59TH ANZSN
ANNUAL SCIENTIFIC MEETING
& AUXILIARY EVENTS
TRANSFORMING
KIDNEY CARE
31 August – 4 September 2024
Adelaide, South Australia
ADELAIDE CONVENTION CENTRE

AKI and biomarkers

Jihyun Yang

Sungkyunkwan University Kangbuk Samsung Hospital

1530 – 1700	PLENARY #8: The Nephrology of Tomorrow
Session Chair	Eoin O'Sullivan
1530 – 1600	AKI AND BIOMARKERS **Dr Jihyun Yang**, Korea University Anam Hospital
1600 – 1630	FROM STEM CELLS TO THERAPIES: ADVANCES IN ENGINEERED KIDNEY TISSUE **Dr Jessica Vanslambrouck**, Murdoch Children's Research Institute
1630 – 1700	THE CUTTING EDGE OF NEPHROLOGY: PERSONALISED MEDICINE IN GLOMERULONEPHRITIS **Associate Professor Simon Jiang**, Australian National University

I have no conflict of interest to declare.

Contents

- Introduction
- Classic biomarker
- Functional/Dynamic biomarker
- Limitation
- Future of the AKI biomarker

Introduction(1)

KDIGO classification		
Stage	**Serum creatinine**	**Urine output**
1	**≥ 0.3mg/dL in 48hr Or x 1.5~1.9↑from baseline**	**<0.5mL/kg/h for 6~12h**
2	**x 2~2.9↑from baseline**	**<0.5mL/kg/h for ≥12hr**
3	**≥ x 3↑from baseline Or > 4mg/dL Or Treatment with RRT Or <18years, eGFR < 35$_{mL/min/1.73\ m^2}$**	**<0.3mL/kg/h ≥ 24hr Or Anuria ≥ 12hr**

Causes of AKI :
exposures and susceptibilities for non-specific AKI

Exposures	Susceptibilities
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female
Burns	Gender
Trauma	Black race
Cardiac surgery (esp. with Cardiopulmonary bypass)	CKD
Major noncardiac surgery	Chronic disease (Heart, lung, liver)
Nephrotoxic drugs	Diabetes mellitus
Radiocontrast agents	Cancer
Poisonous plants and animals	Anemia

No response to medical management → renal/kidney replacement therapy

Kidney International Supplements (2012) 2, 13–18

Introduction(2)

BUN and creatinine

In oliguric AKI … **bolus intravenous furosemide**

Urine microscopy

Kidney injury molecule-1 (KIM-1)

Neutrophil gelatinase associated lipocalin **(NGAL)**

… Measurement of urine and serum levels of structural biomarkers, such as **KIM-1**, and inflammatory markers, such as **NGAL** and **IL-18** may aid in the diagnosis of AKI, although the data are not yet conclusive...

In 2014, the U.S. FDA approved **insulin-like growth factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinase-2 (TIMP-2)** as predictive biomarkers for higher risk of the developme nt of moderate to severe AKI in critically ill patients

Harrison's Principles of Internal Medicine, 21th Chapter 304: Acute Kidney Injury
Goldman-Cecil Internal Medicine, 26th Chapter 112: Acute Kidney Injury
Modififed from Nat Rev Nephrol. 2018;14:217-230

Pseudo AKI due to creatinine metabolism

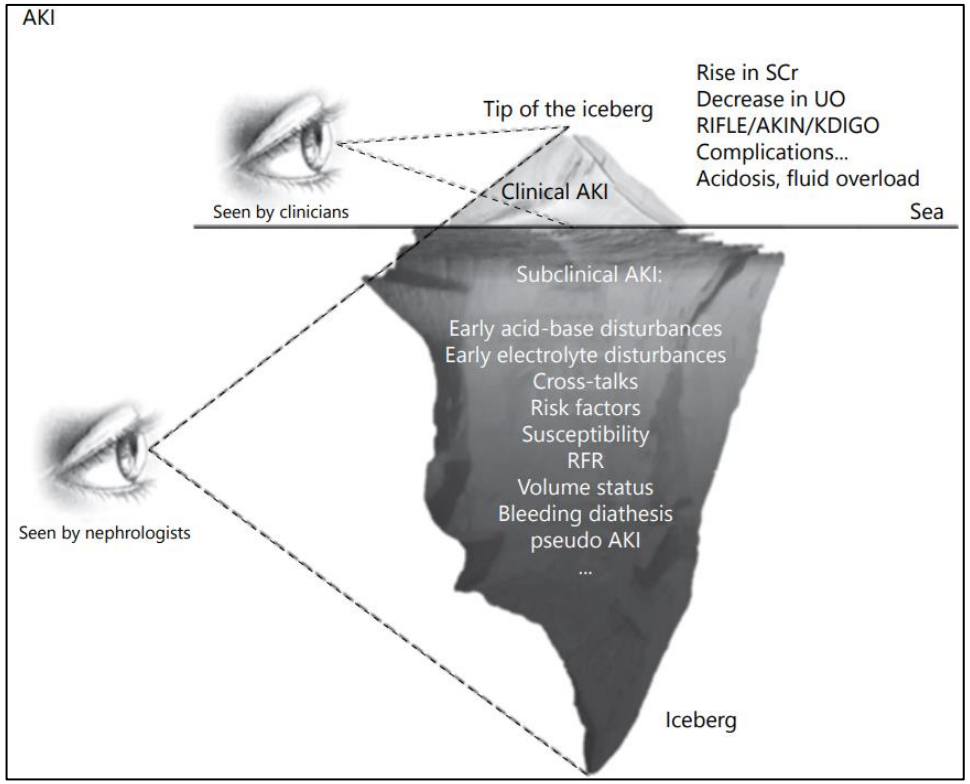
Table 1. Medications associated with pseudo-AKI and hemodynamically mediated AKI

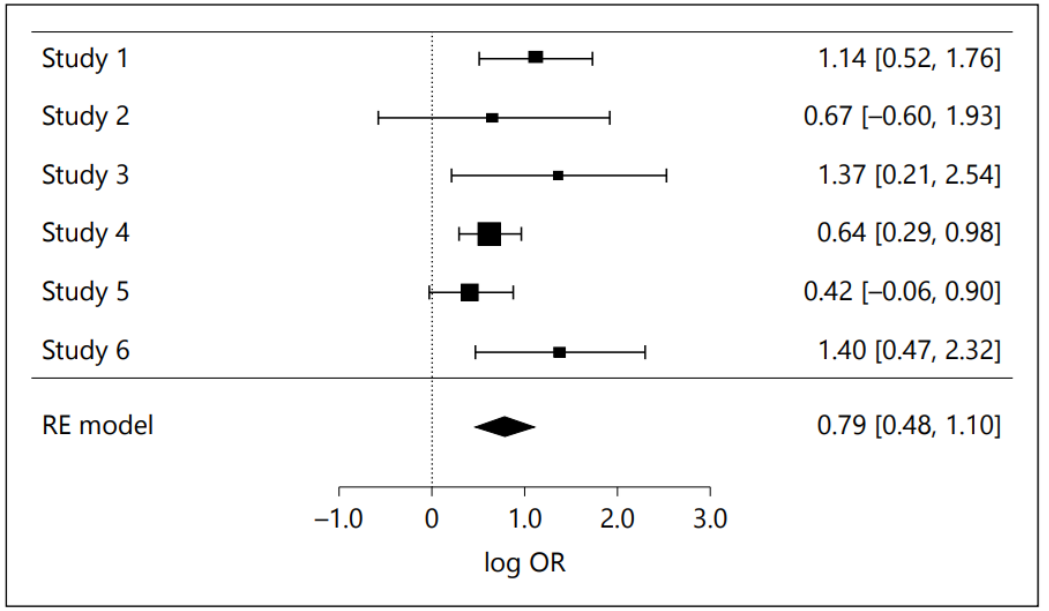
Medication associated with pseudo-AKI	Mechanism of increased serum creatinine	Medications associated with hemodynamically mediated AKI	Mechanism of reduced GFR
• Cimetidine • Trimethoprim • Dronedarone • Cobicistat and dolutegravir • Tyrosine kinase inhibitors (imatinib, bosutinib, sorafenib, sunitinib, crizotinib, gefitinib, and pazopanib) • Pyrimethamine	Decrease creatinine secretion through the proximal tubular cells into the urine	Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers	Inhibit efferent arteriolar vasoconstriction and reduce GFR
Dexamethasone Corticosteroids	Some formulations contain Catabolic state with release of creatine from muscle, which is converted to creatinine	NSAIDs	Inhibit production of vasodilatory prostaglandins with afferent arteriolar vasoconstriction (especially prominent in states of volume depletion, older age, hypercalcemia and effective arterial volume depletion such as cirrhosis, heart failure, nephrotic syndrome)
cefoxitin	Recognized as a creatinine chromagen by the alkaline picrate method of creatinine analysis	SGLT2i inhibitors	Induce vasoconstriction of the afferent arteriole due to tubuloglomerular feedback
Flucytosine	Interferes with enzymatic assay for serum creaetinine determination	Calcineurin inhibitors	Induce vasoconstriction of the afferent arteriole (due to an imbalance between vasoconstrictor agents such as endothelin, thromboxane, and activation of the renin-angiotensin system and decrease of vasodilator factors like prostaglandin E2, Prostacyclin, and nitric oxide)
Calcitriol and alfacalcidol	unclear		
Fenofibrate	Increase metabolic production of creatinine		

CJASN 17(8):p 1220-1233, August 2022

Introduction(4)

Early nephrologist involvement → prevents worsening kidney function, improves survival

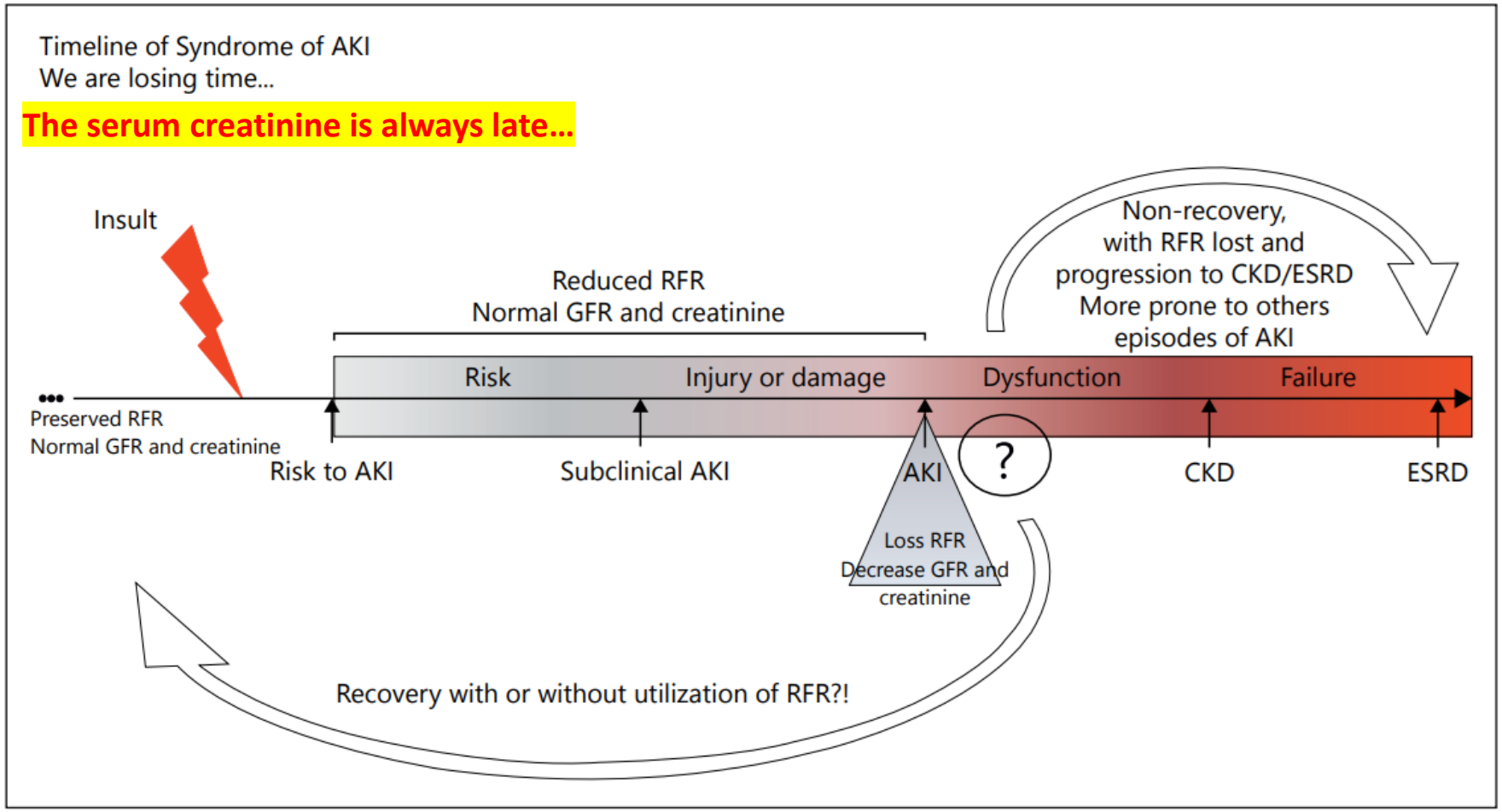




Delayed nephrology consultation → higher mortality in AKI

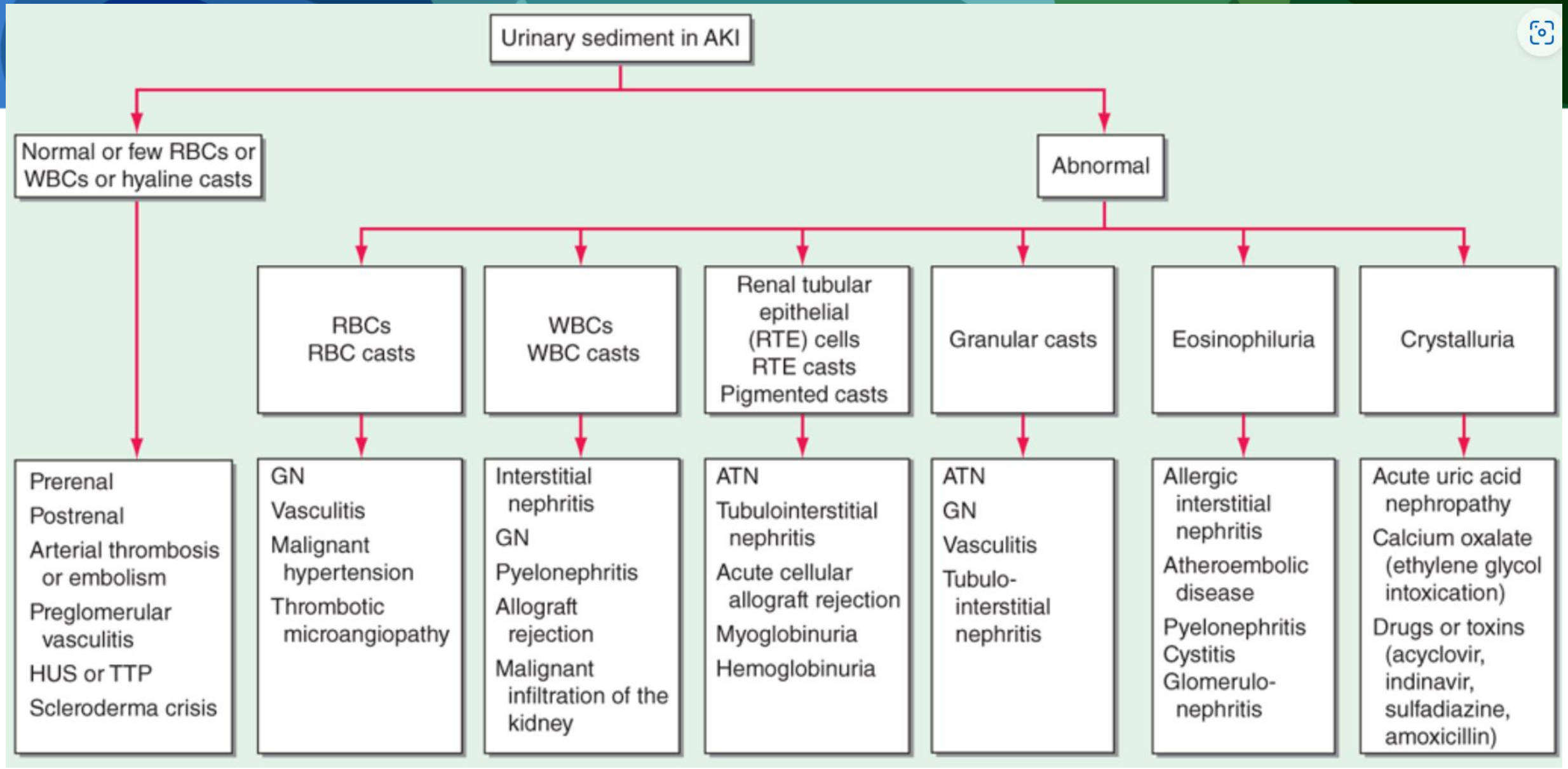
Blood Purif 2017;43:57–67

Introduction(5)



