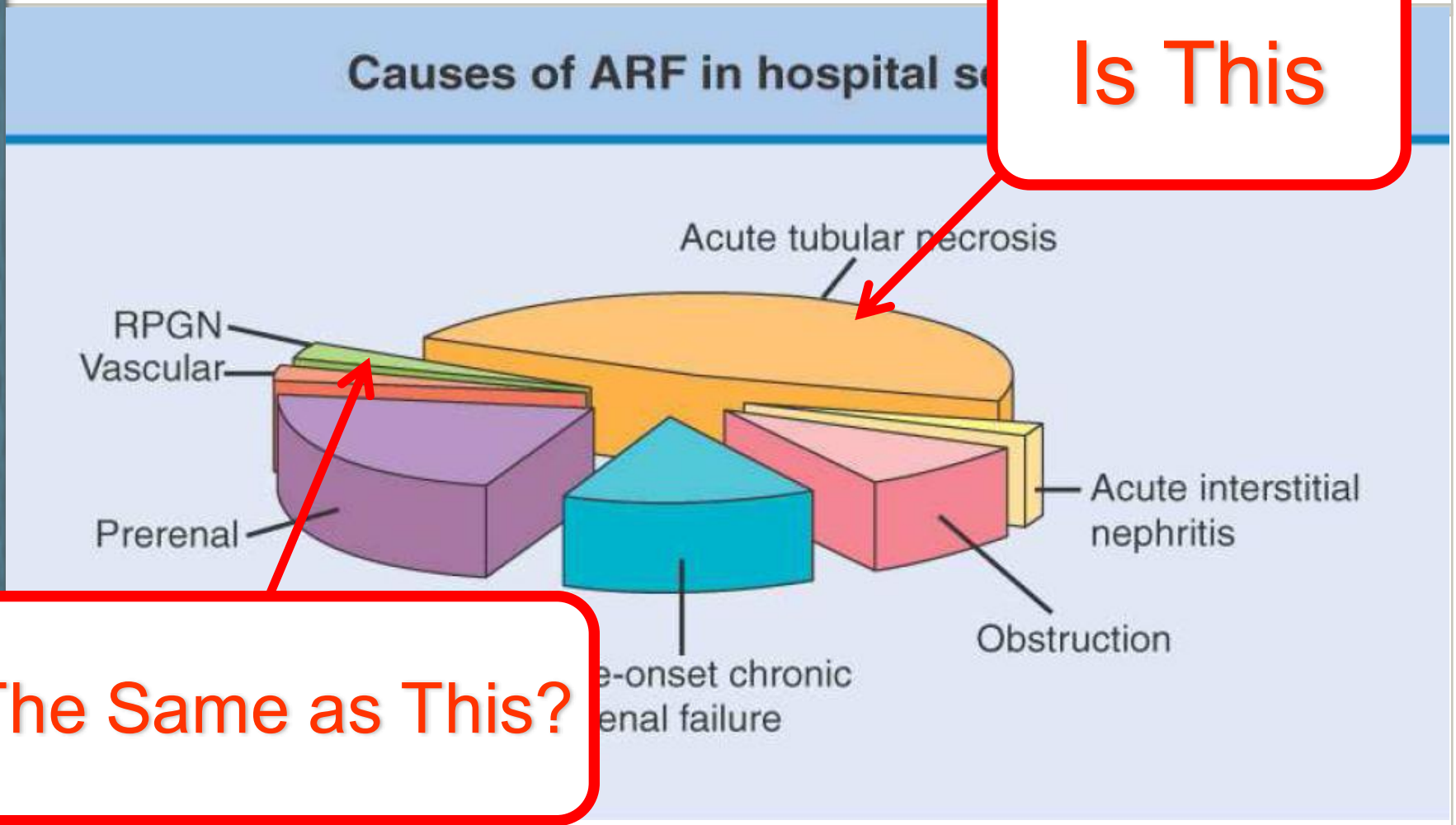
- There was Acute Renal Failure : Remember that?
- Defining it could be relatively straightforward…..
- **"The patient has acute renal failure when I say they have…."**


ARF : Was A Bit like Pornography….
Easy to Recognise….. Hard to Define!

We Now Have Definitions…

Stage	Serum Creatinine	Urine Output
1	≥ 1.5-1.9 times baseline or 0.3 mg/dl (>26.4 µmol/L) increase	< 0.5 ml/kg.h for ≥ 6-12 hrs
2	≥ 2.0-2.9 times baseline	< 0.5 ml/kg.h for ≥ 12 hrs
3	≥ 3.0 times baseline OR increase in creatinine ≥ 4 mg/dl (352 µmol/L) In patients < 18 yrs decrease of eGFR to 35 ml/kg/1.73 m^2	< 0.3 ml/kg.h for ≥ 24 hrs OR Anuria ≥ 12 hrs

Is All AKI Equal?




I'm AKI
No…I'm AKI

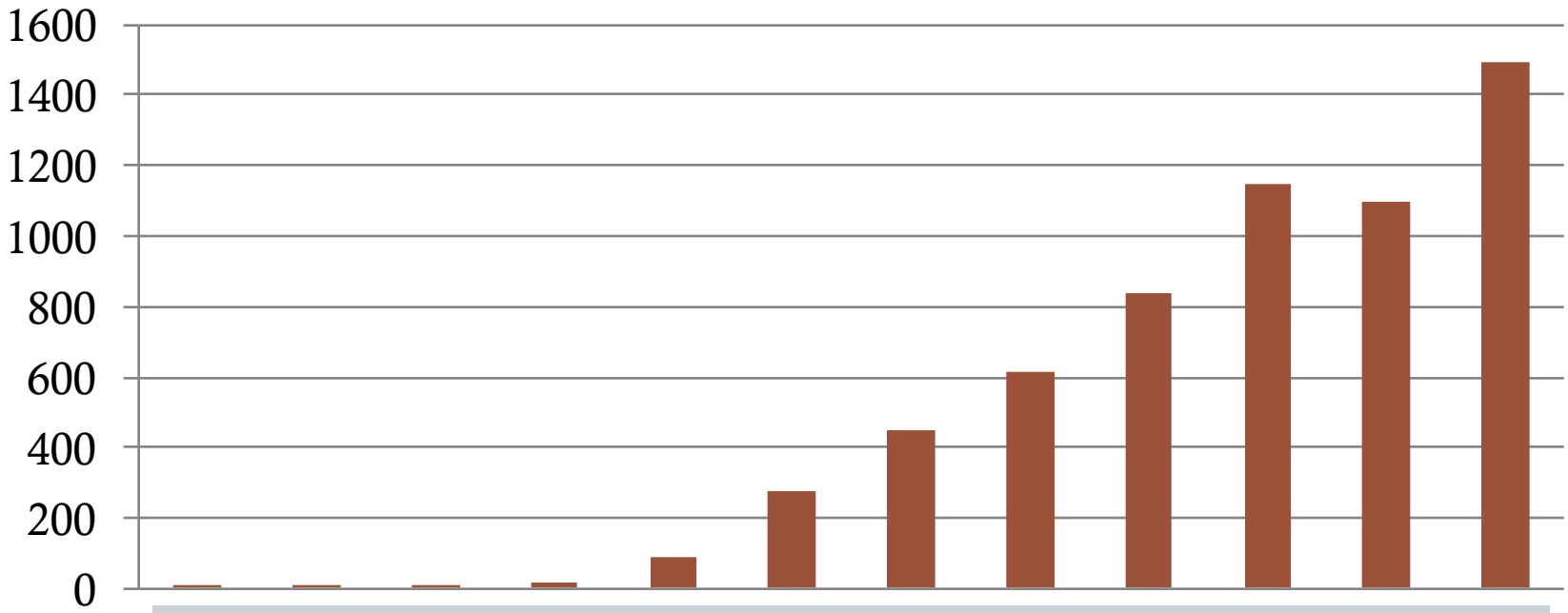
We don't have a Fairy Godmother…

Neil Soni Anaesthesia, 2010, 65, pages 971–979

Why Is AKI Important?

- **Common**
- **High Mortality**
- **Heavy Burden of Illness**
  - **Acute**
  - **'Chronic'**
- **Cost Implications**

AKI : Must be very Important…



More Than 4 Papers a Day..

AKI : A Broad Clinical Syndrome

We Can Define AKI
But Not The Cause

Not One Disease : No One Diagnostic Test

- (e.g., prerenal azotemia, and acute postrenal obstructive nephropathy)

HSE

Health and Safety Executive

Five steps to risk assessment

Step 1
Identify the hazards


AMBULANCE

Step 1
Identify the hazards

Step 2
Decide who might be harmed and how

So Who Is At Risk?

Where Do We Go For Guidance?

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

kidney INTERNATIONAL supplements

141 Pages Long

132 Page Appendix

64 Pages of Tables

KDIGO Clinical Practice Guideline for Acute Kidney Injury

The GRADE System

Table 1 | Implications of the strength of a recommend

Grade*	Patients	Clinicia
Level 1 "We recommend"	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most pa recomm
Level 2 "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Differen differen arrive a with he

- A = High
- B = Moderate
- C = Low
- D = Very Low

National Clinical Guideline Centre

Acute kidney injury

Acute kidney injury

Prevention, detection and management up to the point of renal replacement therapy

271 Pages Long

126 References

Clinical guideline <CG 169>

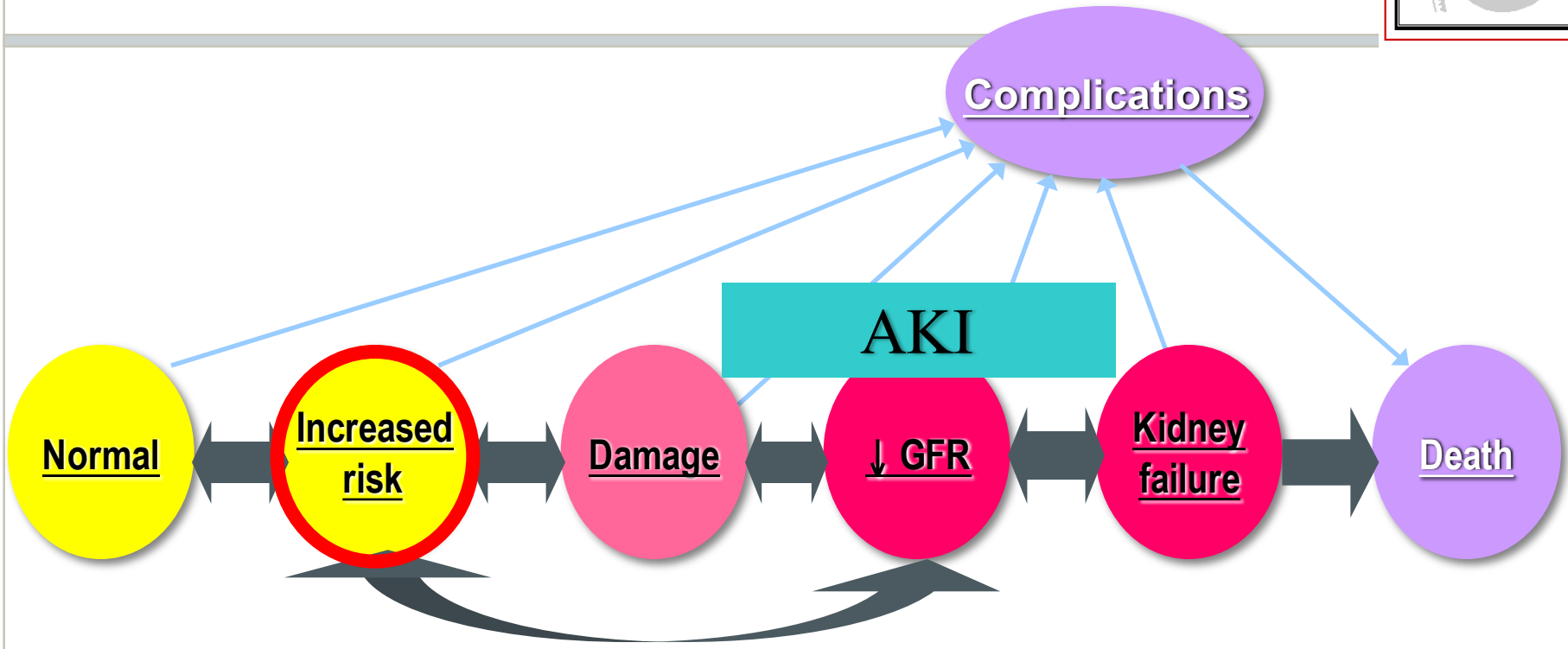
Methods, evidence and recomme

August 2013

Final draft

Commissioned by the National Institute for Health and Care Excellence

Conceptual Model for Acute Kidney Injury (AKI)



