Monitoring of Renal Function in ICU

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1397/02/13

Advantages of Monitoring Kidney Function in the ICU:

- ✓ Early intervention
- ✓ Evaluate the effectiveness of the therapeutic intervention
- ✓ Reduce need for RRT
- ✓ Reduce need of morbidity & mortality

Critical Care Nephrology
Claudio Ronco, Rinaldo Bellomo, John A. Kellum
ISBN: 978-1-4160-4252-5

TABLE 28-2 Incidence and Outcomes of AKI

	Community-Acquired AKI	Hospital-Acquired AKI	ICU-Acquired AKI
Incidence	Low (<1%)	Moderate (2–20%)	High (20–60%)
Cause	Usually single	Single or multiple	Multifactorial
Overall mortality rate	N/A	15–40%	30–90%
Common risk factors	Chronic comorbid conditions, elderly, male gender, sepsis, dehydration, infection, drugs (ACEIs, ARBs, diuretics)	Volume depletion, hypotension, sepsis, low cardiac output, nephrotoxic drugs, radiocontrast dyes	Septic shock, major surgery, multiorgan failure, hypotension, low cardiac output, nephrotoxic drugs

ACEIs, angiotensin-converting enzyme inhibitors; AKI, acute kidney injury; ARBs, angiotensin receptor blockers; ICU, intensive care unit; N/A, not available.

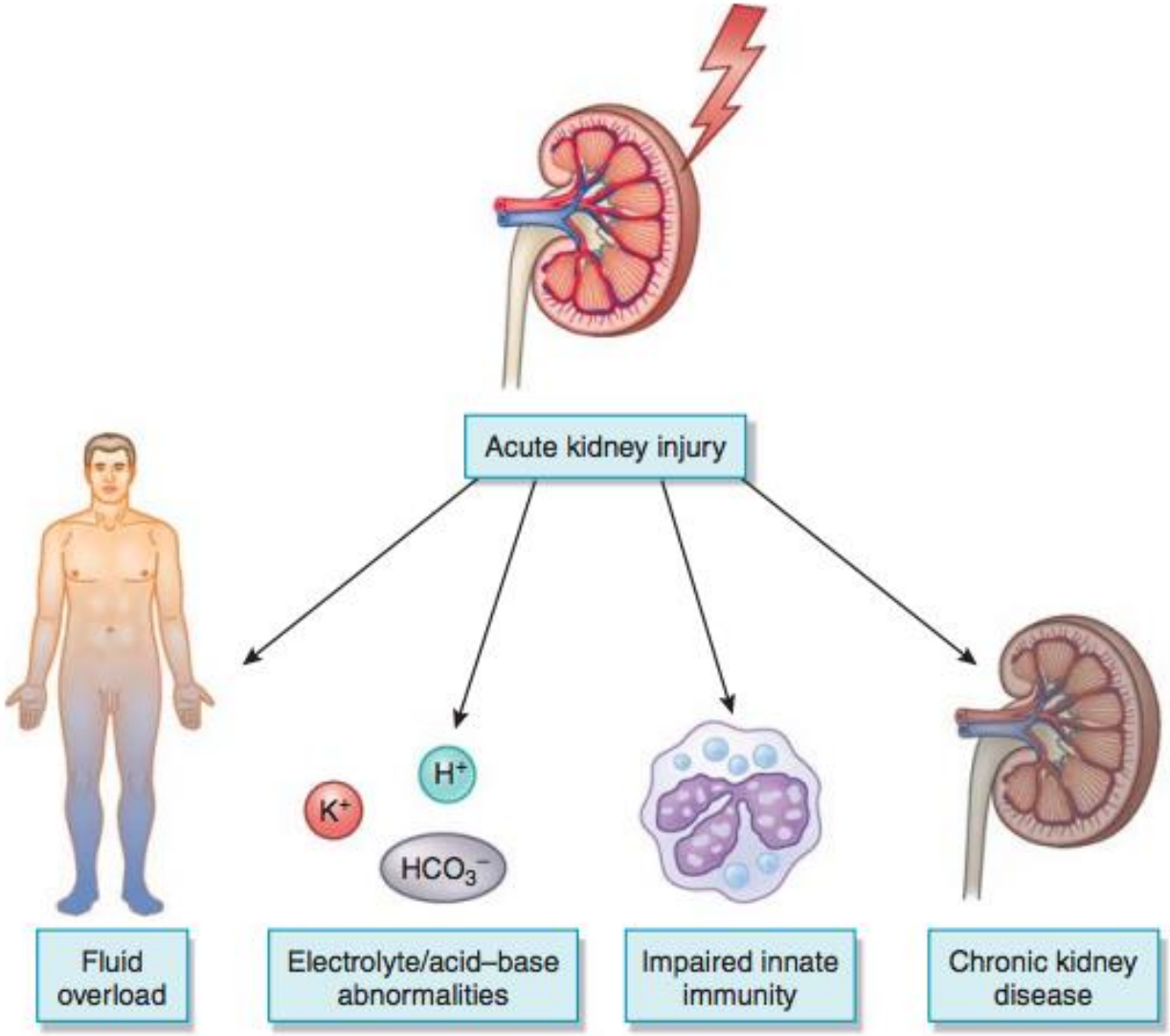

Figure 2 | Acute kidney injury (AKI) can have both immediately recognizable consequences as well as less noticeable or delayed consequences. Fluid overload and electrolyte/acid–base abnormalities represent well known, easily recognized consequences of AKI. Contrary, impaired innate immunity and chronic kidney disease do not manifest themselves immediately.

AKI in the ICU: definition, epidemiology, risk stratification, and outcomes
Kidney International (2012) 81,819-825

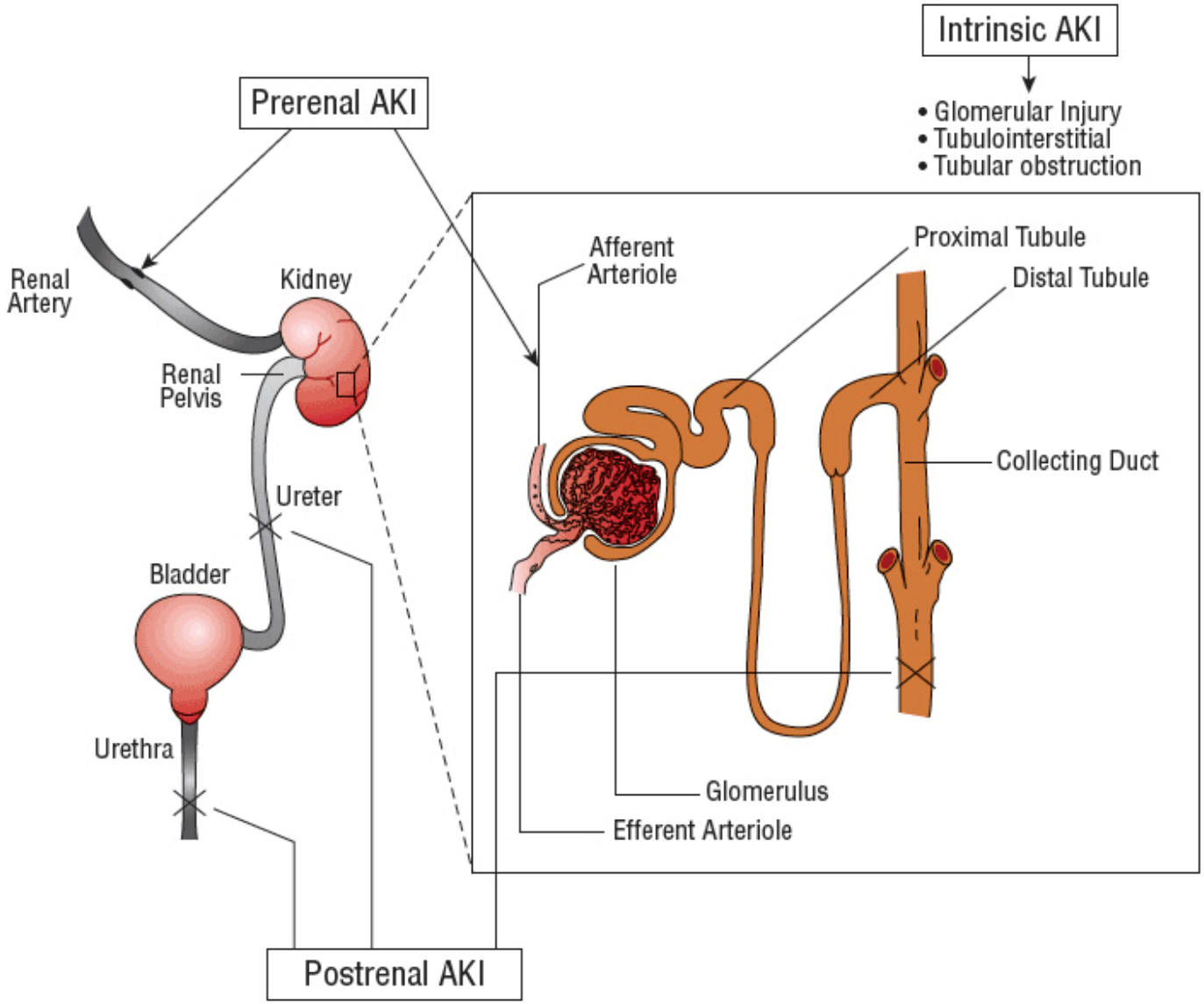

FIGURE 28-2 Physiologic classification of AKI. Blood flows through the afferent arteriole, to the glomerulus, and exits through the efferent arteriole. A decrease in blood flow and renal perfusion can lead to a prerenal reduction in renal function. Under conditions in which renal blood flow is diminished, the kidney maintains glomerular ultrafiltration by vasodilating the afferent arterioles and vasoconstricting the efferent arterioles. Medications that may interfere with these

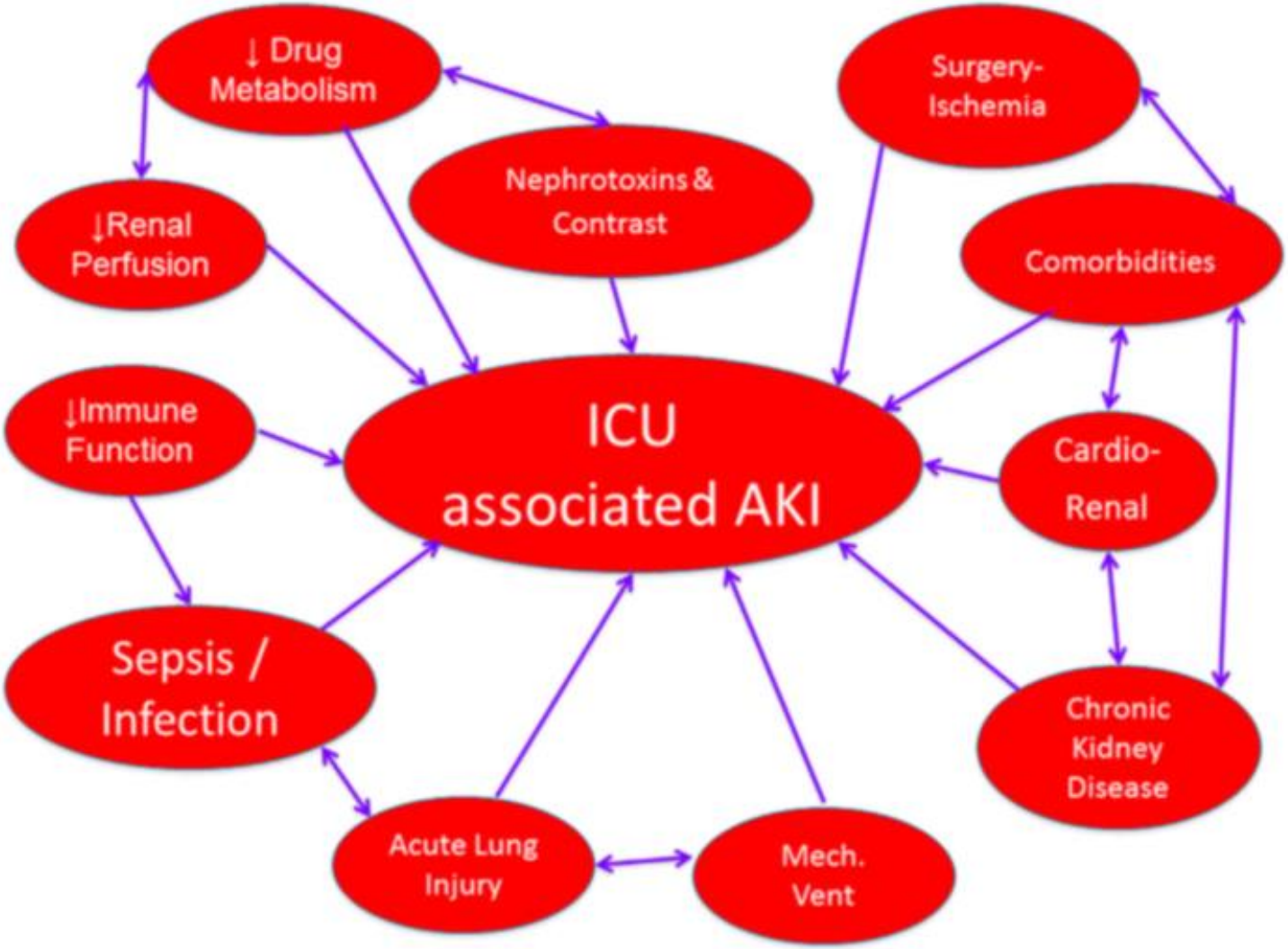

Figure 1. Tangled relationship between AKI, sepsis, and numerous intertwined risk factors and comorbidities. Mech, mechanical.

