Perioperative Acute Kidney Injury

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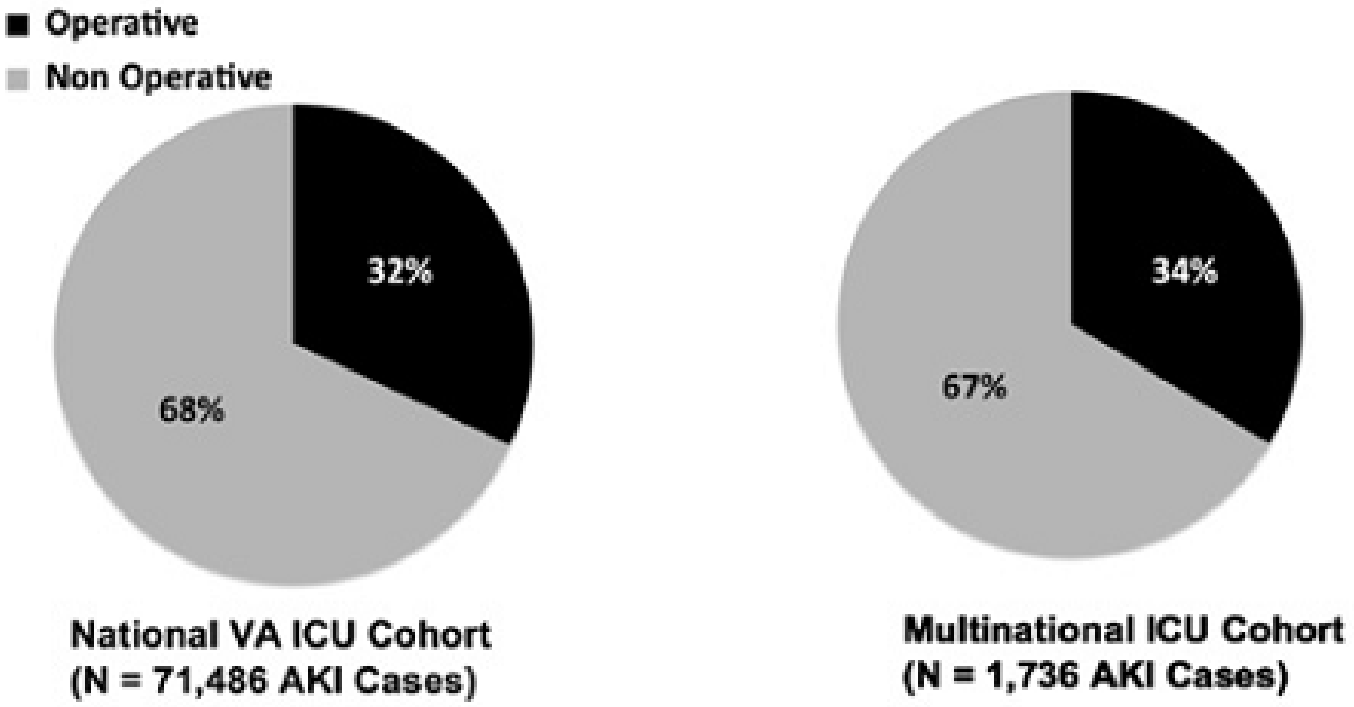
25/5/2014

- Perioperative acute kidney injury
- Dialysis dependent patients

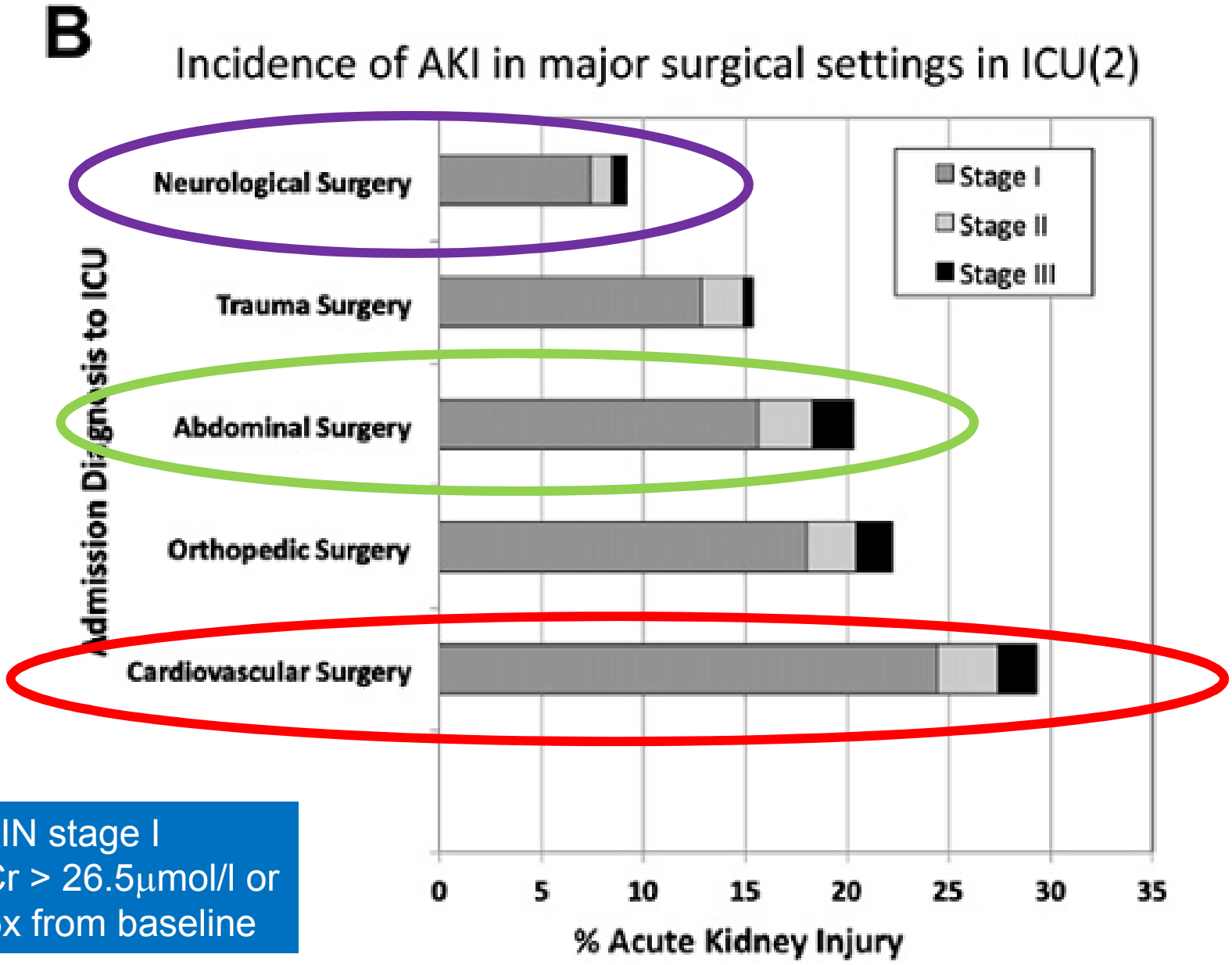
Perioperative Acute kidney injury (AKI) - how common is the problem?

A Proportion of AKI cases attributable to surgical settings.(2, 3)



Crit Care Med.2009;37:2552-2558

JAMA. 2005;294:813-818

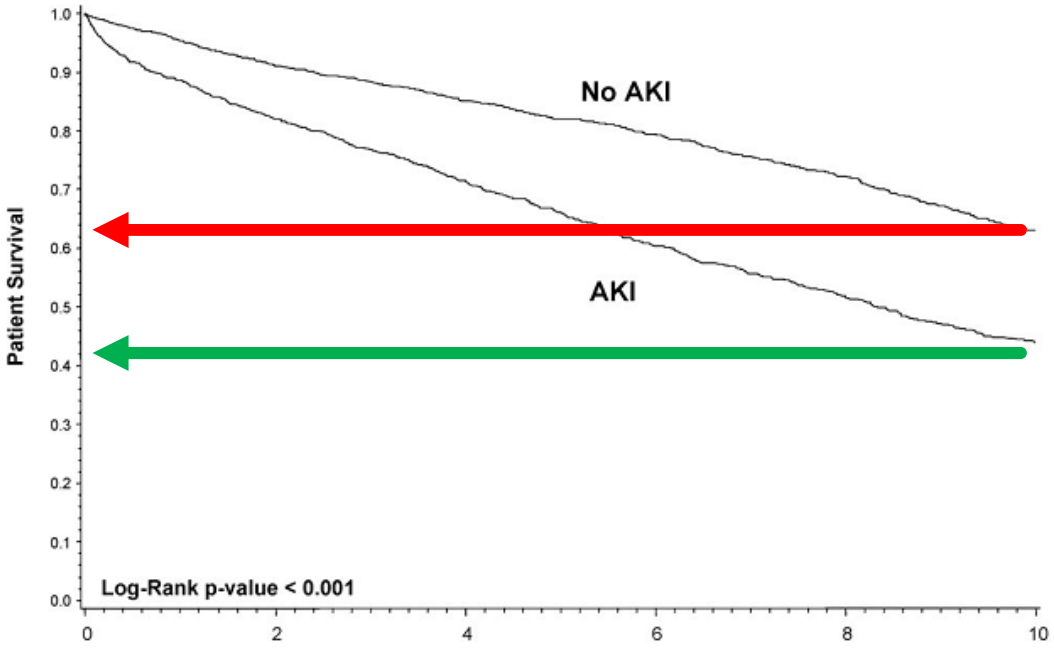


AKIN stage I
↑ Cr > 26.5μmol/l or
1.5x from baseline

Crit Care Med.2009;37:2552-2558

Why perioperative AKI important?

- AKI requiring dialysis is an independent risk factor for death



~3000 patients received CS, survival decrease from 62% to 42%

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

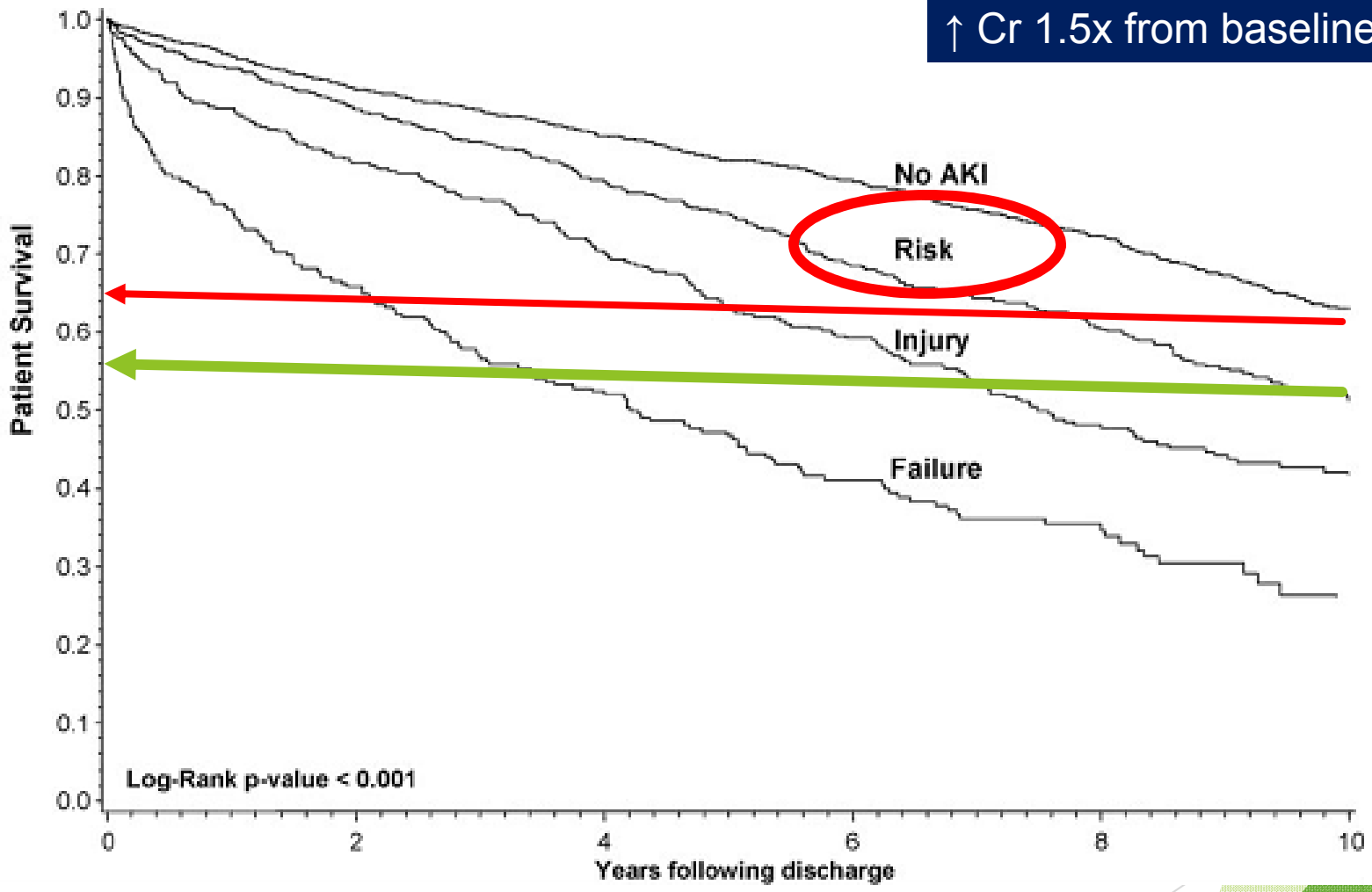
American Heart Association®

Acute Kidney Injury Is Associated With Increased Long-Term Mortality After Cardiothoracic Surgery