Vancouver meeting 2006

Chapter 2.2: Risk assessment

2.2.1: We recommend that patients be stratified for risk of AKI according to their susceptibilities and exposures. (*1B*)

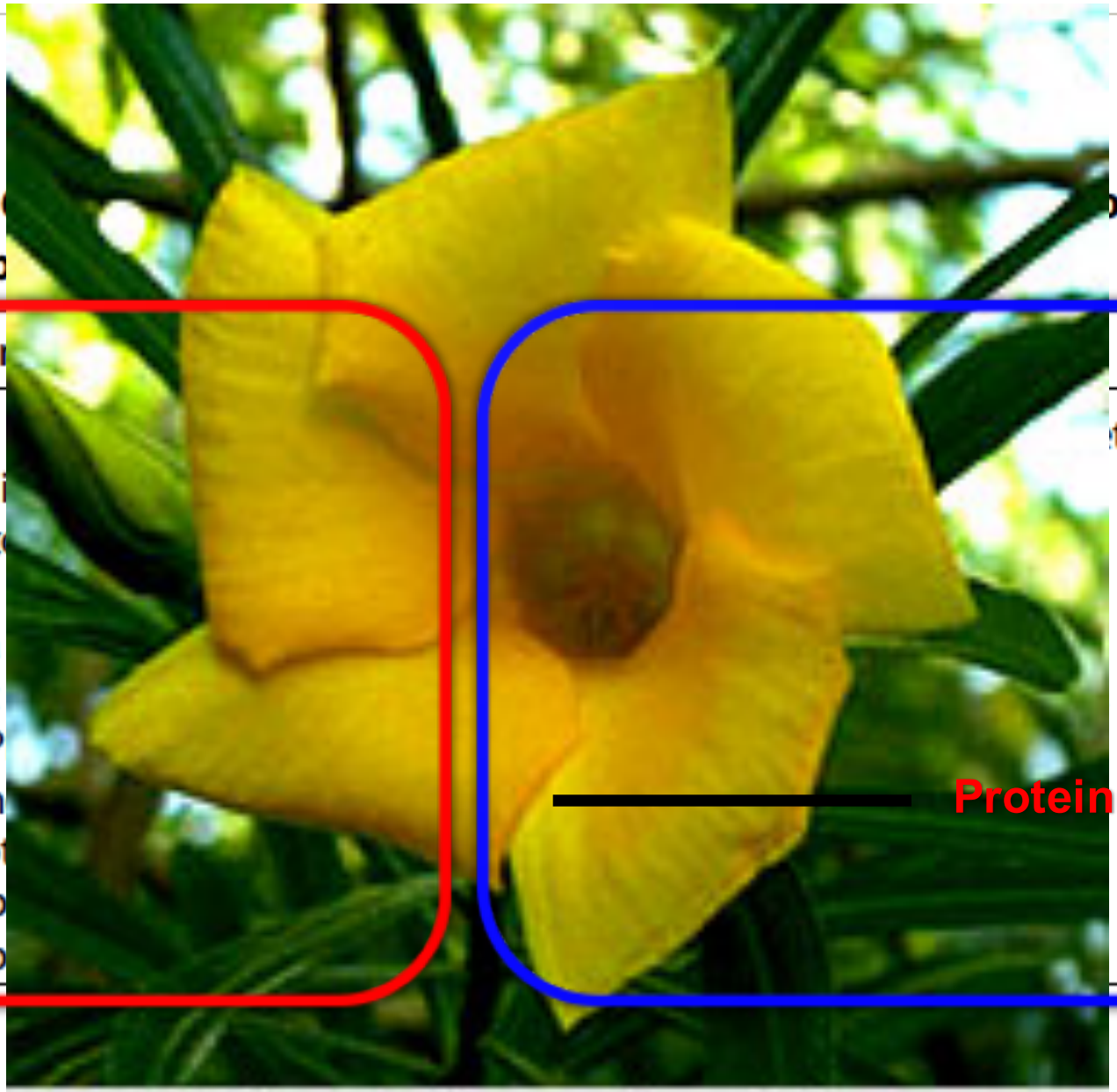
2.2.2: Manage patients according to their susceptibilities and exposures to reduce the risk of AKI (see relevant guideline sections). (*Not Graded*)

2.2.3: Test patients at increased risk for AKI with measurements of SCr and urine output to detect AKI. (*Not Graded*) Individualize frequency and duration of monitoring based on patient risk and clinical course. (*Not Graded*)

Table

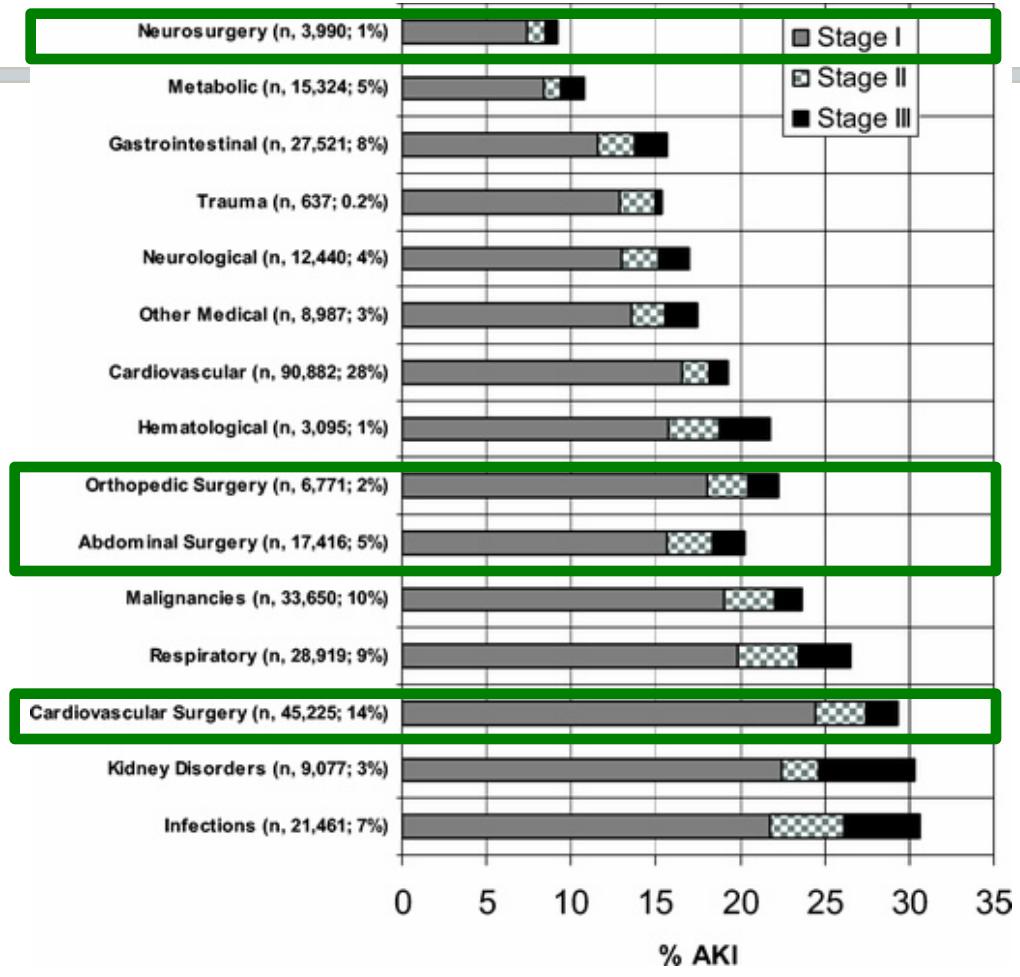
non-sp

Exposu
Sepsis
Critical i
Circulat
Burns
Trauma
Cardiac
with CP
Major n
Nephrot
Radioco
Poisono



Yellow Oleander Flower

Incidence and outcomes of acute kidney injury in intensive care units: A Veterans Administration study



Risk Dependent on Cause

CV Thakar et al, Crit Care Med 2009

Can We Predict AKI??

Common Risk Factors In AKI Scores

- Age, Gender
- Hypotension, Oliguria
- Liver Failure, Hypoalbuminaemia
- Sepsis
- **Mechanical Ventilation**

Poorly Performing Variable Definitions

Author/Study	Year	Number
Mehta	2002	605
Lins	2004	293
Dharan	2005	265
Chertow	2006	618
Demirjian	2011	1122

What about in well defined populations?

- Cardiac Surgery
  - Known Baseline
  - Timed Insult
  - Accurate Data Collection

Variable Endpoints
Not Applicable to the Majority of our Patients

Can We Even Identify AKI?

Original Paper

nephron Clinical Practice

Nephron Clin Pract 2013;123:143–150
DOI: 10.1159/000351509

Received: January 16, 2013
Accepted: April 16, 2013
Published online: July 25, 2013

Identifying the Patient at Risk of Acute Kidney Injury: A Predictive Scoring System for the Development of Acute Kidney Injury in Acute Medical Patients

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Vivien Bewick[c] Mark Dennis[b] Richard Venn[a]

[a]Department of Critical Care, Worthing Hospital, and [b]Department of Performance and Information, Western Sussex Hospitals Trust, Worthing, and [c]School of Computing, Mathematical and Information Sciences, University of Brighton, Brighton, UK