Entanglement of Sepsis, Chronic Kidney Disease, and Other Comorbidities in Patients Who Develop Acute Kidney Injury
Seminars in Nephrology, Vol 35, No 1, Jan 2015, pp 23-37

The best global index for the monitoring of renal function is GFR

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Serum Cr is widely used as a marker of kidney function, but it has well known limitation.

- Dietary intake
- Muscle mass
- No linear correlation between serum Cr & GFR (Serum Cr is normal in subclinical AKI(
- Due to tubular secretion Cr clearance overestimate GFR

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Serum cystatin C

It doesn't depend on:

- Muscle mass
- BMI
- Hydration status
- Gender
- No circadian rhythm, so no need for a 24 hour urine collection .

serum cystatin C levels were able to predict the development of ARF 1 or 2 days earlier than serum Cr

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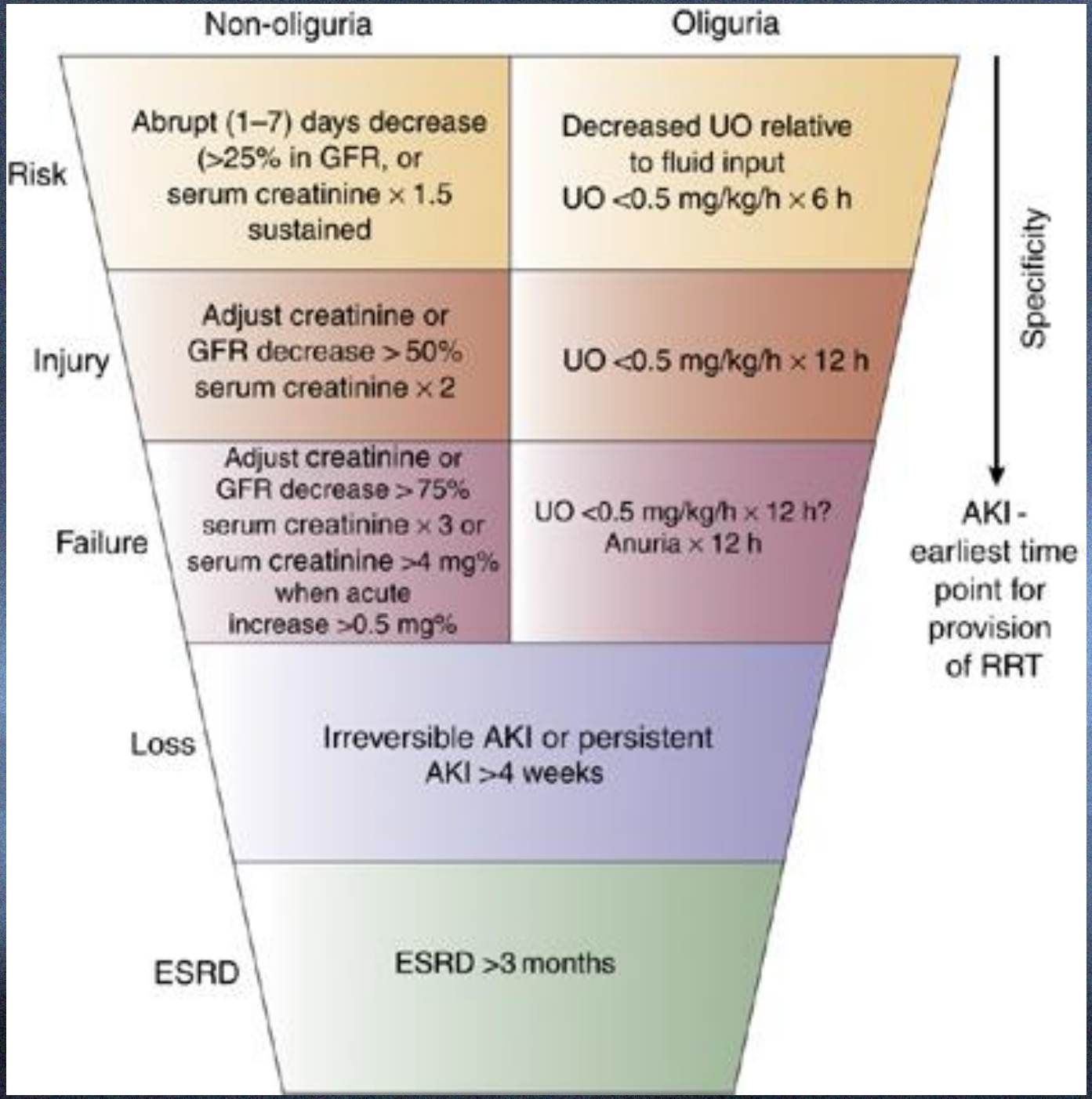
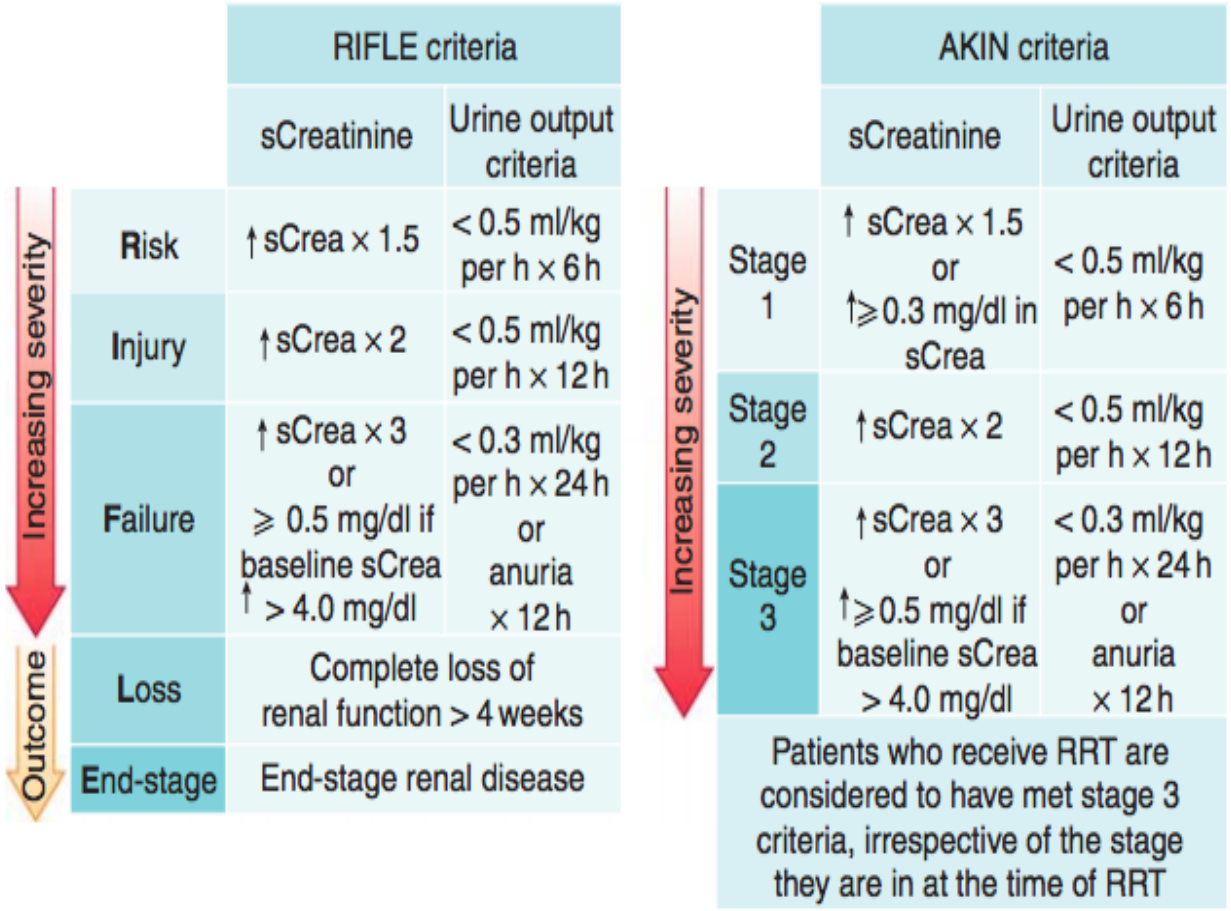

Non-oliguria
Oliguria
Risk
Abrupt (1–7) days decrease (>25% in GFR, or serum creatinine × 1.5 sustained
Decreased UO relative to fluid input UO <0.5 mg/kg/h × 6 h
Injury
Adjust creatinine or GFR decrease > 50% serum creatinine × 2
UO <0.5 mg/kg/h × 12 h
Failure
Adjust creatinine or GFR decrease > 75% serum creatinine × 3 or serum creatinine >4 mg% when acute increase >0.5 mg%
UO <0.5 mg/kg/h × 12 h? Anuria × 12 h
Loss
Irreversible AKI or persistent AKI >4 weeks
ESRD
ESRD >3 months
Specificity
AKI - earliest time point for provision of RRT



	RIFLE criteria	
	sCreatinine	Urine output criteria
Risk	↑ sCrea × 1.5	< 0.5 ml/kg per h × 6 h
Injury	↑ sCrea × 2	< 0.5 ml/kg per h × 12 h
Failure	↑ sCrea × 3 or ⩾ 0.5 mg/dl if baseline sCrea ↑ > 4.0 mg/dl	< 0.3 ml/kg per h × 24 h or anuria × 12 h
Loss	Complete loss of renal function > 4 weeks	
End-stage	End-stage renal disease	

Increasing severity

Outcome

	AKIN criteria	
	sCreatinine	Urine output criteria
Stage 1	↑ sCrea × 1.5 or ↑⩾0.3 mg/dl in sCrea	< 0.5 ml/kg per h × 6 h
Stage 2	↑ sCrea × 2	< 0.5 ml/kg per h × 12 h
Stage 3	↑ sCrea × 3 or ↑⩾0.5 mg/dl if baseline sCrea > 4.0 mg/dl	< 0.3 ml/kg per h × 24 h or anuria × 12 h
Patients who receive RRT are considered to have met stage 3 criteria, irrespective of the stage they are in at the time of RRT		

Increasing severity

Figure 1 | Direct comparison of RIFLE (Risk of renal dysfunction, Injury to the kidney, Failure or Loss of kidney function, and End-stage kidney disease) and Acute Kidney Injury (AKI) Network criteria to classify AKI according to Bellomo *et al.*[7] and Mehta *et al.*,[8] respectively. Note that the original RIFLE criteria also listed glomerular filtration rates as reference, but these do not precisely agree with the changes in serum creatinine and were subsequently removed. For AKI Network criteria, the change in serum creatinine from baseline follows RIFLE, but there is also the option to use a 0.3 mg/dl increase if it is observed to occur within a 48-h period. RRT, renal replacement therapy.