Charles E. Hobson, Sinan Yavas, Mark S. Segal, Jesse D. Schold, Curtis G. Tribble, A. Joseph Layon and Azra Bihorac

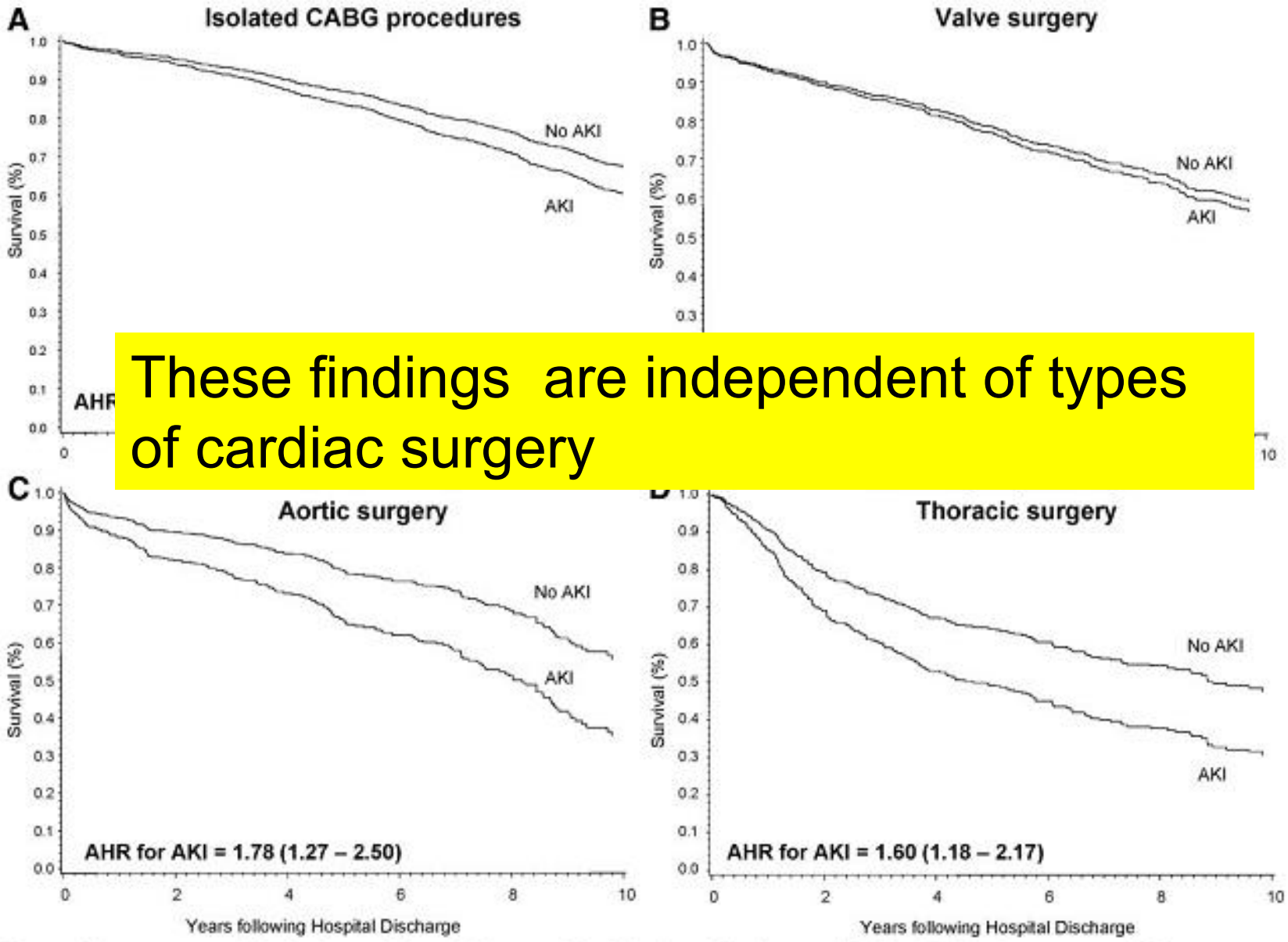
Circulation. 2009;119:2444-2453

RIFLE “Risk”
↑ Cr 1.5x from baseline



Greater AKI severity -> higher mortality
Patient survival differ by 10% comparing no AKI with “Risk”

Circulation. 2009;119:2444-2453



These findings are independent of types of cardiac surgery

Figure 3. Long-term survival of patients with and without an AKI during hospitalization, stratified by individual surgery type. AKI group includes all patients with AKI, regardless of severity. Survival curves are adjusted for the mean level of model covariates listed in Table 2.

Circulation. 2009;119:2444-2453

Long-Term Risk of Mortality and Acute Kidney Injury During Hospitalization After Major Surgery

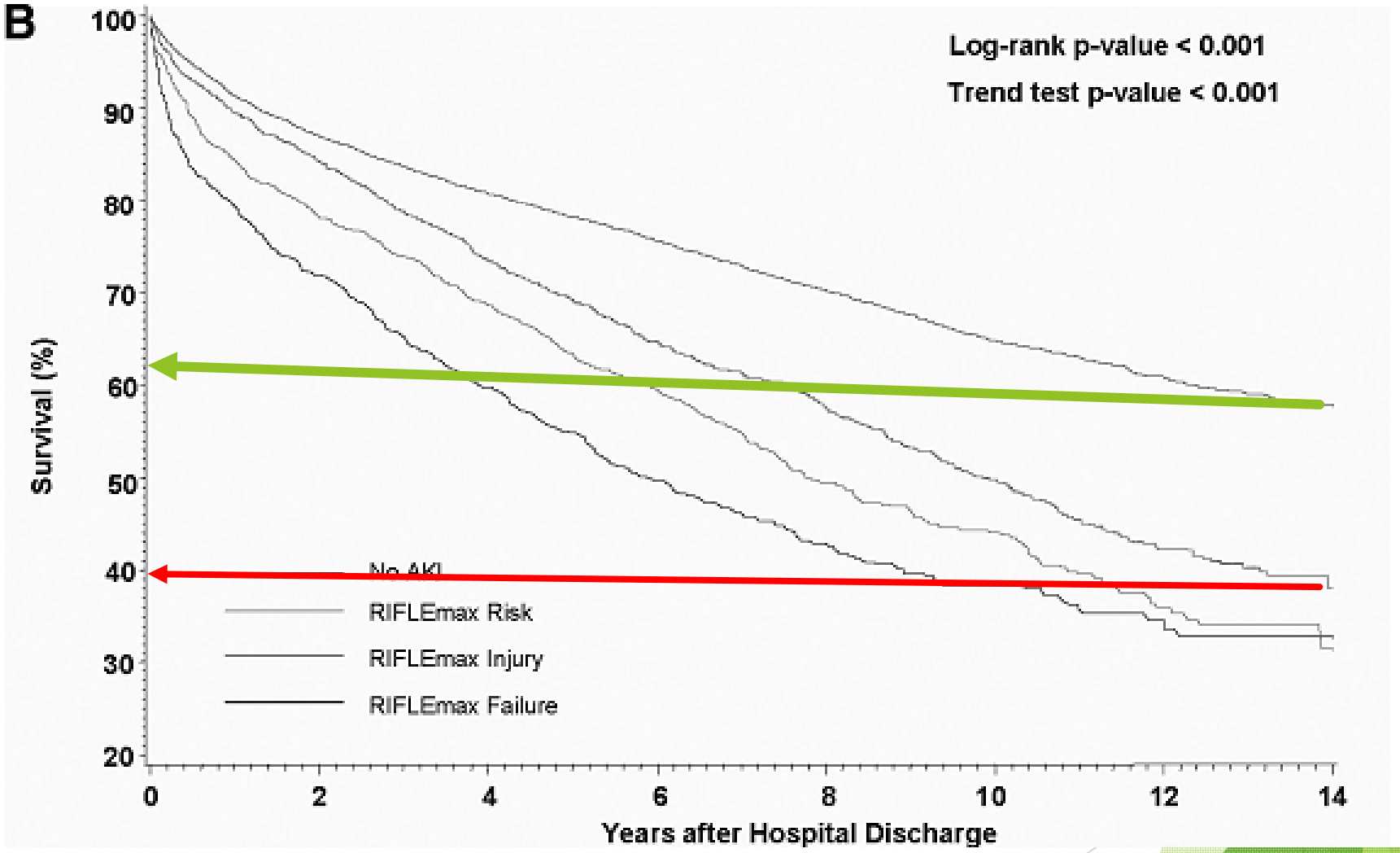
Azra Bihorac, MD, Sinan Yavas, MD,* Sophie Subbiah, BA,* Charles E. Hobson, MD,†*
Jesse D. Schold, PhD,‡ Andrea Gabrielli, MD, A. Joseph Layon, MD,* and Mark S. Segal, MD, PhD‡*

Type of surgery

- Cardiothoracic surgery (n = 3140, 30%)
- Vascular surgery (n = 1725, 16%)
- General surgery (n = 2337, 22%)
- Neurosurgery (n = 3316, 32%)

~10000 surgical patients

(*Ann Surg* 2009;249: 851–858)



Greater AKI severity -> higher mortality
Patient survival differ by 20% comparing no AKI with “Risk”

- Even minimal increases in serum creatinine have been associated with an increase in both short and long-term mortality
- This risk of death is independent from other postoperative complications and co-morbidities
- AKI is related to the subsequent development and progression of chronic kidney disease (CKD), esp. in those with pre-existing renal impairment

Kidney Int 2004,66:1613–1621

Crit Care Med 2002,30:2051–2058

Definition of AKI

- Highly variable (>150 definitions) until recent years
- Risk, Injury, Failure, Loss and End stage (RIFLE) - 2004
- Acute Kidney Injury Network (AKIN) - 2007

Table 3 | Comparison of RIFLE and AKIN criteria for diagnosis and classification of AKI

AKI staging		RIFLE	
Serum creatinine	Urine output (common to both)	Class	Serum creatinine or GFR
Stage 1 Increase of more than or equal to 0.3 mg/dl (≥26.5 μmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg/h for more than 6 hours	Risk	Increase in serum creatinine × 1.5 or GFR decrease >25%
Stage 2 Increased to more than 200% to 300% (>2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours	Injury	Serum creatinine × 2 or GFR decreased >50%
Stage 3 Increased to more than 300% (>3-fold) from baseline, or more than or equal to 4.0 mg/dl (≥354 μmol/l) with an acute increase of at least 0.5 mg/dl (44 μmol/l) or on RRT	Less than 0.3 ml/kg/h for 24 hours or anuria for 12 hours	Failure	Serum creatinine × 3, or serum creatinine >4 mg/dl (>354 μmol/l) with an acute rise >0.5 mg/dl (>44 μmol/l) or GFR decreased >75%
		Loss	Persistent acute renal failure=complete loss of kidney function >4 weeks
		End-stage kidney disease	ESRD >3 months

Note: For conversion of creatinine expressed in SI units to mg/dl, divide by 88.4. For both AKIN stage and RIFLE criteria, only one criterion (creatinine rise or urine output decline) needs to be fulfilled. Class is based on the worst of either GFR or urine output criteria. GFR decrease is calculated from the increase in serum creatinine above baseline. For AKIN, the increase in creatinine must occur in <48 hours. For RIFLE, AKI should be both abrupt (within 1–7 days) and sustained (more than 24 hours). When baseline creatinine is elevated, an abrupt rise of at least 0.5 mg/dl (44 μmol/l) to >4 mg/dl (>354 μmol/l) is sufficient for RIFLE class Failure (modified from Mehta *et al.*[23] and the report of the Acute Dialysis Quality Initiative consortium[22]).

- RIFLE criteria failed to detect 9% of cases that were detected by AKIN criteria. However, the AKIN criteria missed 26.9% of cases detected by RIFLE
- Kidney Disease Improving Global Outcomes (KDIGO) -> new AKI definition (2012)

Kidney International Supplements (2012) **2,** 8–12; doi:10.1038/kisup.2012.7

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

- Increase in SCr by $\geqslant$0.3 mg/dl ($\geqslant$26.5 µmol/l) within 48 hours; or
- Increase in SCr to $\geqslant$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.