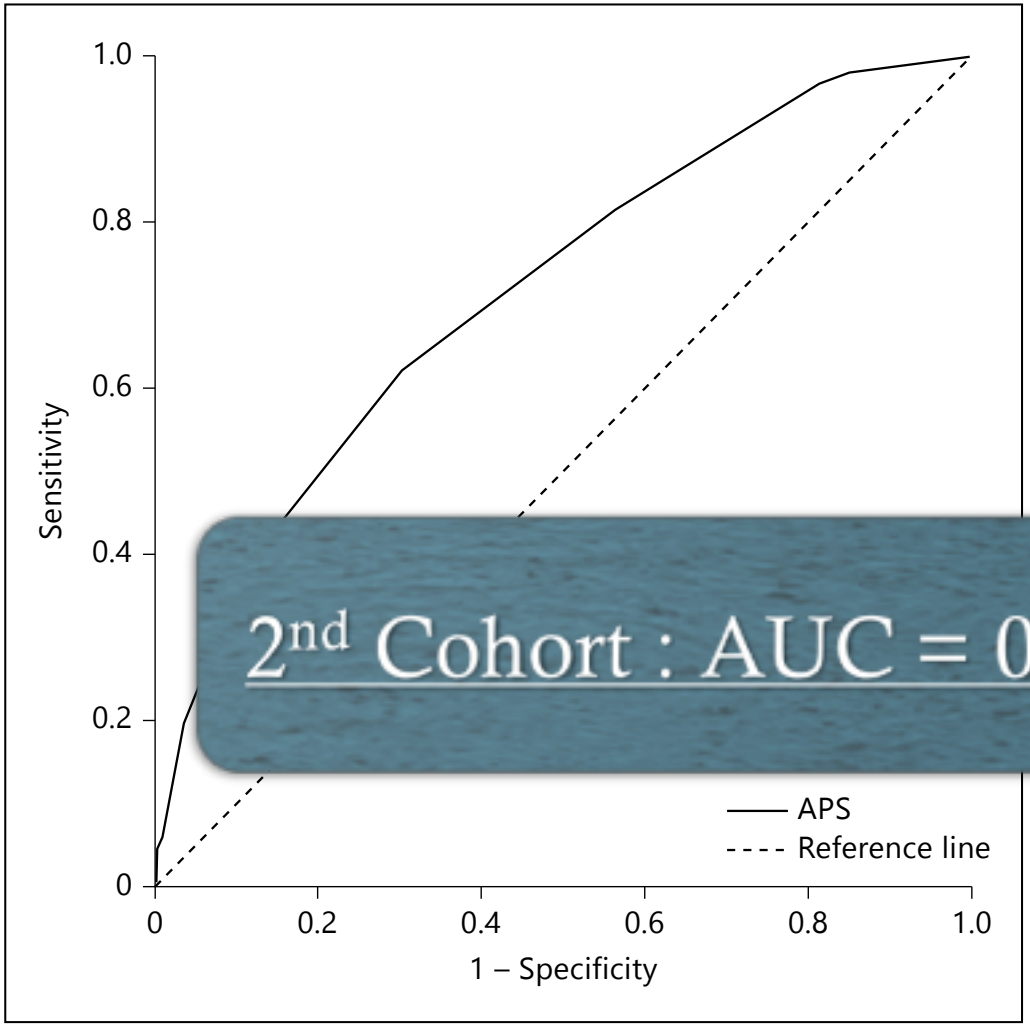


Fig. 2. Receiver operator characteristic curve for the AKI prediction score.

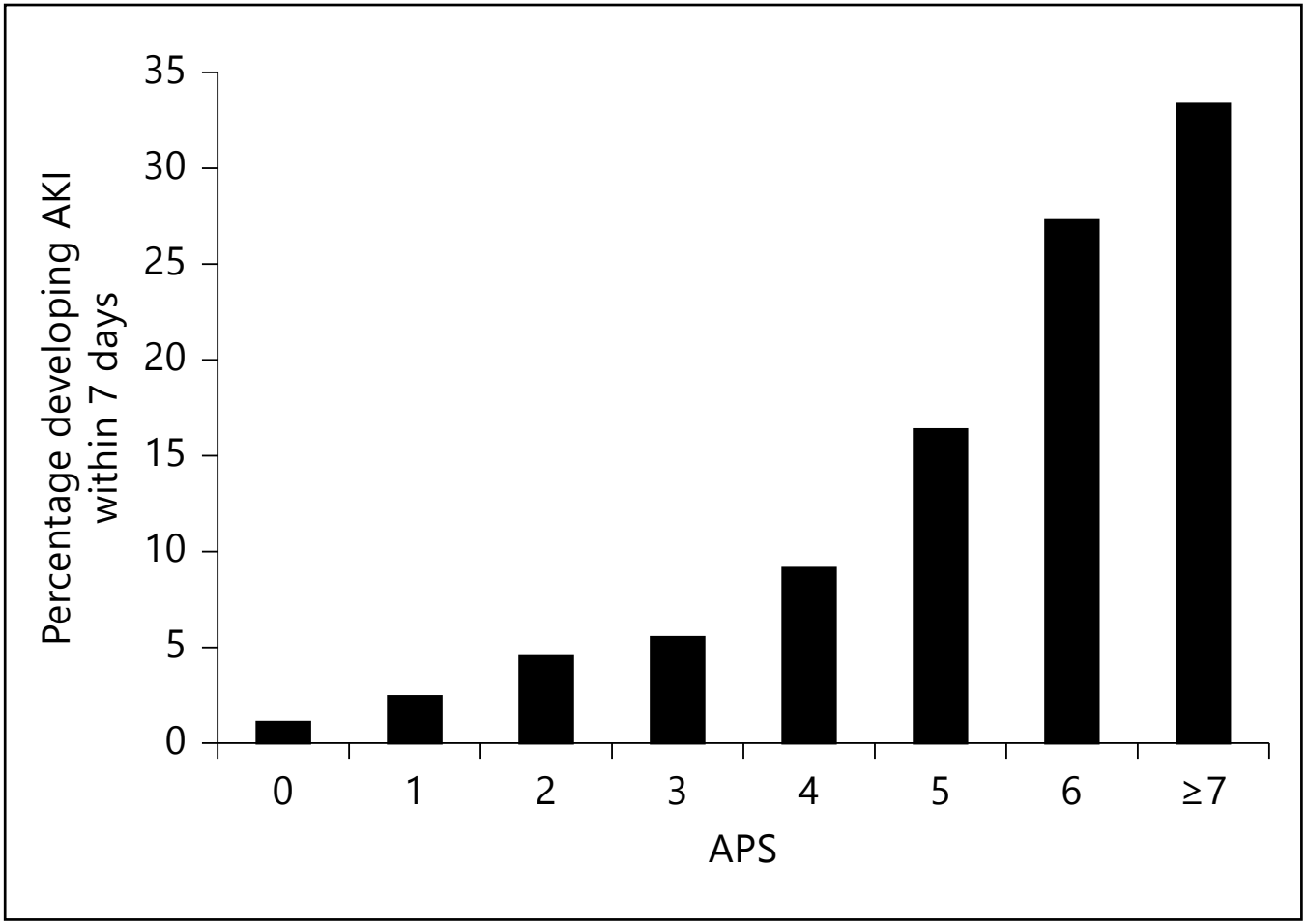
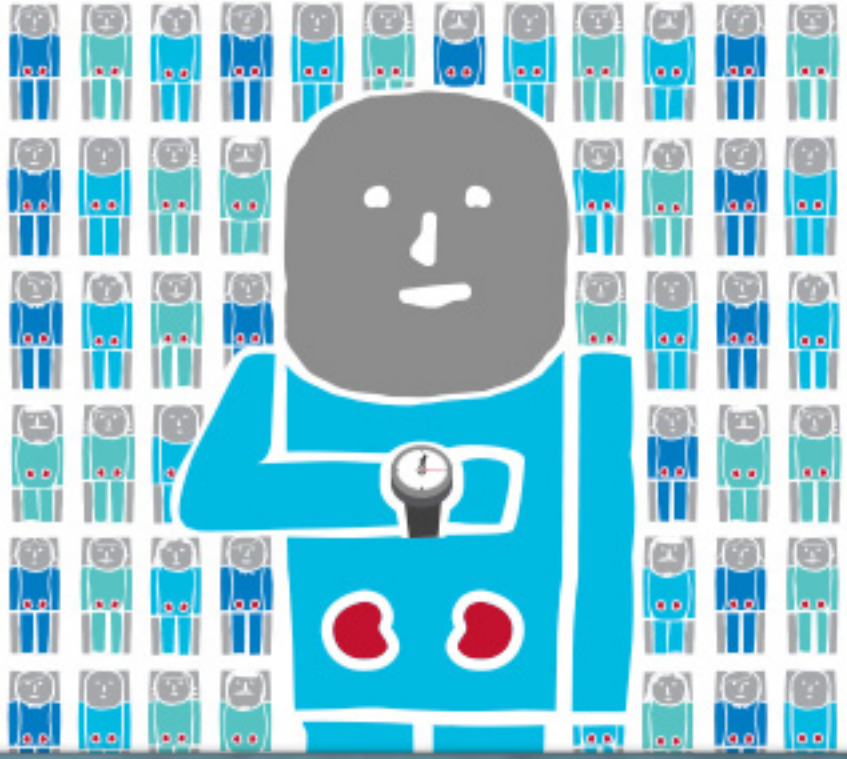


Fig. 3. Percentage of patients developing AKI within 7 days of admission according to the APS.



When At Risk Identified? What Then?

Step 1
Identify the hazards

Step 2
Decide who might be harmed and how

Step 3
Evaluate the risks and decide on precautions

Prevention?

How Do We Prevent AKI??

Don’t Get Admitted to Hospital…

UK Renal Association….

4. Acute Kidney Injury (AKI) (Guidelines AKI 4.1 – 4.5)

Guideline 4.1 – AKI : Management; General Management

We recommend that general supportive measures include optimisation of haemodynamic status by appropriate fluid therapy, administration of vasopressors and/or inotropes and treatment of any underlying sepsis. Nephrotoxic medications should be stopped. (1A)

Guideline 4.2 – AKI : Management; Pharmacological Therapy

We recommend that therapeutic drug dosing must be adapted to altered kinetics in AKI. (1B)

Guideline 4.3 – AKI : Management; Pharmacological Therapy

We recommend that there is no specific pharmacological therapy proven to effectively treat AKI secondary to hypoperfusion injury and/or sepsis. (1B)

Chapter 2.2: Risk assessment

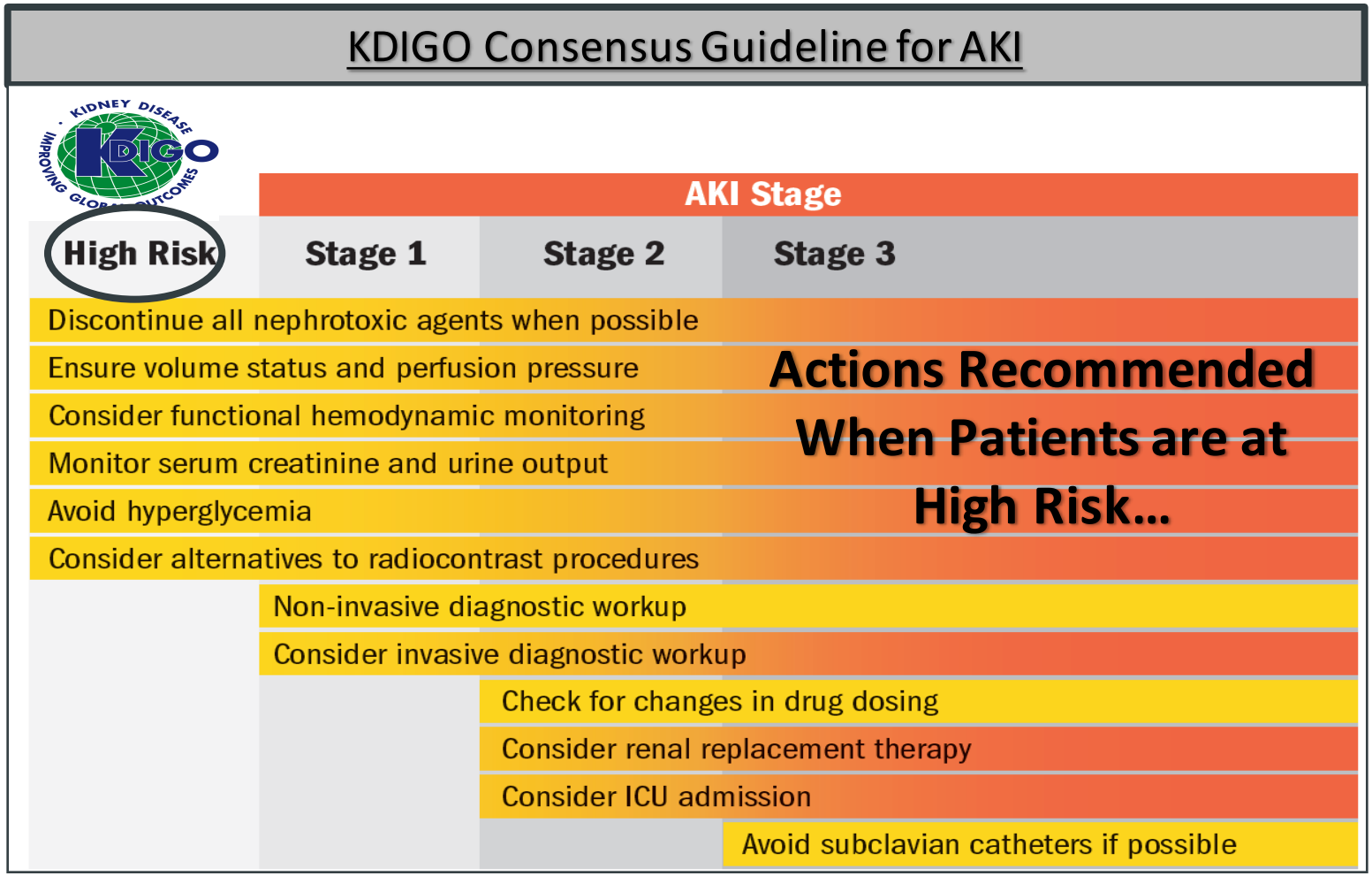
Intensive Care Med (2010) 36:379–380
DOI 10.1007/s00134-009-1683-1