AKI in the ICU: definition, epidemiology, risk stratification, and outcomes
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TABLE 28-3 Diagnostic Parameters for Differentiating Causes of AKIa

Laboratory Test	Prerenal AKI	Intrinsic AKI	Postrenal AKI
Urine sediment	Hyaline casts, may be normal	Granular casts, cellular debris	Cellular debris
Urinary RBC	None	2–4+	Variable
Urinary WBC	None	2–4+	1+
Urine Na (mEq/L or mmol/L)	<20	>40	>40
FE_{Na} (%)	<1	>2	Variable
Urine/serum osmolality	>1.5	<1.3	<1.5
Urine/S_{cr}	>40:1	<20:1	<20:1
BUN/S_{cr} (urea/S_{cr}, SI)	>20 (>80)	~15 (~60)	~15 (~60)
Urine specific gravity	>1.018	<1.012	Variable

AKI, acute kidney injury; BUN, blood urea nitrogen; FE_{Na}, fractional excretion of sodium; S_{cr}, serum creatinine; RBC, red blood cell; WBC, white blood cell.

[a]Common laboratory tests are used to classify the cause of AKI. Functional AKI, which is not included in this table, would have laboratory values similar to those seen in prerenal AKI. However, the urine osmolality-to-plasma osmolality ratios may not exceed 1.5, depending on the circulating levels of antidiuretic hormone.

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ISBN: 978-1-4160-4252-5

TABLE 28-4 Urinary Findings as a Guide to the Etiology of AKI

Type of Urinary Evaluation	Presence of	Suggestive of
Urinalysis	Leukocyte esterases	Pyelonephritis
	Nitrites	Pyelonephritis
	Protein	
	Mild (<0.5 g/day)	Tubular damage
	Moderate (0.5–3 g/day)	Glomerulonephritis, pyelonephritis, tubular damage
	Large (>3 g/day)	Glomerulonephritis, nephrotic syndrome
	Hemoglobin	Glomerulonephritis, pyelonephritis, renal infarction, renal tumors, kidney stones
	Myoglobin	Rhabdomyolysis-associated tubular necrosis
	Urobilinogen	Hemolysis-associated tubular necrosis
Urine sediment	Microorganisms	Pyelonephritis
Cells	Red blood cells	Glomerulonephritis, pyelonephritis, renal infarction, papillary necrosis, renal tumors, kidney stones
	White blood cells	Pyelonephritis, interstitial nephritis
	Eosinophils	Drug-induced interstitial nephritis, renal transplant rejection
	Epithelial cells	Tubular necrosis

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Casts	Granular casts	Tubular necrosis
	Hyaline casts	Prerenal azotemia
	White blood cell casts	Pyelonephritis, interstitial nephritis
	Red blood cell casts	Glomerulonephritis, renal infarct, lupus nephritis, vasculitis
Crystals	Urate	Postrenal obstruction
	Calcium phosphate	Postrenal obstruction

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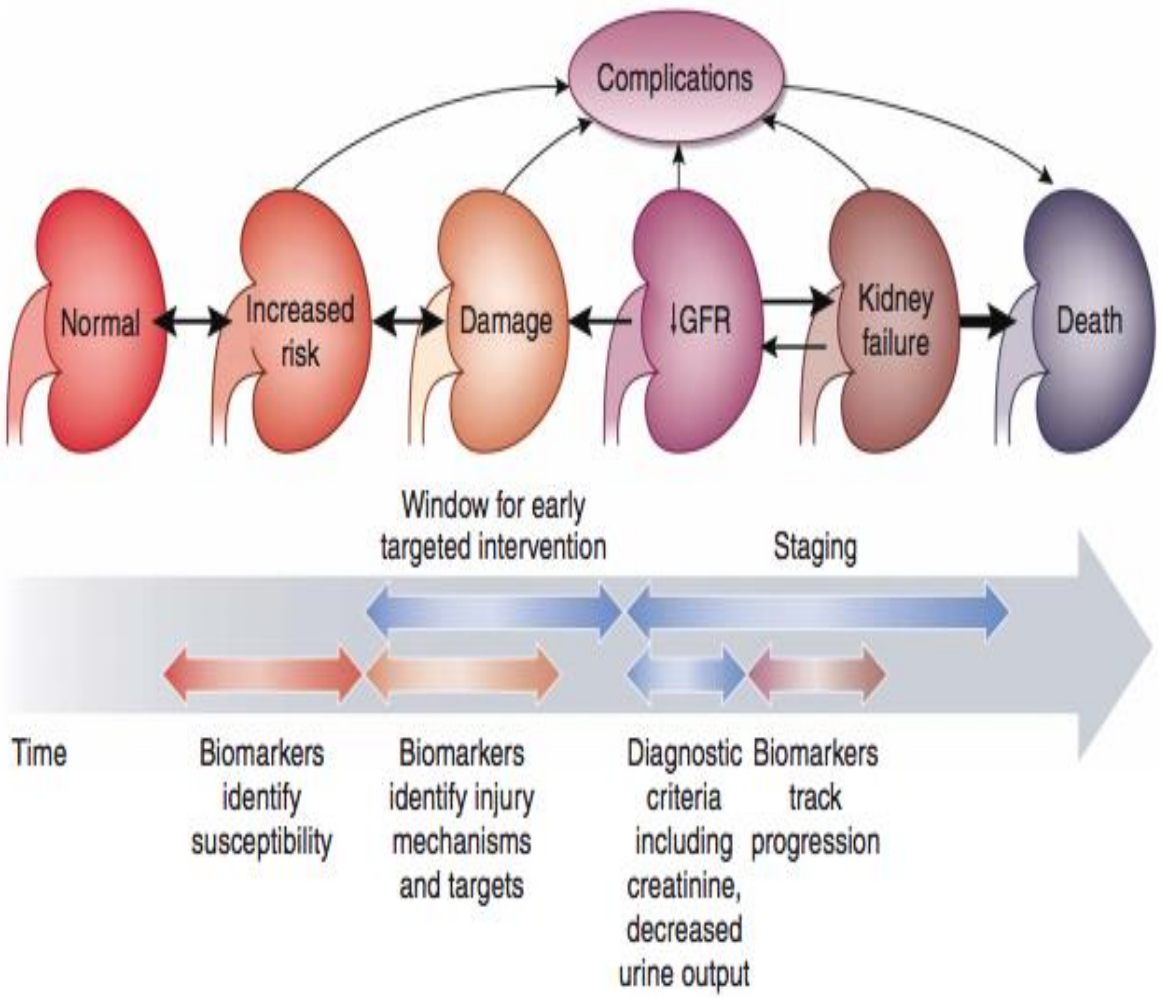
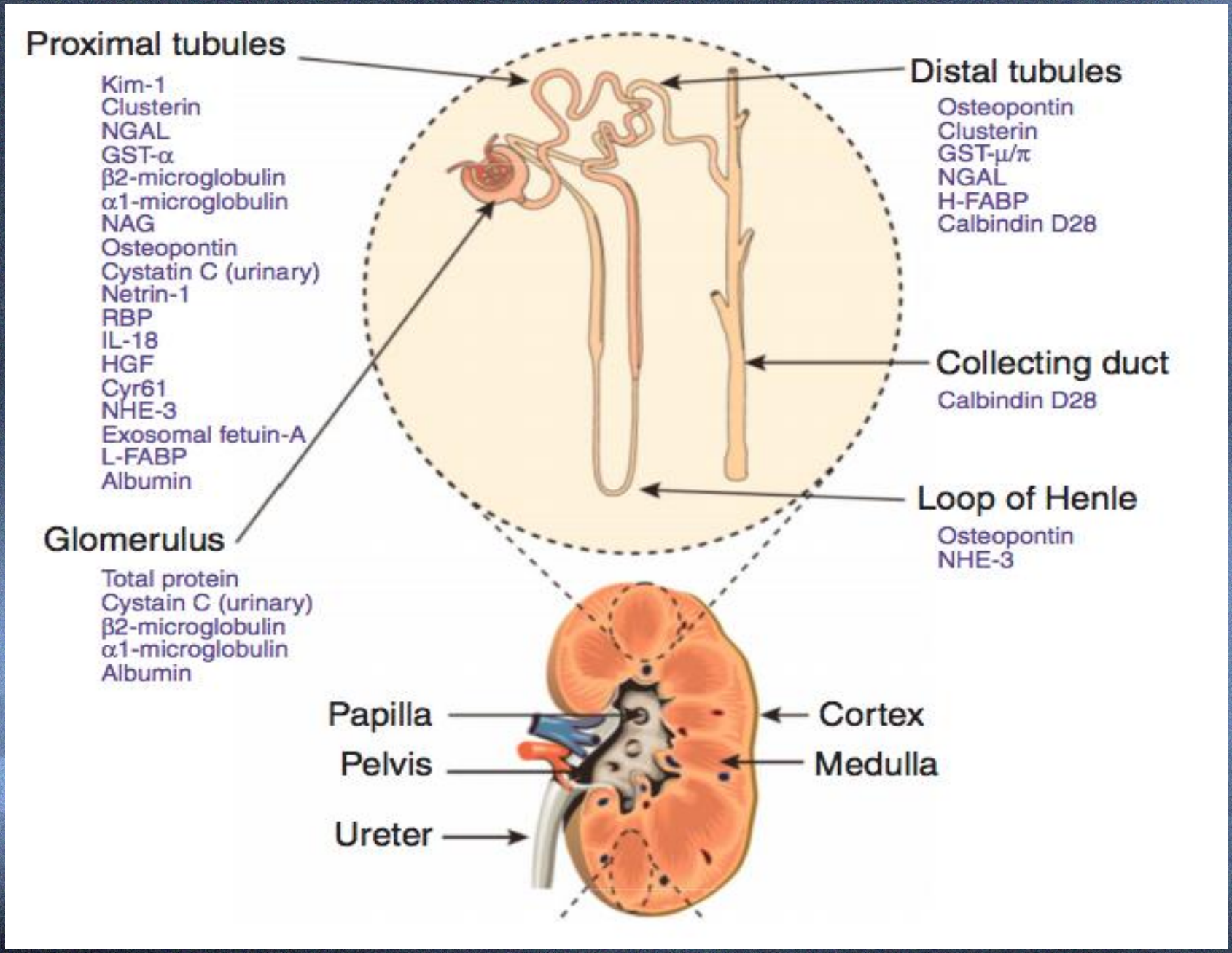


Figure 3 | Potential utilization of biomarkers for acute kidney injury (AKI) I. Several biomarkers are now available for assessing changes in kidney function and detecting kidney damage. They can be utilized for initial diagnosis and staging, differential diagnosis, and prognosis; reprinted with permission from Mehta[16]). GFR, glomerular filtration rate.