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (*Not Graded*)

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR $\geqslant$0.3 mg/dl ($\geqslant$26.5 µmol/l) increase	$<$0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	$<$0.5 ml/kg/h for $\geqslant$12 hours
3	3.0 times baseline OR Increase in serum creatinine to $\geqslant$4.0 mg/dl ($\geqslant$353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients $<$18 years, decrease in eGFR to $<$35 ml/min per 1.73 m^2	$<$0.3 ml/kg/h for $\geqslant$24 hours OR Anuria for $\geqslant$12 hours

Kidney International Supplements (2012) **2,** 8–12; doi:10.1038/kisup.2012.7

Any risk factors that predict development of periop AKI?

Table 2 Factors associated with the development of AKI after cardiac surgery

Patient related factors	Surgical factors
Age	Duration of surgery
Hypertension	Intra-peritoneal surgery
Diabetes Mellitus	Length of CPB
Chronic Obstructive Pulmonary Disease	Cross clamp time
LVF, EF <40%	Hemolysis (cardiac surgery)
Chronic kidney disease	Hemodilution (cardiac surgery)
Emergency surgery	Use of IABP (cardiac surgery)
Sepsis	
Peripheral vascular disease	
Cerebrovascular disease	
Ascites	

EF, ejection fraction; *IABP*, Intra-aortic ump
function.

Cytokines activation
Alter vasomotor tone to kidney -> decrease renal perfusion pressure by 30%
Both induce ischemic reperfusion injury
RBC hemolysis -> direct tubular injury
Microembolization -> renal ischemia

GFR <60ml/min carry much higher risk of AKI postop – benefit from periop optimization

Calvert and Shaw *Perioperative Medicine* 2012, **1**:6

Anesthesiology 2011; 114:964–70

- Three scoring systems (Cleveland Clinic Foundation, Society of Thoracic Surgeons, and Simplified Renal Index) a/v for risk stratification and assess risk of postop RRT

J Am Soc Nephrol.2005;16:162-168
JAMA.2007;297:1801-1809
Circulation.2006;114:2208-2216
Med Clin N Am 97 (2013) 1109–1122

Risk Factor	Score
Female	1
CHF	1
LVEF < 35%	1
Pre-op IABP	2
COPD	1
IDDM	1
Prior Surgery	1
Emergency surgery	2
Surgery Type: Valve only CABG + Valve Other	 1 2 2
Pre-op Creatinine: 1.2 to < 2.1 mg/dl 2.1 mg/dl or greater	 2 5

Score Group	AKI Dialysis
0 - 2	0.4%
3 - 5	2%
6 - 8	8%
9 - 13	21%

Outcome	ROC value
CCF Score	
AKI – Dialysis	0.82
External Validation of CCF Score	
AKI Dialysis	0.86
Stage II or III AKI	0.81

ROC – receiver operating characteristics
CCF – Cleveland Clinic Foundation score

J Am Soc Nephrol.2005;16:162-168

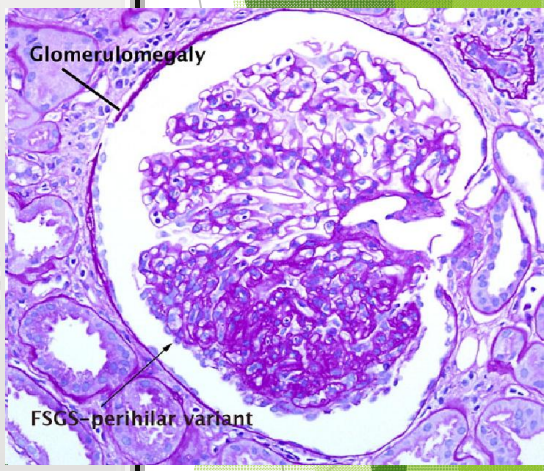
Table 3. Incidence and Risk Factors of AKI After Noncardiovascular Surgery[39]

Risk Factors	Risk Category	AKI Frequency
Age > 59 y	Class I (0 risk factors)	0.3%
BMI > 32	Class II (1 risk factor)	0.5%
Emergency surgery	Class III (2 risk factors)	1.3%
High-risk surgery	Class IV (≥3 risk factors)	4.3%
Peripheral vascular disease		
COPD		
Liver disease		

Anesthesiology.2007;107:892-902

Obesity Induced Changes in Kidneys

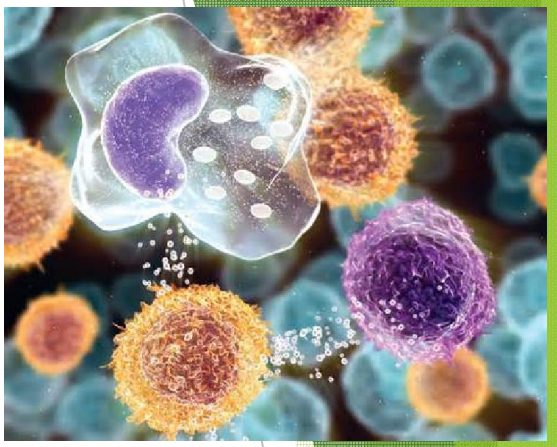
- Normal to high GFR
- Hyperfiltration syndrome
- Glomerular hypertrophy and mesangial hyperplasia
- Obesity related glomerulopathy
- Focal segmental glomerular sclerosis
- Proteinuria

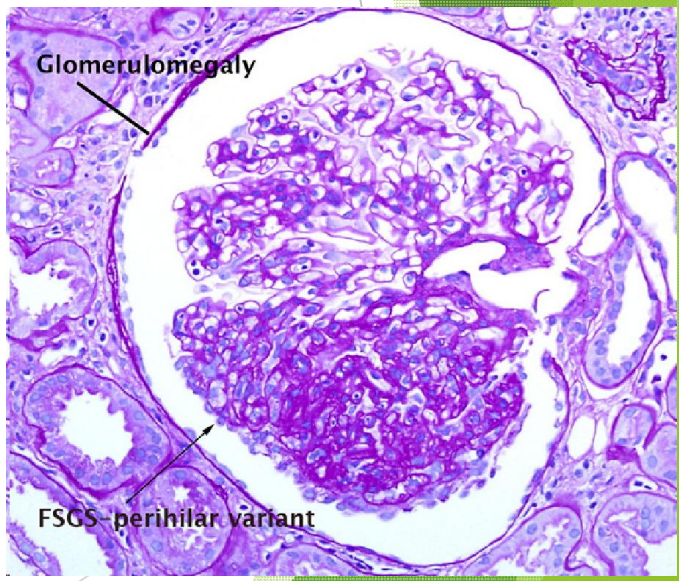


Suneja M, Kumar AB, Obesity and perioperative acute kidney injury: A focused review, J Crit Care (2014)

Obesity and periop AKI

- Retrospective analysis of 351 000 patients from the American College of Surgeons National Surgical Quality Improvement database -> 2-3X increase risk of periop AKI
- Obesity can be viewed as a chronic low-grade inflammatory status with increase circulating proinflammatory cytokines (including adipokines)
- Increased oxidative stress
- Hemodynamic optimization and drug dosing in periop period more difficult in obese patients





Suneja M, Kumar AB, Obesity and perioperative acute kidney injury: A focused review, J Crit Care (2014)

- RIFLE, AKIN and KDIGO all diagnose AKI according to serum creatinine and urine output
- Urine output measurement, non-automated process ->can be highly inaccurate
- Serum creatinine is neither sensitive nor specific, tending to represent a functional change rather than being a true marker of kidney injury

Cr is affected by multiple factors

- Age
- Malnutrition
- Ethnicity
- Gender
- Muscle mass
- Medications
  - Trimethoprim, cimetidine
- Protein intake

Renal biomarkers

Acronym/ abbreviation	Legend
AP	Alcaline phosphatase
α_1MG	Alpha 1 microglobulin
$\alpha_1$acidGP	Alpha 1 acid glycoprotein
B_2MG	Beta 2 microglobulin
Cystatin C	Cystatin C
FENA	Fractional excretion of sodium
GGTP	Gamma glutamyl transpeptidase
αGST	Alpha glutathione S transferase
πGST	Pi glutathione S transferase
HGF	Hepatocyte Growth Factor
IL-6	Interleukin 6
IL-8	Interleukin 8
IL-10	Interleukin 10
IL-18	Interleukin 18
KIM-1	Kidney injury molecule 1
LFABP	Liver-type fatty acid-binding protein
NGAL	Neutrophil gelatinase-associated lipocalin
NAG	*N*-Acetyl beta glucosaminidase
PAI-1	Plasminogen activator inhibitor 1
PCX	Podocalyxin
RBP	Retinol-binding protein
sTNFR-I	Soluble tumour necrosis factor receptor I
sTNFR-II	Soluble tumour necrosis factor receptor II
TNFα	Tumour necrosis factor alpha
11k-TXB_2	11-keto-Thromboxane B_2
vWF	Von Willebrand factor

Nephrol Dial Transplant (2013) 28: 254–273

Biomarkers for AKI

IGFBP7 Insulin-like Growth Factor Binding Protein 7 (Urine)	Inducer of G1 cell cycle arrest expressed by injured tubular cells. Cell cycle stopped via its own receptor
TIMP-2 Tissue inhibitor Metalloproteinases-2 (Urine)	Inducer of G1 cell cycle arrest expressed by injured tubular cells. Cell cycle stopped via its own receptor
NGAL Neutrophil gelatinase-associated lipocalin (Blood/urine)	Protein expressed in neutrophils and prox/distal renal tubule cells; binds and traffics free iron and is upregulated in the setting of renal tubular ischaemia
IL-18 Interleukin-18 (Urine)	Inflammatory cytokine found in macrophages and proximal tubule cells that is upregulated in the setting of renal ischemic injury
Cystatin C (Blood/urine)	Cysteine protease inhibitor freely filtered at glomerulus that is normally reabsorbed by prox tubule cells and appears in the urine in the setting of tubular injury
KIM-1 (Kidney Injury Molecule) (Urine)	Type 1 cell membrane glycoprotein that is shed into the urine following proximal tubule injury

- NGAL measured in >7000 patients after cardiac surgery can predict the subsequent development of AKI (AUC 0.7–0.8)
- Performance of urine NGAL is slightly better than plasma NGAL
- Urine NGAL was the only biomarker with predictive value as early as 2 h postoperatively

Ann Clin Biochem OnlineFirst, published on February 11, 2014

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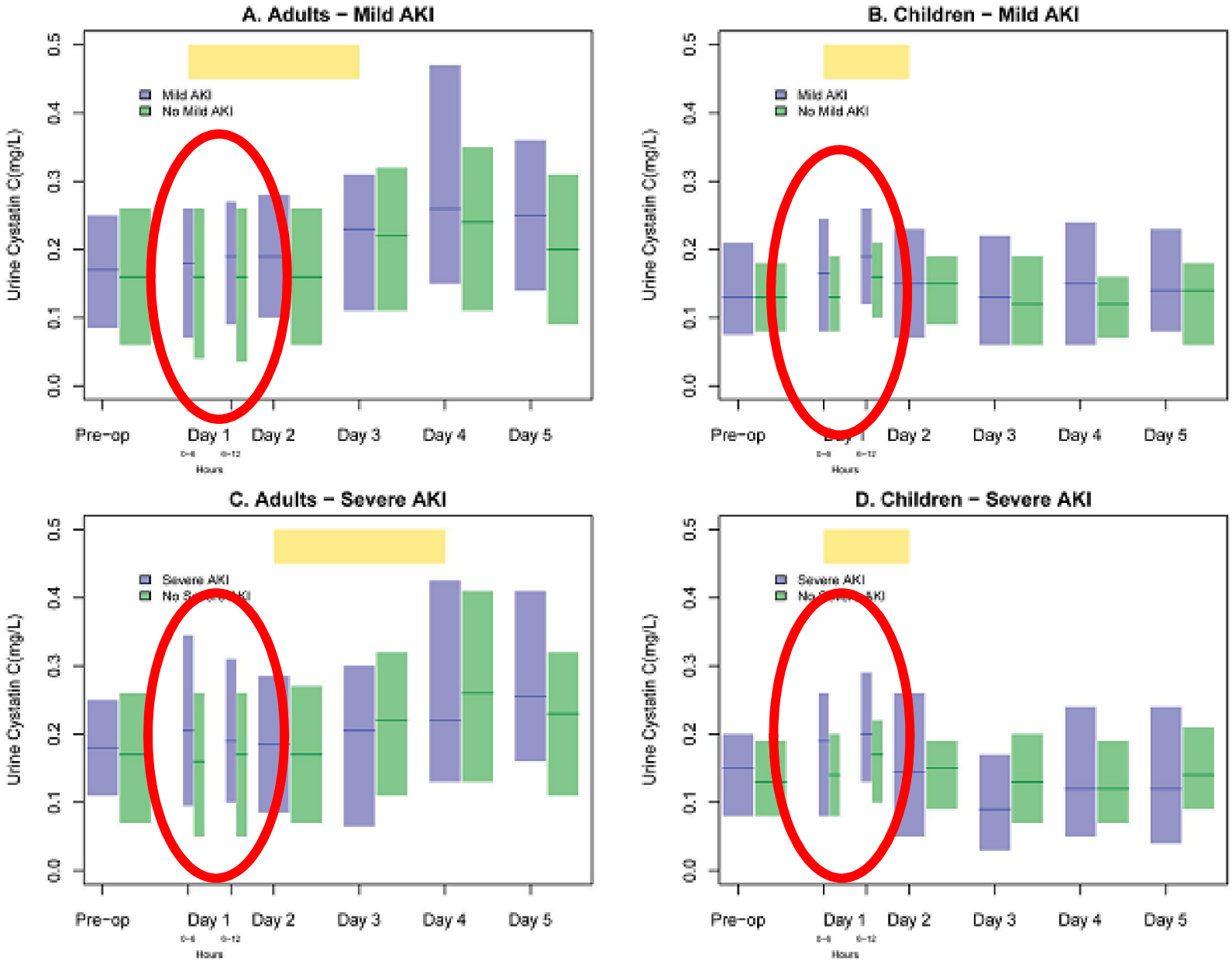
KIM-1 (Kidney Injury Molecule) (Urine)	Type 1 cell membrane glycoprotein that is shed into the urine following proximal tubule injury

Correlated well with GFR

Published in final edited form as:
Am J Kidney Dis. 2013 May ; 61(5): 730–738. doi:10.1053/j.ajkd.2012.12.006.