EDITORIAL

Andrew Davenport

Clinical guidelines for the protection of kidney function and prevention of acute kidney injury in the intensive care unit: common sense rather than magic bullets?

Stage Based Management Options

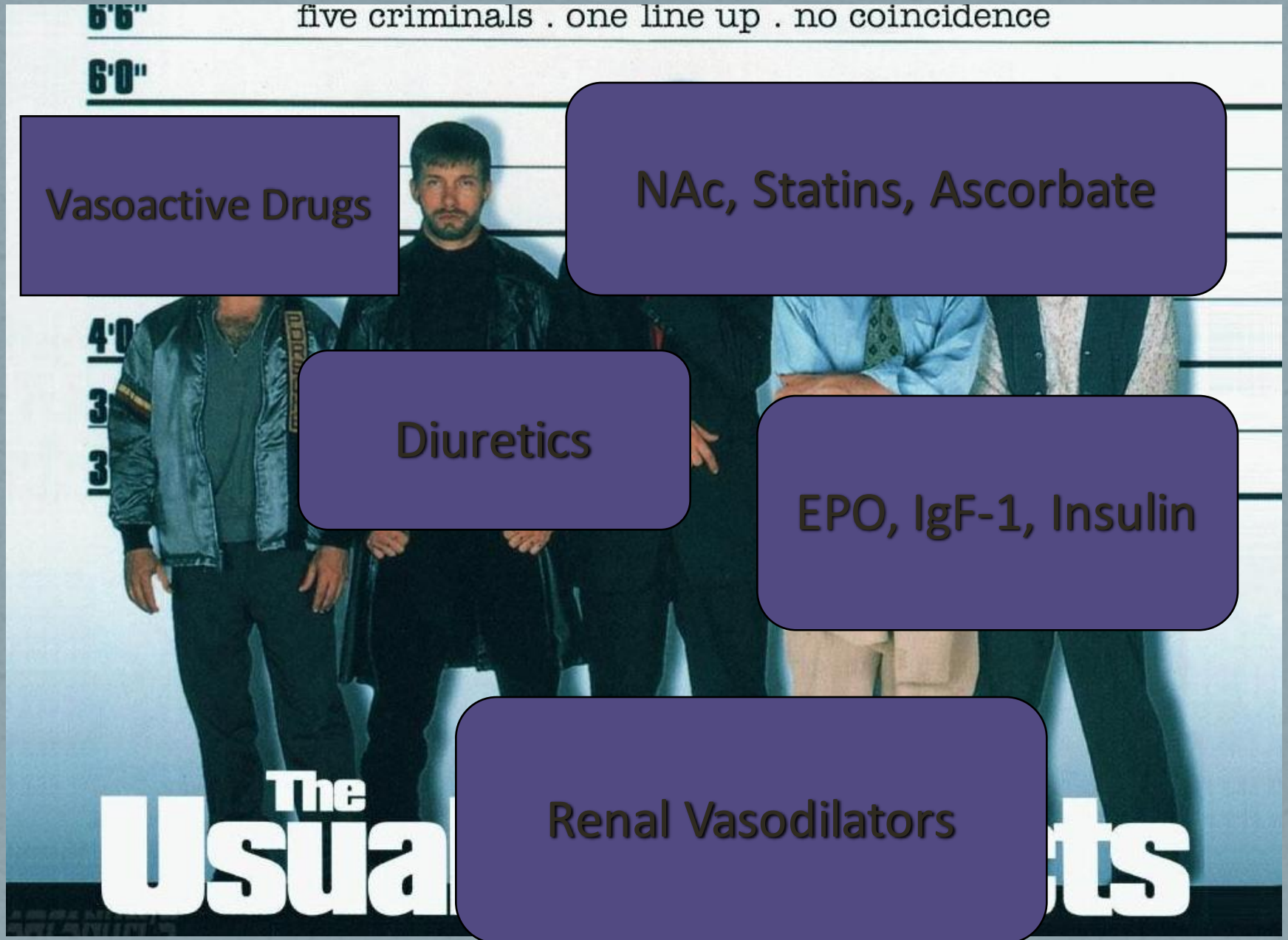


KDIGO: Kidney Disease Improving Global Outcomes; Kidney International Supplements (2012) 2, 1; doi: 0.1038/kisup.2012.1; MacLeod A. NCEPOD report on acute kidney injury- must do better. Lancet 2009; 374: 1405-1406

Preventing AKI

- Often (always) multifactorial
- Can we expect to find a 'cure-all'?

- **What has been Tried?**



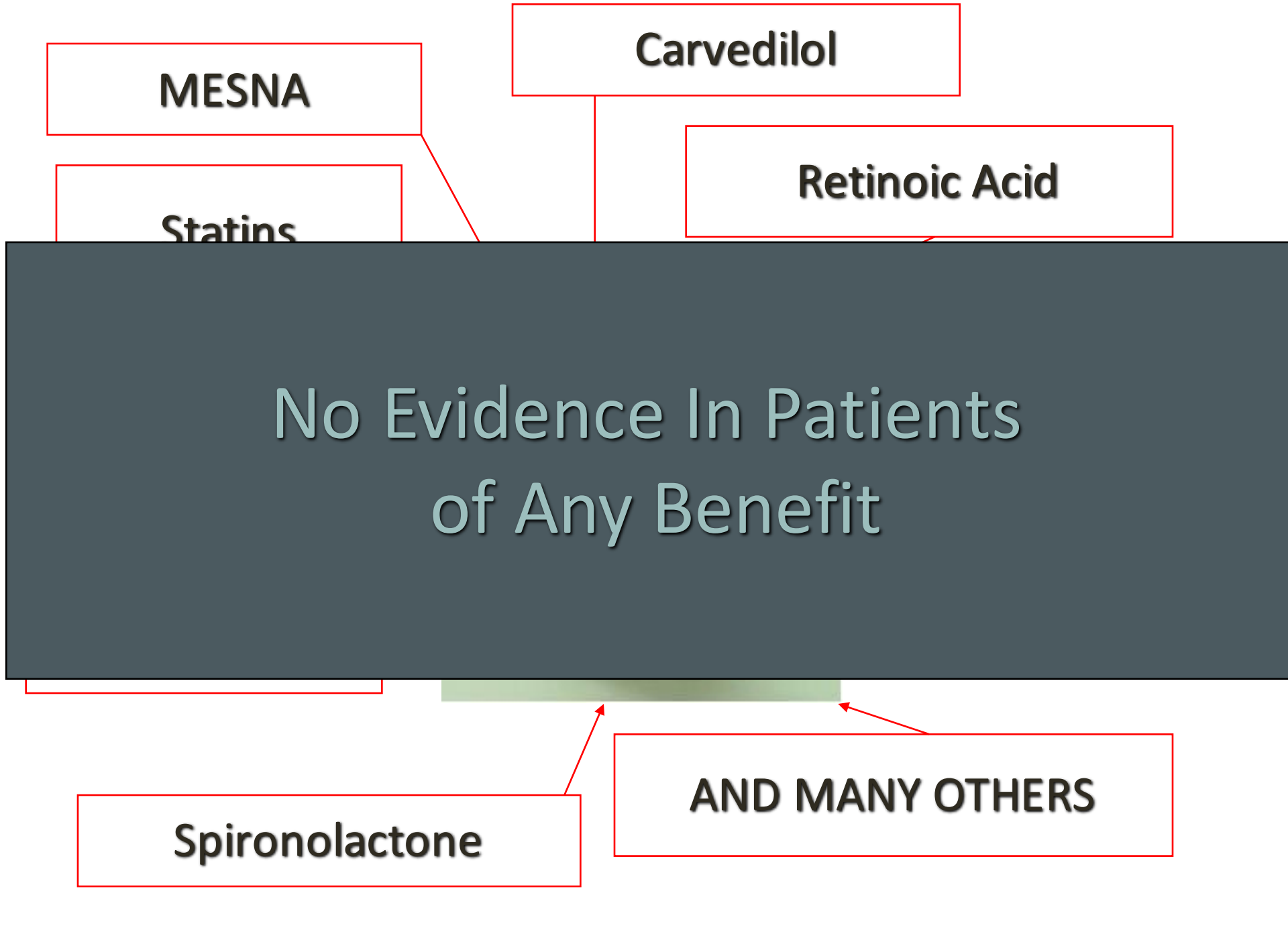
Vasoactive Drugs

NAc, Statins, Ascorbate

Diuretics

EPO, IgF-1, Insulin

Renal Vasodilators


Carvedilol
MESNA
Retinoic Acid
Statins
No Evidence In Patients of Any Benefit
Spironolactone
AND MANY OTHERS

Preventing AKI: Fluids

- Fluid replacement : Must be a good thing

Despite the recognition of volume depletion as an important risk factor for AKI, there are no randomized controlled trials (RCTs) that have directly evaluated the role of fluids vs. placebo in the prevention of AKI. However, RCTs mostly in the field of CI-AKI have

Not entirely surprising…

Preventing AKI: Colloids?

CONCLUSIONS

In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. (Funded by the National Health and Medical Research Council of Australia and others; CHEST ClinicalTrials.gov number, NCT00935168.)

Evidence that colloids increase the need for RRT…

Which Fluid…..

Key messages

- It has been hypothesized that hyperoncotic colloid solutions may damage the kidney. A meta-analysis of randomized controlled trials was performed to test this hypothesis.
- Hyperoncotic albumin decreased the odds of acute kidney injury by 76% and of death by 48%.
- Hyperoncotic hydroxyethyl starch increased the odds of acute kidney injury by 92% and of death by 41%.
- Hyperoncotic colloids *per se* do not appear to be harmful to the kidney.
- Renal effects may be specific to the particular colloid molecule.