Potential use of biomarkers in acute kidney injury: report and summary of recommendations from the 10th Acute Dialysis Quality Initiative consensus conference
Kidney International (2014) 85, 513-521



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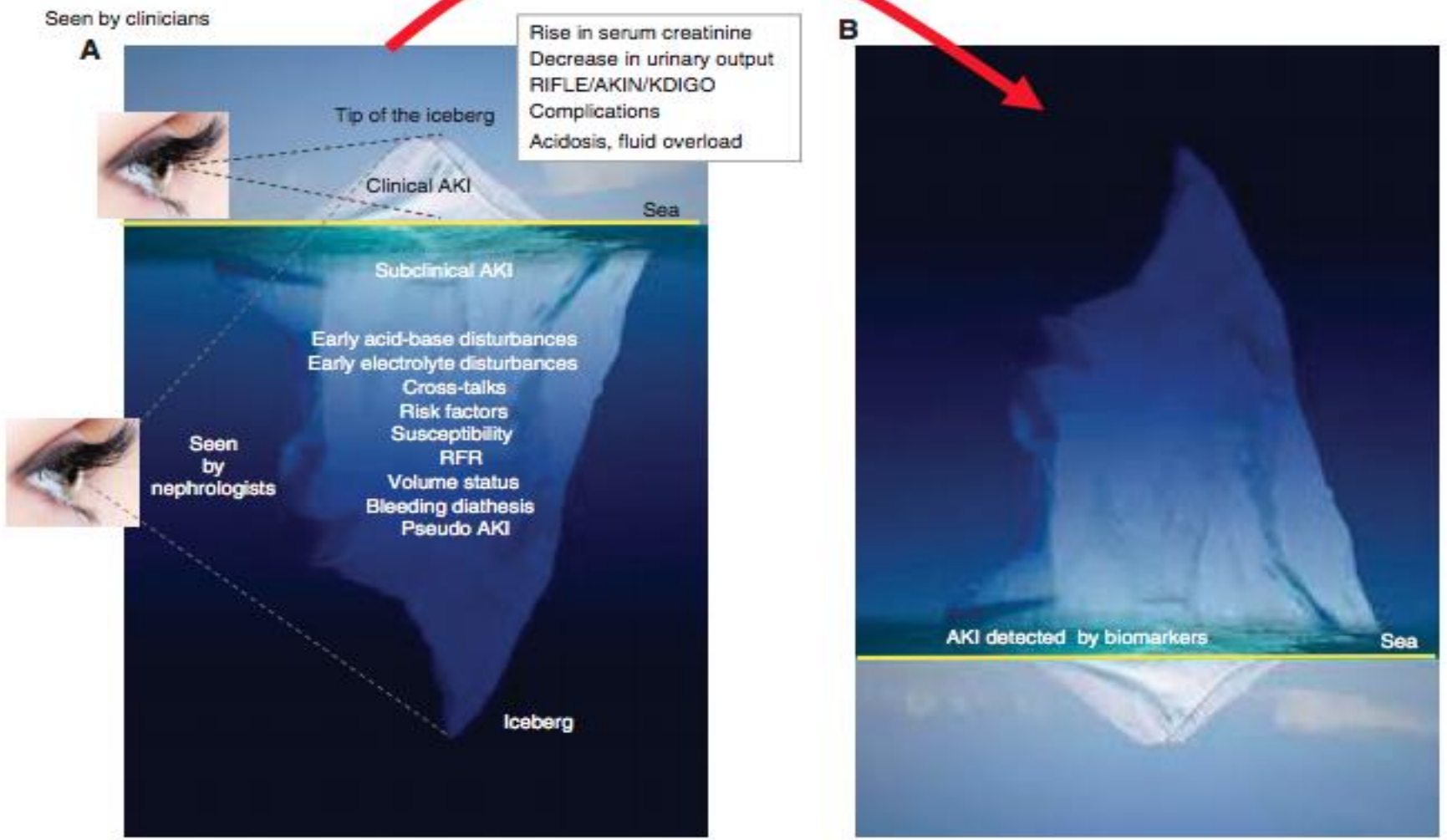

Figure 1: The iceberg of AKI.
Hidden conditions under the cover of the tip of the iceberg when traditional criteria are adopted (A). Improvement in AKI diagnosis by using biomarkers (B). From Reference 2, modified.

Biomarkers of acute kidney injury: a step forward

Clin Chem Lab Med 2017; 55(8): 1071–1073

TABLE 28-5 Advantages and Disadvantages of Novel Clinical Biomarkers of AKI

Biomarker	Source	Description	Advantages	Disadvantages
Cystatin C	Plasma Urine	Endogenous cysteine proteinase filtered by the glomeruli and catabolized by proximal tubules	Well studied as a marker of stable GFR Commercial assay available	Levels altered in the presence of systemic inflammation, thyroid disease, patient demographics Nonspecific marker of GFR Delayed increase in concentrations postinsult (8–12 hours) compared with other biomarkers
IL-18	Urine	Proinflammatory cytokine expressed by proximal tubules after renal injury	Marker of ischemic AKI	Inconsistent performance across different patient populations Unknown impact of systemic inflammation on urinary levels
KIM-1	Urine	Glycoprotein expressed by proximal tubules after renal injury	Commercial urine test available Early marker of ischemic AKI	Not widely studied in different patient populations
NGAL	Plasma Urine	Epithelial protein filtered by the glomeruli and reabsorbed by the proximal tubules	Commercial test available Highly sensitive and specific in select populations	Decreased specificity in patients with CKD and other comorbidities

AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; IL-18, interleukin-18; KIM-1, kidney injury molecule-1; NGAL, neutrophil gelatinase–associated lipocalin.

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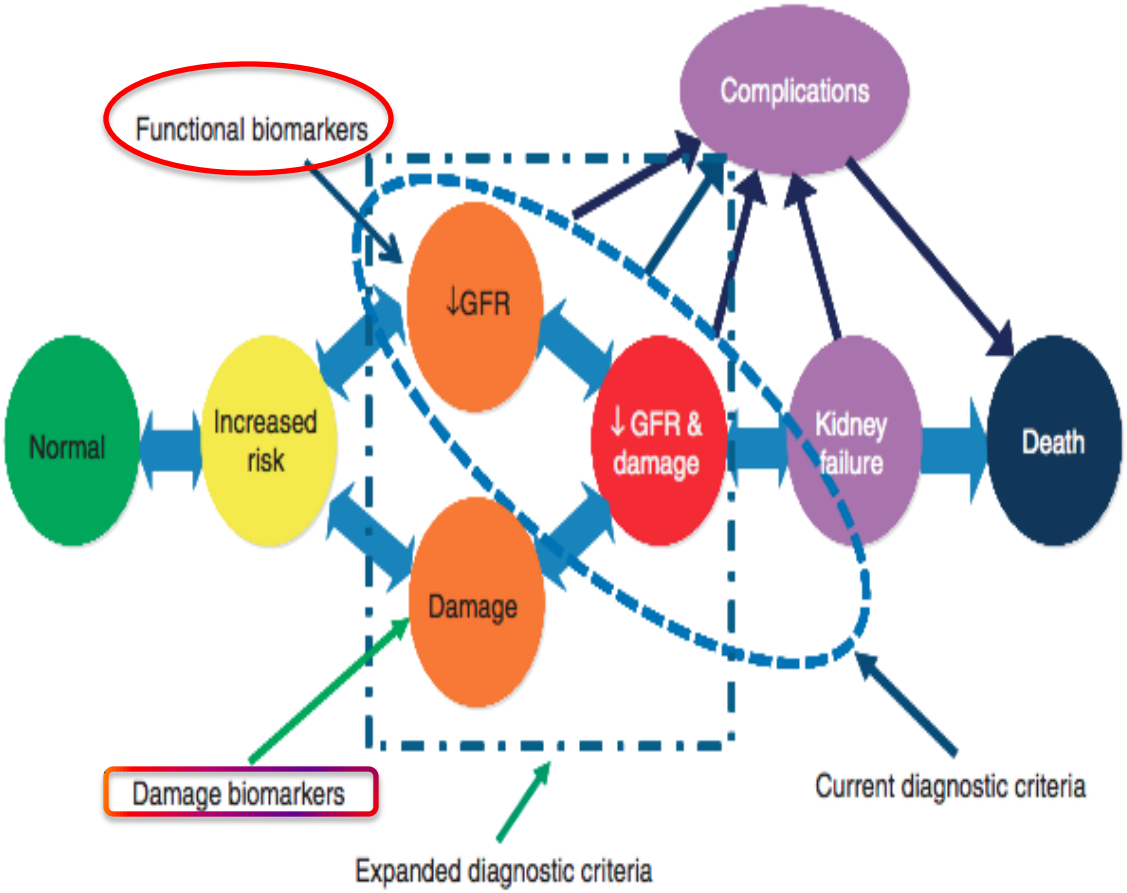

Figure 5 | Modified conceptual model of acute kidney injury. The availability of specific biomarkers permits recognition of kidney damage separately from changes in kidney function. Kidney damage and changes in function may precede each other or occur concurrently. The time sequence of events depends on the nature and duration of the insult and the underlying state of health of the kidney. Consequently, we propose a modified conceptual framework to include evidence of isolated kidney damage as a potential criterion for diagnosis of AKI. The timing of diagnosis will depend on the frequency with which specific biomarkers of kidney damage and function are assessed.

Functional Biomarkers: Cr & UOP

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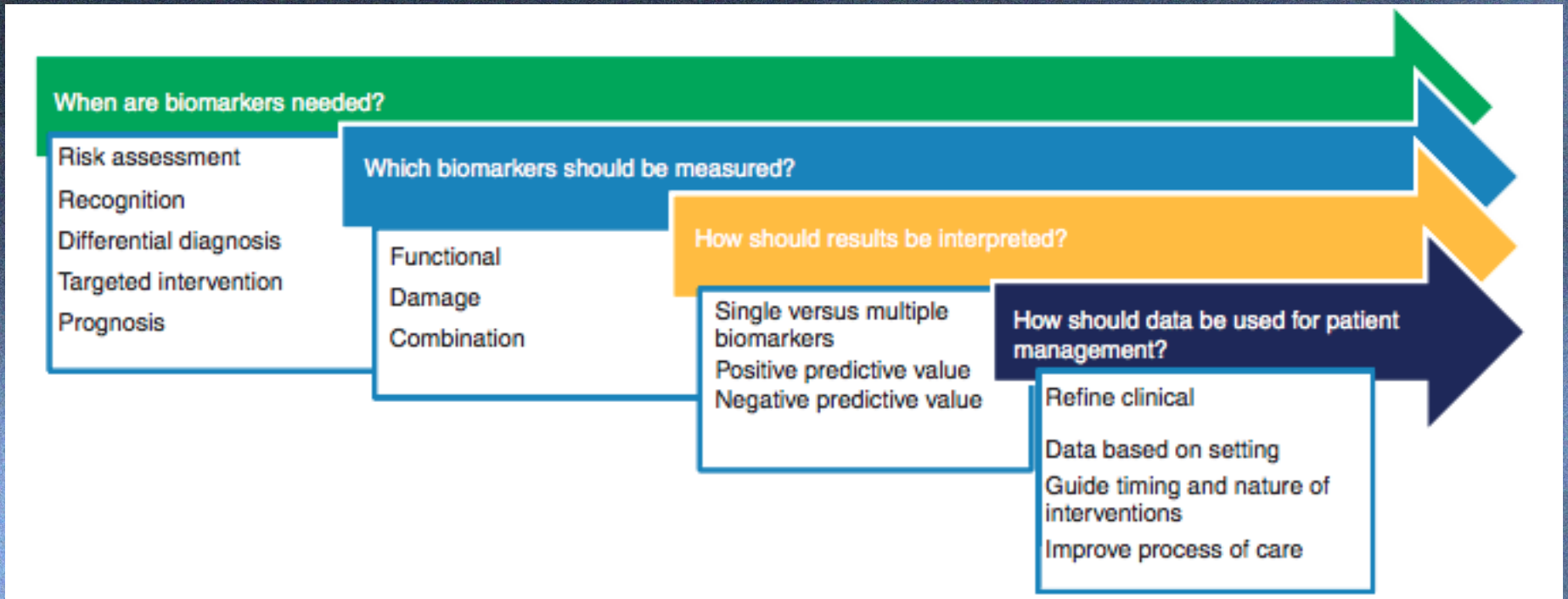

Figure 1 | Clinical need for biomarkers to improve management of acute kidney injury. Several components typically need to be considered for each decision that guides biomarker utilization. These key issues are pertinent for the efficient adoption of biomarkers in clinical practice.