1500 patients

Urinary Cystatin C and Acute Kidney Injury After Cardiac Surgery



- Urinary CysC measured in the early post-operative period (0–6 and 6–12 hours postoperatively) correlated with both mild and severe AKI in adults and children. However after analyses were adjusted for other clinical factors the effect was attenuated
- Urinary CysC values are not significantly associated with the development of AKI following cardiac surgery in adults and children.

Am J Kidney Dis. 2013 May ; 61(5): 730–738

Biomarkers for AKI

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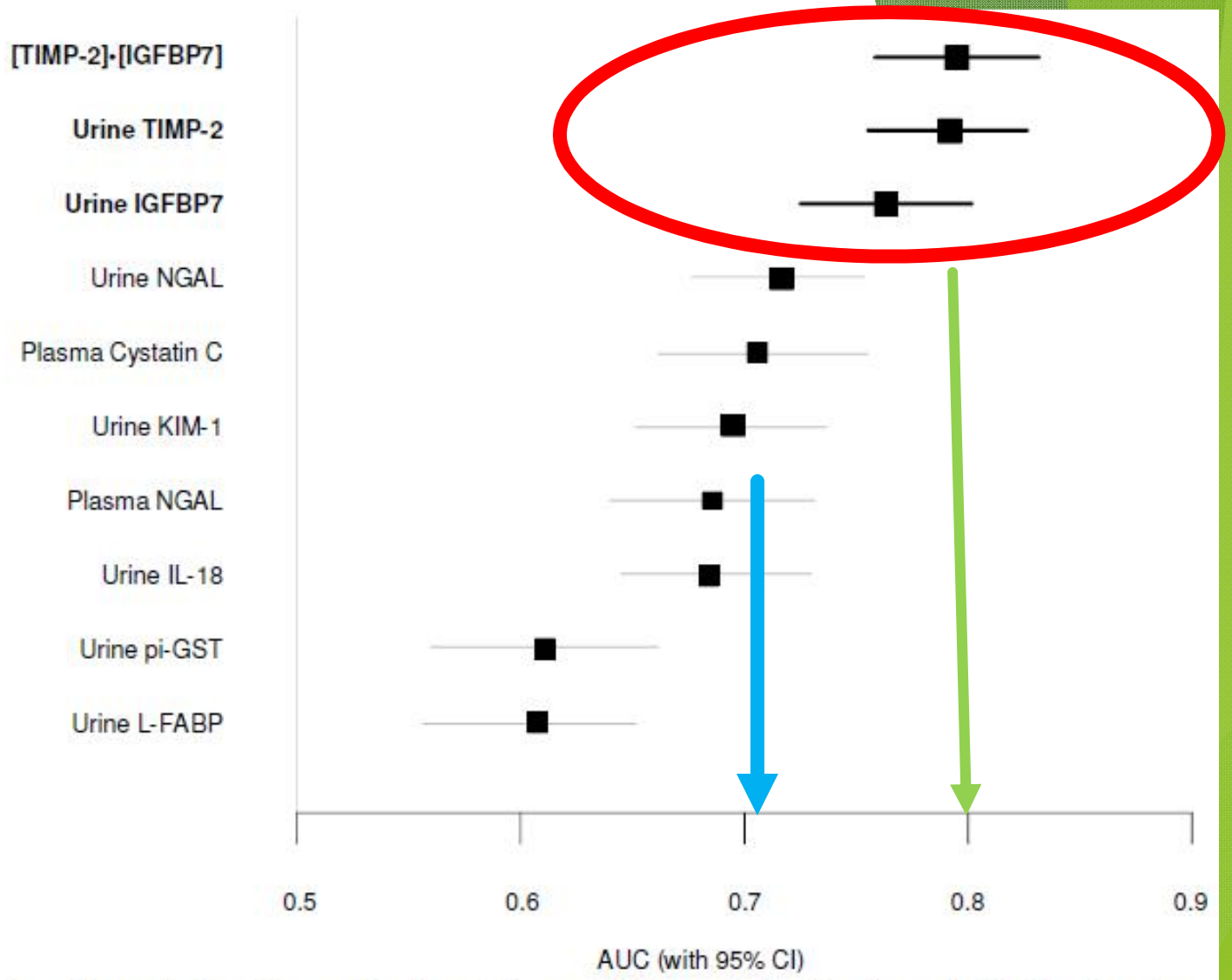
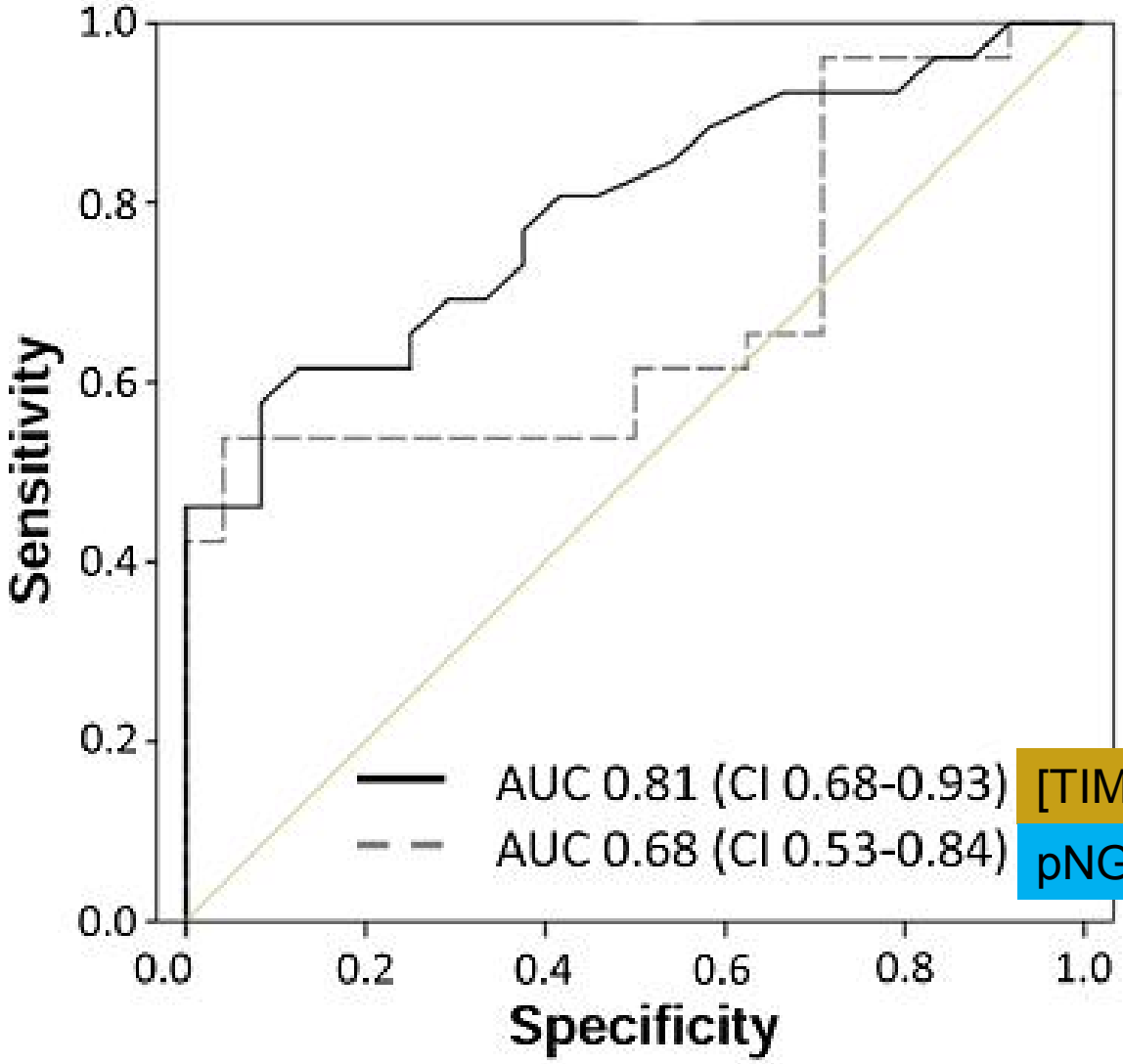


Figure 2 Area under the receiver-operating characteristics curve (AUC) for novel urinary biomarkers and existing biomarkers of acute kidney injury for the primary Sapphire study endpoint (KDIGO stage 2 or 3 within 12 hours of sample collection). Samples were collected within 18 hours of enrollment. The AUC for urinary [TIMP-2]·[IGFBP7] is larger than for the existing biomarkers (*P* value <0.002). IGFBP7, insulin-like growth factor-binding protein 7; IL-18, interleukin-18; KIM-1, kidney injury marker-1; L-FABP, liver fatty acid-binding protein; NGAL, neutrophil gelatinase-associated lipocalin; pi-GST, pi-Glutathione S-transferase; TIMP-2, tissue inhibitor of metalloproteinases-2.

744 Critical ill patients

Kashaniet al. Critical Care 2013,17:R25



[TIMP-2]*[IGFBP7]

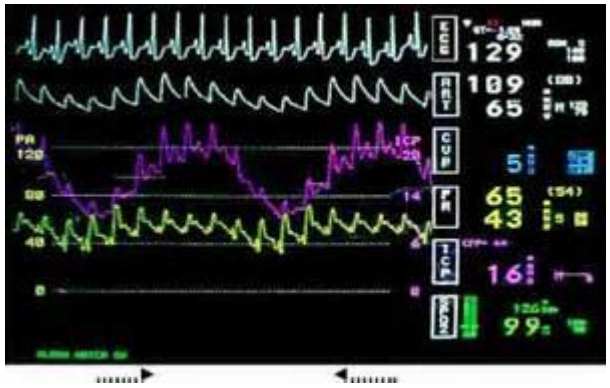
pNGAL

50 patients received cardiac surgery

PLoS One. 2014 Mar 27;9(3)

Preventive measures for AKI

- Maintenance of normal renal perfusion is very important
- 80% of patients experiencing postoperative AKI having an episode of hemodynamic instability



Does perioperative hemodynamic optimization protect renal function in surgical patients? A meta-analytic study

Nicola Brienza, MD, PhD; Maria Teresa Giglio, MD; Massimo Marucci, MD; Tommaso Fiore, MD

Table 2. Intervention details of analyzed studies and renal outcome definition

Author	Timing of Optimization	Goals of Optimization	Modality of Optimization	Definition of Acute Kidney Injury
Bender et al (35)	Preop from the morning of surger for 16 hrs postop	CI $\geq$2.8 L·min^{-1}·m^{-2}, 8 $\leq$ PAOP $\geq$ 14 mmHg, SVR $\leq$1100 dyne·sec/cm^5	Fluids, blood, dopamine, NTP	Increase in baseline creatinine by >1 mg/dL
Berlauk et al (36)	Preop from 12 or 3 hrs before surgery for 18 hrs postop	CI $\geq$2.8 L·min^{-1}·m^{-2}, 8 $\leq$ PAOP $\leq$ 15 mm Hg, SVR $\leq$1100 dyne·sec/cm^5	Fluids, dopamine or dobutamine, NTP, NTG	UO <0.5 mL·kg^{-1}·hr^{-1} for 5 hrs and/or rise in baseline creatinine by >0.5 mg/dL and/or need of RRT
Bishop et al (37)	Postop within 6 hrs after surgery for at least 48 hrs	CI $\geq$4.5 L·min^{-1}·m^{-2}, DO_2 $\geq$670 mL·min^{-1}·m^{-2}, VO_2 $\geq$166 mL·min^{-1}·m^{-2}	Fluids, blood, dobutamine (starting at 5 µg·kg^{-1}·min^{-1})	Creatinine $\geq$2 mg/dL or, with preexisting renal disease, creatinine twice than admission
Bonazzi et al (38)	Preop from the day before surgery to the end of the 2nd postop da	CI >3.0 L·min^{-1}·m^{-2}, DO_2 >600 mL·min^{-1}·m^{-2}, 10 <PAOP <18 mmHg, SVR <1450 dyne·sec/cm^5	Fluids, dobutamine (starting from 2.5 µg·kg^{-1}·min^{-1}), NTG	Worsening of preop function with oliguria requiring high dose furosemide (>250 mg/die) and/or need of RRT
Boyd et al (39)	Preop from ICU admission before surgery for 24 hrs postop	DO_2 >600 mL·min^{-1}·m^{-2}	Fluids, blood, dopexamine (starting at 0.5 µg·kg^{-1}·min^{-1} to a maximum of 8 µg·kg^{-1}·min^{-1})	UO <500 ml/24 hrs despite adequate PAOP
Chytra et al (28)[a]	Postop from ICU admission for 12 hrs postop	SV optimization with FTc between 0.35 and 0.4 sec	Fluids, blood	Need of RRT
Donati et al (40)	Intraop up to 24 hrs postop	O_2ERe ([Sao_2–$Scvo_2$] /SaO_2) <27%	Fluids, blood, dobutamine (starting at 3 up to 15	Creatinine >2 mg/dL or need of RRT