AKI : Acute kidney injury, CKD : chronic kidney disease, ESRD : end-stage renal disease, GFR : glomerular filtration rate, RFR : renal function reserve

Fig 316.6) Interpretation of urinary sediment findings in acute kidney injury



Urine indices used in the differential diagnosis of prerenal AKI and ATN

Diagnostic Index	Prerenal AKI	ATN
Fractional excretion of sodium (%)	<1 [a]	>2 [a]
Urine sodium concentration (mmol/L)	<20	>40
Urine creatinine-to-plasma creatinine ratio	>40	<20
Urine urea nitrogen-to-plasma urea nitrogen ratio	>8	<3
Urine specific gravity	>1.018	~1.010
Urine osmolality (mOsm/kg H_2O)	>500	~300
Plasma BUN-to-creatinine ratio	>20	<10-15
Renal failure index, $U_{Na}/(U_{Cr}/P_{Cr})$	<1	>1
Urine sediment	Hyaline casts	Muddy brown granular casts

- If CKD, diuretics : urine Na excretion over 40 mEq/L
- If HRS, high-dose diuretics : urine Na excretion less than 20 mEq/L

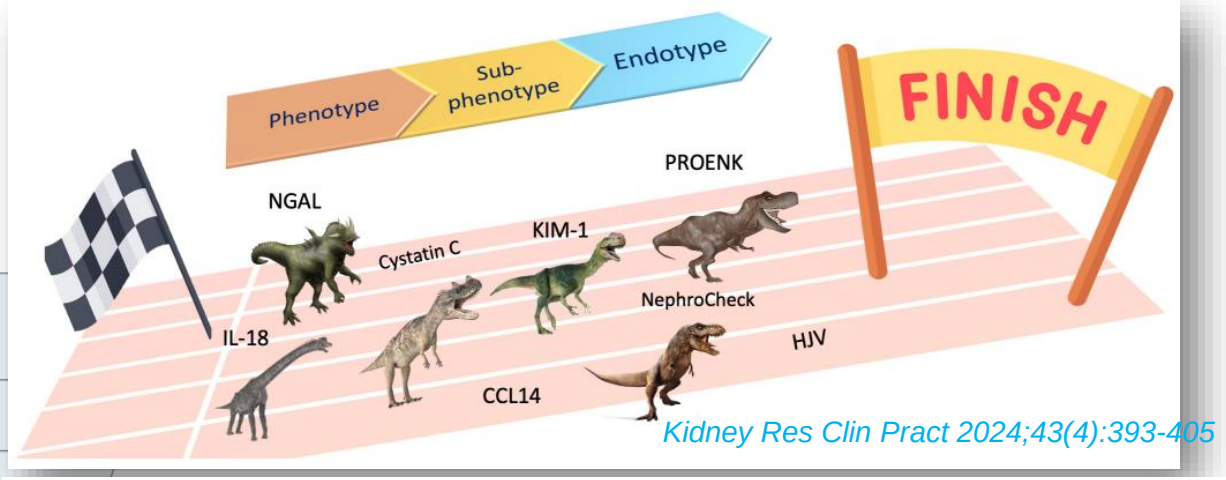
Brenner and Rector's The Kidney, 29, 940-977.e15

Classic Biomarker (1)

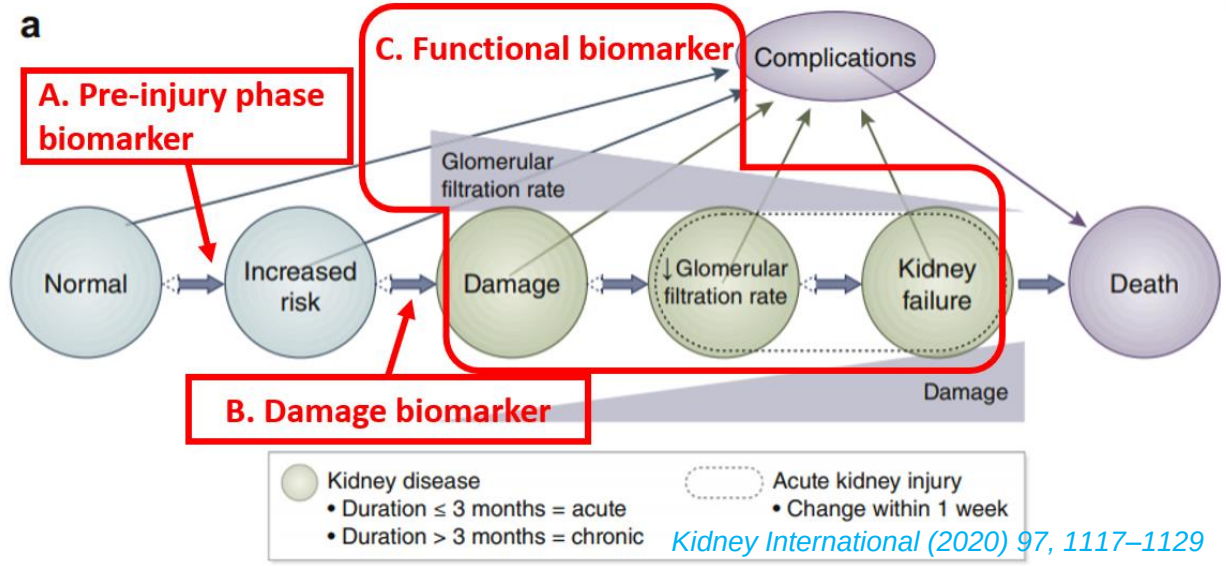
Proposed New Definitions of Acute Kidney Injury

Functional criteria	Stage	Damage criteria
No change or sCr level increase <0.3 mg/dL and no UO criteria	1S	Biomarker positive
Increase of sCr level by ≥0.3 mg/dL for ≤48 h or ≥150% for ≤7 days and/or UO <0.5 mL/kg/h for >6 h	1A	Biomarker negative
	1B	Biomarker positive
Increase of sCr level by >200% and/or UO <0.5 mL/kg/h for >12 h	2A	Biomarker negative
	2B	Biomarker positive
Increase of sCr level by >300% (≥4.0 mg/dL with an acute increase of ≥0.5 mg/dL) and/or UO <0.3 mL/kg/h for >24 h or anuria for >12 h and/or acute KRT	3A	Biomarker negative
	3B	Biomarker positive

JAMA Network Open. 2020;3(10):e2019209



Kidney Res Clin Pract 2024;43(4):393-405



Kidney International (2020) 97, 1117–1129

Classic Biomarker (2)

Proximal tubule
- Albumin
- IL-18
- GST-α (urinary)
- Clusterin
- Cystatin C (urinary)
- KIM-1
- α-1 Microglobulin
- β-2 Microglobulin
- NGAL
- HGF
- Netrin-1
- Osteopontin
- NHE-3
- Cyr61
- L-FABP
- Exosomal fetuin-A
- NAG
- RBP
- NHE-3

Glomerulus
- Albumin
- Total protein
- α-1 Microglobulin
- β-2 Microglobulin
- Cystatin C (urinary)

Loop of Henle
- Osteopontin
- NHE-3

Distal tubules
- GST-μ/π
- NGAL
- Osteopontin
- Clusterin
- H-FABP
- Calbindin D-28

Collecting duct
- Calbindin D-28

Preinjury biomarkers
- IGFBP-7 @
- TIMP-2 @
- DKK1–4 (DKK-3)* (serum, urinary)
- Hemojuvelin (HJV) (urinary)
- Micro-RNAs (U) (urinary)
- Wnt (serum, urinary)

Others
- Cytochrome-C (urinary)
- Epidermal growth factor (urinary)
- Malondialdehyde (urinary)

How fast, useful, and reliable?

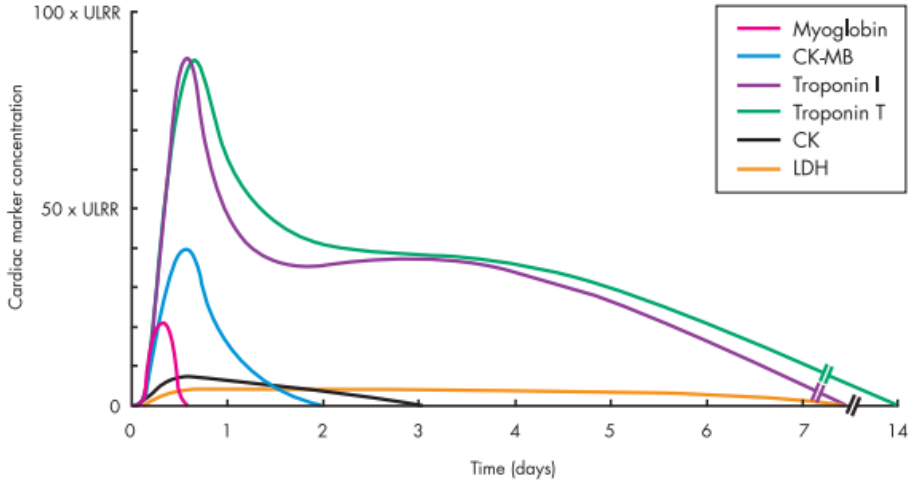
Indian J Crit Care Med. 2020 Apr; 24(Suppl 3): S90–S93

AKI biomarker	Stress marker	Damage marker	Functional marker	Potential role in clinical practice
ALP (2008)		Urine (U)		Diagnosis, Severity of AKI
Calprotectin (2011)		U		Diagnosis
C-C- motif Chemokine ligand-14 (2020)		U		Recovery
Chitinase 3-like protein 1 (2016)		U and Plasma (P)		Diagnosis
Cystatin C (2008)			P	Diagnosis, Severity
Dickkopf-3 (2019)	U			Risk assessment, prediction
α –transferase S-transferase (2010)		U		Diagnosis
π glutathione S-transferase (2008)		U		Diagnosis
Hepatocyte growth factor (2008)		P		Severity, Recovery
Hepcidin (2015)		U and P		Diagnosis, Severity
TIMP-2*IGFBP7 (2013)	U			Prediction, Diagnosis, Severity
Interleukin-18 (2008)		U		Prediction, Diagnosis
Kidney injury molecule-1 (2008)		U		Prediction, Diagnosis, Severity
Liver-type fatty acid-binding protein (2015)		U and P		Diagnosis
microRNA (2019)		U and P		Diagnosis
Monocyte chemoattractant peptide-1 (2017)		U		Severity
N-acetyl-β-Dglucosaminidase (2014)		U		Diagnosis
Neutrophil gelatinase-associated lipocalin (2008)		U and P		Diagnosis, Severity
Netrin-1 (2010)		U		Diagnosis
Osteopontin (2011)		P		Diagnosis, Severity
Proenkephalin A (2019)			P	Diagnosis, Severity, Recovery
Retinol binding protein (2014)		P		Diagnosis?
Tumor necrosis factor (2015)		P		Diagnosis

JAMA Network Open. 2020;3(10):e2019209

Classic Biomarker (4)

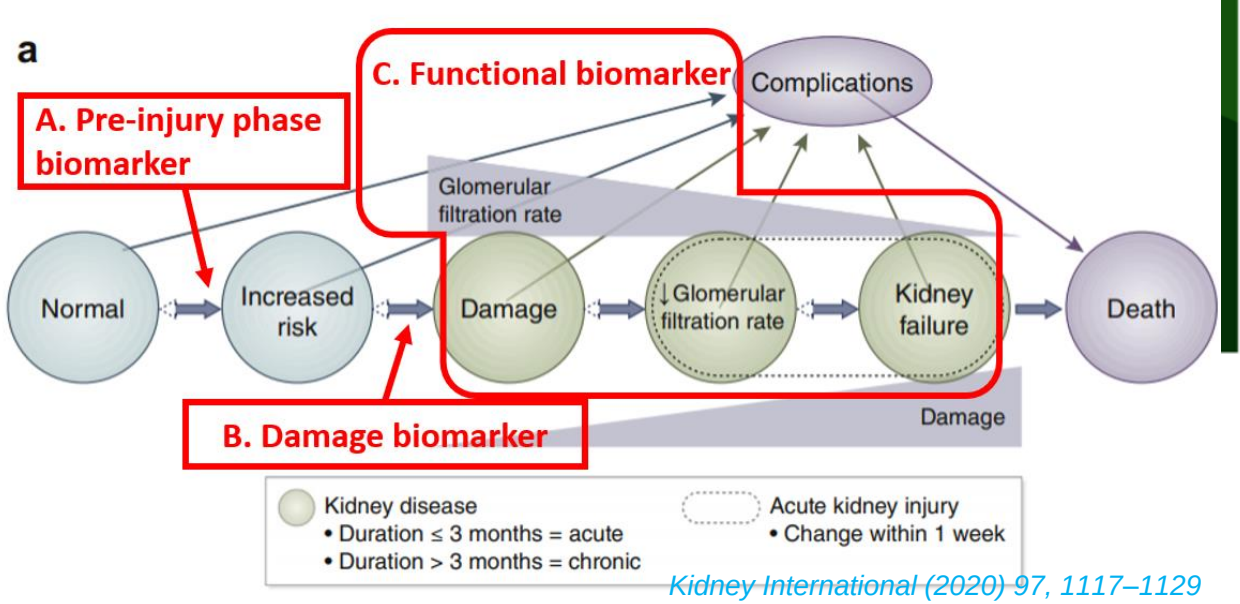
vs Cardiac biomarkers



Protein	Molecular mass (kD)	First detection	Duration of detection	Sensitivity	Specificity
Fatty acid binding protein	12	1.5-2 (h)	8-12	+++	++
Myoglobin	16	1.5-2	8-12	+++	+
CK-MB	83	2-3	1-2	+++	+++
Troponin I	33	3-4	7-10	++++	++++
Troponin T	38	3-4	7-14	++++	++++
CK	96	4-6	2-3	++	++
Aspartate transaminase	~103	6-10	3-5	++	+
LDH	135	6-10	5-7	++	+

Heart 2004;90:99–106

AKI biomarkers?