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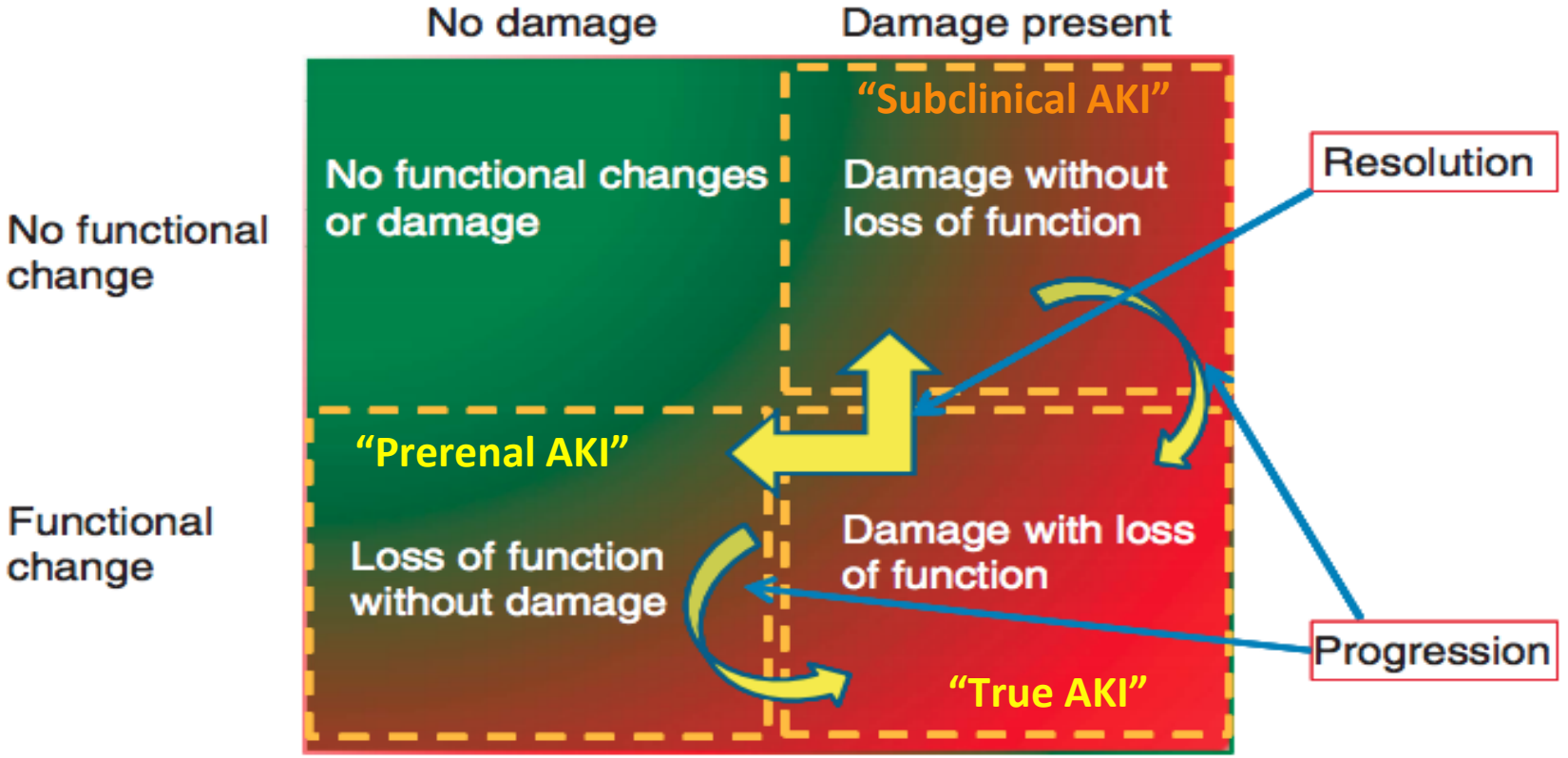

Figure 4 | Proposed framework for evaluating acute kidney injury (AKI) based on biomarkers. A combination of kidney functional and damage markers simultaneously provides a simple method to stratify patients with AKI. At initial presentation, patients would be evaluated in terms of these two domains, and then could be assessed over time to monitor their transitions across the domains. From http://www.ADQI.org, used with permission.

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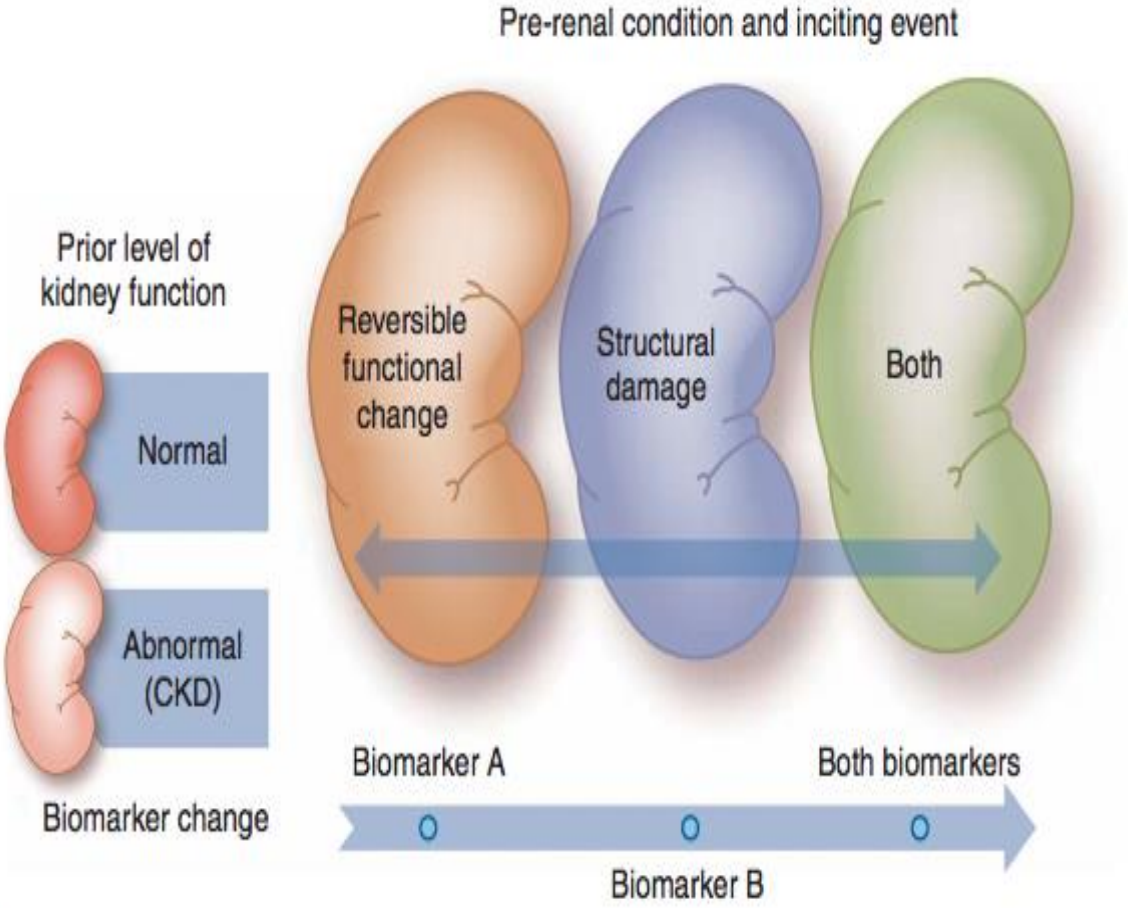

Figure 7 | Utilization of functional and damage markers concurrently to manage patients with acute kidney injury (AKI) and chronic kidney disease (CKD). The utilization of biomarkers to evaluate changes in kidney function in the presence of preexisting CKD offers unique challenges. A combination of function and damage markers can be used to evaluate patients as shown in Figure 4. However, the thresholds for biomarkers will likely be different based on the underlying preexisting level of renal function. This distinction will be important mechanistically to define outcomes and understand the pathophysiology; modified from Mehta[36].

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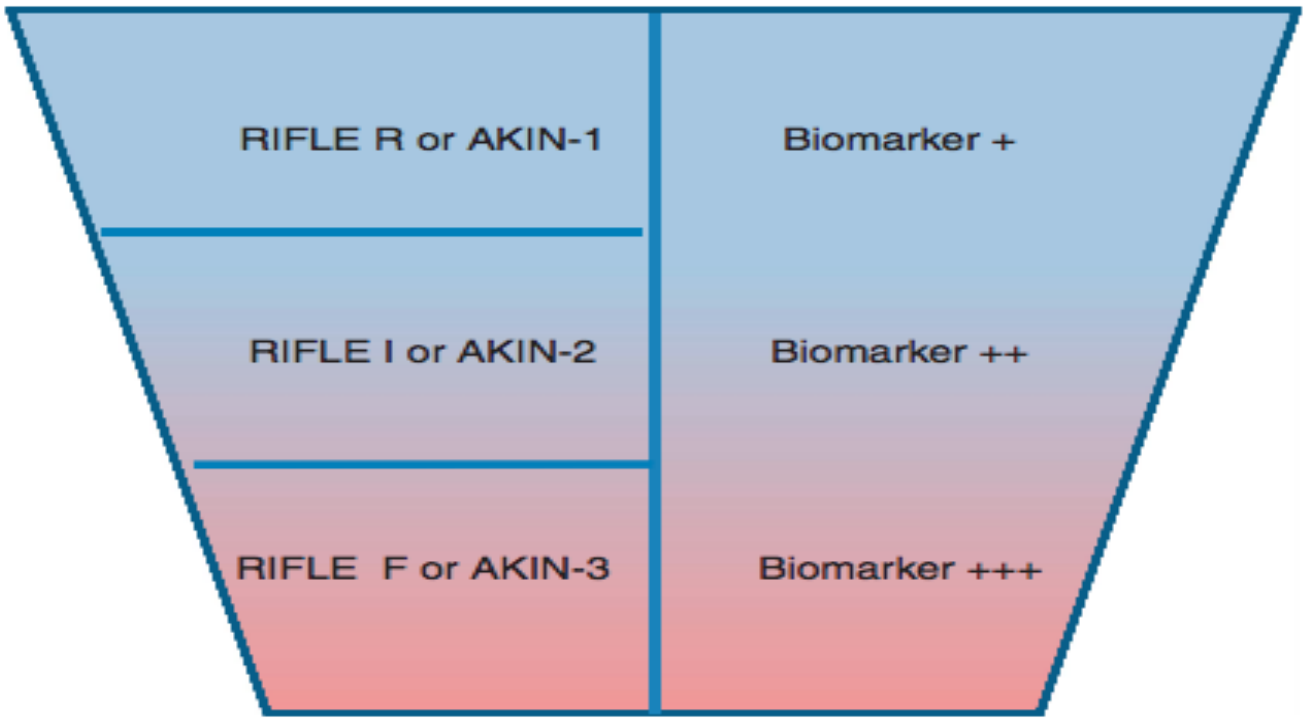

Figure 6 | Proposed new criteria for acute kidney disease (AKI) diagnosis and staging using biomarkers. New criteria for AKI diagnosis are displayed. In order to diagnose AKI, selecting the worst criterion (function (RIFLE/AKIN) or damage) is recommended. In the appropriate clinical setting, this new damage biomarker criterion will enhance the ability of RIFLE/AKIN to define AKI. There are currently insufficient injury biomarker data to support staging of AKI; however, AKI stages based on renal function changes are suggested to remain. The semiquantitative trend for increasing biomarker severity associated with increasing kidney damage is suggested by the literature and is displayed by the darkening background color and the symbols +/++/+++. *Adapted from RIFLE/AKIN criteria. AKIN, Acute Kidney Injury Network. From http://www.ADQI.org, used with permission.

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Box 3: Measures to Prevent Acute Renal Failure in Hospitalized Patients

- Prevent hypotension, and correct it rapidly when it does occur.
- Evaluate renal function before any surgery.
- Avoid prescribing nephrotoxic drugs.
- Correct volume deficits or electrolyte imbalances, especially before surgery.
- Replace traditional contrast agents with nonionic contrast, and use contrast sparingly.
- Treat infection quickly.
- Treat oliguria quickly.