20 trials, 4000 surgical patients

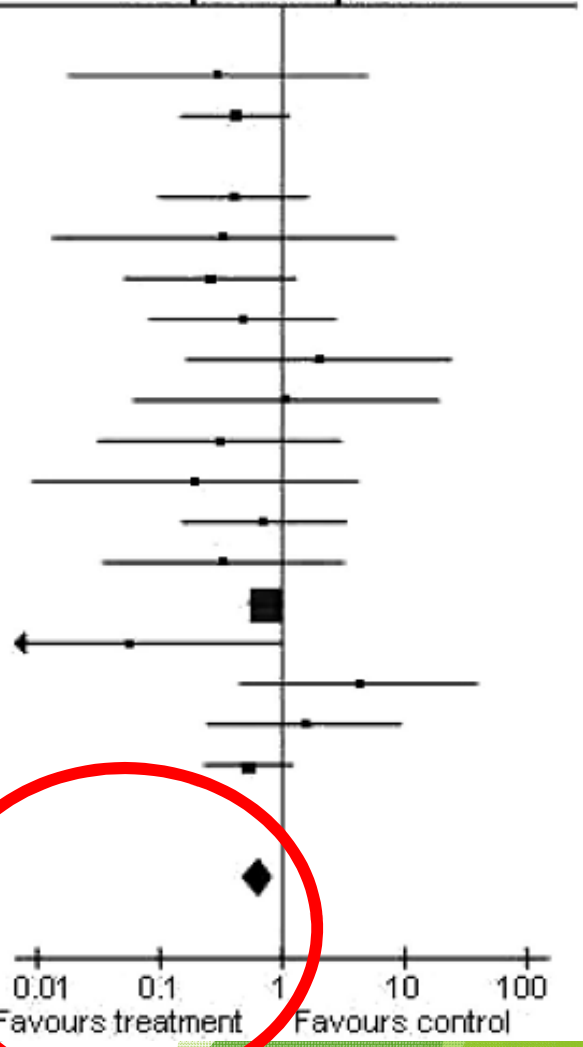
Crit Care Med 2009; 37:2079–2090

Outcome: **POSTOPERATIVE ACUTE KIDNEY INJURY**

Studies	Treatment Events	Treatment Total	Control Events	Control Total	Odds Ratio M-H, Random, 95% CI
Bender [28]	0	51	0	53	Not estimable
Berlauk [29]	1	68	1	21	0.30 [0.02, 4.99]
Bishop [30]	6	50	16	65	0.42 [0.15, 1.16]
Bonazzi [31]	0	50	0	50	Not estimable
Boyd [32]	3	53	7	54	0.40 [0.10, 1.65]
Chytra [33]	0	80	1	82	0.34 [0.01, 8.41]
Donati [34]	2	68	7	67	0.26 [0.05, 1.30]
Gan [35]	2	50	4	50	0.48 [0.08, 2.74]
Lobo [36]	2	19	1	18	2.00 [0.17, 24.19]
Malhotra [37]	1	13	1	14	1.08 [0.06, 19.31]
McKendry [38]	1	89	3	85	0.31 [0.03, 3.05]
Noblett [39]	0	51	2	52	0.20 [0.01, 4.19]
Pearse [40]	3	62	4	60	0.71 [0.15, 3.32]
Polonen [41]	1	196	3	197	0.33 [0.03, 3.22]
Sandham [42]	70	941	95	965	0.74 [0.53, 1.02]
Shoemaker [26]	0	28	14	60	0.06 [0.00, 0.98]
Valentine [43]	4	60	1	60	4.21 [0.46, 38.86]
Wakeling [44]	3	64	2	64	1.52 [0.25, 9.45]
Wilson [45]	16	92	13	46	0.53 [0.23, 1.24]
Ziegler [46]	0	32	0	40	Not estimable
Total (95% CI)		**2117**		**2103**	**0.64 [0.50, 0.83]**
Total events	115		175		

Heterogeneity: Tau² = 0.00; Chi² = 12.45, df = 16 (P = 0.71); I² = 0%

Test for overall effect: Z = 3.37 (P = 0.0007)



Crit Care Med 2009; 37:2079–2090

Outcome: **POSTOPERATIVE ACUTE KIDNEY INJURY IN HIGH AND LOW RISK PATIENTS**

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Odds Ratio M-H, Random, 95% CI
high risk					
Bishop [30]	6	50	16	65	0.42 [0.15, 1.16]
Boyd [32]	3	53	7	54	0.40 [0.10, 1.65]
Chytra [33]	0	80	1	82	0.34 [0.01, 8.41]
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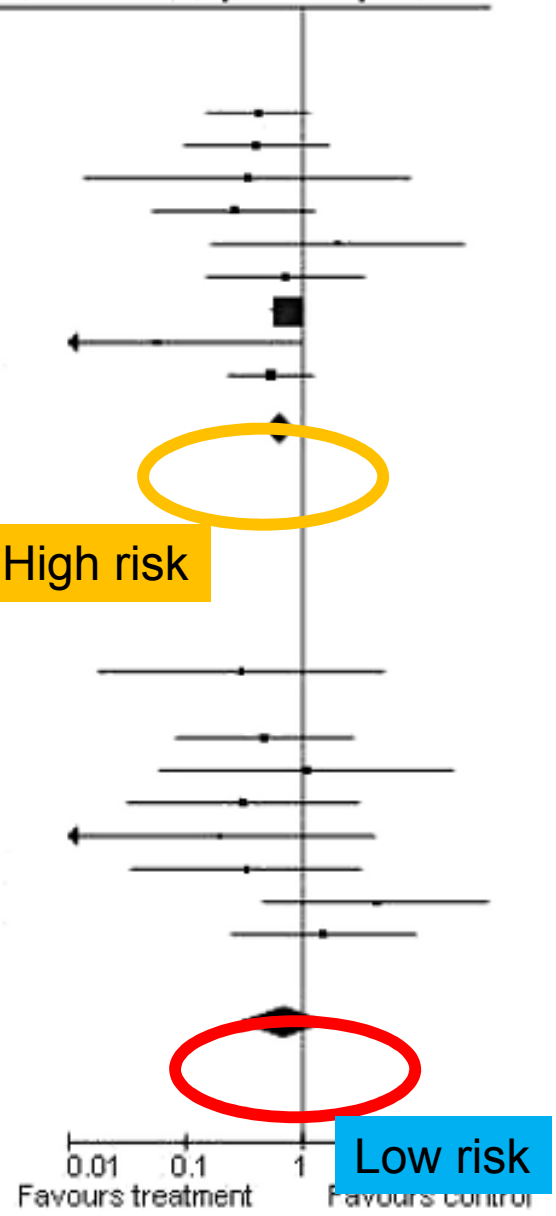
Pearse [40]	3	62	4	60	0.71 [0.15, 3.32]
Sandham [42]	70	941	95	965	0.74 [0.53, 1.02]
Shoemaker [26]	0	28	14	60	0.06 [0.00, 0.98]
Wilson [45]	16	92	13	46	0.53 [0.23, 1.24]
Subtotal (95% CI)		**1393**		**1417**	**0.64 [0.49, 0.84]**
Total events	102		158		
Heterogeneity: Tau² = 0.00; Chi² = 7.05, df = 8 (P = 0.53); I² = 0%					
Test for overall effect: Z = 3.25 (P = 0.001)					
low risk					
Bender [28]	0	51	0	53	Not estimable
Berlauk [29]	1	68	1	21	0.30 [0.02, 4.99]
Bonazzi [31]	0	50	0	50	Not estimable
Gan [35]	2	50	4	50	0.48 [0.08, 2.74]
Malhotra [37]	1	13	1	14	1.08 [0.06, 19.31]
McKendry [38]	1	89	3	85	0.31 [0.03, 3.05]
Noblett [39]	0	51	2	52	0.20 [0.01, 4.19]
Polonen [41]	1	196	3	197	0.33 [0.03, 3.22]
Valentine [43]	4	60	1	60	4.21 [0.46, 38.86]
Wakeling [44]	3	64	2	64	1.52 [0.25, 9.45]
Ziegler [46]	0	32	0	40	Not estimable
Subtotal (95% CI)		**724**		**686**	**0.69 [0.31, 1.54]**
Total events	13		17		
Heterogeneity: Tau² = 0.00; Chi² = 5.40, df = 7 (P = 0.61); I² = 0%					
Test for overall effect: Z = 0.90 (P = 0.37)					



Crit Care Med 2009; 37:2079–2090

Patient related factors
Age
Hypertension
Diabetes Mellitus
Chronic Obstructive Pulmonary Disease
LVF, EF <40%
Chronic kidney disease
Emergency surgery
Sepsis
Peripheral vascular disease
Cerebrovascular disease
Ascites

Calvert and Shaw *Perioperative Medicine* 2012, **1**:6

Anesthesiology 2011; 114:964–70

Nephrotoxic agents

- NSAID - stop 3 days before OT
- ACEI/ ARB (esp. in volume depleted patients and those on diuretics) – W/H on morning of surgery (esp. in those for non-HF use)
- Antibiotics (aminoglycosides, high dose penicillin and quinolones)
- IV contrast -> use iso-osmolar and low-osmolar non-ionic contrast

Anesthesiology 2007; 106:218–225

J Hosp Med 2008; 3:319–325.

Hydroxyethyl starch

- Increase risk of AKI and requirement of RRT in critically ill patients
- ESICM recommend not to use HES with molecular weight ≥ 200 kDa and/or degree of substitution >0.4

Mutter TC, Ruth CA, Dart AB. Cochrane Database Syst Rev. 2013 Jul 23;7:CD007594.

European Society of Intensive Care Medicine. Intensive Care Med. 2012 Mar;38(3):368-83.

British Journal of Anaesthesia **112** (1): 25–34 (2014)
Advance Access publication 17 September 2013 · doi:10.1093/bja/aet303

BJA

REVIEW ARTICLES

Incidence of postoperative death and acute kidney injury associated with i.v. 6% hydroxyethyl starch use: systematic review and meta-analysis

Study or subgroup	HES Events	HES Total	Control Events	Control Total	Weight	Risk difference M–H, fixed, 95% CI
Cardiac surgery						
Lee and colleagues[29]	1	53	0	53	26.5%	0.02 [–0.03, 0.07]
Ooi and colleagues[33]	0	45	0	45	22.5%	0.00 [–0.04, 0.04]
Subtotal (95% CI)		**98**		**98**	**49.0%**	**0.01 [–0.02, 0.04]**
Total events	1		0			
Heterogeneity: χ^2=0.33, df=1 (P=0.56); I^2=0%						
Test for overall effect: Z=0.58 (P=0.56)						
Non-cardiac/mixed surgery						
Diehl and colleagues[22]	2	33	0	27	14.8%	0.06 [–0.04, 0.16]
Godet and colleagues[24]	8	32	7	33	16.2%	0.04 [–0.17, 0.24]
Hung and colleagues[27]	0	41	0	39	20.0%	0.00 [–0.05, 0.05]
Subtotal (95% CI)		**106**		**99**	**51.0%**	**0.03 [–0.04, 0.10]**
Total events	10		7			
Heterogeneity: χ^2=1.87, df=2 (P=0.39); I^2=0%						
Test for overall effect: Z=0.78 (P=0.43)						
Total (95% CI)		**204**		**197**	**100.0%**	**0.02 [–0.02, 0.06]**
Total events	11		7			
Heterogeneity: χ^2=2.21, df=4 (P=0.70); I^2=0%						
Test for overall effect: Z=0.95 (P=0.34)						
Test for subgroup differences: χ^2=0.22, df=1 (P=0.64); I^2=0%						

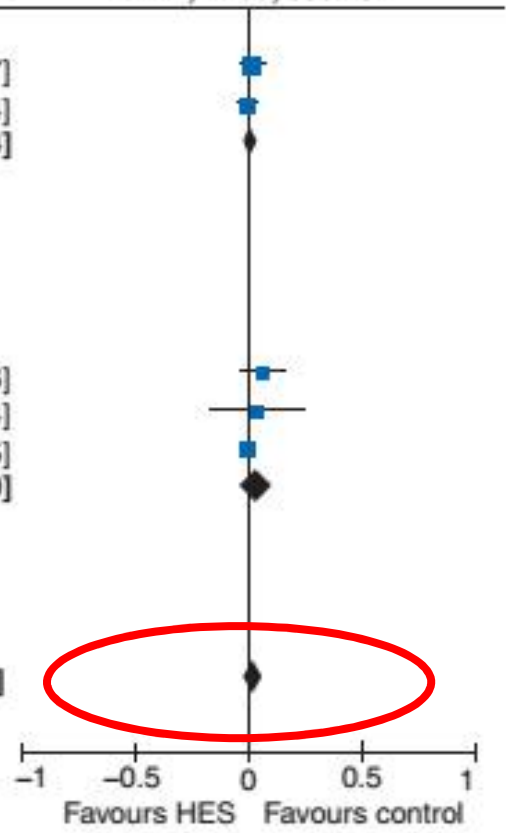


Fig 3 Forest plot of acute kidney injury.