Kidney International (2020) 97, 1117–1129

Protein	Molecular mass (kD)	First detection	Duration of detection	Sensitivity	Specificity
Liver-type fatty acid binding protein (L-FABP)	14	1	IR : 24h CIN :72h-2wks	+++	+?
IL-18	22	1	24h?	+++	+?
NGAL	25-45	1	12h (3-6?) Urinary : 2h	+++	+?
KIM-1	38.7	3-6	12-7days	+++	+?
TIMP-2 and IGFBP7	TIMP-2=21 IGFBP7 = 29	4	12-24h	+++	+?
Cystatin C	13	12	24h	+++	+?
Pro-enkephalin (Pro-ENK)/penKid	4.6	24-48h	During AKI	+++	83.1%

Classic Biomarker application: biomarker-guided therapeutic approach

Functional criteria	Stage	Damage criteria
No change or sCr level increase <0.3 mg/dL and no UO criteria	1S	Biomarker positive
Increase of sCr level by ≥0.3 mg/dL for ≤48 h or ≥150% for ≤7 days and/or UO <0.5 mL/kg/h for >6 h	1A	Biomarker negative
	1B	Biomarker positive
Increase of sCr level by >200% and/or UO <0.5 mL/kg/h for >12 h	2A	Biomarker negative
	2B	Biomarker positive
Increase of sCr level by >300% (≥4.0 mg/dL with an acute increase of ≥0.5 mg/dL) and/or UO <0.3 mL/kg/h for >24 h or anuria for >12 h and/or acute KRT	3A	Biomarker negative
	3B	Biomarker positive

Cardiac surgery

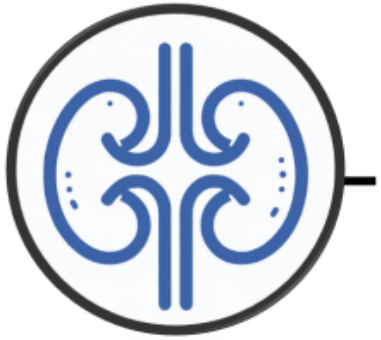
Urinary [TIMP-2]-[IGFBP7] KDIGO care bundle intervention
Lower occurrence of moderate to severe AKI

Hepatorenal syndrome

① Urinary NGAL: predict the treatment response
② Urinary NGAL: predictor of in-hospital mortality

Cardiorenal syndrome

① Aggressive volume removal: NAG, KIM-1, NGAL did not increase risks of post-discharge mortality or rehospitalization
② Galectin-3, ST2, FGF-23, suPAR, miRNA, GDF-15, and NAG: kidney disease progression
③ L-FABP and suPAR: predict AKI
④ ST2 and NAG: diuretic resistance



AIN

① Urine TNF-alpha and IL-9 level are higher
② IL-9: predict treatment response from corticosteroid
③ Urinary CXCL9 was identified and validated
④ Urinary CXCL9-to-creatinine ratios

Kidney Res Clin Pract 2024;43(4):393-405

Early diagnosis and prognosis prediction

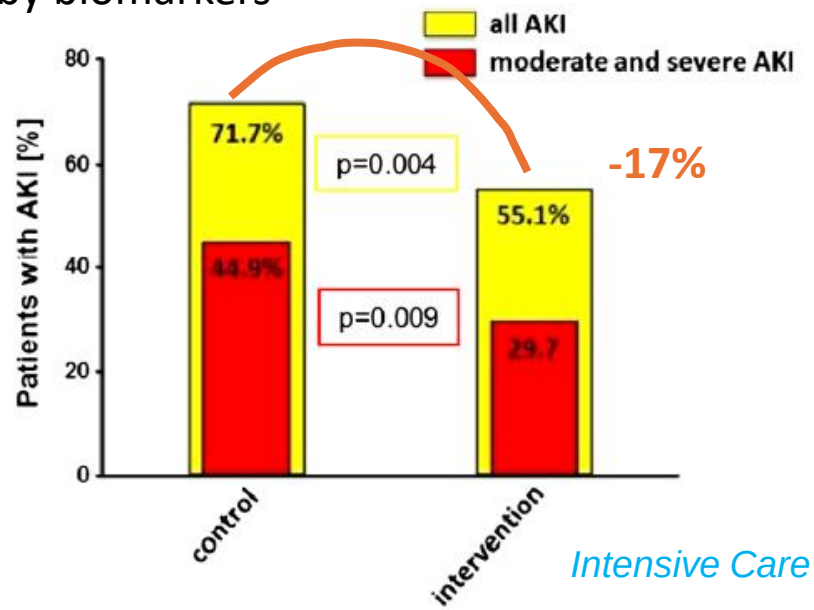
Pre-injury phase biomarkers, NephroCheck® = TIMP-2*IGFBP7

BigpAK RCT : Biomarker-guided intervention to prevent AKI after major surgery

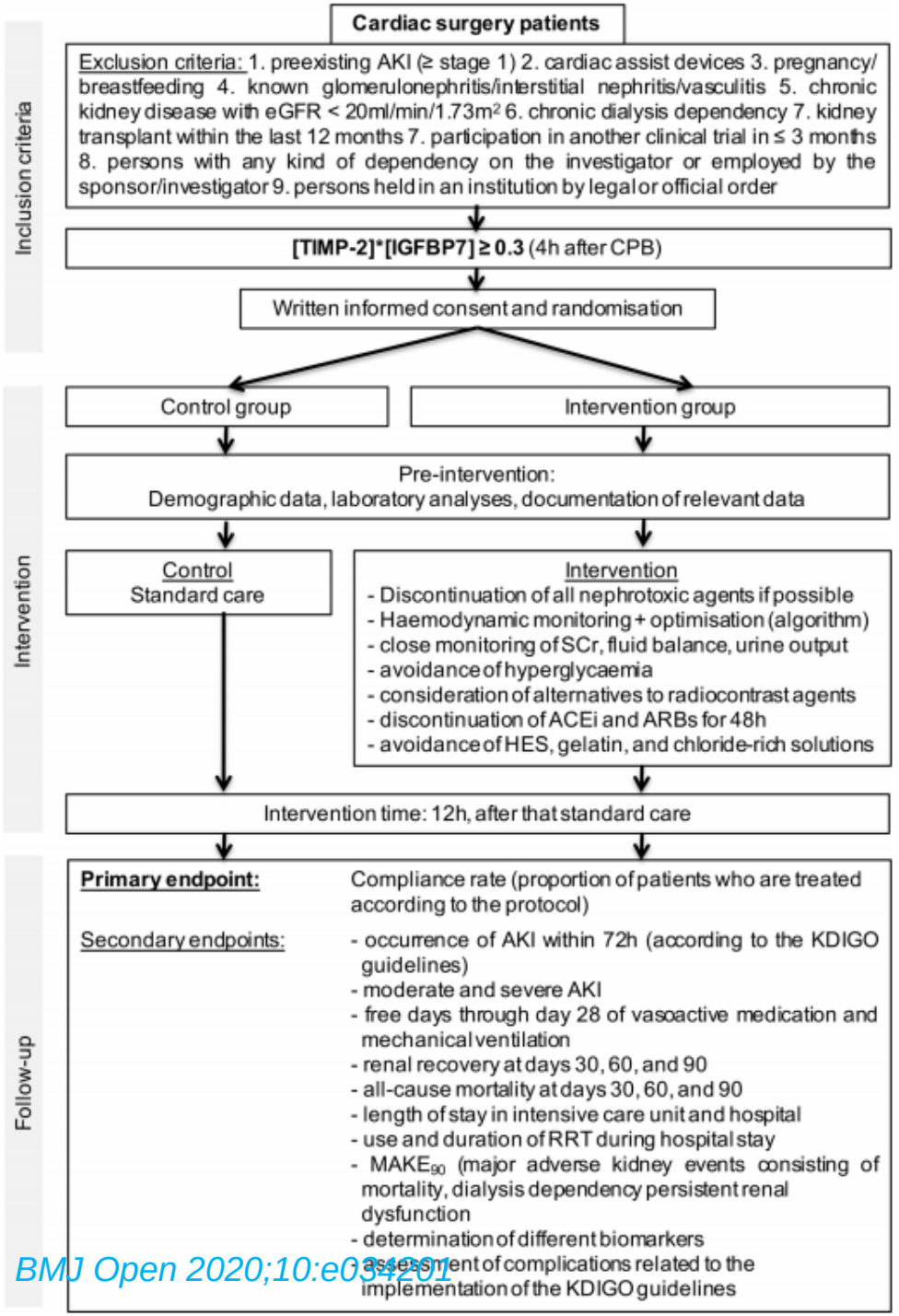
- Reduced incidence of AKI 27.1% vs 48% (*P* = 0.03)
- Reduced **-13%** of moderate and severe AKI (*P* = 0.04)
- Creatinine elevation more than 25% of baseline (*P* = 0.01)
- Reduced length of ICU and hospital stay (*P*= 0.04)

Ann Surg 2018;267:1013–1020

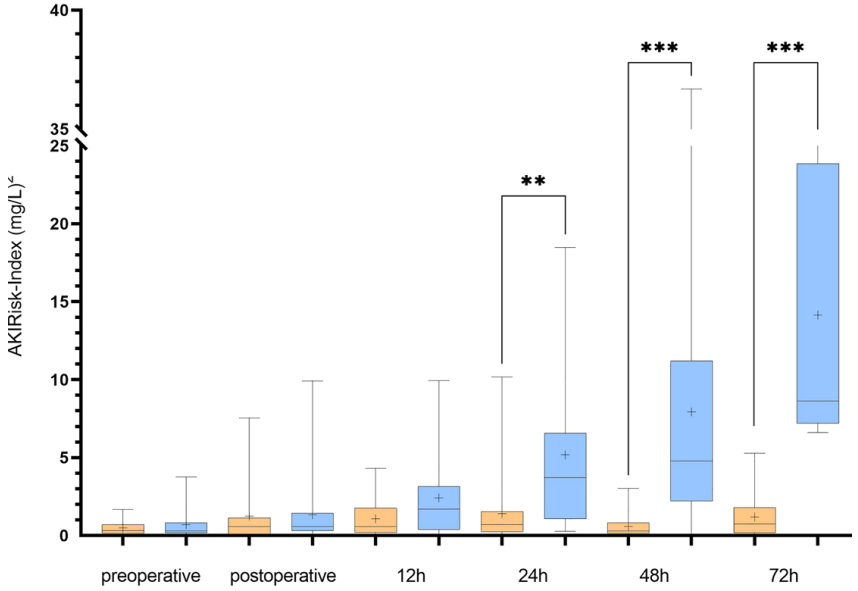
PrevAKI RCT : Cardiac surgery-associated AKI prevention by AKI high risk patie nt identified by biomarkers