TABLE 28-6 KDIGO Recommendations for Prevention and Treatment of AKI

Drug	Indication	Recommended for Prevention	Recommended for Treatment	Comments
ANP	AKI	No (2C)	No (2B)	
Diuretics	AKI	No (1B)	No (2C)	Acceptable if managing concurrent fluid overload
Dopamine (1–3 mcg/kg/min)	AKI	No (1A)	No (1A)	
Fenoldopam	AKI CI-AKI	No (2C) No (1B)	No (2C)	
Isotonic saline IV	AKI CI-AKI	Yes (2B) Yes (1A)	Yes (2B)	For AKI: recommended in the absence of hemorrhagic shock
NAC	AKI CI-AKI	No (2D) Yes (2D)		For CI-AKI: give in combination with isotonic saline
RRT	AKI CI-AKI	 No (2C)	Yes (NG)	
Sodium bicarbonate IV	CI-AKI	Yes (1A)		
Theophylline	CI-AKI	No (2C)		
Vasopressors	AKI	Yes (1C)	Yes (1C)	Recommended in combination with fluids in vasomotor shock

AKI, acute kidney injury; ANP, atrial natriuretic peptide; CI-AKI, contrast-induced acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes; NAC, *N*-acetylcysteine; RRT, renal replacement therapy.
Strength of recommendation levels: 1, recommended; 2, suggested; NG, not graded.
Quality of supporting evidence: A, high; B, moderate; C, low; D, very low.

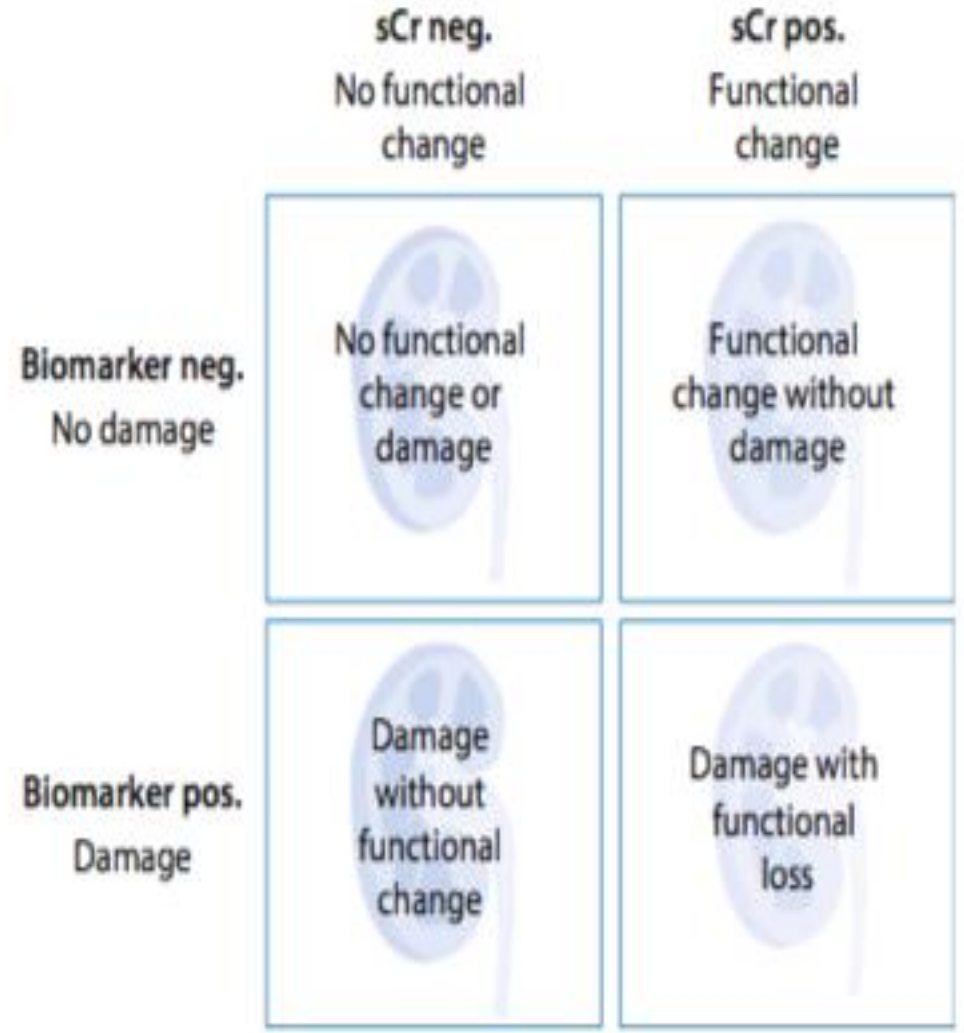


Fig. 2 Diagnosis of AKI using functional and damage biomarkers. To diagnose AKI earlier, functional and damage biomarkers facilitate the process. It is obvious that a patient's condition may change and that a change from one phase to another is possible. *pos.*: positive; *neg.*: negative; *sCr*: serum creatinine

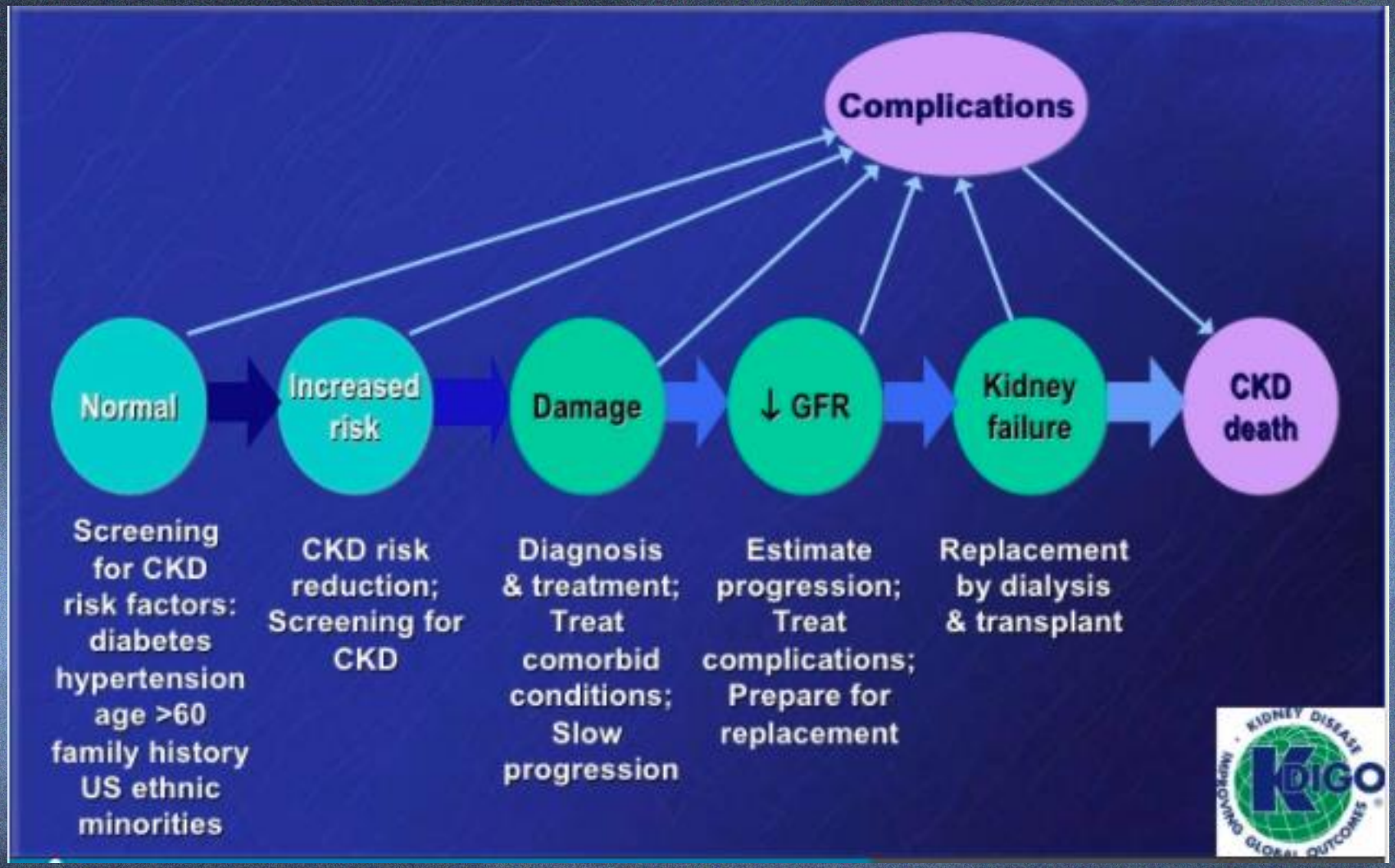
2017
Annual Update in Intensive Care and Emergency Medicine 2017
ISBN 978-3-319-51908-1

TABLE 28-1 RIFLE, AKIN, and KDIGO Classification Schemes for Acute Kidney Injury[a]

RIFLE Category	S_{cr} and GFR[b] Criteria	Urine Output Criteria
Risk	S_{cr} increase to 1.5-fold or GFR decrease >25% from baseline	<0.5 mL/kg/h for ≥6 hours
Injury	S_{cr} increase to twofold or GFR decrease >50% from baseline	<0.5 mL/kg/h for ≥12 hours
Failure	S_{cr} increase to threefold or GFR decrease >75% from baseline, or S_{cr} ≥4 mg/dL (≥354 µmol/L) with an acute increase of at least 0.5 mg/dL (44 µmol/L)	Anuria for ≥12 hours
Loss	Complete loss of function (RRT) for >4 weeks	
ESKD	RRT >3 months	
AKIN Criteria	**S_{cr} Criteria**	**Urine Output Criteria**
Stage 1	S_{cr} increase ≥0.3 mg/dL (≥27 µmol/L) or 1.5- to 2-fold from baseline	<0.5 mL/kg/h for ≥6 hours
Stage 2	S_{cr} increase >2- to 3-fold from baseline	<0.5 mL/kg/h for ≥12 hours
Stage 3	S_{cr} increase >3-fold from baseline, or S_{cr} ≥4 mg/dL (≥354 µmol/L) with an acute increase of at least 0.5 mg/dL (≥44 µmol/L), or need for RRT	<0.3 mL/kg/h for ≥24 hours or anuria for ≥12 hours
KDIGO Criteria	**S_{cr} Criteria**	**Urine Output Criteria**
Stage 1	S_{cr} increase ≥0.3 mg/dL (≥27 µmol/L) or 1.5–1.9 times from baseline	<0.5 mL/kg/h for 6–12 hours
Stage 2	S_{cr} increase 2–2.9 times from baseline	<0.5 mL/kg/h for ≥12 hours
Stage 3	S_{cr} increase three times from baseline, or S_{cr} ≥4 mg/dL (≥354 µmol/L), or need for RRT, or eGFR[c] <35 mL/min/1.73 m^2 (<0.34 mL/s/m^2) in patients <18 years	Anuria for ≥12 hours

AKIN, Acute Kidney Injury Network; ESKD, end-stage kidney disease; eGFR, estimated glomerular filtration rate; h, hours; KDIGO, Kidney Disease: Improving Global Outcomes; RIFLE, Risk, Injury, Failure, Loss of Kidney Function, and End-Stage Kidney Disease; RRT, renal replacement therapy; S_{cr}, serum creatinine.