5 studies, ~400 patients

British Journal of Anaesthesia **112** (1): 25–34 (2014)

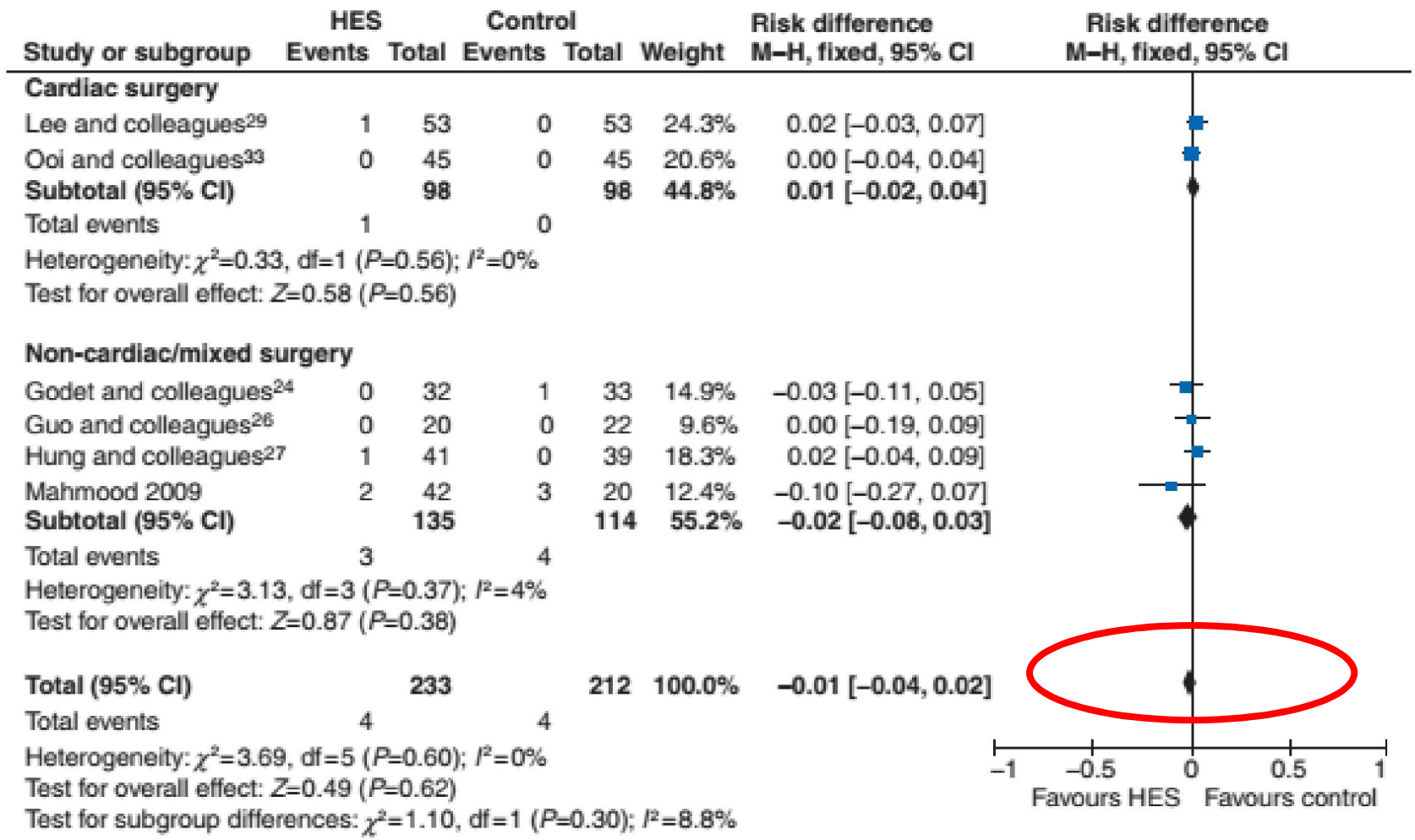
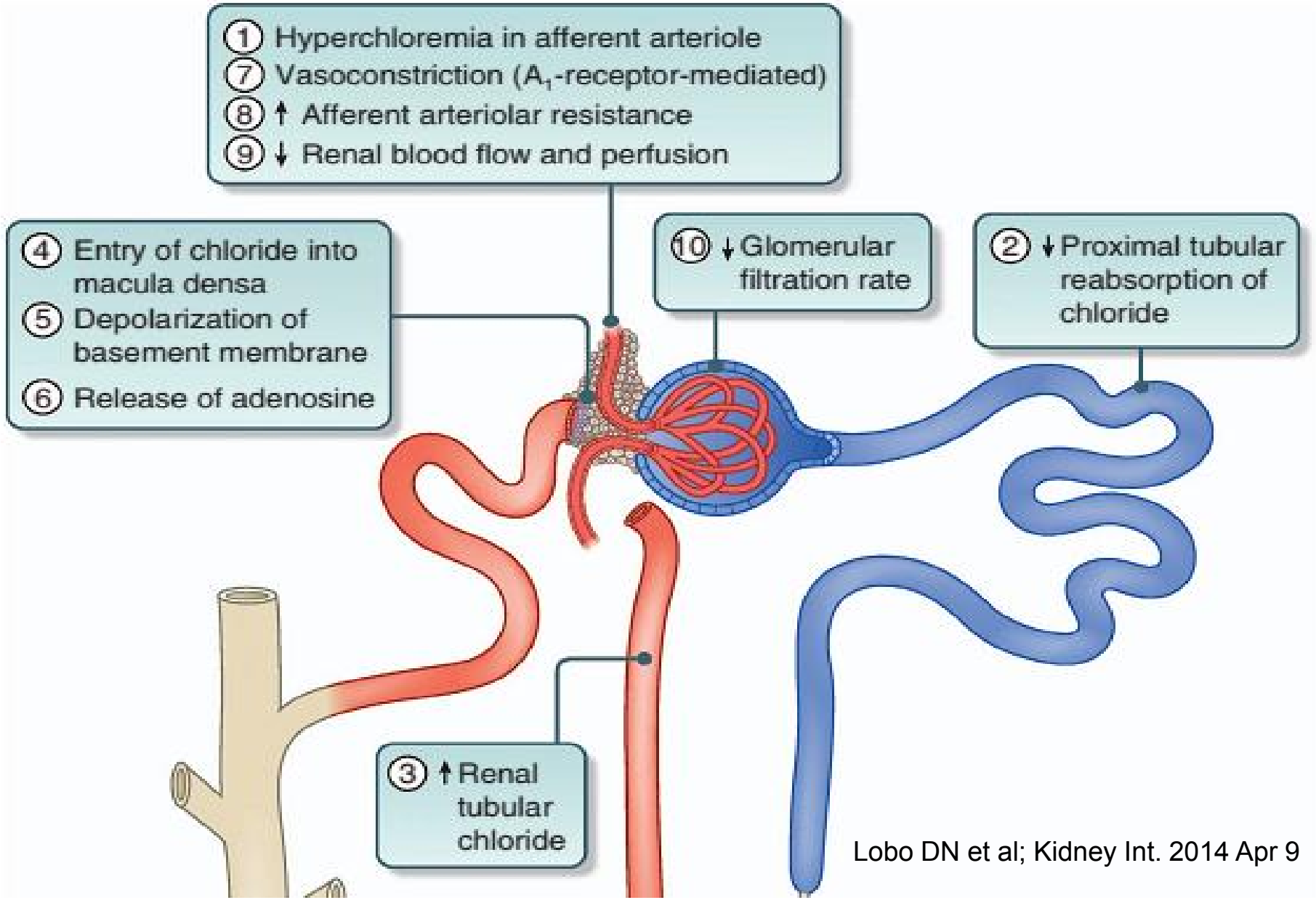


Fig 4 Forest plot of renal replacement therapy.

Is NS safe?



Lobo DN et al; Kidney Int. 2014 Apr 9

- Multiple trials (most of them observational) comparing NS with balanced crystalloid
- More likely to develop AKI and require RRT
- Also more infective complications, blood transfusion requirement
- +/- higher mortality

Anesth Analg 2013; 117: 412–421.
Ann Surg 2012;255: 821–829
JAMA 2012;308: 1566–1572
Crit Care Med2011;39: 2419–2424

Transfusion and AKI in cardiac surgery

- 18 observational studies
- Exact pathophysiology not clear
- Erythrocytes undergo irreversible morphological and biochemical changes during storage
- After transfusion, they can promote
  - pro-inflammatory state
  - impair tissue oxygen delivery
  - exacerbate tissue oxidative stress

British Journal of Anaesthesia 109(S1): i29–i38 (2012)

Interventions for protecting renal function in the perioperative period

- Dopamine
- Fenoldopam
- Diuretics
- Calcium channel blockers
- Atrial natriuretic peptide
- N-acetyl cysteine
- Statin
- Erythropoietin (EPO)

Dopamine

- Infusions of dopamine were used as treatment in 11 studies (~600 patients)
- No difference for the following:
  - Rate of AKI
  - Dopamine associated with small decrease of CrCl level 24-48hr postop

Heart Fail Rev (2011) 16:553–567

Fenoldopam

- 4 studies with ~450 patients
- Decrease requirement of RRT
- Increase CrCl postop
- However, 2 studies compare fenoldopam with dopamine and dopamine use may associate with decrease of CrCl

Heart Fail Rev (2011) 16:553–567

Diuretics

- 5 trials, 250 patients
- No difference for the following:
  - Rate of AKI
  - Urine output 24 hours after operation
  - Creatinine clearance at 24hrs
- use Lasix has been shown to be not only ineffective but also detrimental, associated with higher postoperative Cr level and needs for RRT

Heart Fail Rev (2011) 16:553–567

Cochrane Database Syst Rev. 2013 Sep 11;9:CD003590.

Calcium Channel Blocker

- Six trials, 172 patients
- E.g. diltiazem, nicardipine and felodipine
- No difference for the following:
  - Rate of AKI
  - Urine output 24 hours after operation
  - Creatinine clearance at 24hrs
  - Free water clearance 24 hours

Cochrane Database Syst Rev. 2013 Sep 11;9:CD003590.

Atrial Natriuretic Peptide

- 4 trials, 865 patients
- May have some AKI protective effect OR 0.23, 95% CI 0.08 to 0.64)
- Significant reduction in the need for RRT was seen in postcardiac surgical patients with decompensated CHF who received low-dose infusions of recombinant human ANP
- No difference for the following:
  - Urine output 24 hours after operation
  - Creatinine clearance at 24hrs

Cochrane Database Syst Rev. 2013 Sep 11;9:CD003590.

NAC

- 5 trials with 600 patients
- No difference for the following:
  - Rate of AKI
  - Urine output 24 hours after operation

Cochrane Database Syst Rev. 2013 Sep 11;9:CD003590.