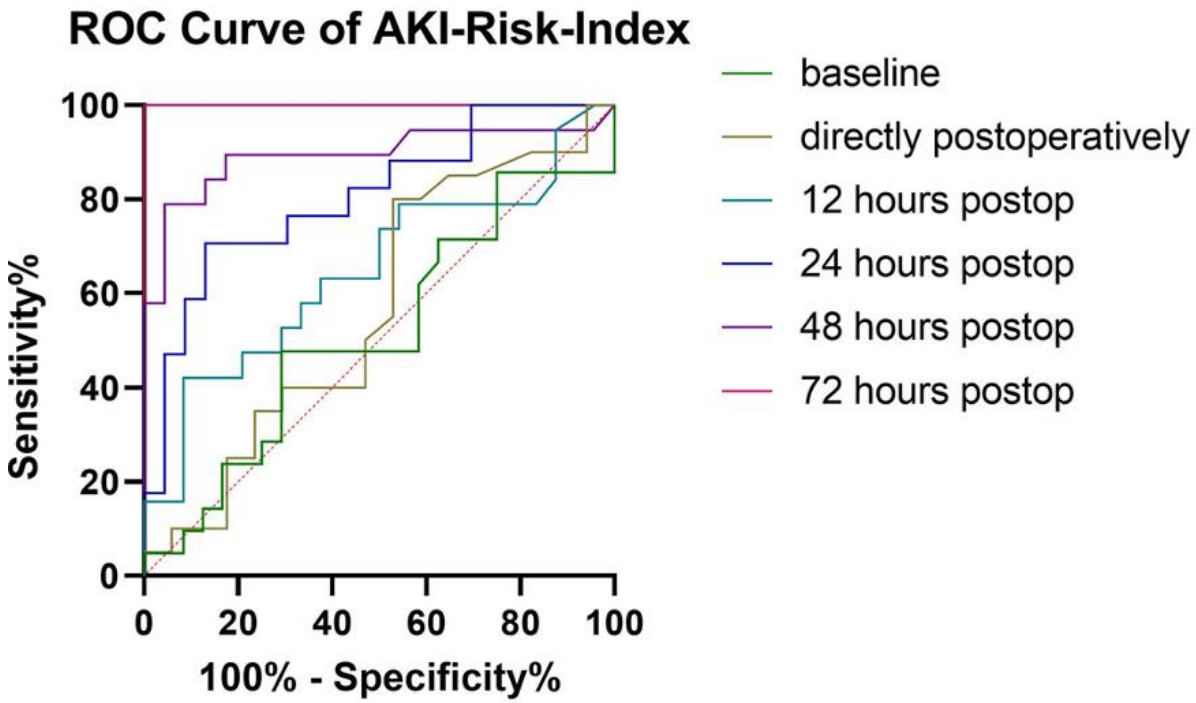
Intensive Care Med (2017) 43:1551–1561

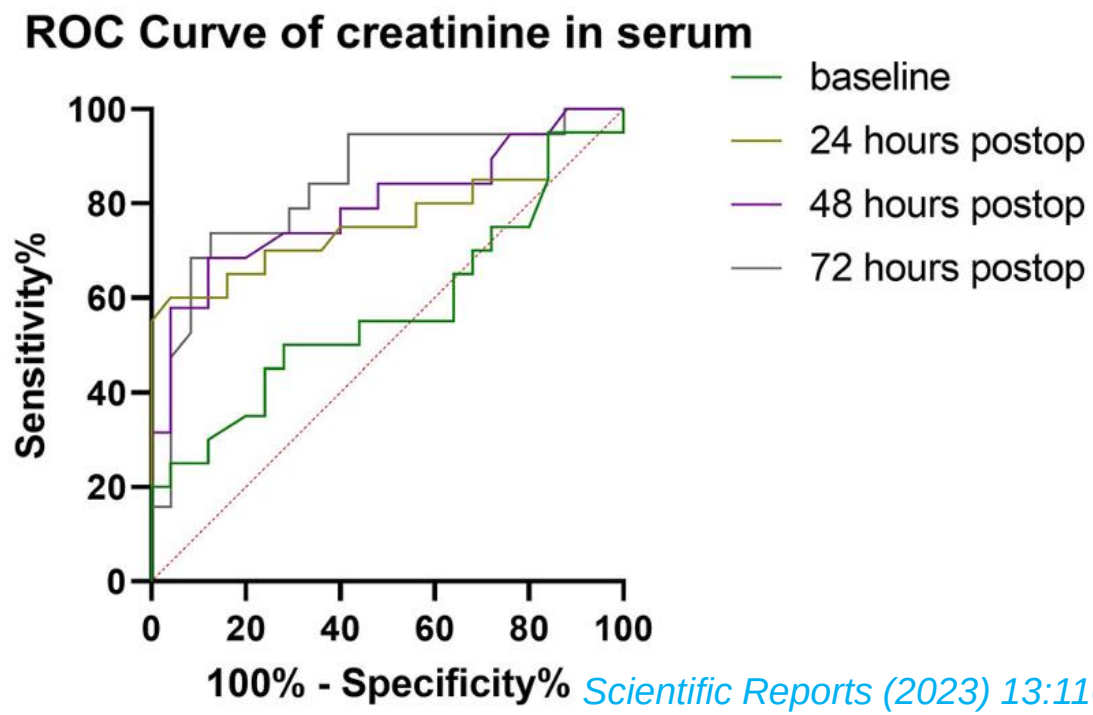


BMJ Open 2020;10:e034201



	Time point	AUC	95% CI	*p* value	Cut-off	Se (%)	Sp (%)	Likelihood ratio
AKIRisk Index	Preoperative	0.5149	0.34–0.69	0.87	> 0.15	80.95	25.00	1.079
	Postoperative	0.5647	0.37–0.76	0.50	> 0.26	80.00	47.06	1.511
	12 h	0.6480	0.48–.82	0.099	> 0.14	84.21	12.50	0.9624
	24 h	0.8056	0.67–0.95	0.001	> 0.81	82.35	56.52	1.894
	48 h	0.8947	0.78–1	< 0.001	> 1.23	84.21	86.96	6.456
	72 h	1.000	1–1	< 0.001	> 5.96	100	100	
Creatinine in serum	Preoperative	0.5740	0.4–0.75	0.40	> 0.77	85.00	16.00	1.012
	24 h	0.7640	0.61–0.92	0.003	> 1.36	80.00	44.00	1.429
	48 h	0.7958	0.65–0.94	< 0.001	> 1.32	84.21	52.00	1.754
	72 h	0.8410	0.72–0.97	< 0.001	> 1.31	84.21	66.67	2.526





Scientific Reports (2023) 13:11096

Early diagnosis and prognosis prediction

Pre-injury phase biomarkers, NephroCheck® = TIMP-2*IGFBP7, *candidate?*

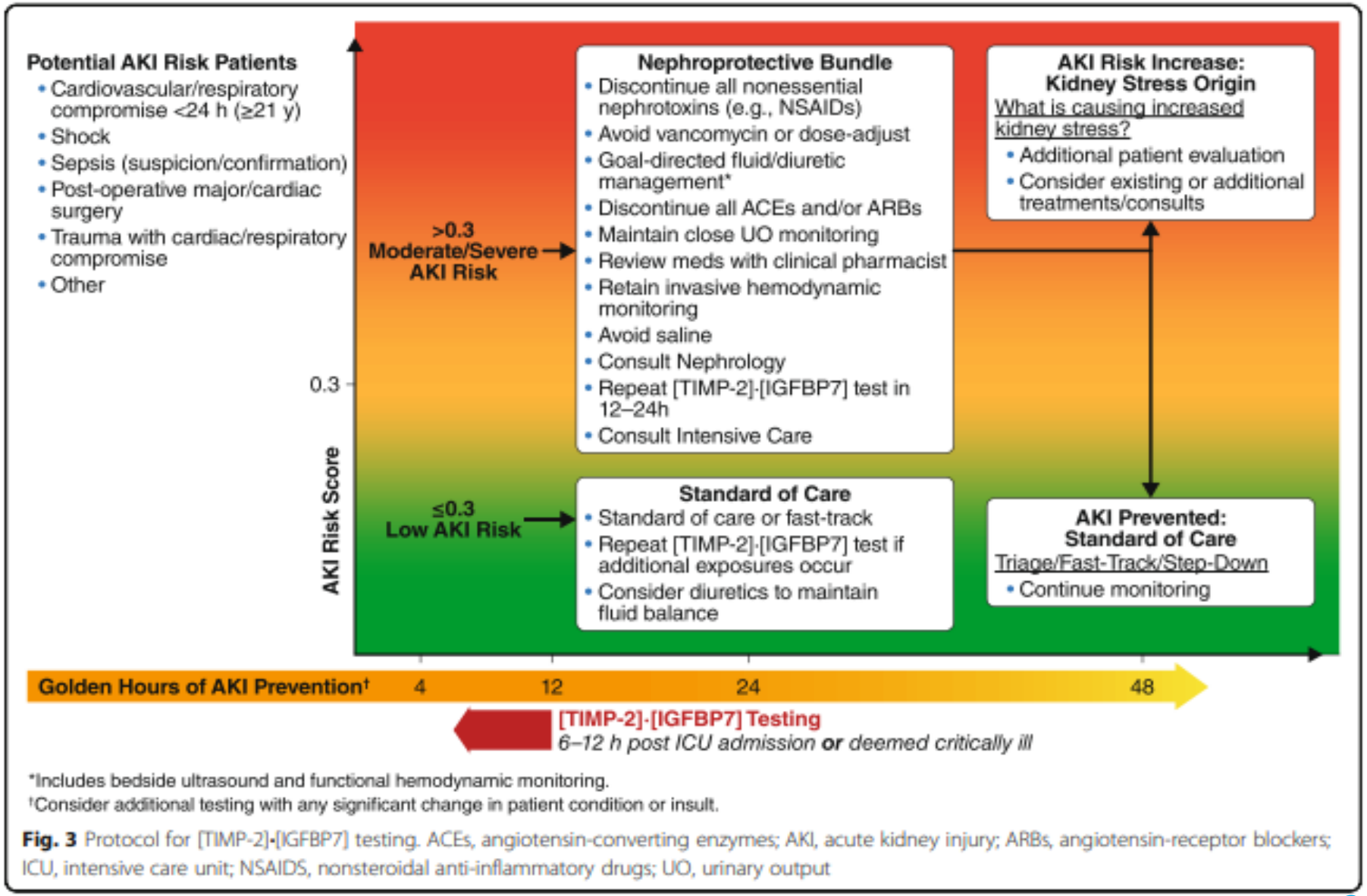
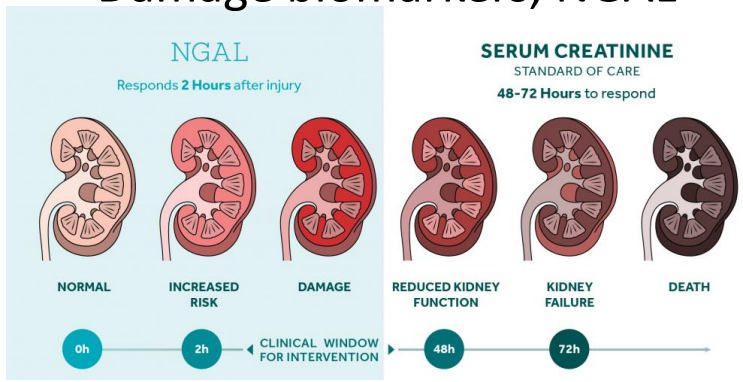


Fig. 3 Protocol for [TIMP-2]·[IGFBP7] testing. ACEs, angiotensin-converting enzymes; AKI, acute kidney injury; ARBs, angiotensin-receptor blockers; ICU, intensive care unit; NSAIDS, nonsteroidal anti-inflammatory drugs; UO, urinary output

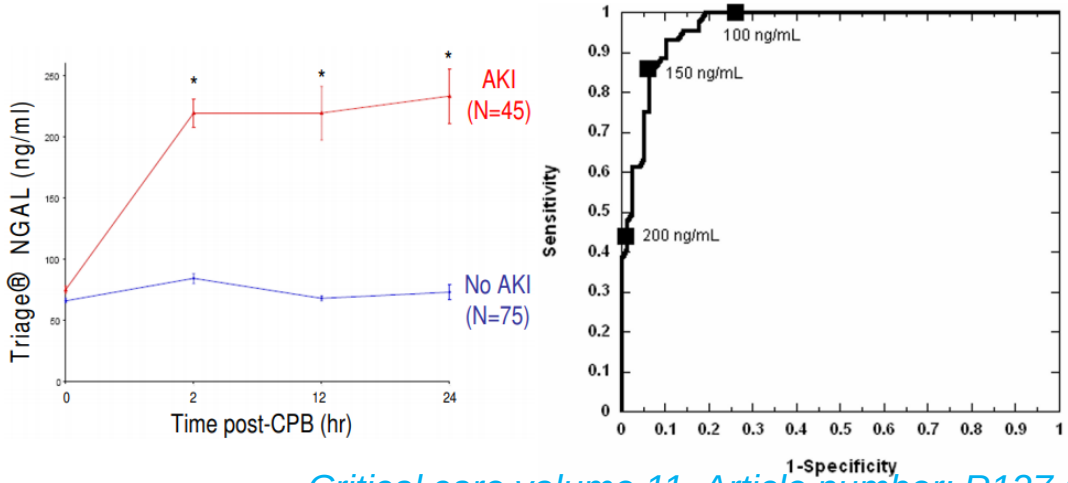
Guzzi et al. Critical Care (2019) 23:225

Early diagnosis and prognosis prediction

Damage biomarkers, NGAL

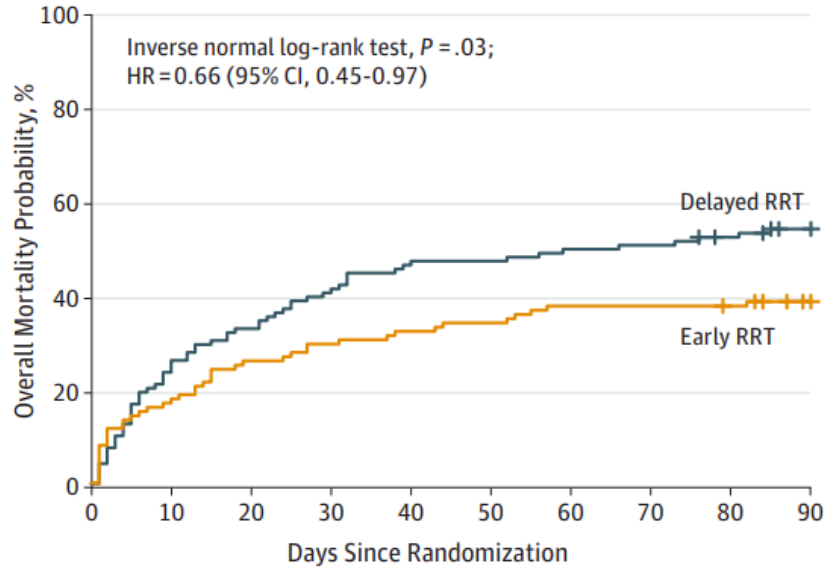


Plasma neutrophil gelatinase-associated lipocalin predicts acut e kidney injury, morbidity and mortality after pediatric cardiac s urgery: a prospective uncontrolled cohort study



Critical care volume 11, Article number: R127 (2007)

Figure 2. Mortality Probability Within 90 Days After Study Enrollment for Patients Receiving Early and Delayed Initiation of Renal Replacement Therapy (RRT)



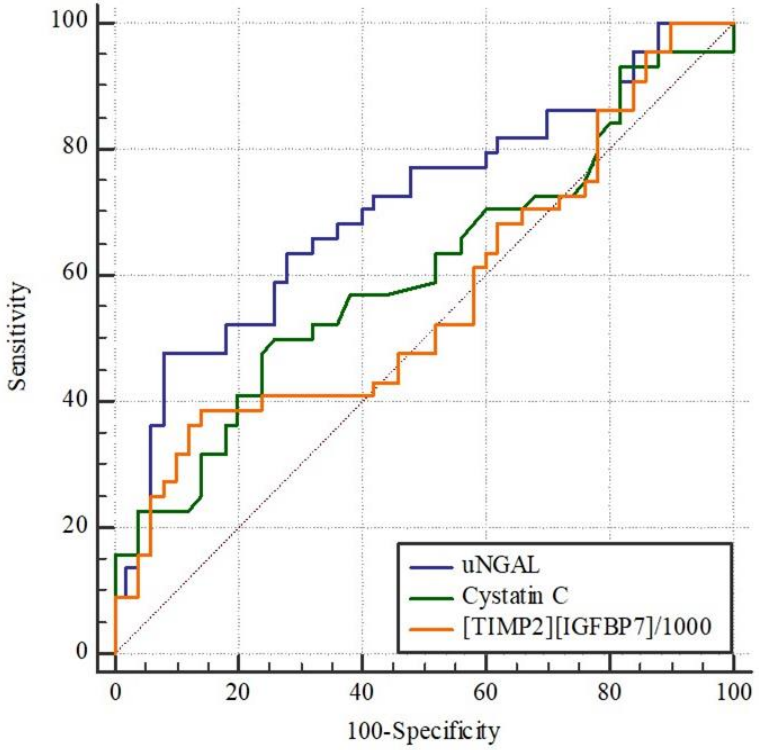
No. at risk										
Early RRT	112	92	82	78	75	73	69	69	66	55
Delayed RRT	119	90	79	70	63	62	59	58	54	48

KDIGO indicates Kidney Disease: Improving Global Outcomes. In the delayed group, 18 patients had an absolute indication for RRT. The median (quartile 1 [Q1], quartile 3 [Q3]) duration of follow-up was 90 days (Q1, Q3: 90, 90) in the early group and 90 days (Q1, Q3: 90, 90) in the delayed group. The vertical ticks indicate censored cases.