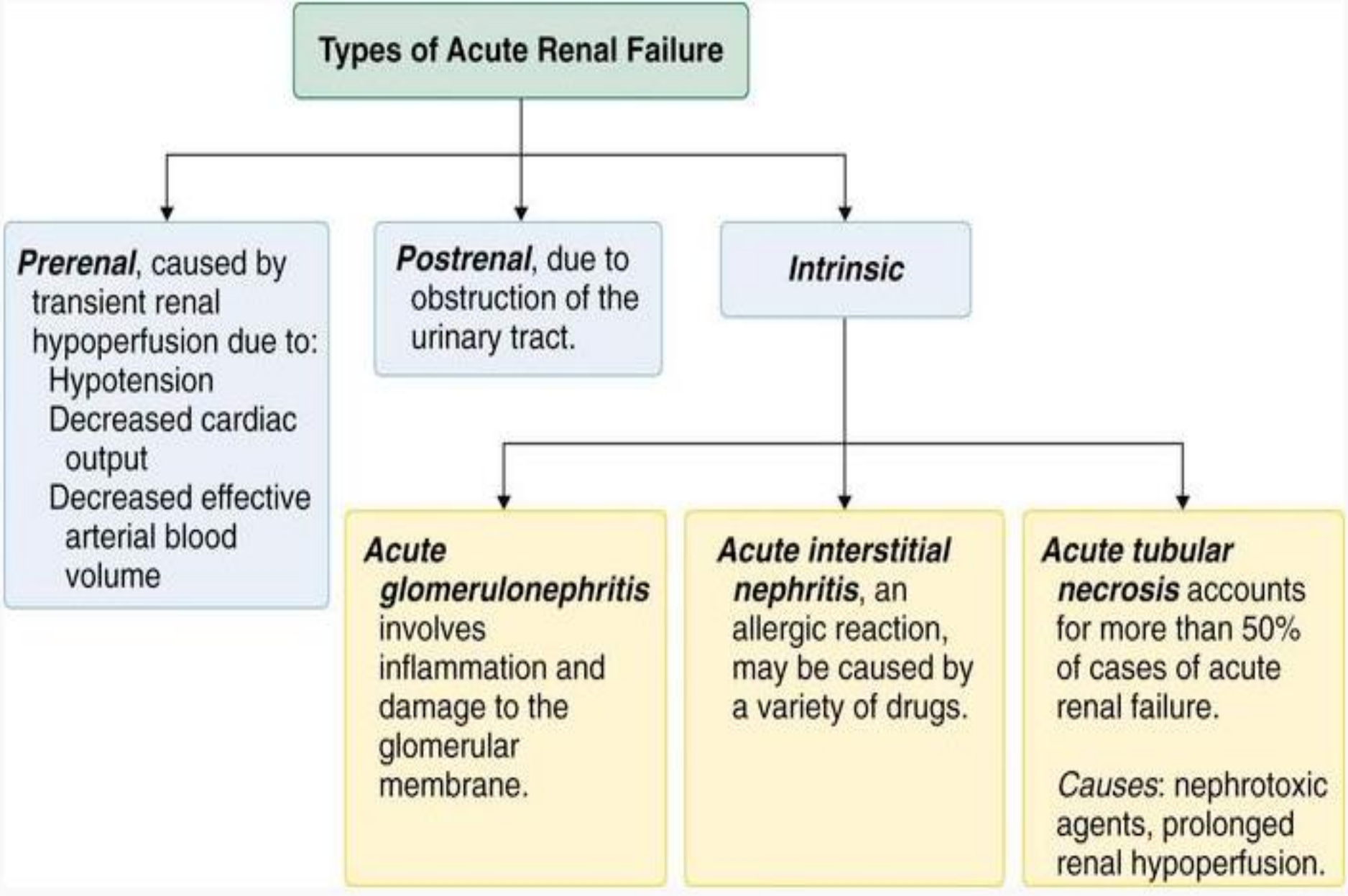
[a]For all staging systems, the criterion that leads to worst possible diagnosis should be used.
[b]GFR calculated using the Modification of Diet in Renal Disease (MDRD) equation.
[c]GFR calculated using the Schwartz formula.

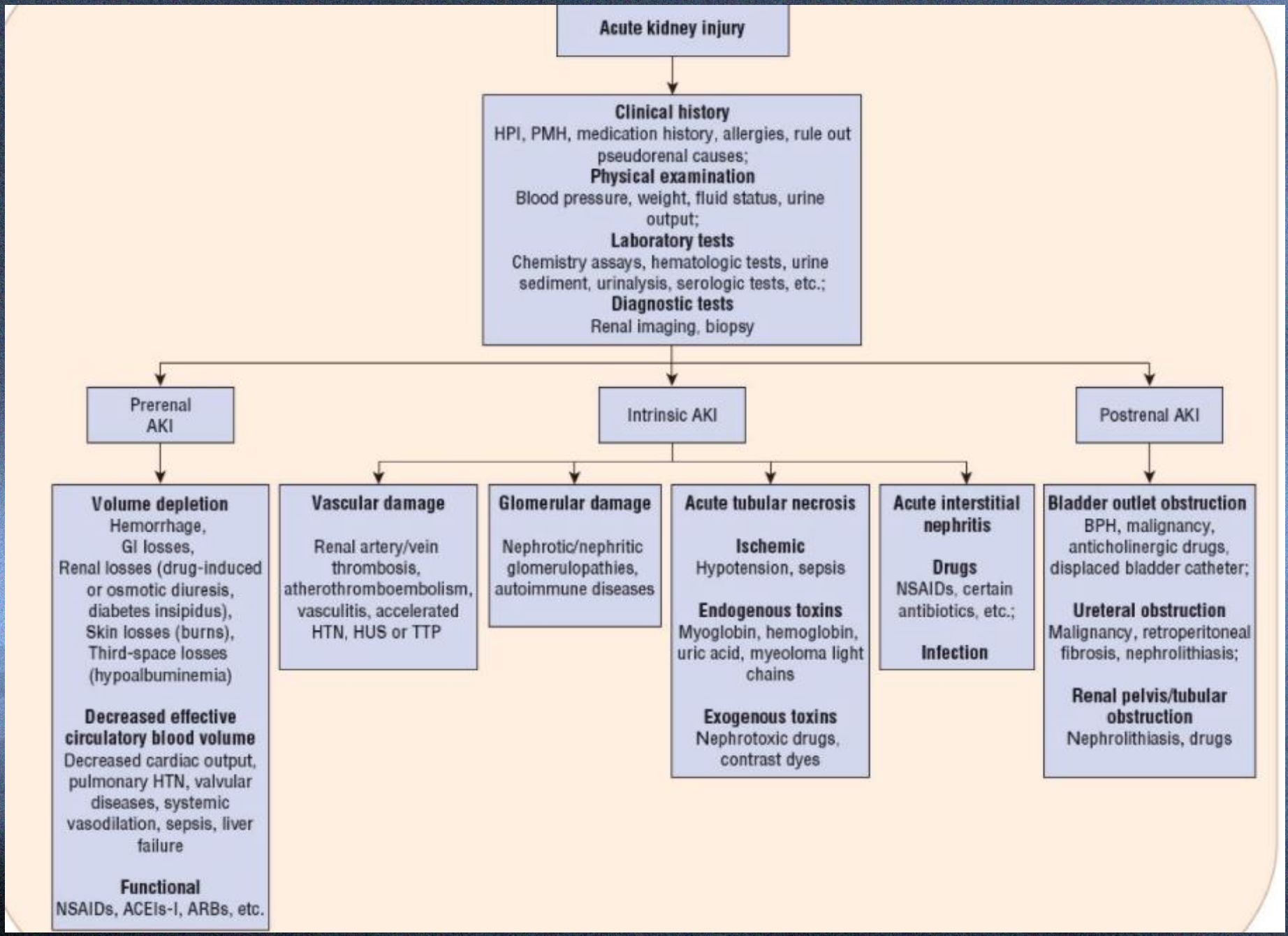

Complications
Normal
Increased risk
Damage
↓ GFR
Kidney failure
CKD death
Screening for CKD risk factors: diabetes hypertension age >60 family history US ethnic minorities
CKD risk reduction; Screening for CKD
Diagnosis & treatment; Treat comorbid conditions; Slow progression
Estimate progression; Treat complications; Prepare for replacement
Replacement by dialysis & transplant
KDIGO

Box 2: Evaluation of Patients With Acute Renal Failure

1. Review records, perform history and physical examination
   - Findings that suggest prerenal causes:
     - Volume depletion
     - Congestive heart failure
     - Severe liver disease or other edematous states
   - Findings that suggest postrenal causes:
     - Palpable bladder or hydronephrotic kidneys
     - Enlarged prostate
     - Abnormal pelvic examination
     - Large residual bladder urine volume
     - History of renal calculi, perform ultrasound to screen for urinary tract obstruction)
   - Findings that suggest intrinsic renal disease:
     - Exposure to nephrotoxic drugs or hypotensive
     - Recent radiographic procedures with contrast
2. Examine the urine sediment
   - If no abnormalities: suspect prerenal or postrenal azotemia
   - If eosinophils: suspect acute interstitial nephritis
   - If red blood cell casts: suspect glomerulonephritis or vasculitis
   - If renal tubular epithelial cells and muddy brown casts: suspect acute tubular necrosis
3. Calculate urinary indices
   - Findings that suggest prerenal azotemia or glomerulonephritis:
     - Urinary sodium concentration <20 mEq/L
     - Urine : plasma creatinine ratio >30
     - Renal failure index <1
     - Renal failure index = (urinary sodium concentration × plasma creatinine concentration)/urinary creatinine concentration
     - Urine osmolality >500 mOsm/kg
   - Findings that suggest acute tubular necrosis or postrenal azotemia:
     - Urinary sodium concentration >40 mEq/L
     - Urine:plasma creatinine ratio <20
     - Renal failure index >1
     - Urine osmolality <400 mOsm/kg

	Serum Creatinine Criteria			Urine Output Criteria
	RIFLE	AKIN	KDIGO	
1—R	>1.5 × baseline or GFR decrease >25%	≥0.3 mg/dL increase or ≥1.5–2 × baseline	1.5–1.9 × baseline or >0.3 mg/dL increase (within 48 h)	<0.5 mL/kg/h for 6–12 h
2—I	>2 × baseline or GFR decrease >50%	>2–3 × baseline	2–2.9 × baseline	<0.5 mL/kg/h for 12 h
3—F	>3 × baseline or Cr >4 mg/dL with an acute rise >0.5 mg/dL	>3 × baseline or ≥4.0 mg/dL with acute increase of ≥0.5 mg/dL or initiation of RRT	3 × baseline or increase in serum Cr ≥4 mg/dL or initiation of RRT	<0.3 mL/kg/h for 24 h or anuria for 12 h
L	*Loss of renal function >4 wk*			
E	*End-stage renal disease*	*← Outcome classes for RIFLE criteria*		


Types of Acute Renal Failure
Prerenal, caused by transient renal hypoperfusion due to:
Hypotension
Decreased cardiac output
Decreased effective arterial blood volume
Postrenal, due to obstruction of the urinary tract.
Intrinsic
Acute glomerulonephritis involves inflammation and damage to the glomerular membrane.
Acute interstitial nephritis, an allergic reaction, may be caused by a variety of drugs.
Acute tubular necrosis accounts for more than 50% of cases of acute renal failure.
Causes: nephrotoxic agents, prolonged renal hypoperfusion.