Statin

- 17 observational studies, 46000 patients
- Lower mortality in statin users
- No difference on incidence of AKI
- In isolated CABG patients, statin decrease requirement of RRT

Interactive CardioVascular and Thoracic Surgery 17 (2013) 345–352

Erythropoietin

- Provide immunomodulating effect and organ protection against ischemia-reperfusion injury
- Pilot trial showed some beneficial effect
- Three RCTs, 278 CS patients give conflicting results (two negative vs one positive)

Crit Care. 2013 Oct 24;17(5):R254
BMC Nephrol. 2013 Jul 5;14(1):136
BMC Nephrol. 2012 Oct 3;13:132
Am J Nephrol. 2009;30(3):253-60

Conclusion

- No reliable evidence from the available literature suggests that interventions during surgery can protect the kidneys from damage (ANP/ Fenoldopam may be helpful)
- Variation of AKI definition may contribute to this findings
- Use of standard definition or renal biomarker may offer some help on this issue

The End

Perioperative management of dialysis dependent patients

Hong Kong Journal of Nephrology (2013) 15, 28–43

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.hkjn-online.com

HONG KONG RENAL REGISTRY

Hong Kong Renal Registry Report 2012

HO YW et al; HKJN (2013) 15, 25-43

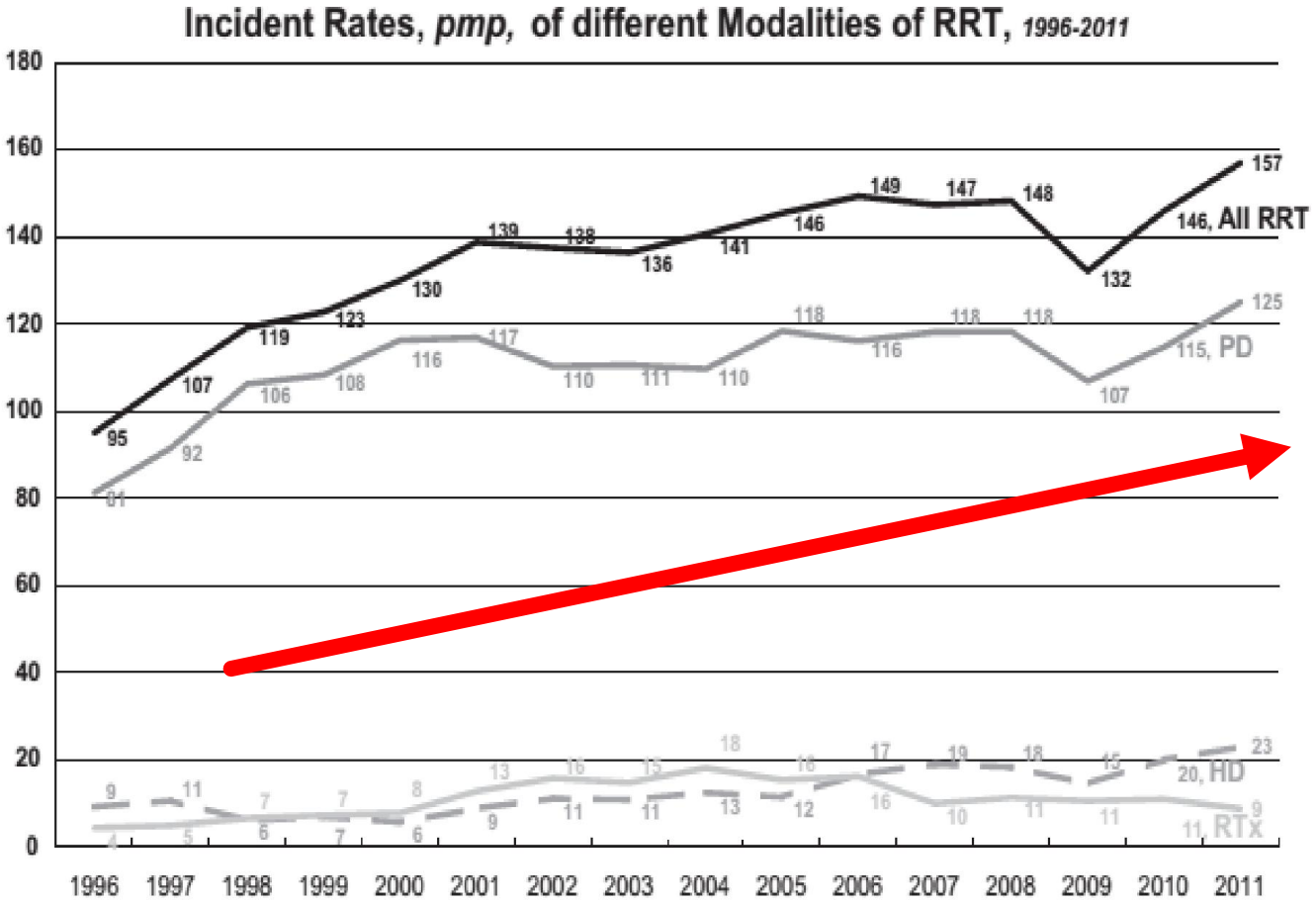
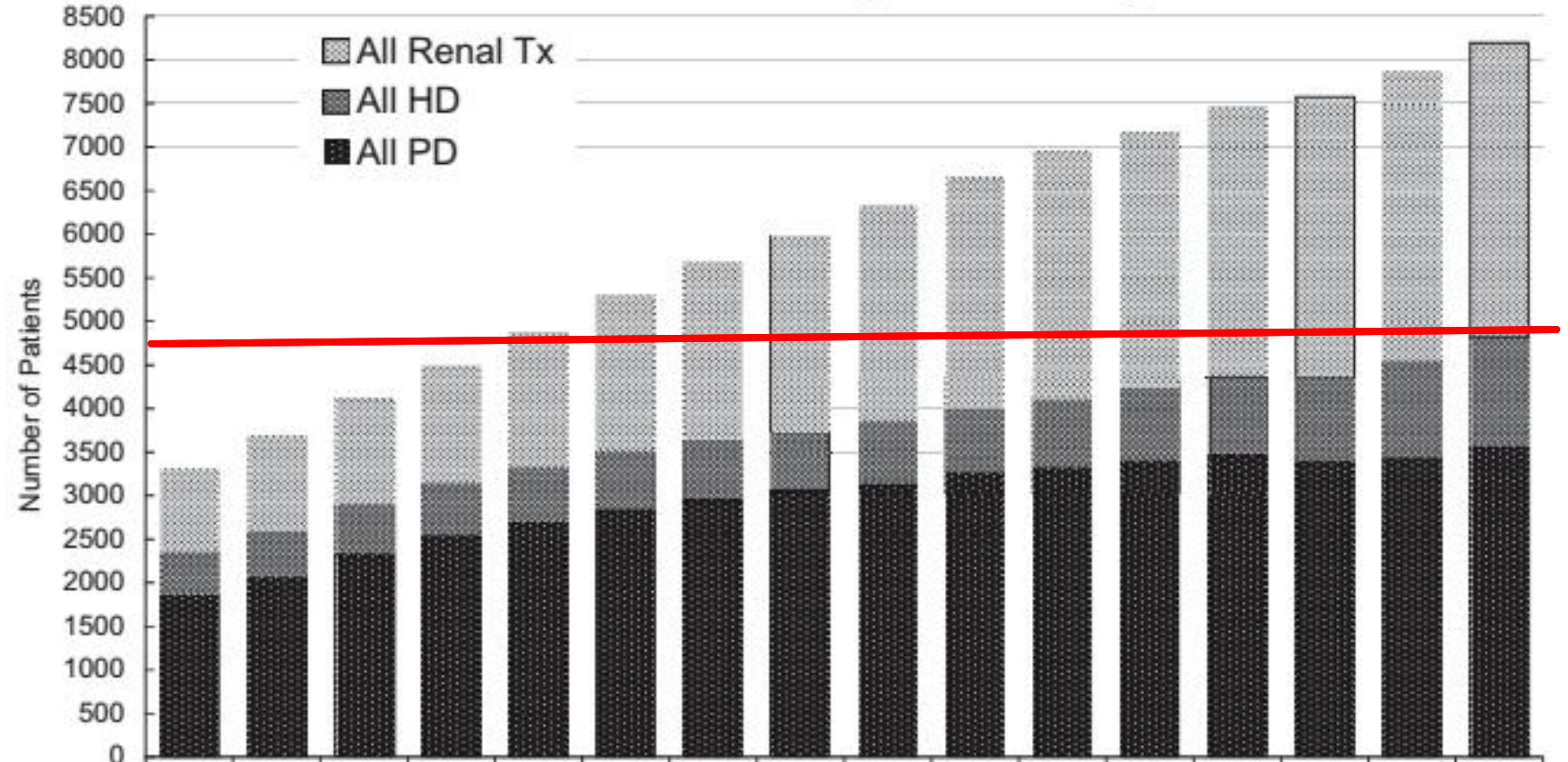


Figure 1 Incident rates (per million population) by calendar year of patients accepted into renal replacement therapy (RRT) programs, 1996–2011. All = all patients on renal replacement therapy; HD = hemodialysis; PD = peritoneal dialysis; RTx = renal transplant.

HO YW et al; HKJN (2013) 15, 25-43

Prevalence of All RRT, *as of 31/12 each year*



	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
All Renal Tx	956	1088	1202	1361	1554	1795	2048	2255	2462	2653	2835	2923	3095	3234	3320	3378
All HD	491	524	572	582	618	656	672	670	695	714	780	842	903	945	1100	1246
All PD	1865	2069	2338	2555	2705	2850	2961	3054	3161	3279	3328	3406	3462	3401	3437	3573

HO YW et al; HKJN (2013) 15, 25-43

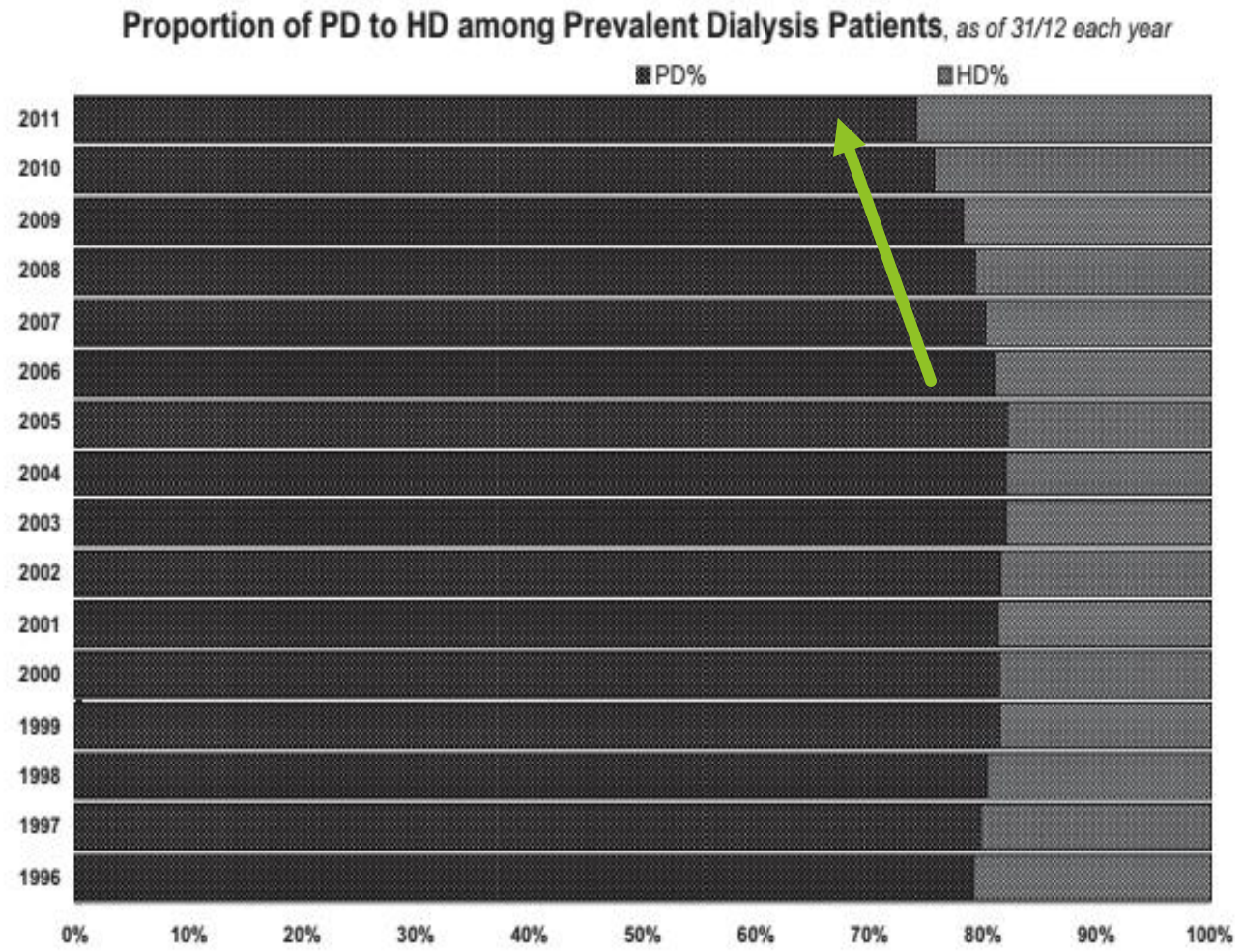


Figure 10 Peritoneal dialysis/hemodialysis (PD/HD) ratio for all registered patients in Hospital Authority, including HD in charitable and private centers, 1996–2011.

