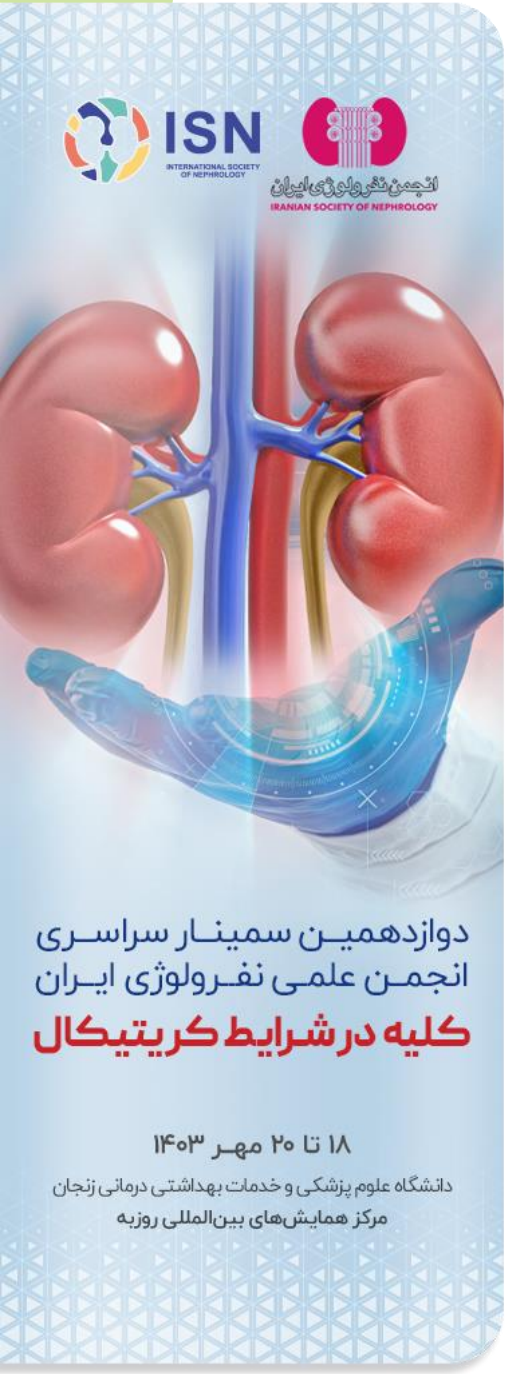

AKI in the ICU

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AKI
Definition

abrupt decrease in kidney function

over the course of

hours to days.

AKI
Clinical manifestation related with

- retention of waste products
- disruption homeostasis of:

  Fluid / electrolyte / acid-base
- and reduced clearance of toxins - drugs

AKI
DIAGNOSTIC CRITERIA

Traditionally, based on

Rise in serum Cr

or

Fall in urine output.

- Serum creatinine and urine output are surrogate markers GFR

Advantage:

widely available & easy to measure.

TABLE 5.1 Classifications of Acute Kidney Injury

	RIFLE (2004)[4]			AKIN (2007)[1]			KDIGO (2012)[11]	
AKI Class	SCr or GFR	Urine Output	AKI Stage	SCr	Urine Output	AKI Stage	SCr	Urine Output
Risk	SCr × 1.5 times or GFR decrease < 25% from baseline (in a 7-d period)	<0.5 mL/kg/hr for ≥6 hr	1	Increase ≥0.3 mg/dL (26.5 μmol/L) in 48 hr or × 1.5-2 times baseline in a 7-d period	<0.5 mL/kg/hr for ≥6 hr	1	Increase ≥0.3 mg/dL (26.5 μmol/L) in 48 hr or ×1.5-2 times baseline in a 7-d period	<0.5 mL/kg/hr for ≥6 hr
Injury	SCr × 2 or GFR decrease <50%	<0.5 mL/kg/hr for ≥12 hr	2	2-3 times baseline	<0.5 mL/kg/hr for ≥12 hr	2	2.0-2.9× baseline	<0.5 mL/kg/hr for ≥12 hr
Failure	SCr × 3 or ≥4.0 mg/dL (with an acute increase of at least 0.5 mg/dL) or GFR decrease >75%	<0.3 mL/kg/hr for ≥24 hr or anuria for ≥12 hr	3	>3 times baseline or ≥4.0 mg/dL (with an acute increase of at least 0.5 mg/dL) or initiation of KRT	<0.3 mL/kg/hr for ≥24 hr or anuria for ≥12 hr	3	3.0× baseline or ≥4.0 mg/dL or initiation of KRT	<0.3 mL/kg/hr for ≥24 hr or anuria for ≥12 hr

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; GFR, glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; RIFLE, Risk, Injury, Failure, Loss, End-stage; KRT, kidney replacement therapy; SCr, serum creatinine.

Several studies in various patient populations have confirmed an association between the different AKI classifications and short- and longterm outcomes

LIMITATIONS AND CHALLENGES OF CURRENT AKI CRITERIA

- S.Cr and U.output are markers of excretory function only.
- Not indicate early structural changes
- Not provide any information about any other roles of the kidney (metabolic, endocrine, or immunologic)
- Not renal specific.