Simplified Severe Sepsis Protocol: A Randomized Controlled Trial of Modified Early Goal–Directed Therapy in Zambia*

Andrews, Ben MD[1,2,3]; Muchemwa, Levy MBChB[3]; Kelly, Paul MD, FRCP[4]; Lakhi, Shabir MBChB, MMed, MPH[3,5]; Heimburger, Douglas C. MD, MS, FACP[1]; Bernard, Gordon R. MD[6]

Interventions: Simplified Severe Sepsis Protocol consisting of up to 4 L of IV fluids within 6 hours, guided by jugular venous pressure assessment, and dopamine and/or blood transfusion in selected patients. Control group was managed as usual care. Blood cultures were collected and early antibiotics administered for both arms.

Simplified Severe Sepsis Protocol received significantly more IV fluids in the first 6 hours (2.7 L vs 1.7 L, $p = 0.002$). The study was stopped early because of high mortality rate among patients with hypoxemic respiratory failure in the intervention arm (8/8, 100%)

Section 3: Prevention and Treatment of AKI

FLUIDS

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*)

Diuretics

Rationale

- Reduced O_2 Consumption
- Increased Tubular Flow
- Increased Urea Excretion
- Volume Management

High-dose Furosemide in patients with Established AKI

Table 2. Study End Points in the Population Assessable for Efficacy With Stratification According to SAPS

	Furosemide (n = 166)	Placebo (n = 164)	Significance (*P*)
Patients alive at the end of the study (n = 221)			
SAPS ≤15	60	67	0.36*
SAPS >15	47	47	
Total	107	114	
Deaths (n = 109)			
SAPS ≤15	16	11	
SAPS >15	43	39	
Total	59	50	
No. of RRT sessions			
SAPS ≤15	5.6 ± 5.5	5.7 ± 4.5	0.37†
SAPS >15	7.3 ± 5.3	7.9 ± 5.6	
Total	6.5 ± 5.4	6.9 ± 5.3	
Time on RRT (d)	11.4 ± 8.6	12.4 ± 8.7	0.21†
Time to achieve a serum creatinine level <2.26 mg/dL without RRT (d)	19.7 ± 40.6	21.4 ± 65.1	0.99†
Time to achieve a 2-L/d diuresis (d)	5.7 ± 5.8	7.8 ± 6.8	0.004†

Cantarovic F, Am J Kidney Dis 2004

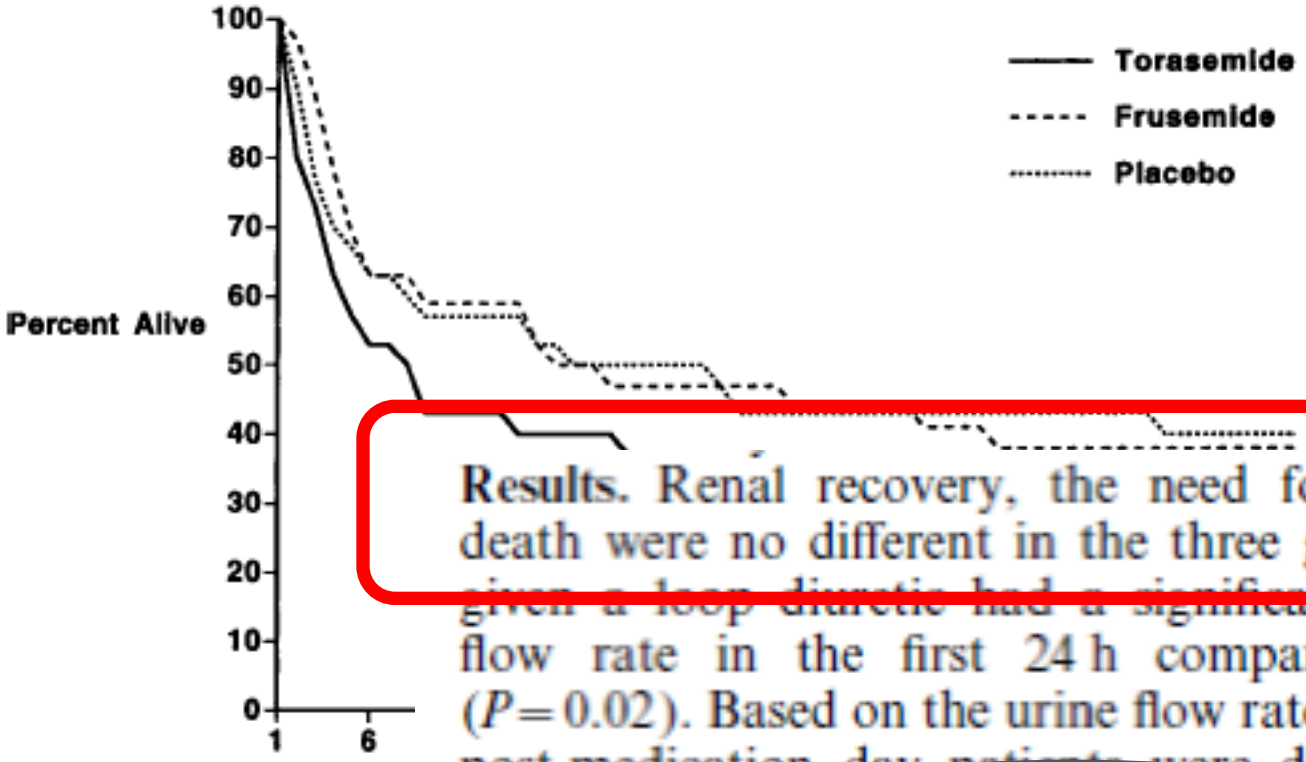


Fig. 1. Actuarial survival for the

Results. Renal recovery, the need for dialysis, and death were no different in the three groups. Patients given a loop diuretic had a significant rise in urine flow rate in the first 24 h compared to placebo ($P=0.02$). Based on the urine flow rate during the first post-medication day patients were divided into two groups—oliguric (< 50 ml/h) and non-oliguric (≥ 50 ml/h). Non-oliguric patients had a significantly lower mortality than oliguric patients (43% *vs* 69%, $P=0.01$). However, they were less ill (APACHE II score 17.2 *vs* 20.6, $P=0.008$) and had less severe renal failure at entry (creatinine clearance 14 ml/min *vs* 4 ml/min, $P<0.0001$).

Conclusion. The use of loop diuretics in oliguric patients with ARF can result in a diuresis. There is no evidence that these drugs can alter outcome.

Chapter 3.4: The use of diuretics in AKI

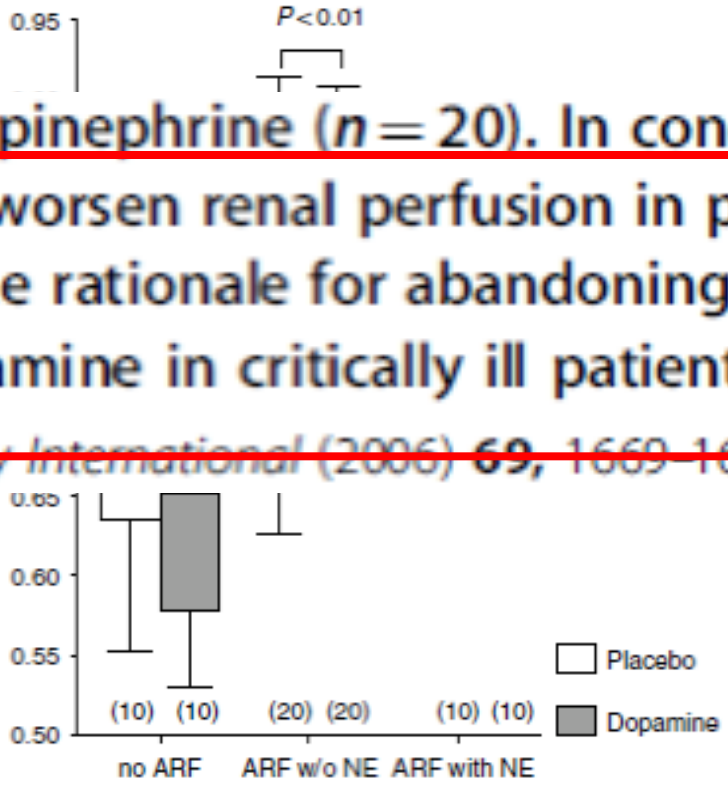
3.4.1: We recommend not using diuretics to prevent AKI. (*1B*)

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

Dopamine

- Rationale
- ? Preferential Renal Vasodilatation
- ?Evidence

Effect of ´low-dose´ dopamine on Renal Resistive Index



norepinephrine ($n = 20$). In conclusion 'low-dose' dopamine can worsen renal perfusion in patients with ARF, which adds to the rationale for abandoning the routine use of 'low-dose' dopamine in critically ill patients.

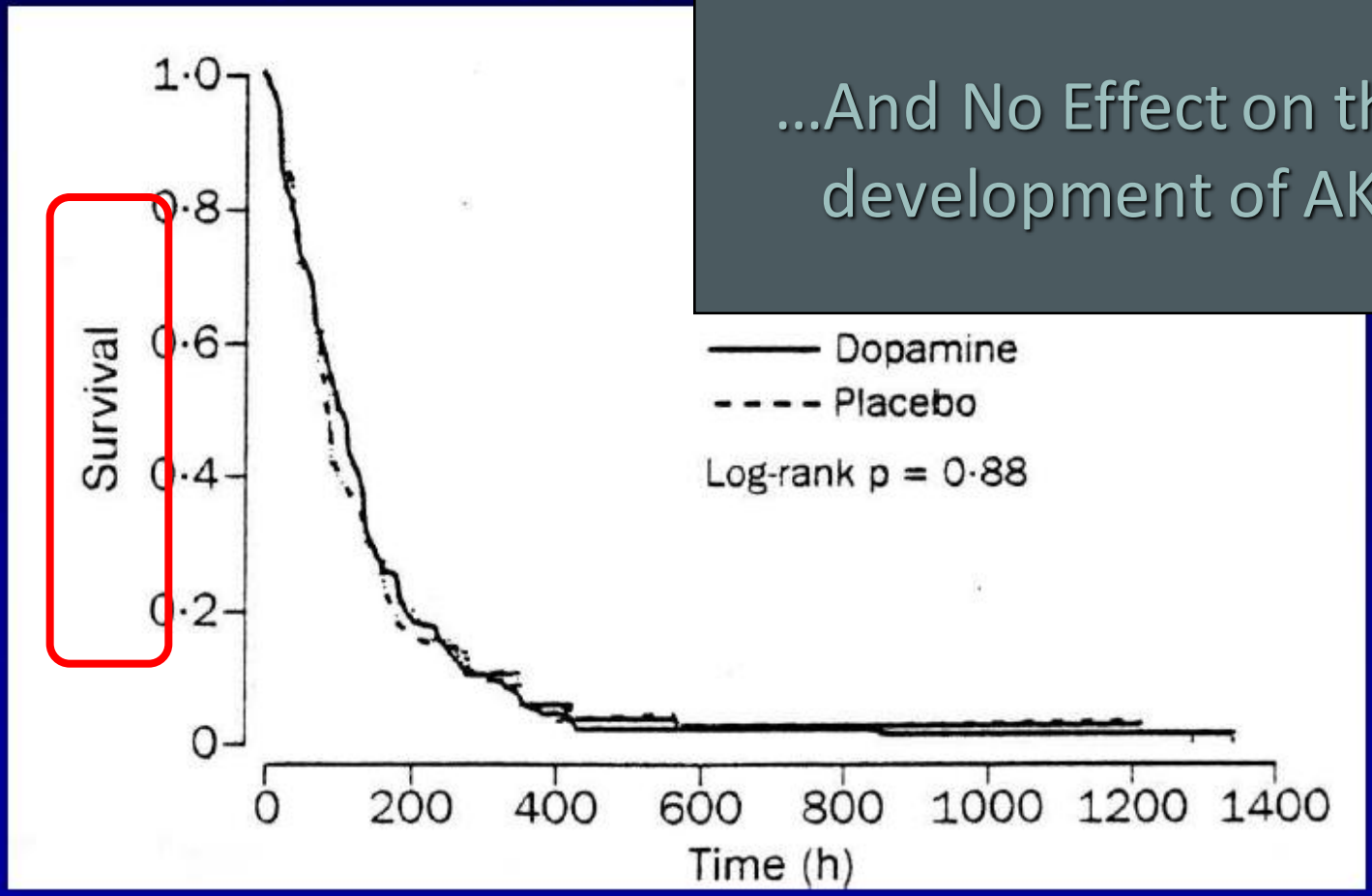
Kidney International (2006) **69**, 1669–1674. doi:10.1038/sj.ki.5000310;

Figure 5 | Effect of dopamine on RI values in patients with and without norepinephrine (NE) infusion.