JAMA. 2016;315(20):2190-2199

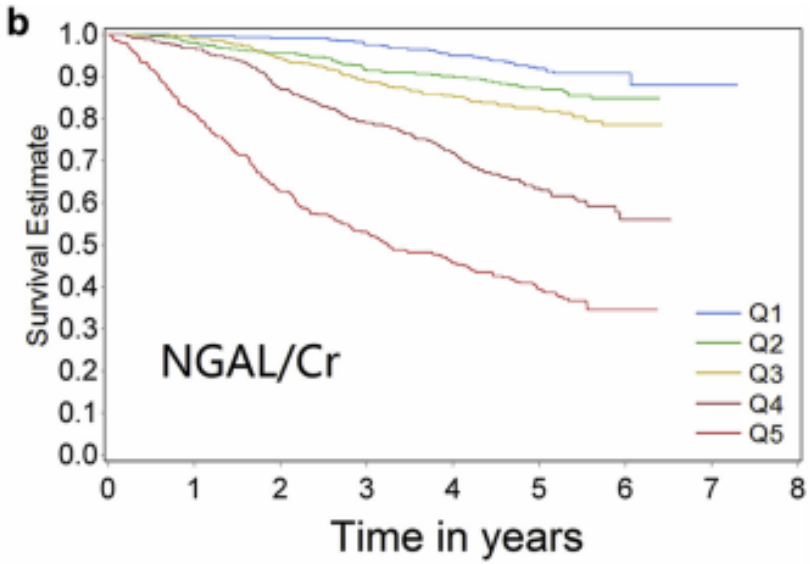
Early diagnosis and prognosis prediction

Damage biomarkers, NGAL



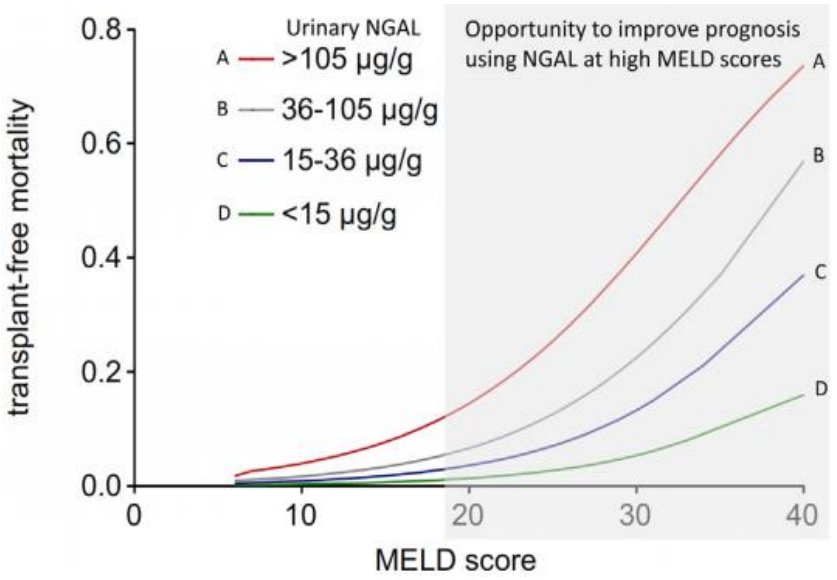
Prediction of AKI in decompensated liver cirrhosis patients

Scientific reports (2019) 9:14508



Prediction of CKD progression (unadjusted cox regression)

Kidney International (2017) 91, 196–203



MELD using NGAL/Cr for predicting 28 -day transplant-free mortality

Journal of hepatology, 2016, Jul. 65. 1: 57-65

Early diagnosis and prognosis prediction

plasma pro-enkephalin (pro-ENK)

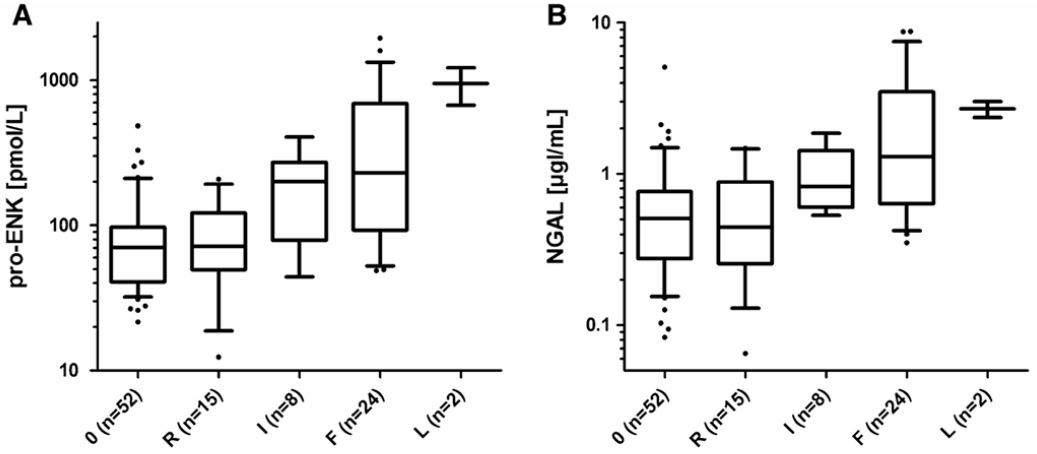
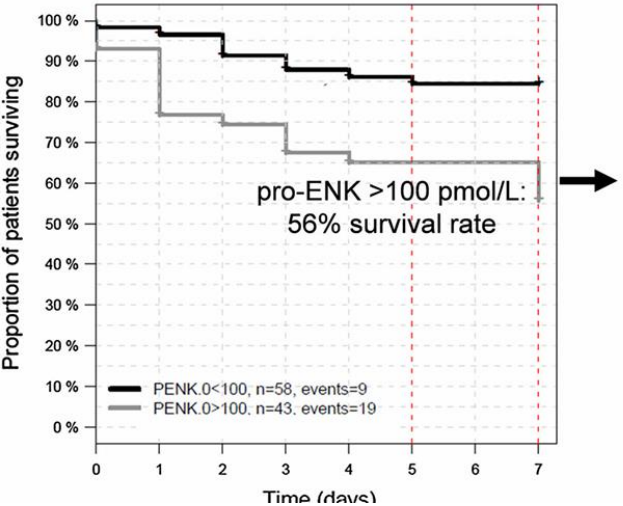
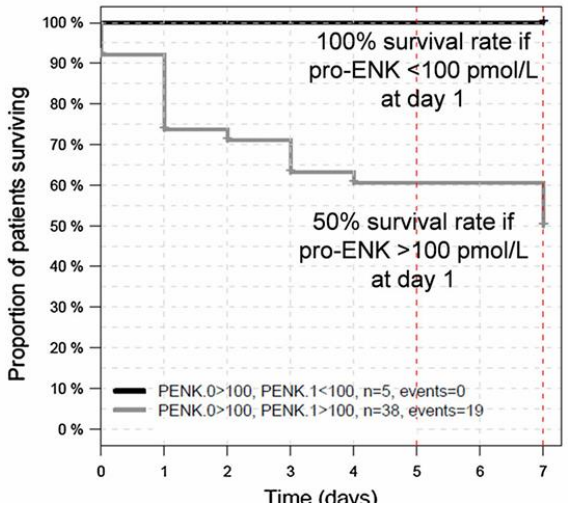
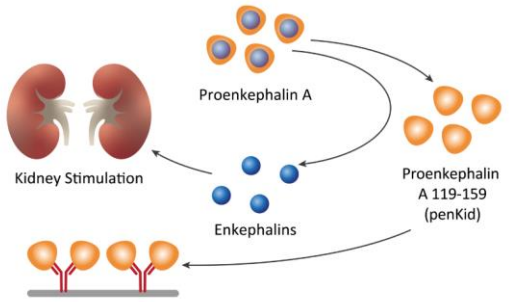


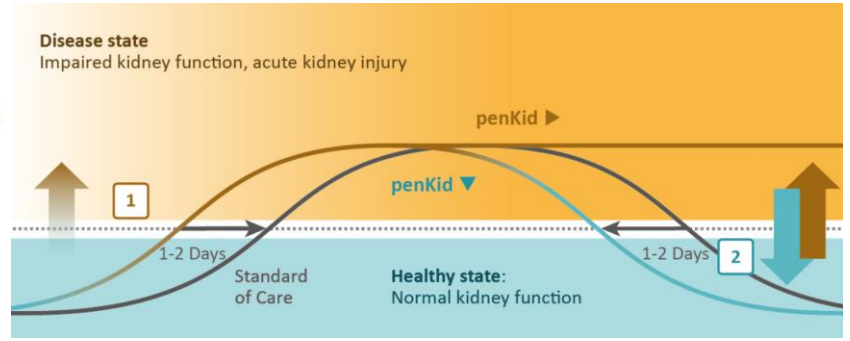
Fig. 2 Concentration of pro-ENK (**a**) and NGAL (**b**) in patients according to the RIFLE criteria. Plasma levels of both markers were determined for all patients on admission and are shown here for patient subgroups according to presence and severity of AKI using the RIFLE criteria (*box* 25th–75th percentile, *whiskers* 10th–90th percentile). The upper normal limits are 80 pmol/l (pro-ENK) and 0.1 µg/ml (NGAL). *pro-ENK* proenkephalin, *NGAL* neutrophil gelatinase-associated lipocalin, *RIFLE* risk, injury, failure, loss of function, end-stage renal disease, *AKI* acute kidney injury



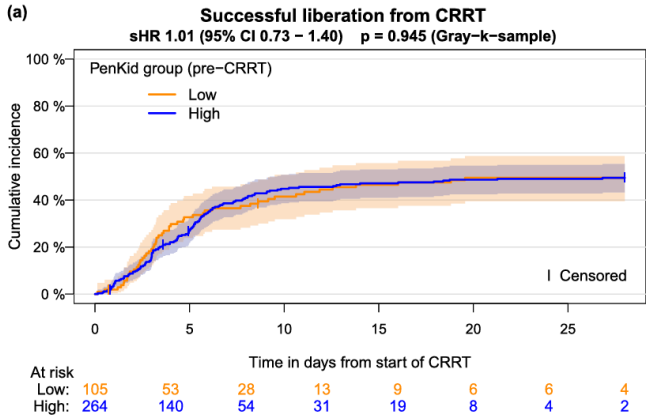


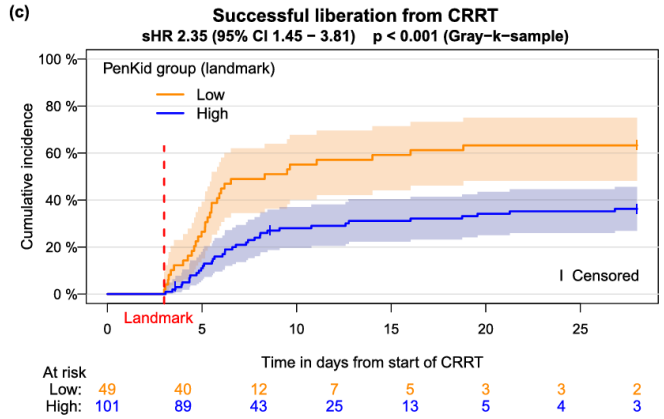
2015 Dec;28(6):717-24

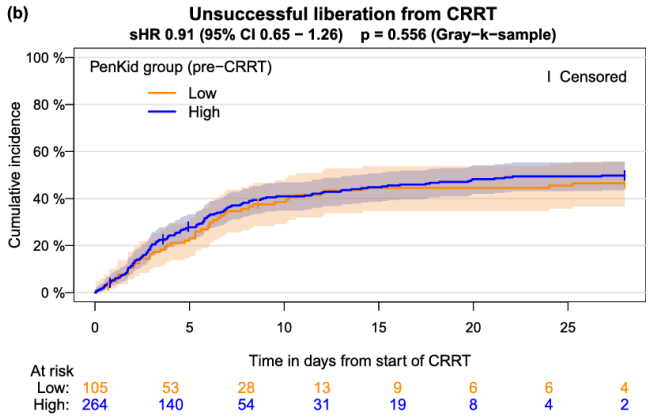


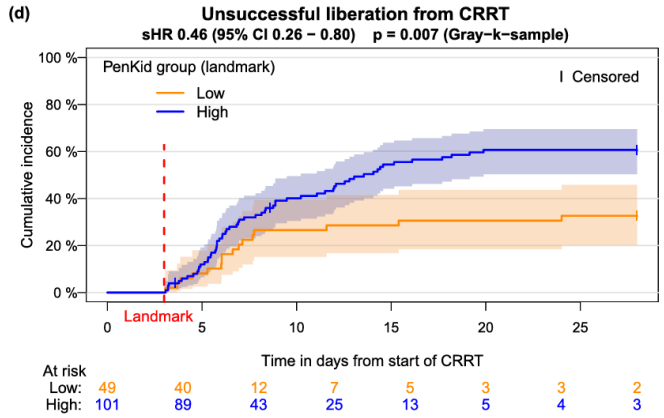


https://sphingotec.com/



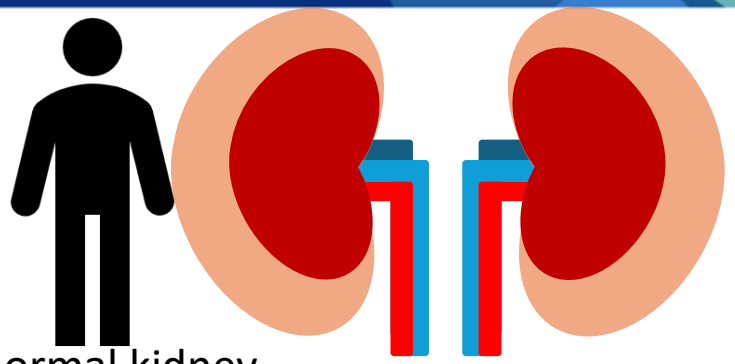




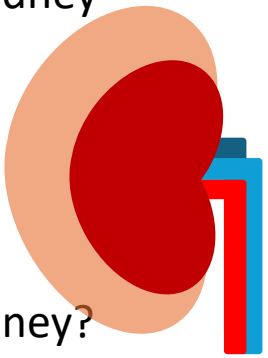


von Groote et al. Critical Care, (2023) 27:276

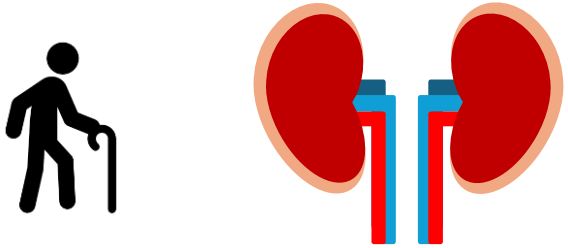
Functional/dynamic biomarker



Normal kidney

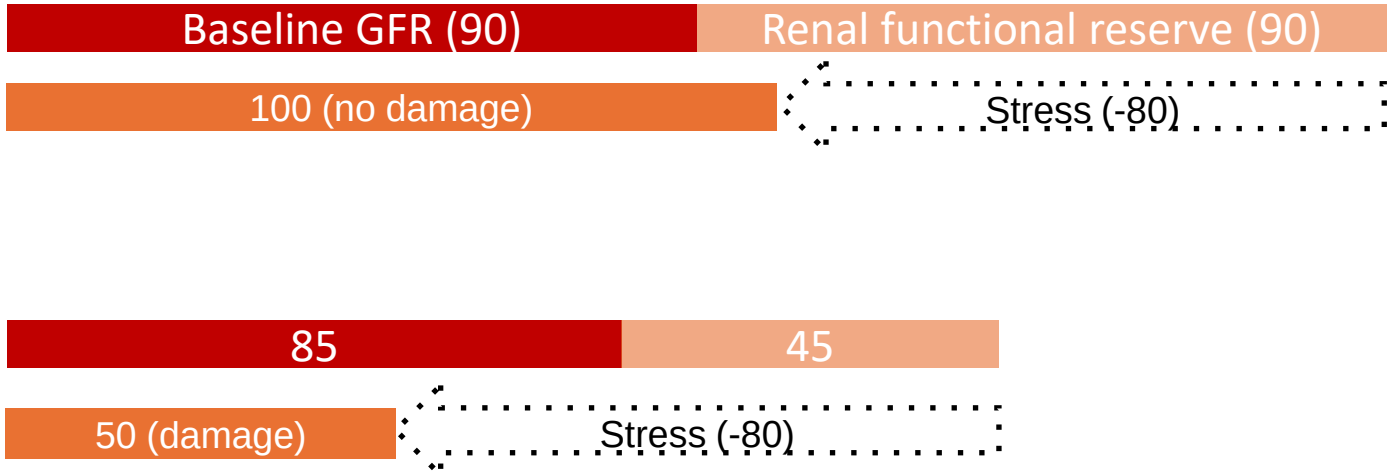


Single kidney?