Acute kidney injury
Clinical history
HPI, PMH, medication history, allergies, rule out pseudorenal causes;
Physical examination
Blood pressure, weight, fluid status, urine output;
Laboratory tests
Chemistry assays, hematologic tests, urine sediment, urinalysis, serologic tests, etc.;
Diagnostic tests
Renal imaging, biopsy
Prerenal AKI
Intrinsic AKI
Postrenal AKI
Volume depletion
Hemorrhage, GI losses, Renal losses (drug-induced or osmotic diuresis, diabetes insipidus), Skin losses (burns), Third-space losses (hypoalbuminemia)
Decreased effective circulatory blood volume
Decreased cardiac output, pulmonary HTN, valvular diseases, systemic vasodilation, sepsis, liver failure
Functional
NSAIDs, ACEIs-I, ARBs, etc.
Vascular damage
Renal artery/vein thrombosis, atherothromboembolism, vasculitis, accelerated HTN, HUS or TTP
Glomerular damage
Nephrotic/nephritic glomerulopathies, autoimmune diseases
Acute tubular necrosis
Ischemic
Hypotension, sepsis
Endogenous toxins
Myoglobin, hemoglobin, uric acid, myeloma light chains
Exogenous toxins
Nephrotoxic drugs, contrast dyes
Acute interstitial nephritis
Drugs
NSAIDs, certain antibiotics, etc.;
Infection
Bladder outlet obstruction
BPH, malignancy, anticholinergic drugs, displaced bladder catheter;
Ureteral obstruction
Malignancy, retroperitoneal fibrosis, nephrolithiasis;
Renal pelvis/tubular obstruction
Nephrolithiasis, drugs

$$FE_{Na} = \frac{\text{excreted Na}}{\text{filtered Na}} \times 100 = \frac{U_{vol} \times U_{Na}}{GFR \times S_{Na}} \times 100$$

$$GFR = \frac{U_{vol} \times U_{cr}}{S_{cr} \times t}$$

$$FE_{Na} = \frac{U_{Na} \times S_{cr} \times 100}{U_{cr} \times S_{Na}}$$

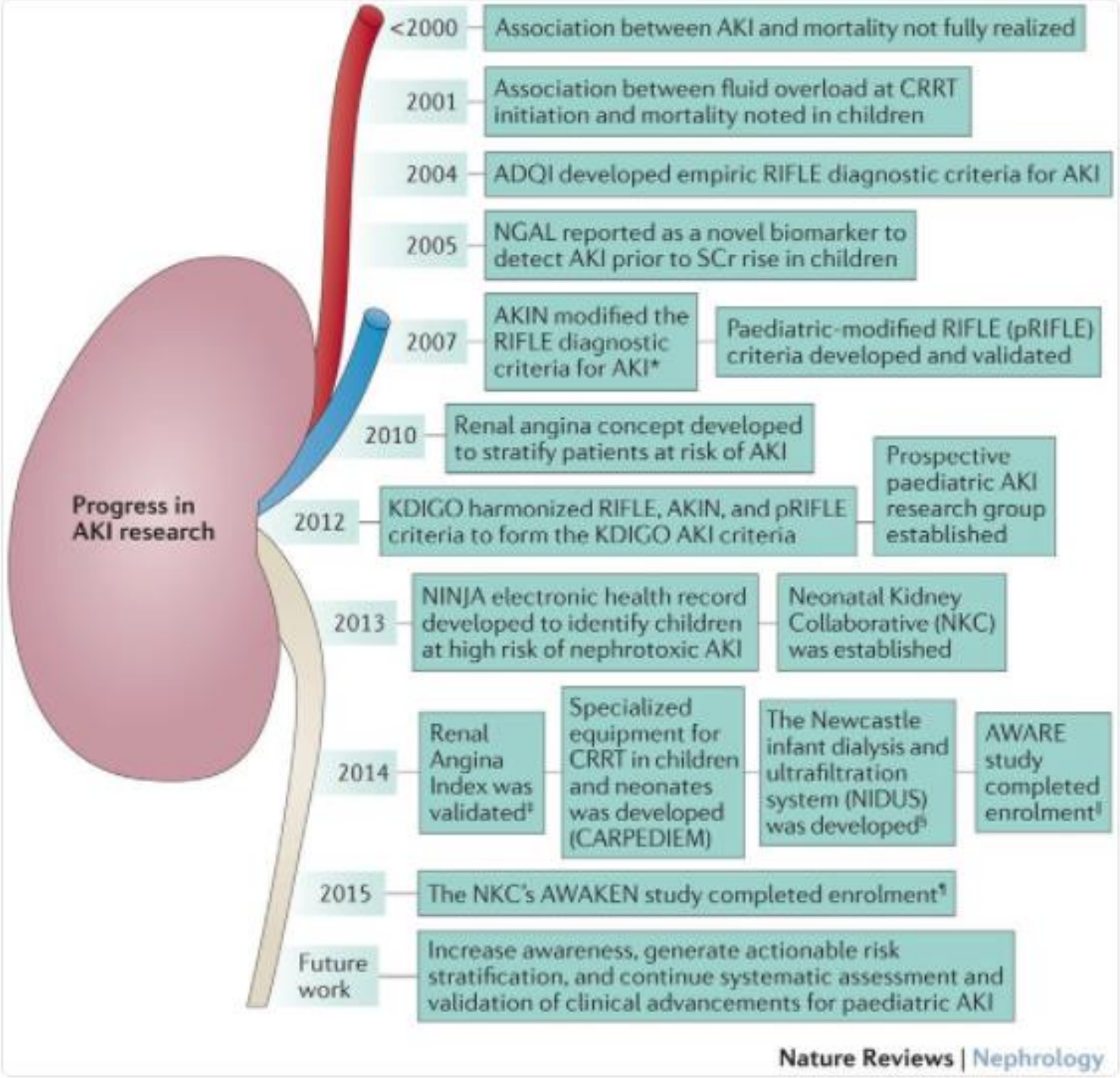
Cardiac surgery associated (CSA) acute kidney tubular damage

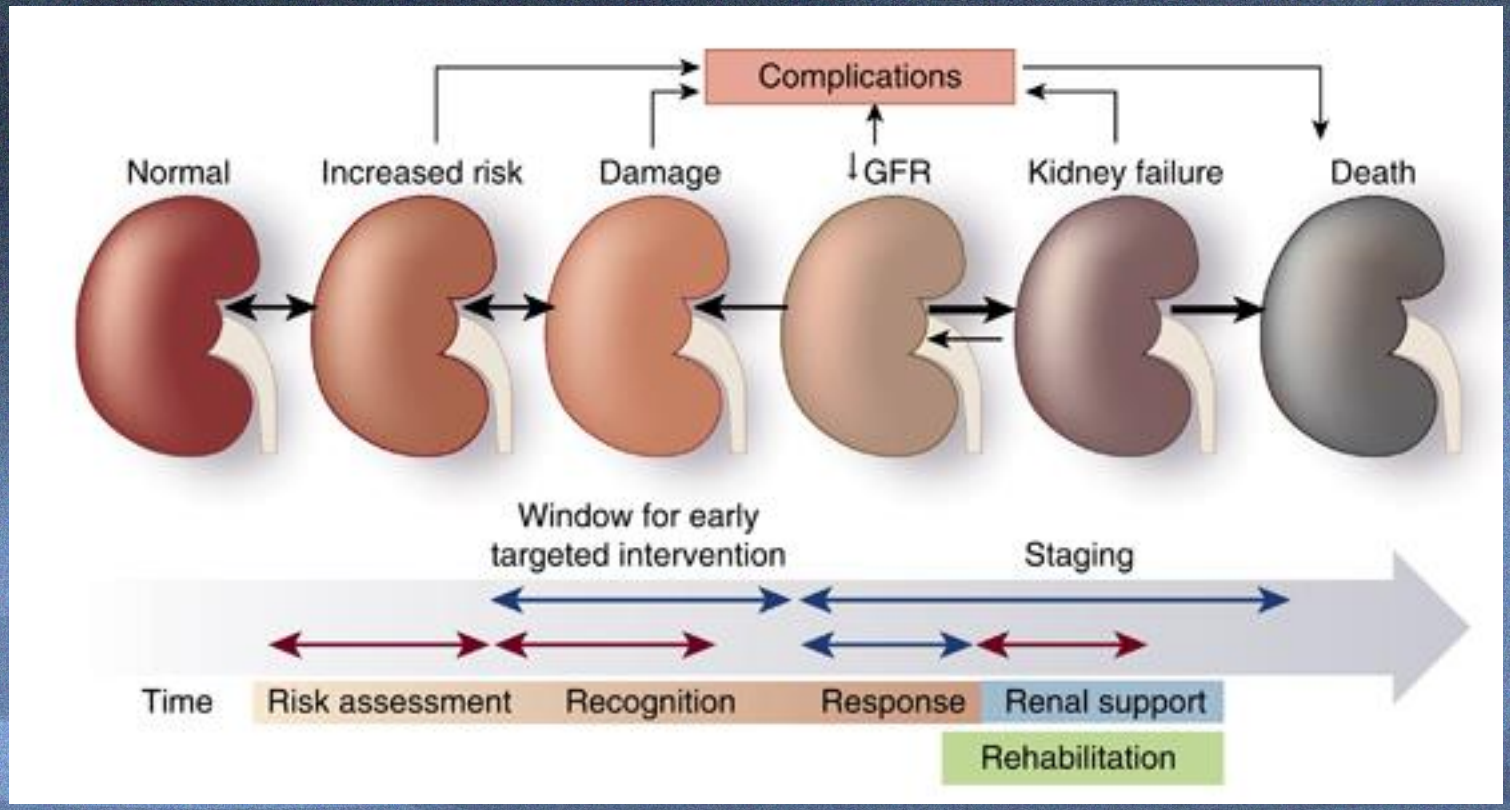
Concentration Sample	[ng/mL]		Delta (Δ) NGAL at following measurement	CSA-NGAL Score	
uNGAL	<50			0	Tubular damage unlikely
pNGAL	<100				
uNGAL	50 - <150			1	Tubular damage possible
pNGAL	100 - <200				
uNGAL	150 - <1000	or	Δ > 100 + second value ≥ 125	2	Tubular damage
pNGAL	200 - <1000	or	Δ > 100 + second value ≥ 150		
uNGAL	>1000			3	Severe tubular damage
pNGAL					

CSA-NGAL Score based management considerations

Acute kidney tubular damage in cardiac surgery

ACTION	CSA-NGAL 0 Tubular damage unlikely	CSA-NGAL 1 Tubular damage possible	CSA-NGAL 2 Tubular damage	CSA-NGAL 3 Severe tubular damage
Pre-operative	Continue with operation		Continue with operation with focus on AKI progression	Consider postponing operation or continue with intensified focus on AKI progression
NGAL follow-up	Only 4-6h post surgery	YES – until damage has subsided		
sCreatinine	Standard care (daily)		Every 12 hours	Every 6 hours
Urine output	Standard care		Strict Ins and Outs review Every 6h	Monitor hourly urine output
Venous Oxygen saturation	Standard Care	Target SVO_2 > 60% Review SVO_2 trend every 3h		Target SVO_2 > 60% Hourly review of SVO_2 trend
Nephrotoxic medication	Standard care		Consider alternatives Adjust dosing	Move to alternatives if possible Close attention to renal responses
Patient location	Discharge to floor from ICU as per standard care	Discharge to floor from ICU	Consider step-down unit	Consider keeping patient in ICU
Expert consultation	Standard care		Consider Nephrology consult	Nephrology consult Consider RRT


Progress in AKI research
<2000
Association between AKI and mortality not fully realized
2001
Association between fluid overload at CRRT initiation and mortality noted in children
2004
ADQI developed empiric RIFLE diagnostic criteria for AKI
2005
NGAL reported as a novel biomarker to detect AKI prior to SCr rise in children
2007
AKIN modified the RIFLE diagnostic criteria for AKI*
Paediatric-modified RIFLE (pRIFLE) criteria developed and validated
2010
Renal angina concept developed to stratify patients at risk of AKI
2012
KDIGO harmonized RIFLE, AKIN, and pRIFLE criteria to form the KDIGO AKI criteria
Prospective paediatric AKI research group established
2013
NINJA electronic health record developed to identify children at high risk of nephrotoxic AKI
Neonatal Kidney Collaborative (NKC) was established
2014
Renal Angina Index was validated‡
Specialized equipment for CRRT in children and neonates was developed (CARPEDIEM)
The Newcastle infant dialysis and ultrafiltration system (NIDUS) was developed§
AWARE study completed enrolment‖
2015
The NKC's AWAKEN study completed enrolment¶
Future work
Increase awareness, generate actionable risk stratification, and continue systematic assessment and validation of clinical advancements for paediatric AKI
Nature Reviews | Nephrology


Complications
Normal
Increased risk
Damage
↓GFR
Kidney failure
Death
Window for early
targeted intervention
Staging
Time
Risk assessment
Recognition
Response
Renal support
Rehabilitation