Lauschke A, Kidney Int 2006

DOPAMINE DOES NOT PREVENT AKI

RCT - dopamine 2μg/kg/min throughout ITU stay



…And No Effect on the development of AKI

Lancet 2000;356:2139

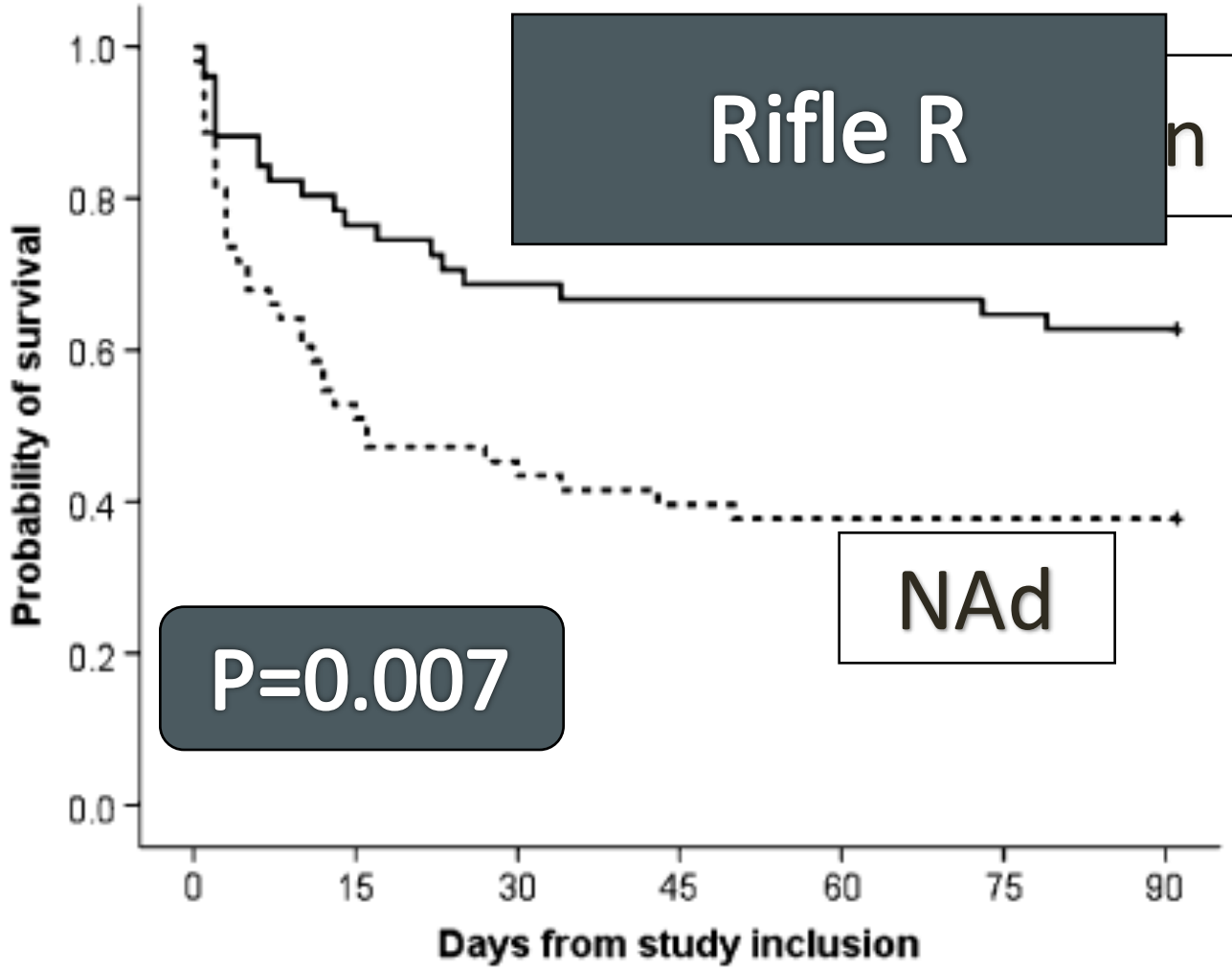
Chapter 3.5: Vasodilator therapy: dopamine, fenoldopam, and natriuretic peptides

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

3.5.2: We suggest not using fenoldopam to prevent or treat AKI. (*2C*)

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

What of Vasoconstrictors?



Section 3: Prevention and Treatment of AKI

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*)

Other Candidates?

• IGF-1	• Not Recommended
• ANP	• Not Recommended
• Fenoldapam	• Not Recommended
• NAc	• Not Recommended
• EPO	• Not Recommended

Insulin

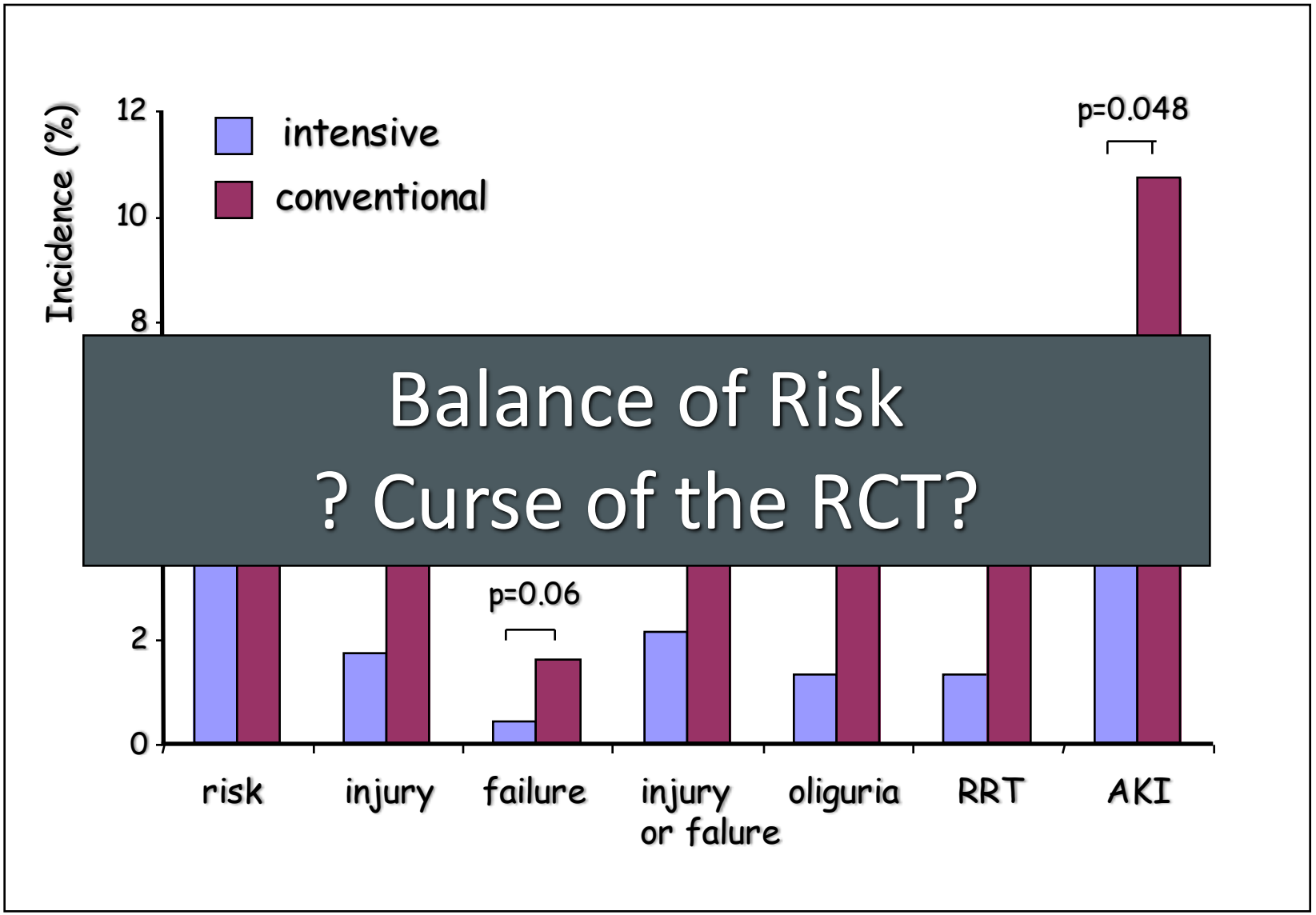
- Pooled analysis failed to confirm early beneficial effects of IIT
- NICE-Sugar found that IIT increased mortality
  - BG target 4.5-6.0 higher mortality than ≤ 9.99
- The end for IIT?

Glycemic control and nutritional support

3.3.1: In critically ill patients, we suggest insulin therapy targeting plasma glucose 110–149 mg/dl (6.1–8.3 mmol/l). (*2C*)