Elderly with chronic kidney disease?

Renal functional reserve(RFR) - baseline GFR according to patients characteristics



Same stress, different consequence

Renal functional reserve

- Furosemide stimulation test (FST)

Table 5. Prediction of the composite of AKIN stage 3 and death

Biomarker	AUC±SEM	*P* Value for Biomarker Alone	*P* Value Compared With FST alone	AUC of Biomarker and FST±SEM	*P* Value for Biomarker and FST Compared With FST Alone
FST (2-hr UOP)	0.81±0.06	<0.0001	NA	NA	NA
Urine NGAL	0.69±0.06	0.006	0.07	0.82±0.06	0.89
Urine IL-18	0.63±0.07	0.07	0.009	0.82±0.06	0.87
Urine KIM-1	0.64±0.06	0.04	0.04	0.82±0.06	0.81
Uromodulin	0.54±0.07	0.58	0.004	0.85±0.06	0.31
Urine IGFBP-7	0.65±0.08	0.07	0.19	0.79±0.08	0.80
Urine TIMP-2	0.66±0.08	0.06	0.18	0.80±0.08	0.75
Urine IGFBP-7×TIMP-2	0.68±0.08	0.03	0.27	0.78±0.08	0.93
Urine Creatinine	0.54±0.07	0.56	0.007	0.83±0.06	0.23
Urine ACR	0.50±0.07	0.96	0.002	0.82±0.06	0.32
FeNa	0.49±0.07	0.84	0.009	0.80±0.06	0.31
Plasma NGAL	0.69±0.08	0.03	0.27	0.80±0.08	0.76

NA, not applicable; ACR, albumin-to-creatinine ratio.

J Am Soc Nephrol 26: 2023–2031, 2015

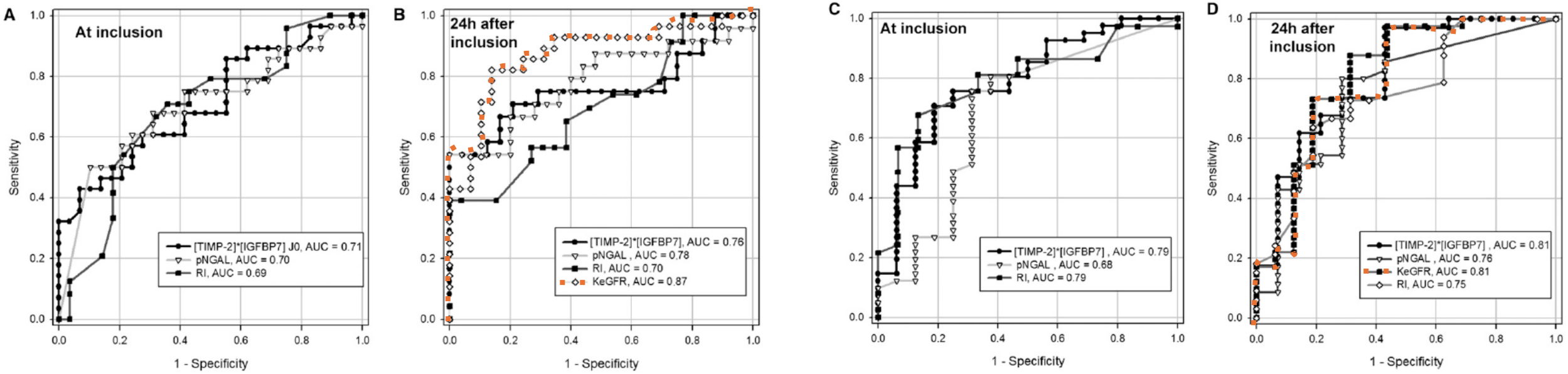
Renal functional reserve

- Kinetic eGFR

$$\text{Kinetic eGFR} = \frac{\text{Baseline sCr} \times \text{eGFR}}{(\text{sCr(H0)}+\text{sCr(H24)})/2} \times \left(1 - \frac{24 \times (\text{sCr(H24)} - \text{sCr(H0)})}{24 \times 133}\right)$$

Renal recovery

Adverse renal outcome



- Renal resistative index (RI)
  - Early AKI detection or to differentiate transient or persistent AKI in ICU
  - Contrast-enhanced ultrasonography associates low mechanical index US and microbubble-based contrast agents to assess organ perfusion
  - Poor performance, interobserver variability was as high as 25%, discordant changes 25%

Clin J Am Soc Nephrol 10: 1900–1910, 2015

Limitation (1)

Still, *serum creatinine* is the best AKI biomarker

AKI = not a disease, more like syndrome

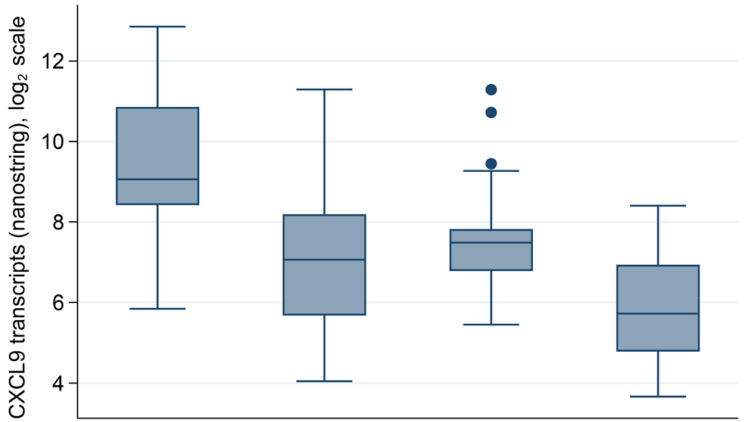
In real world, AKI arise due to multifactorial etiology, in heterogenous population, and creatinine based definition has also limitation.

Protein	Low specificity
Cystatin C	Old age, corticosteroids, hyperthyroidism, inflammation, neoplasia, smoking and alcohol consumption
Liver-type fatty acid binding protein	↑ anemia in nondiabetic patients
IL-18	Autoimmune diseases, myocardial function, emphysema, metabolic syndromes, psoriasis, inflammatory bowel disease, hemophagocytic syndromes, macrophage activation syndrome, sepsis
NGAL	↑Sepsis, CKD, UTI and the lack of general specific cutoff values
KIM-1	↑ chronic proteinuria and inflammatory diseases
TIMP-2 and IGFBP7	↑ diabetes

Limitation (2)

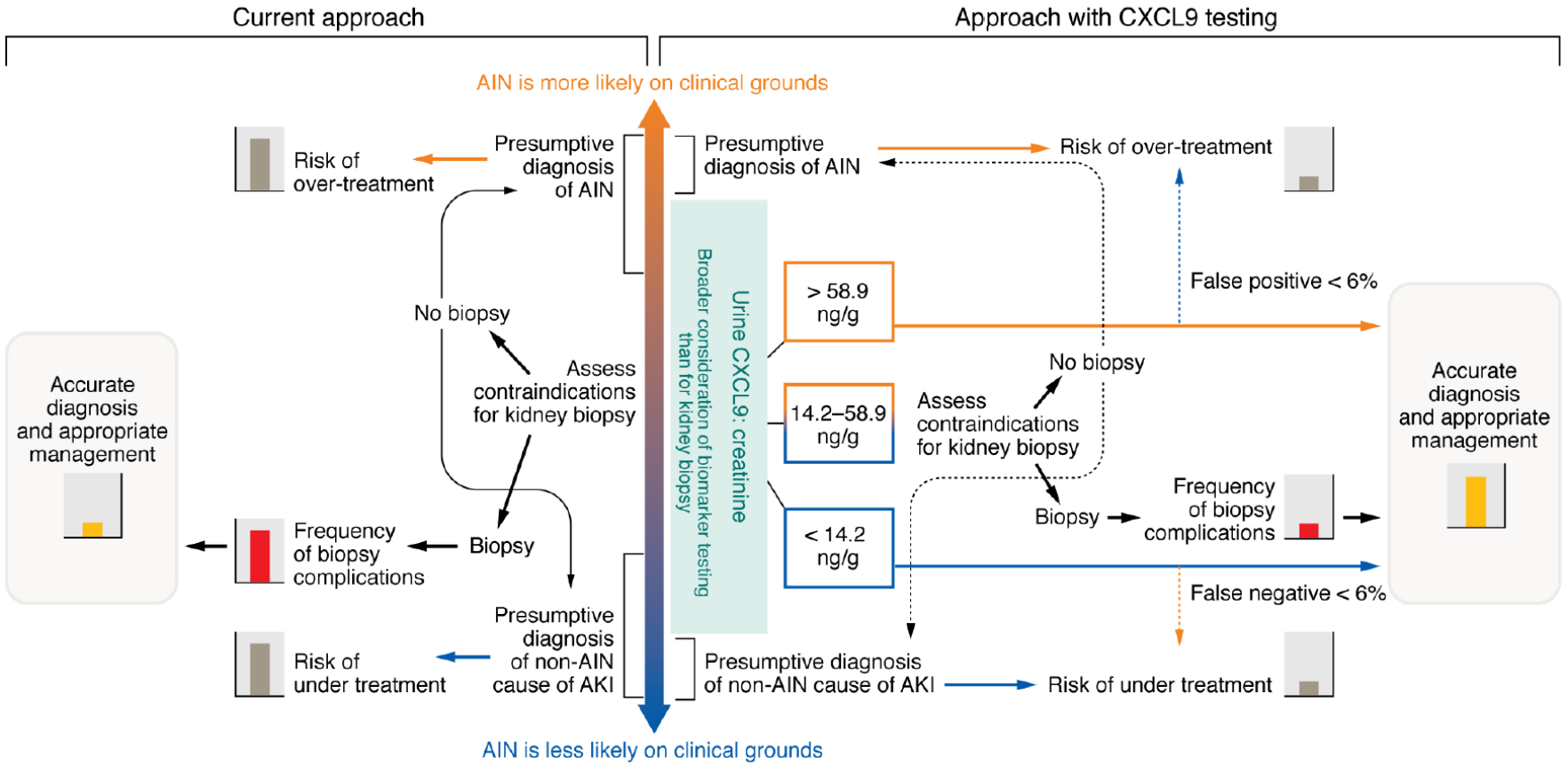
- Organ specificity
- Poor specificity
- Cut-off value validation

Future of the AKI biomarker (1)



Comparison	CXCL-9 mRNA fold difference (AIN vs. control)	*P* value
AIN vs. ATI	4.0	5.7×10^{-4}
AIN vs. DKD	3.0	4.0×10^{-4}
AIN vs. control	10.1	4.0×10^{-5}
AIN vs. all controls	3.9	5.8×10^{-6}

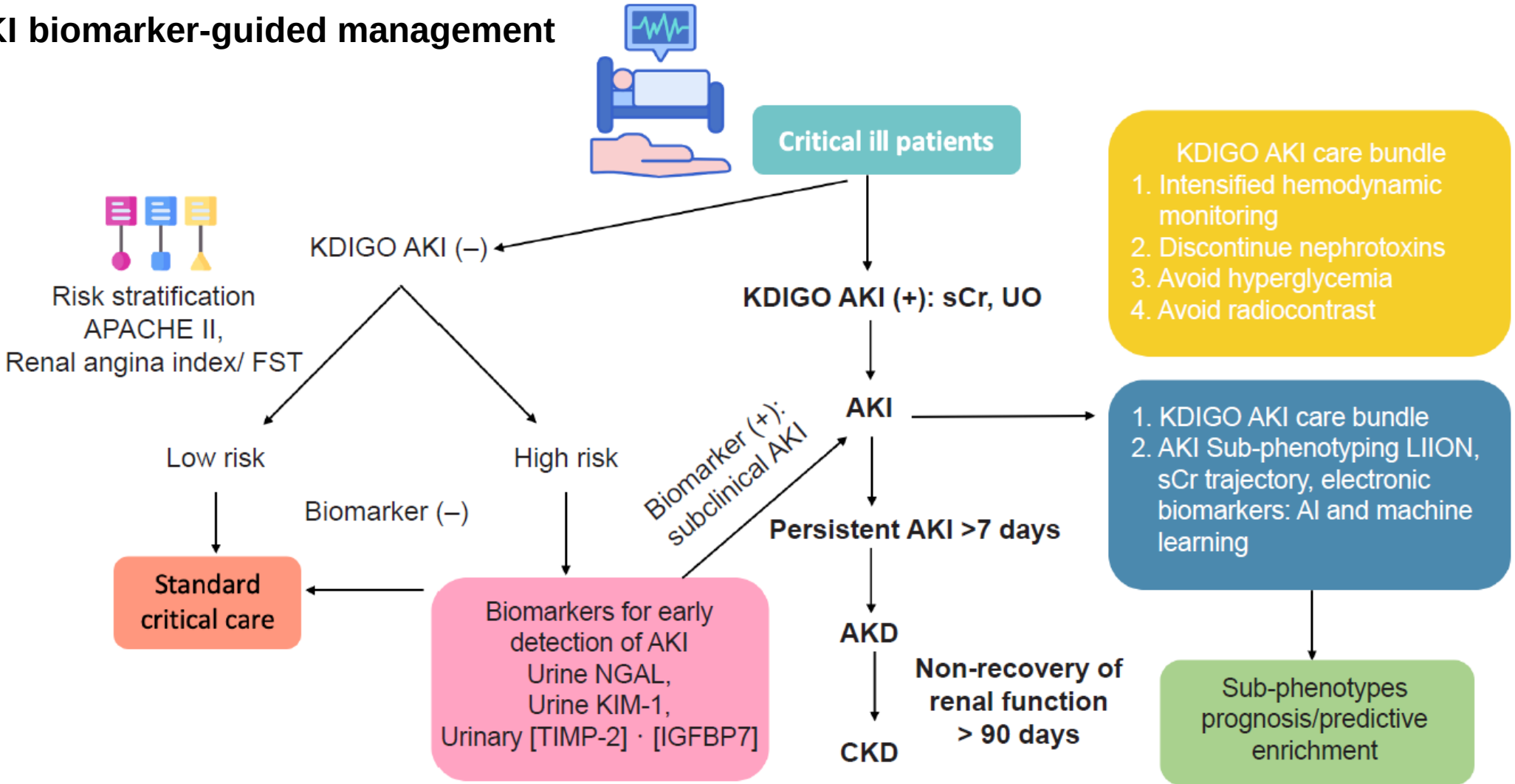
J Clin Invest. 2023;133(13):e168950



J Clin Invest. 2023;133(13):e171431

Future of the AKI biomarker (2)