HO YW et al; HKJN (2013) 15, 25-43

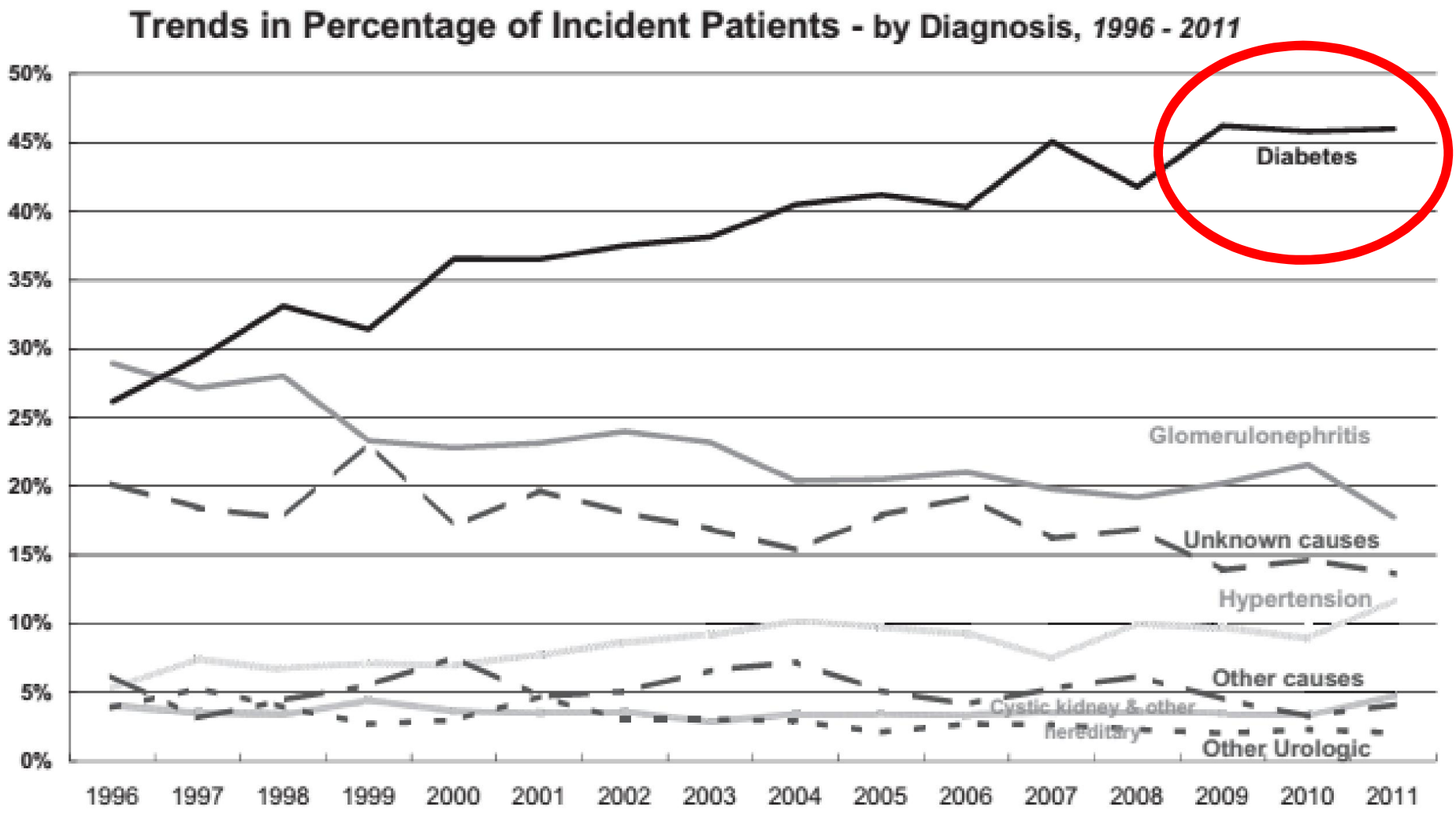


Figure 6 Diagnosis distribution (% incident counts) of patients, 1996–2011.

HO YW et al; HKJN (2013) 15, 25-43

TABLE 1. Comorbid conditions in incident HD dialysis patients starting dialysis between 2003 and 2008

Comorbidity	Number	Percentage (%)	Median age (years)
Angina	1845	16.9	71.3
MI in past 3 months	339	3.1	70.7
MI > 3 months ago	1304	11.9	70.8
CABG/angioplasty	837	7.7	69.0
Cerebrovascular disease	1,177	10.8	71.1
Diabetes (not listed as PRD)	977	9.1	70.9
COPD	855	7.9	70.8
Liver disease	329	3.0	60.0
Claudication	957	8.7	70.6
Ischemic/neuropathic ulcers	410	3.7	62.6
Angioplasty/vascular graft	411	3.8	71.4
Amputation	248	2.3	61.3
Smoking	1629	15.3	61.2
Malignancy	1457	13.3	72.0

Modified from (4).

Trainor D et al; Seminar in dialysis 2011; 24(3); 314-26

In order to limit the potential cardiovascular risk…

You should pay attention to the following issues during periop assessment

Dialysis Adequacy

- Cannot be assumed simply from the patient's biochemical results
- Kt/V of 1.2 for three times weekly dialysis
- Increased catabolic statues can occur during perioperative period which may required higher Kt/v level (e.g. alternate

Am J Kidney Dis 48(Suppl.1):S2– S90, 2006

Anemia

- Inadequate erythropoietin production is the major factor that results in anemia ESRF patients (resistance…catabolic / inflammatory condition)
- Target Hb level of 11-12g/dl with iron therapy and EPO
- Adjustment of EPO in periop period

Am J Kidney Dis 50:471–530, 2007

Why don’t we transfuse up the patients?

- Alloimmunization can occur against RBC or HLA antigens
- risk of sensitization after blood transfusion varies from 2% to over 25%, with even higher rates seen in patients with multiple transfusion

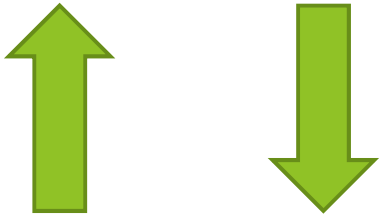
Semin Dial. 2012 Sep-Oct; 25(5): 539–544.

- Reduces the chance of a patient receiving a transplant
- increase the risk of having a higher percentage of panel reactive activity
- The presence of circulating donor-specific anti-HLA antibodies has been associated with hyperacute rejection, antibody-mediated rejection and an increased risk of graft failure

Other transfusion related complications

- Circulatory overload
- Transfusion associated ALI
- hyperkalemia

Blood pressure and fluid status



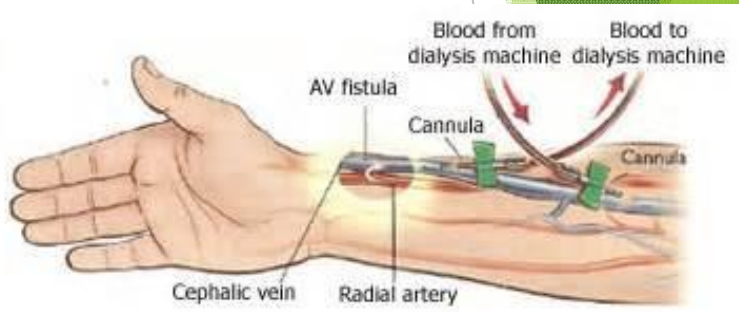
- Achieving the correct dry weight with optimization of fluid removal during preop HD sessions
- Adjusting the dose of antihypertensive drugs

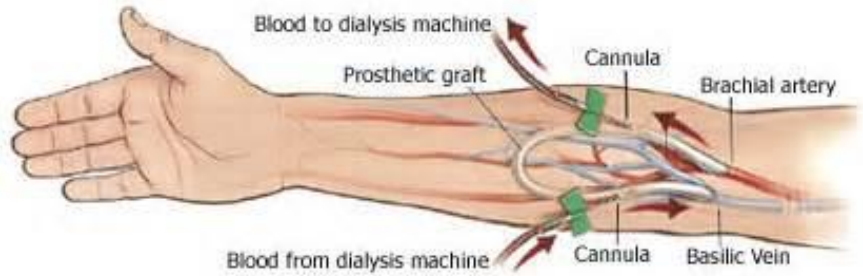
Nutrition

- Malnutrition is common
  - Dialysis inadequacy
  - Chronic inflammation
  - Medication side effects
- Poor wound healing, increase risk of wound infection
- EN/ PN support + adequate dialysis should be considered

Vascular access

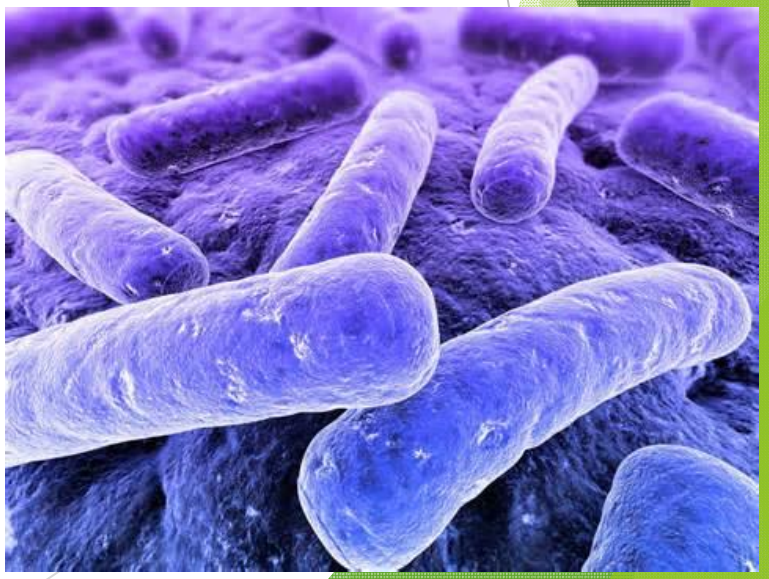
- Difficult vascular access
- Presence of central venous stenosis / thrombosis should be noted
- HD catheter should not be used except in emergency
- Assess AVF / AVG function





Infection control

- Patients with end-stage renal disease are at increased risk of bacterial colonization and infection by resistant bugs (MRSA/ VRE/ ESBL)
- impact on the order of the operating list and use of prophylactic antibiotic



Bleeding risk

- Contributed by PLT dysfunction, anemia, reduced von Willebrand factor activity, use of anti-PLT agents for CV complications
- clopidogrel should be discontinued 7 days prior to surgery

- Decrease bleeding risk by
  - Adequate dialysis
  - Aim Hb level ~10
  - DDAVP 0.3 mcg/kg releases factor VIII and VWF from the endothelium (last 4-12hr)
  - Cryoprecipitate (last for 12-24hr)
  - conjugated estrogen administration (0.6 mg/kg daily for 5 days) (peak effect 5-7d later)

Drugs

- Propofol: no significant change of pharmacokinetic in patients with ESRF – good induction agent
- Sevoflurane may react with carbon dioxide absorbents to produce a substance called Compound A, which is nephrotoxic in rat models -> has been used in renal disease and dialysis-dependent ESRD patients w/o problems

Drugs

- Patients with ESRF have below normal levels of plasma cholinesterase
- prolongation of action of the depolarizing muscle relaxant suxamethonium and the non-depolarizing relaxant mivacurium
- significant hyperkalemic response to suxamethonium is not observed in chronic renal failure provided the preoperative otassium level is within normal limits

Drugs

- non-depolarizing muscle relaxant drug atracurium and the stereoisomer cis-atracurium undergo a process called Hofmann elimination – good NMB
- clinical effects of the amino-steroid muscle relaxant drugs vecuronium and rocuronium are significantly prolonged in renal failure because of reduced clearance -> should be avoided

TABLE 3. Characteristics of opioids and their metabolites in renal failure and dialysis

Opioid	Metabolism	Metabolites (IA) = inactive (A) = active	Excretion	Accumulation in renal failure	Removed by HD	Safety profile in HD patient
Morphine	Hepatic	Normorphine (IA) Morphine-3-glucuronide, (IA) Morphine-6-glucuronide (A)	Renal	Yes	Yes	Reduce dose and increase interval. Extreme caution required
Fentanyl	Hepatic	Norfentanyl (IA)	Renal (7% unchanged)	Parent compound may accumulate	No	Safe – reduce dose
Alfentanil	Hepatic	Noralfentanil (IA)	Renal	No	No	Safe – reduce dose because of increased free fraction
Remifentanil	Blood & tissue esterases	GR90291 (IA)	Renal	No	No	Safe
Codeine	Hepatic with polymorphism	Codeine-6-glucuronide (A) Norcodeine (IA) Morphine (A) Normorphine (IA) Morphine-3-glucuronide, (IA) Morphine-6-glucuronide (A)	Renal	Yes	Limited data	Avoid – serious adverse effects have been reported
Oxycodone	Hepatic with polymorphism	Noroxycodone (IA) Oxymorphone (A) Conjugated oxymorphone (IA)	Renal	Yes	No data	Ideally avoid. If used, reduce dose and increase interval. Extreme caution required
Tramadol	Hepatic	O-dimethyl-tramadol (A)	Renal	Yes	Yes	Avoid – lowered seizure threshold and altered mental status
Meperidine	Hepatic	Normeperidine (A) Normeperidinic acid Meperidinic acid	Renal (5% unchanged)	Normeperidine accumulates	No (normeperidine)	Avoid – metabolite accumulation causes seizures
Methadone	Hepatic		Renal and fecal	–	No	Appears safe
Hydromorphone	Hepatic	Hydromorphone-3-glucoronide (neuro-excitation)	Renal	Yes	Yes	Neuro-excitation possible. Use lower dose or longer interval. If used, additional dose may be needed after HD

HD, hemodialysis.

Seminars in Dialysis—Vol 24, No 3 (May–June) 2011 pp. 314–326

Postoperative renal support

- Hemodialysis should ideally be delayed until the risk of fluid shifts, and hemorrhage has fallen
- Citrate or predilutional CRRT vs heparin free HD

The End