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

Intensive Insulin Therapy and AKI



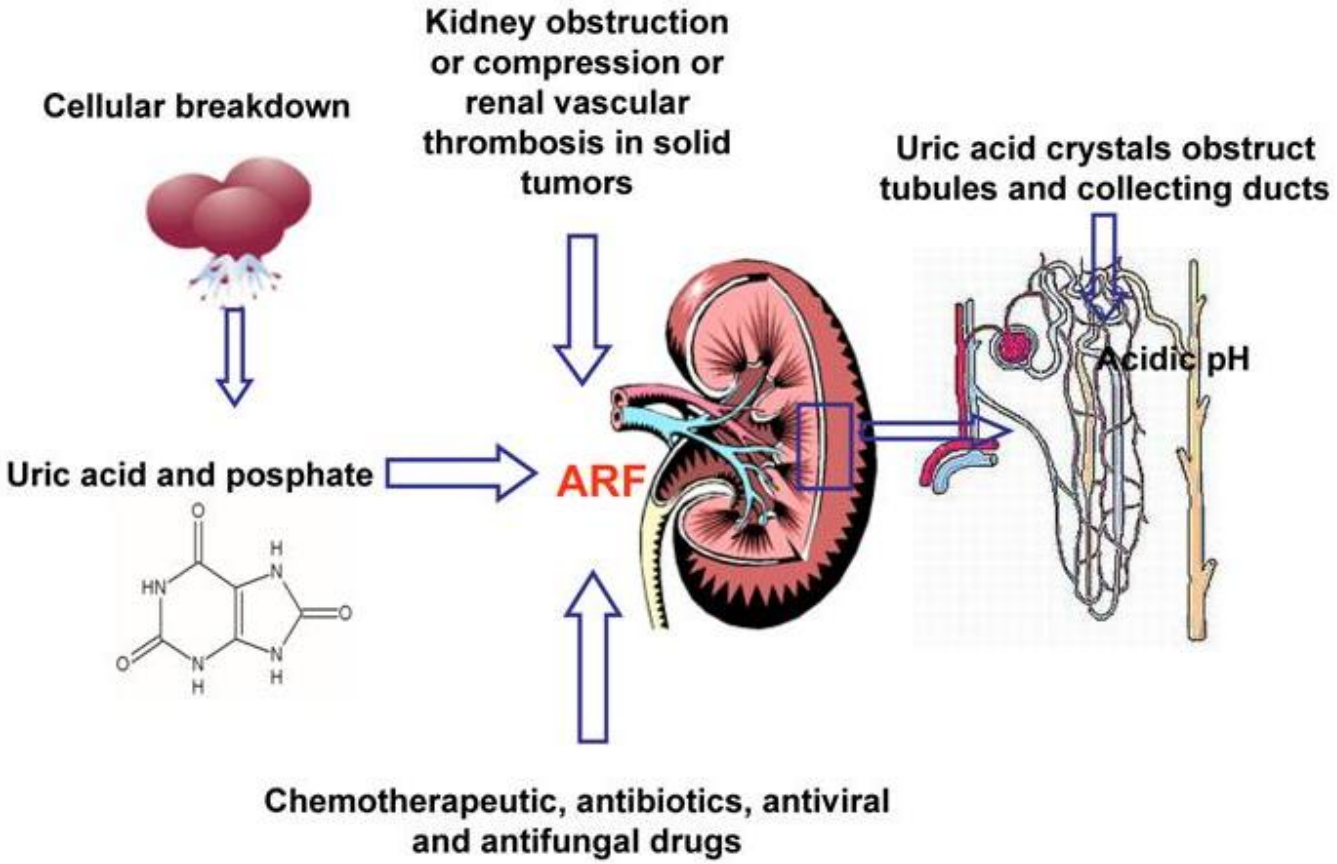
M. Schetz, JASN 2008

Glycemic control and nutritional support

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

3.3.4: We suggest administering 0.8–1.0 g/kg/d of protein in noncatabolic AKI patients without need for dialysis (*2D*), 1.0–1.5 g/kg/d in patients with AKI on RRT (*2D*), and up to a maximum of 1.7 g/kg/d in patients on continuous renal replacement therapy (CRRT) and in hypercatabolic patients. (*2D*)

What About Well Defined Conditions?

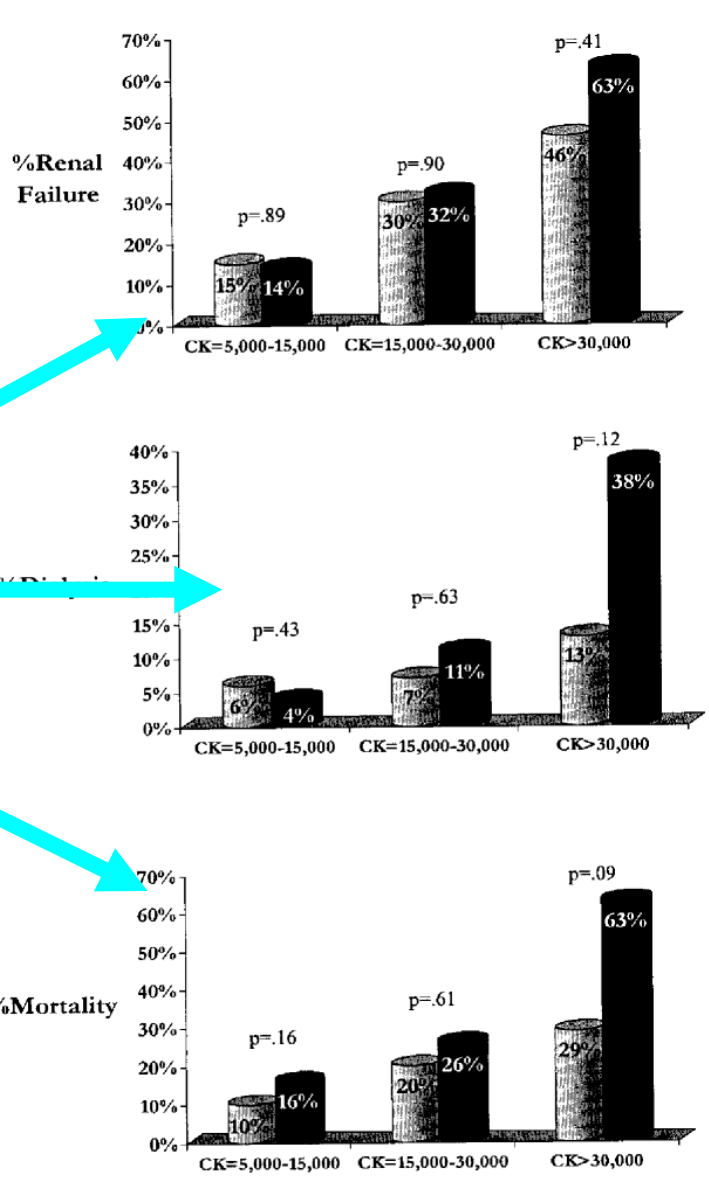


Rhabdomyolysis

- Should be easy
- Identifiable (mostly)
- Biomarker (of sorts)
- Bicarbonate/Mannitol/Frusemide
- ?Evidence

Therapy for Rhabdomyolysis

No Difference in:
% Renal Failure
% Dialysis
% Mortality



Brown C et al.
J Trauma 2004; 30 : 1191-96

Therapy for Rhabdomyolysis

Table 4. Comparative Studies on Preventive and Therapeutic Regimens in Rhabdomyolysis.

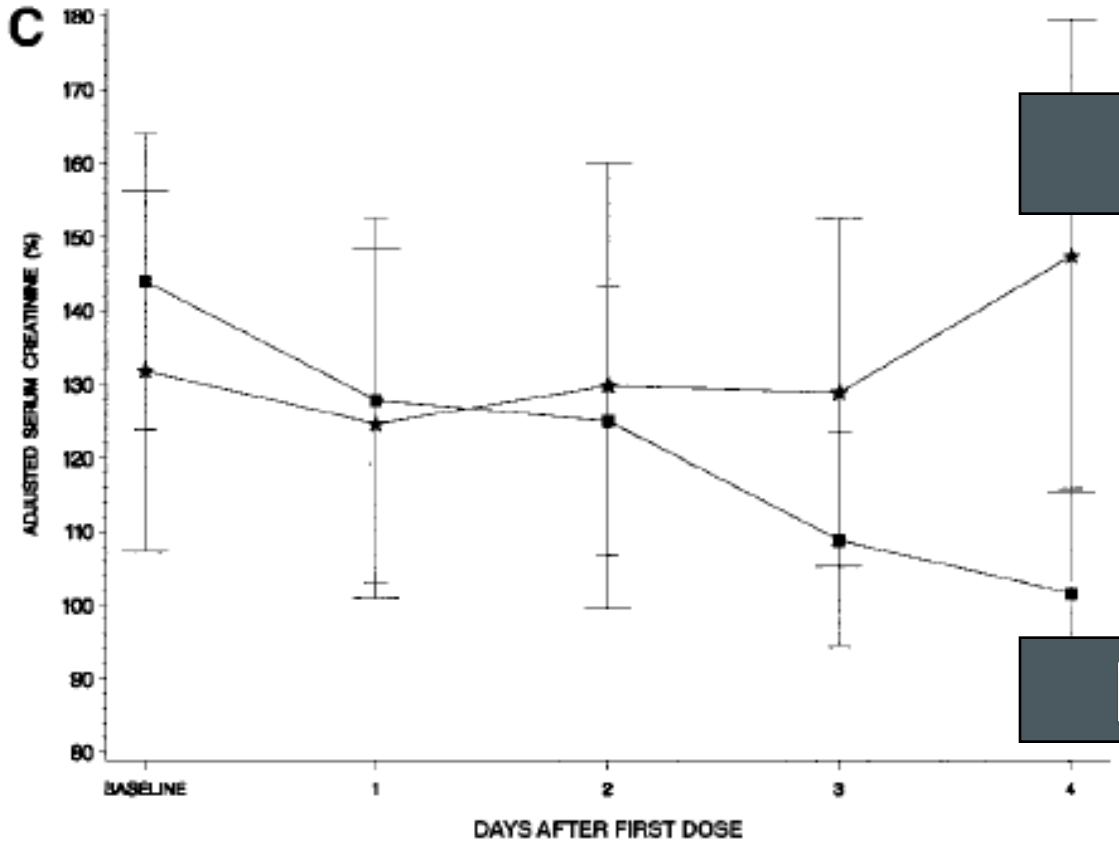
Study	Study Design	Patient Group	No. in Sample	Therapeutic Strategy	Outcome in Patients with Acute Kidney Injury
Shimazu et al.[34]	Retrospective	Patients with the crush syndrome	14	Late vs. early initiation of therapy; high (>10 liters for 48 hours) vs. low volume of hydration	Better if therapy initiated early; high volume of hydration better
Gunal et al.[35]	Retrospective	Patients with the crush syndrome	16	Early vs. late treatment with normal saline followed immediately by bicarbonate	Better if treatment initiated early
Homsi et al.[36]	Retrospective	Patients in the intensive care unit	24	Normal saline vs. normal saline plus bicarbonate and mannitol	No difference
Brown et al.[37]	Retrospective	Patients with trauma	2083	Normal saline vs. bicarbonate plus mannitol	No difference
Cho et al.[38]	Prospective, randomized	Patients with intoxication from doxylamine	28	Ringer's lactate vs. normal saline; bicarbonate if urine pH is <6.5	No effect on peak creatine kinase level or recovery with Ringer's lactate as compared with normal saline; more bicarbonate needed with normal saline than with Ringer's lactate

NEJM 2009

Tumour Lysis Syndrome

- TLS characterized by Severe
  - Hyperuricemia
  - Hyperphosphatemia
  - Hyperkalemia
  - Hypocalcemia,
  - Acute Kidney Injury

Rasburicase



Allopurinol

Rasburicase

Goldman Blood 2001 97; 2998-3003

Rasburicase

- Rasburicase Group
  - Adjusted SCr **fell** from 144% to 102%
- Allopurinol Group
  - Adjusted SCr **rose** from 132% to 147%

  - No difference in need for RRT
  - Peak Uric Acid reduced ($p<.0001$)
  - Mean Uric acid AUC less ($p<.0001$)

Goldman Blood 2001 97; 2998-3003

Preventing AKI…..

- Beset by Problems:
- An incomplete understanding of the underlying pathophysiologic mechanisms
- The lack of robust early markers for AKI, and hence an unacceptable delay in initiating therapy

Management ??

- Hypovolemia -> Volume Expansion
- Hypotension -> Volume Expansion, Vasopressors
- CHF -> Inotropes, Inodilators (e.g. levosimendan)
- Nephrotoxins -> Stop
- ACE/ARB -> Stop

WG Nephrology of ESICM (Joannidis et al , Intensive Care Med 2009)

- Age -> ?
- Gender -> ?


At Present….Is this the best we can hope for?
NIHILISM
Believing in nothing can be exhausting.
ODDCULTURE.COM

Section 3: Prevention and Treatment of AKI

PROTOCOLIZED HEMODYNAMIC MANAGEMENT

3.1.3: We suggest using protocol-based management of hemodynamic and oxygenation parameters to prevent development or worsening of AKI in high-risk patients in the perioperative setting (*2C*) or in patients with septic shock (*2C*).

How Do I Know When I Have Given Enough Fluid?