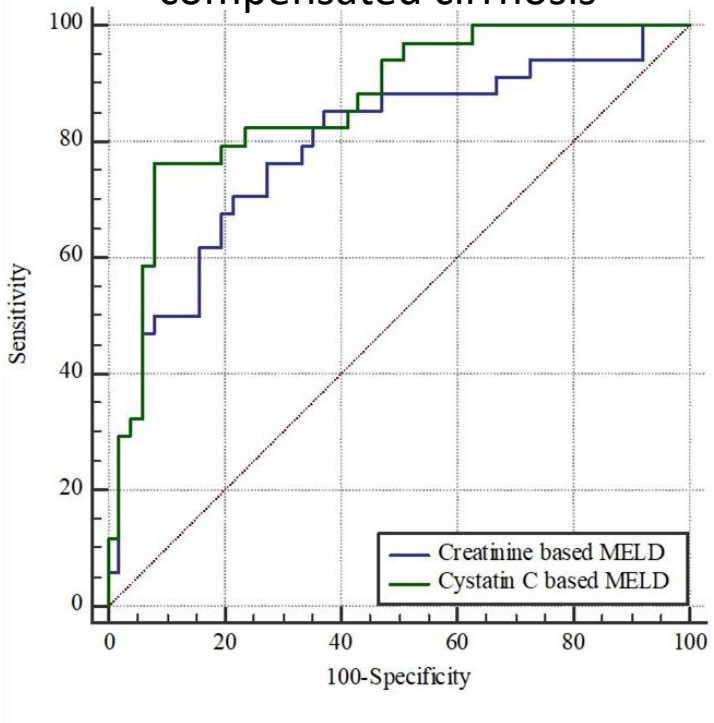
AKI biomarker-guided management



Future of the AKI biomarker (3)

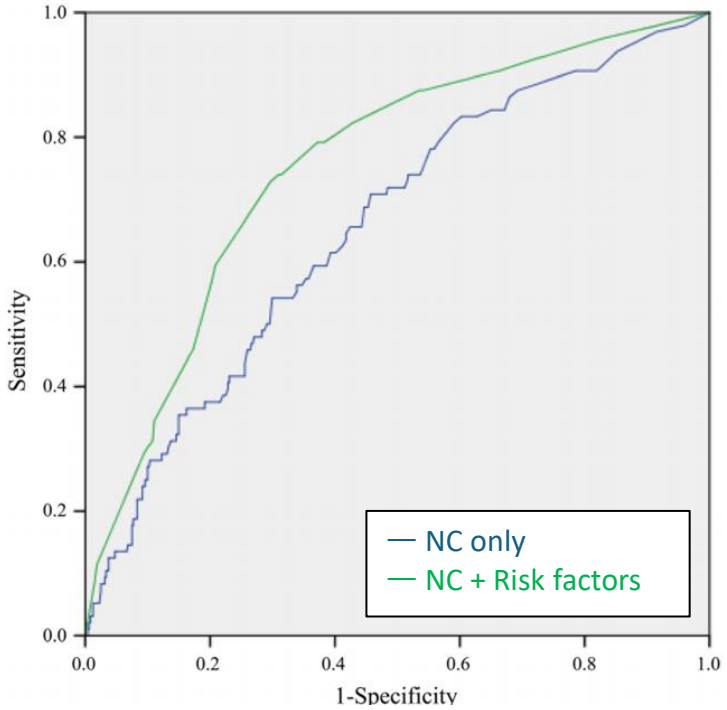
Multimarker strategy

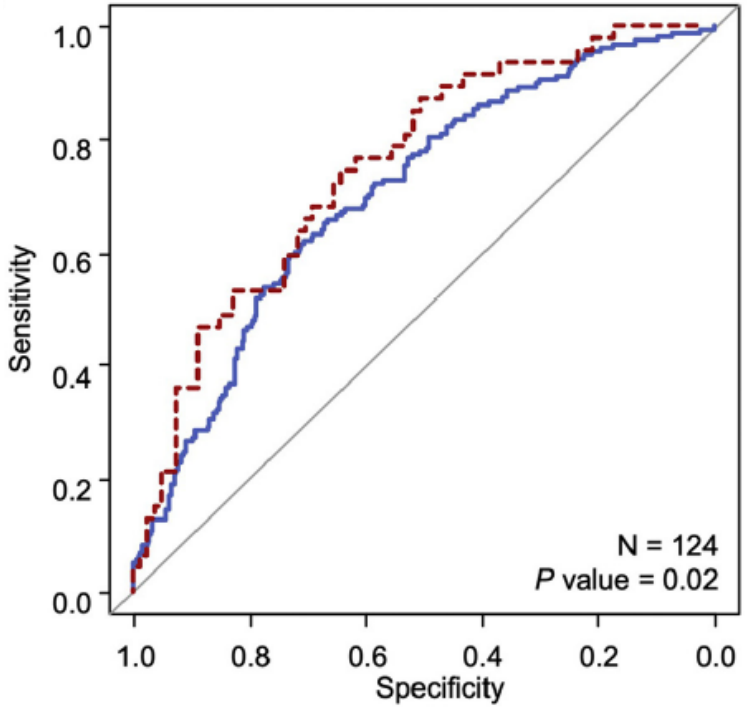
Better prediction for mortality in de compensated cirrhosis



Scientific reports (2019) 9:14508

Better prediction for severe AKI





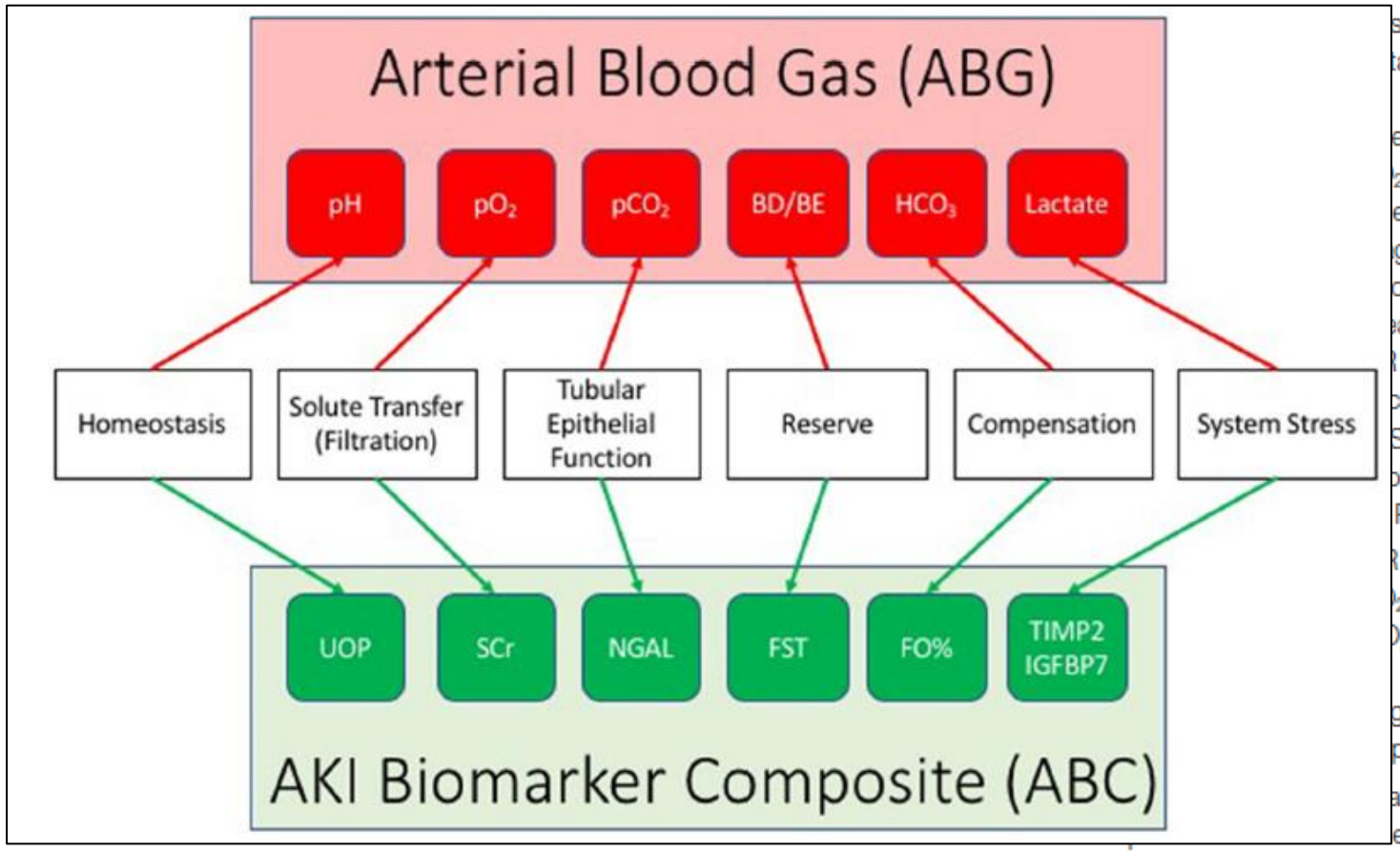
Predictors of severe AKI
Combination with NephroCheck
+ risk factors : age > 65 years, CKD and high Procalcitonin

Clinical model (AUC-ROC = 0.71)
Clinical model + TIMP-2*IGFBP7 + NGAL at 6 h (AUC-ROC = 0.74)

Jia et al. BMC Nephrology (2020) 21:540
Kidney Int Rep (2020) 5, 839–850

TABLE 1 | Comparison of common diagnostics used for ICU syndromes.

Syndrome	Prevalence in ICU patients	Effective management	Risk stratification	Diagnosis	Surveillance and therapeutic monitoring
Sepsis					sical Exam tate e deficit or excess 2 e Output gulation Profile ocardiogram eactive protein calcitonin S Oximetry okine profile POCUS
ARDS					 2 2
AKI					g Ultrasound piratory Secretions atinine e Output

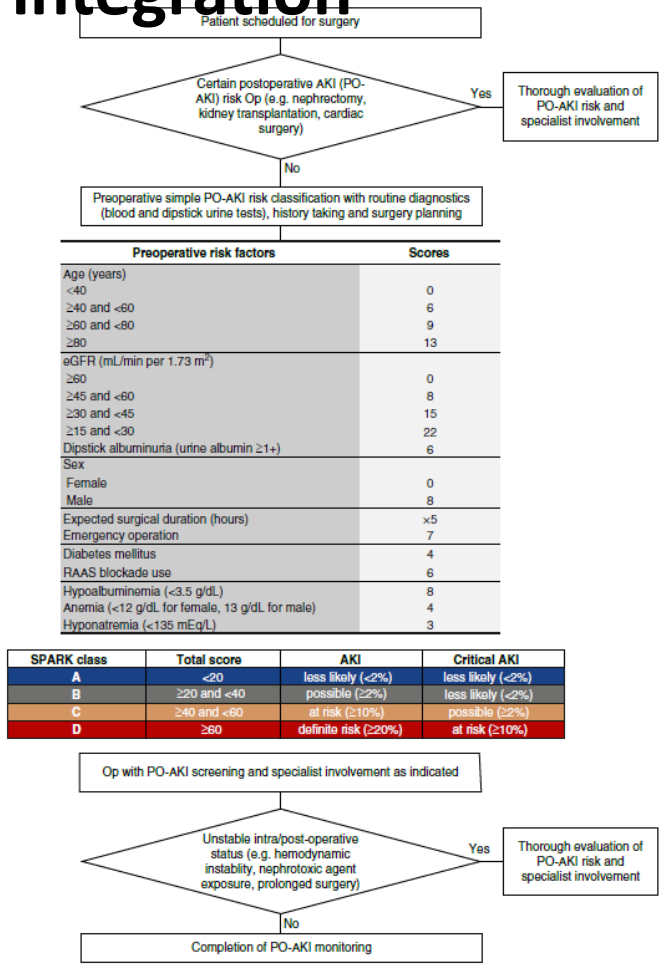


Common ICU injury syndromes with associated characteristics related to prevalence, management and detection. APACHE-III = Acute Physiology, Age, Chronic Health Evaluation. SOFA, Sequential Organ Failure Assessment; PRISM, Pediatric Risk of Mortality; PELOD, Pediatric Logistic Organ Dysfunction; PIM, Pediatric Index of Mortality; HR, heart rate; RR, respiratory rate; MAP, mean arterial pressure; WBC, white blood cell count; SvO_2, venous oxygen saturation; GS, gram stain; CSF, cerebrospinal fluid; Cx, culture; ESR, erythrocyte sedimentation rate; NIRS, near infrared spectroscopy; IVC POCUS, inferior vena cava point of care ultrasound; OI, oxygenation index; S/F, saturation of oxygen/fraction of inspired oxygen; P/F, partial pressure of oxygen/fraction of inspired oxygen; CXR, chest radiograph; CT, computed tomograph; SpO_2, oxygen saturation; pCO_2, partial pressure of carbon dioxide.