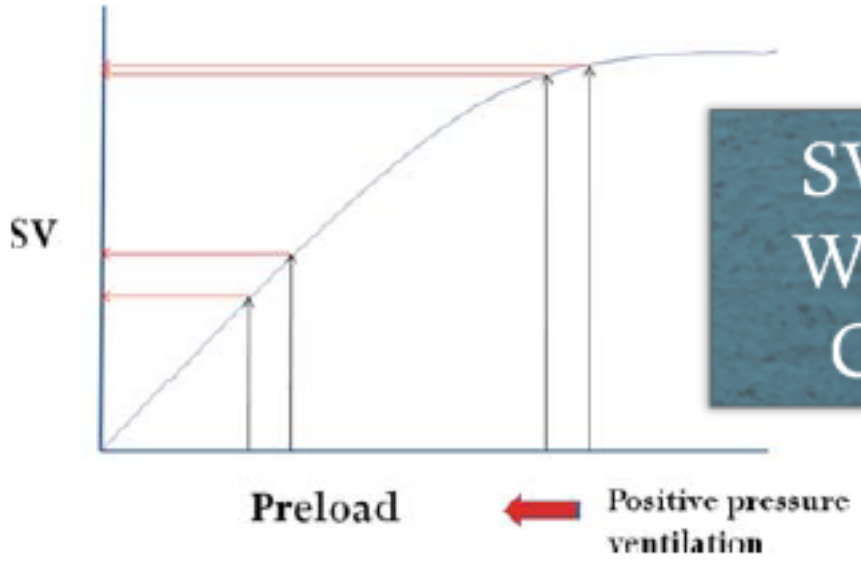
IS MY PATIENT FLUID RESPONSIVE?

The only reason to give a patient a fluid challenge is to increase stroke volume. The concept of "filling up the tank" is meaningless and reflects a poor understanding of human physiology.

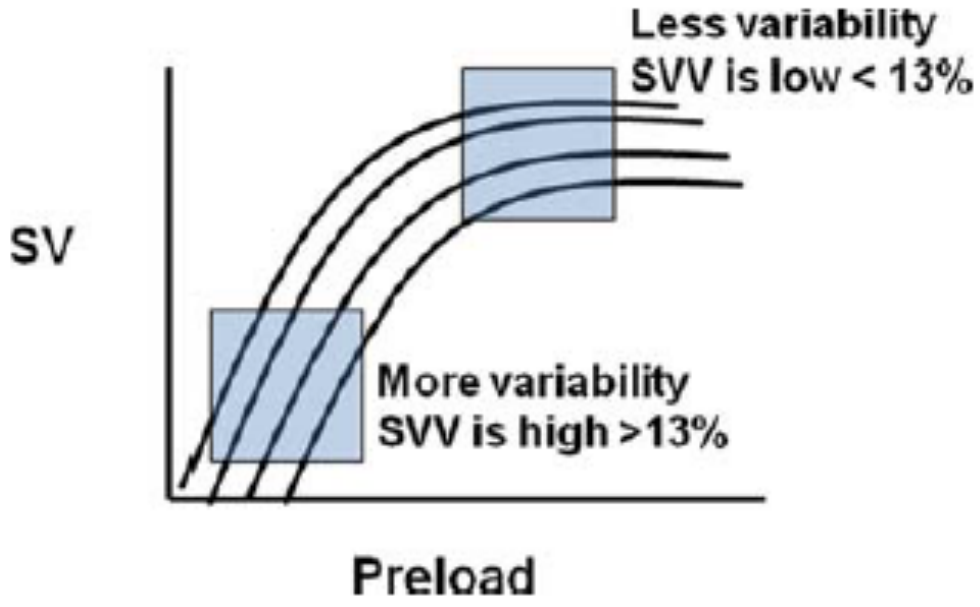
CVP not related to BV (AUC 0.56)

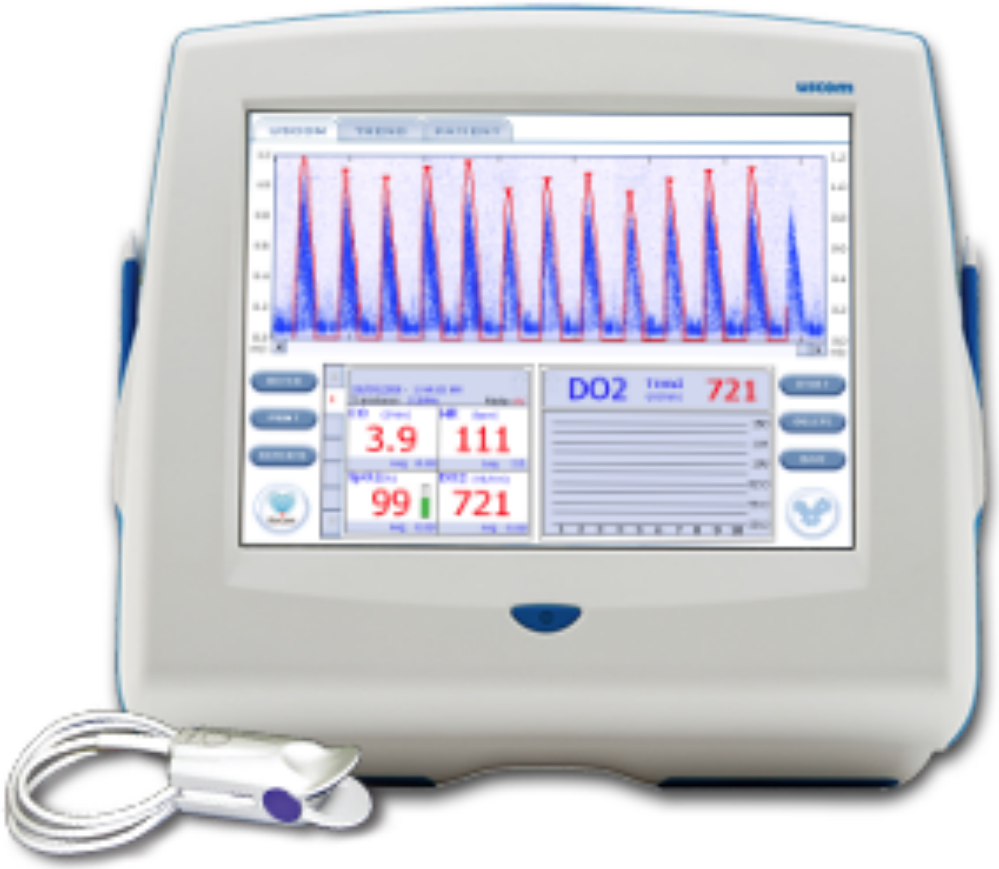
Dynamic Measurements : SVV/PPV

Passive Leg Raise ?



SVV Reduced When Starling Curve 'Flat'

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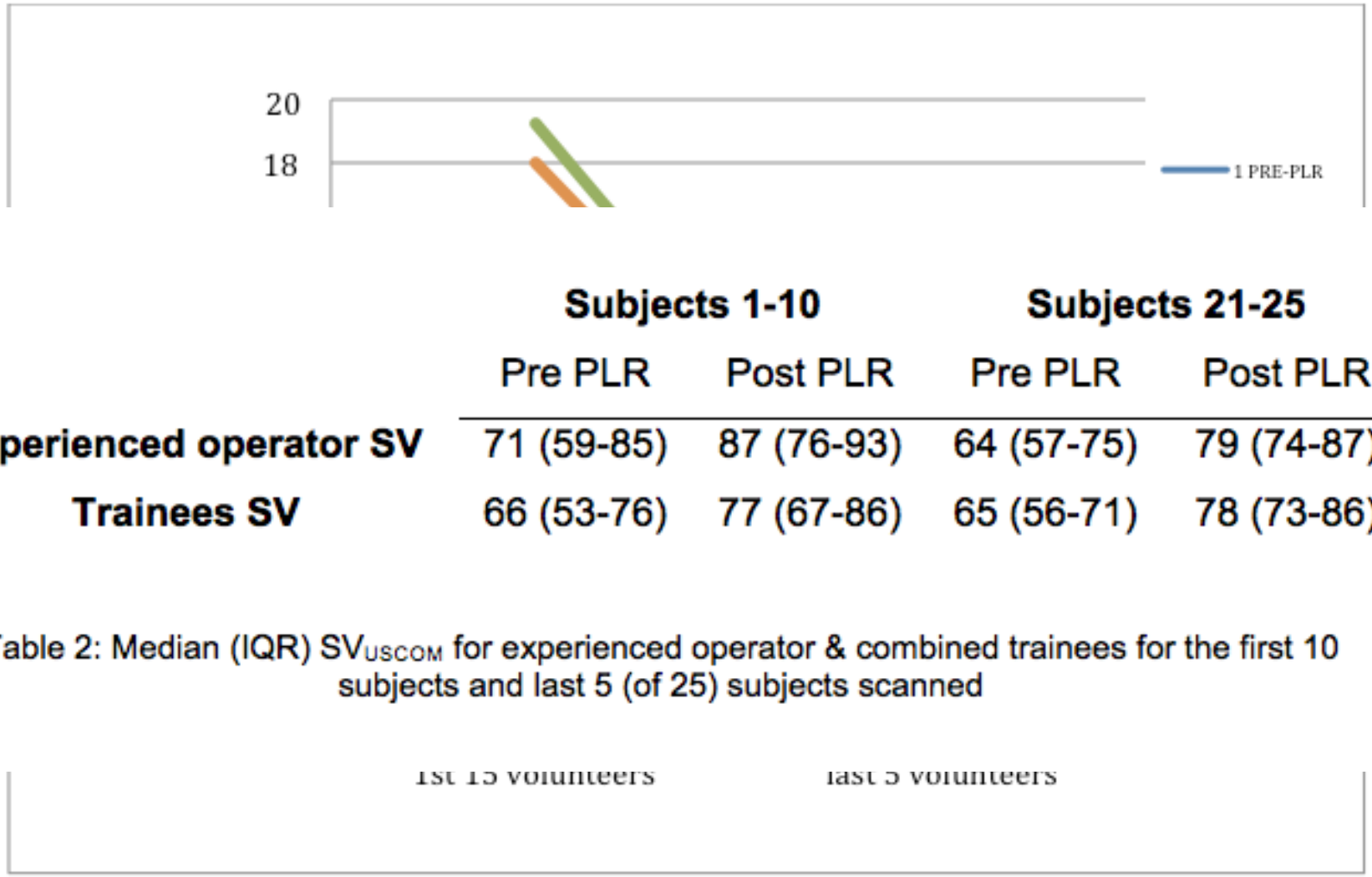

	Subjects 1-10		Subjects 21-25	
	Pre PLR	Post PLR	Pre PLR	Post PLR
Experienced operator SV	71 (59-85)	87 (76-93)	64 (57-75)	79 (74-87)
Trainees SV	66 (53-76)	77 (67-86)	65 (56-71)	78 (73-86)

Table 2: Median (IQR) SV_{USCOM} for experienced operator & combined trainees for the first 10 subjects and last 5 (of 25) subjects scanned

Figure 1 – Mean percentage difference in SV during training between the 4 trainees & the experienced operator comparing 1st 15 volunteers & the last 5 volunteers (includes pre and post PLR differences).

Conclusions:

- Use Haemodynamic Monitoring
- Resist repeated fluid challenges to soft endpoints
- Consider early RRT to prevent/treat fluid overload
- Better data is needed to guide fluid resuscitation particularly in sepsis


I used to think this……

Invitation to participate

Prevalence in **E**urope of **A**cute and **C**hronic Kidney Disease in the ICU **E**nvironment

PEACE

Aims:

- epidemiology of AKI and CKD, defined by RRT in ICU patients
- modalities of RRT
- indications for initiation of RRT
- who is performing RRT.
- renal outcomes and 28-d, ICU, and hospital mortality.

Info: AKI section

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Thank You For Listening