Front. Pediatr. 2020. 7:535

Future of the AKI biomarker (4)

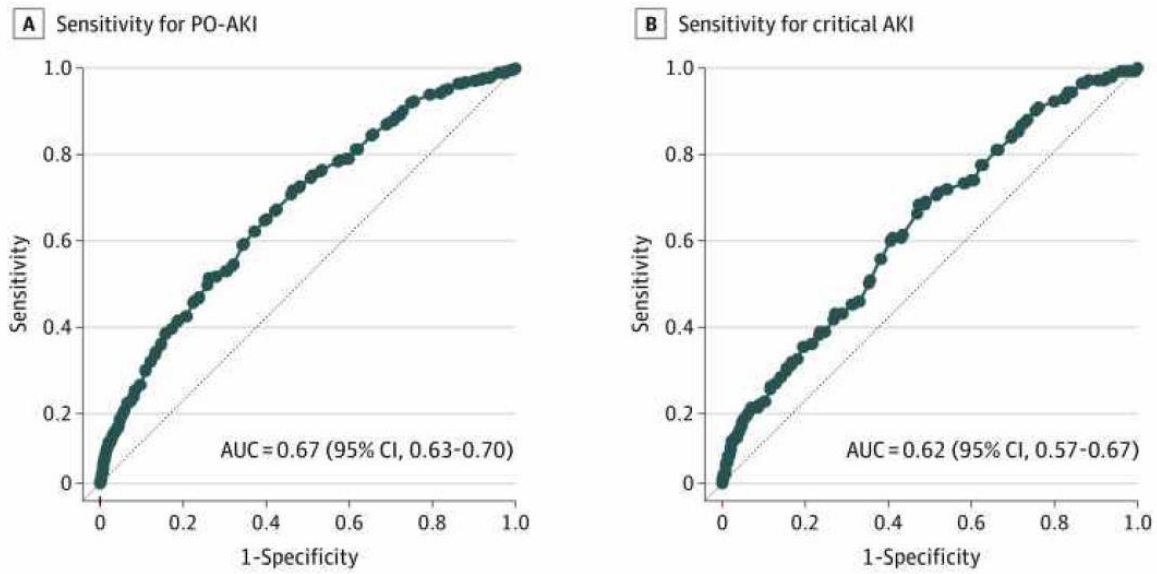
- **AI integration**



Preoperative risk factors	Scores
Age (years)	
<40	0
≥40 and <60	6
≥60 and <80	9
≥80	13
eGFR (mL/min per 1.73 m^2)	
≥60	0
≥45 and <60	8
≥30 and <45	15
≥15 and <30	22
Dipstick albuminuria (urine albumin ≥1+)	6
Sex	
Female	0
Male	8
Expected surgical duration (hours)	×5
Emergency operation	7
Diabetes mellitus	4
RAAS blockade use	6
Hypoalbuminemia (<3.5 g/dL)	8
Anemia (<12 g/dL for female, 13 g/dL for male)	4
Hyponatremia (<135 mEq/L)	3

SPARK class	Total score	AKI	Critical AKI
A	<20	less likely (<2%)	less likely (<2%)
B	≥20 and <40	possible (≥2%)	less likely (<2%)
C	≥40 and <60	at risk (≥10%)	possible (≥2%)
D	≥60	definite risk (≥20%)	at risk (≥10%)

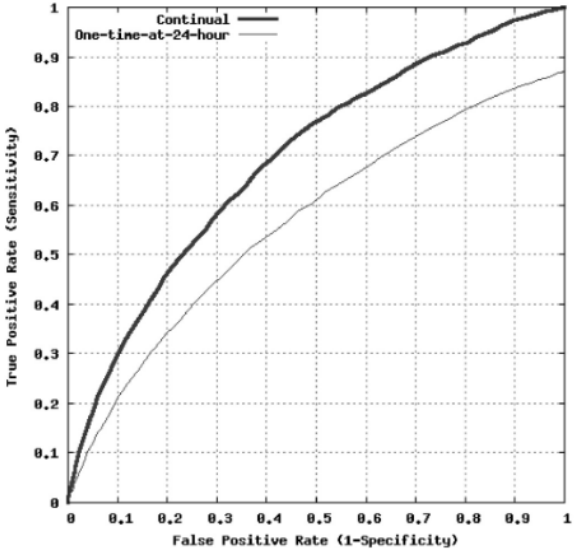
Figure 4. Perioperative PO-AKI risk evaluation strategy on the basis of the suggested SPARK classification. Op, operation; RAAS, renin-angiotensin-aldosterone system.



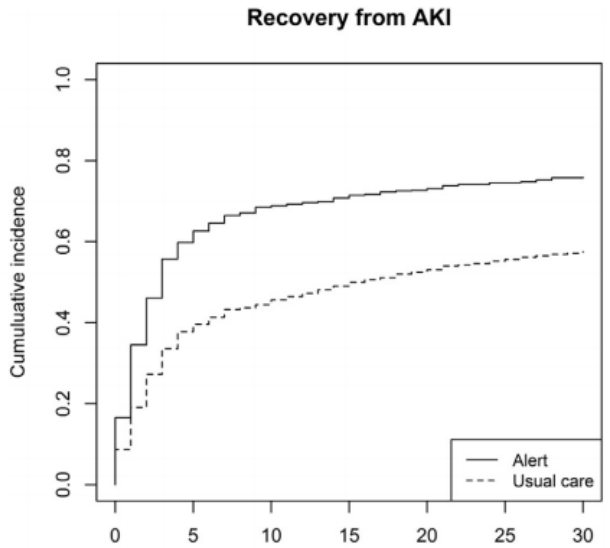
J Am Soc Nephrol 30: 170–181, 2019

JAMA Netw Open. 2021 Oct; 4(10):e2127362

Developing AKI scoring system or EMR-based alert system



Computeres in Biology and Medicine 116 (2020) 103580



AJKD Vol 71 | Iss 1 | January 2018

Real-Time Prediction of AKI in Hospitalized Adults: Implementation and Proof of Concept

Study Design

All Hospitalized Adults

Single Tertiary Care Hospital

Nov 2017 – Apr 2019

12 EHR Variables

AKI Prognostic Model

>15% Risk?

Pre-AKI Alert

Findings

All 2856 Patients with >15% Predicted Risk

Mean Predicted AKI %	Observed AKI %
19.1%	18.9% (540)

- Lower blood pressure with AKI
- Lower O_2 Sat with AKI
- No difference in nephrotoxins with AKI

100 of 2856 Patients Assessed with Biomarkers

- More hyaline casts with AKI
- Lower FE_{Urea} with AKI

CONCLUSION: A real-time Acute Kidney Injury risk model was successfully integrated into the Electronic Health Record.

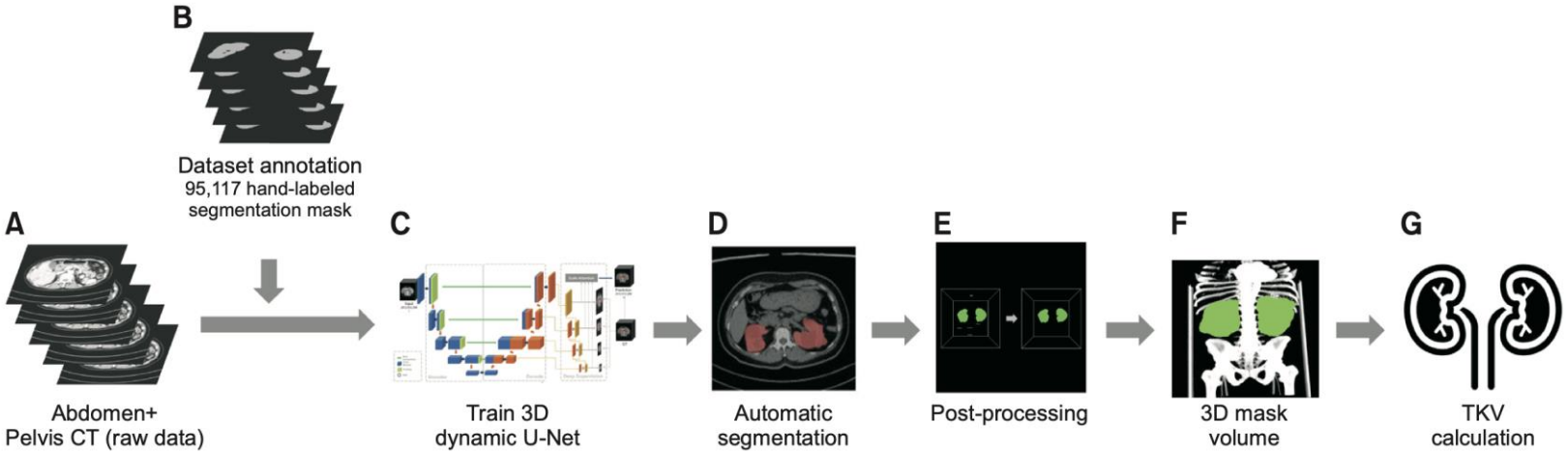
Ugochukwu Ugwuowo, Yu Yamamoto, Tanima Arora, et al (2020)

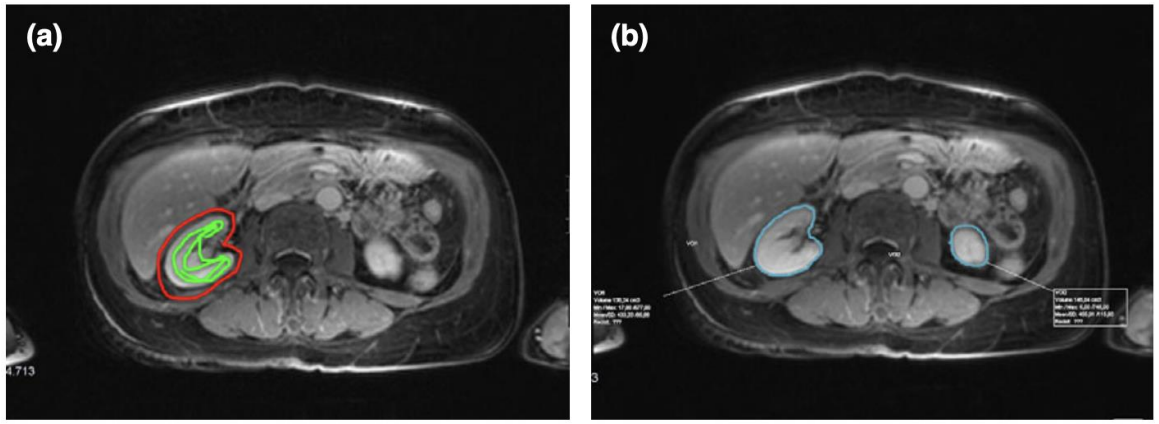
@AJKDonline | DOI: 10.1053/j.ajkd.2020.05.003

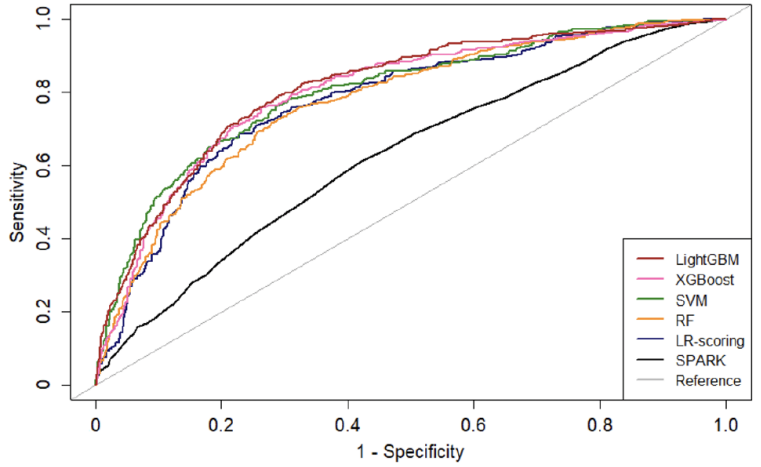
AJKD

AJKD VOLUME 76, ISSUE 6, P806-814.E1, DECEMBER 01, 2020

Future of the AKI biomarker (5)

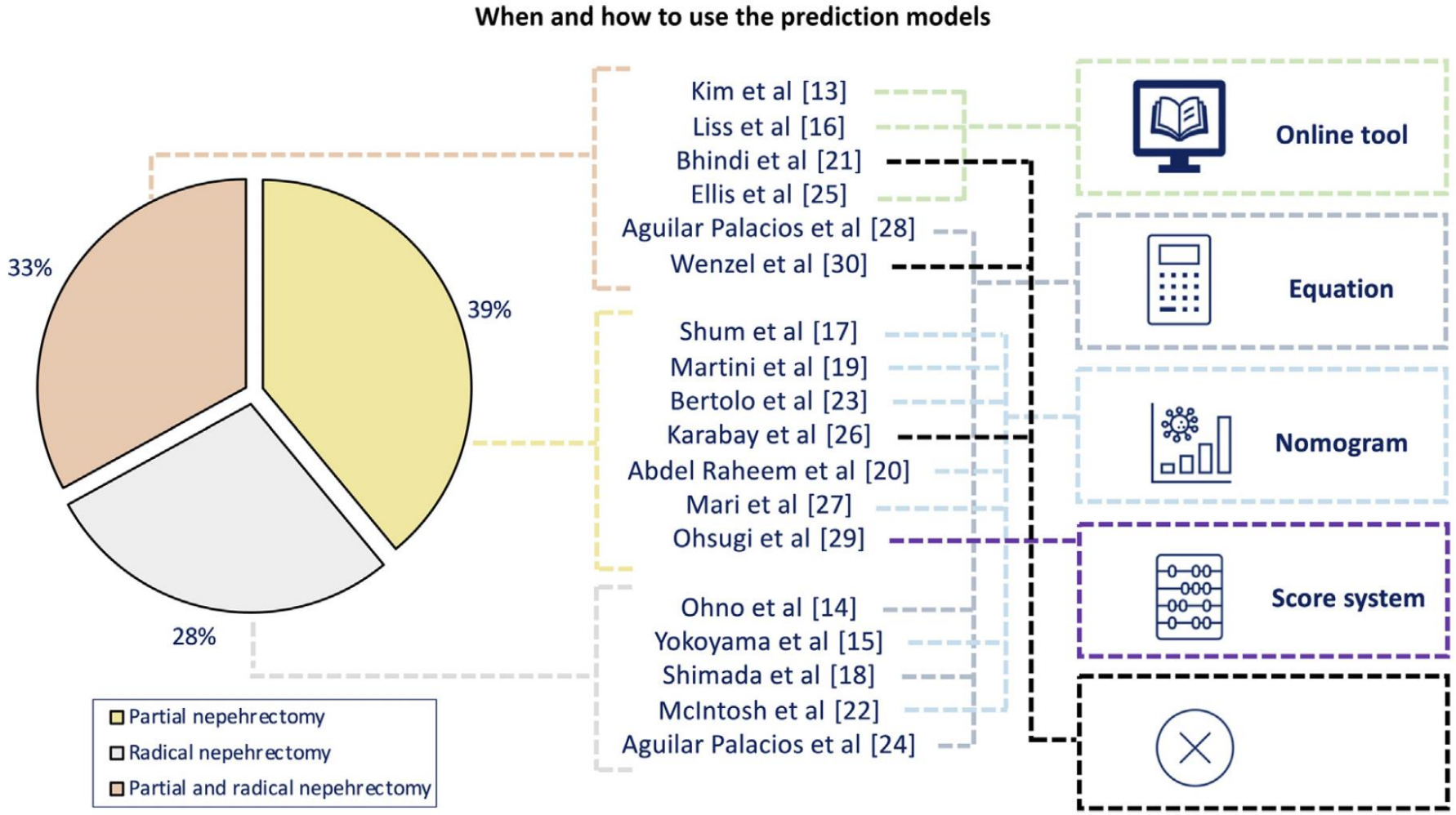






Scientific reports (2021) 11:15704
Investig Clin Urol 2023;64:255-264.
Transplantation international (2018);31:773-780

Future of the AKI biomarker (6)



European urology oncology 6 (2023) 137-147

Take home message

- We need AKI Biomarkers
- …. with diagnostic/prognostic value
- AKI Biomarkers have limitations
- Multiple sources of information must be integrated for the best management.