Creatinin Disadvantage

The key factors that affect serum creatinine concentration are as follows:

- Liver function
- Muscle bulk
- Age
- Race
- Sepsis (falls in Cr production)
- Volume distribution (volume overload)
- drugs (compete with creatinine tubular secretion (i.e., cimetidine and trimethoprim)

LIMITATIONS OF URINE OUTPUT CRITERIA

Oliguria and the duration of oliguria are also associated with increased mortality

It may be appropriately reduced in the setting of:

- fluid depletion
- antidiuretic hormone (ADH) release
- diuretics.

ACUTE KIDNEY DISEASE & DISORDERS

- conditions that are characterized by acute functional and structural changes of the kidneys

<90days

and other conditions that do not meet the CKD criteria

AKI

- Some patients have a slow but persistent (creeping) rise in serum creatinine over days or weeks without fulfilling the consensus criteria for AKI.

AKD

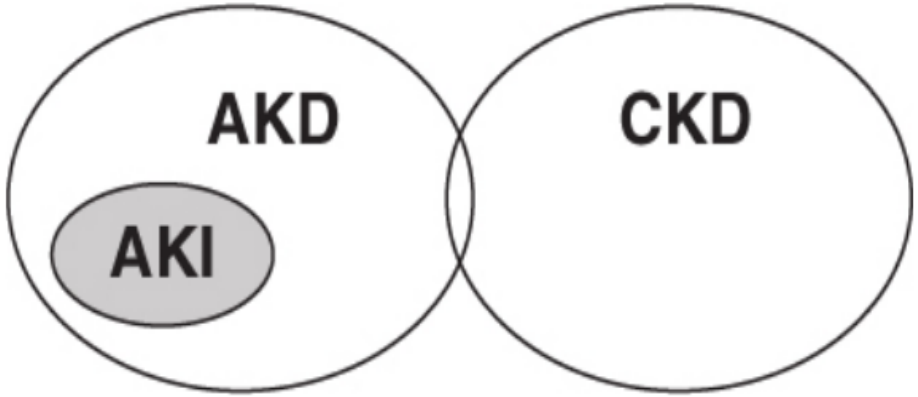

FIGURE 5.1: Acute kidney injury as a subset of acute kidney diseases and disorders. AKD, acute kidney diseases and disorders; AKI, acute kidney injury; CKD, chronic kidney disease.

From Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1-138.

In fact, AKD is more common than AKI and is associated with significant long-term complications.

Similar to AKI, AKD syndromes comprise multiple different etiologies and rarely occur in isolation

usually in the context of other acute illnesses and often on the background of profound chronic comorbidities.

ETIOLOGIES OF ACUTE KIDNEY INJURY

AKI is multifactorial
occurring simultaneously or sequentially

Mechanisms :

- Hemodynamic instability
- Microcirculatory dysfunction
- Formation of microvascular thrombi
- Endothelial dysfunction
- Inflammation
- Tubular cell injury
- Autoimmune processes
- Hypersensitivity immune reactions
- Renal venous congestion
- Obstruction
- Intra-abdominal hypertension

AKI
COMMON ETIOLOGIES

Hypoperfusion

The kidneys receive up to 25% of cardiac output. Conditions that compromise systemic perfusion, such as

- **Hypovolemia**
- **Cardiac failure**
- **Systemic vasodilatation**

can potentially lead to functional AKI. It is often reversible

but

prolonged hypoperfusion can result in acute tubular ischemia.

Sepsis-Associated AKI

Sepsis-associated AKI is common in critically ill patients, 50%

Normal or increased global renal blood flow.

Pathophysiologic :

- Macrovascular and microvascular alterations
- Endothelial dysfunction and capillary leak
- Inflammation
- Tubular injury
- Intrarenal shunting.

Cardiac Surgery-Associated AKI

AKI is a common complication following cardiac surgery, 45%

The pathogenesis is multifactorial:

- Cardiopulmonary bypass
- Cross-clamping of the aorta
- High doses of exogenous vasopressors contribute
- Cholesterol embolization
- Neurohormonal activation
- Hemolysis (release of free hemoglobin and free iron)

Drug-Induced AKI

Approximately 20% of the drugs prescribed in ICU

Hospital mortality rates 18% and 50%

Mechanisms
Drug-Induced Nephrotoxicity

TABLE 5.4 Mechanisms Involved in Drug-Induced Nephrotoxicity

	Mechanism of Nephrotoxicity	Examples
Hemodynamic alteration	Vasoconstriction of afferent arteriole	NSAIDs Vasopressors Calcineurin inhibitors
	Vasodilatation of efferent arteriole	ACE-I ARBs
Vascular damage	Thrombotic microangiopathy	Chemotherapeutic agents ARBs IFN-α Ticlopidine mTOR inhibitors Calcineurin inhibitors

Mechanisms
Drug-Induced Nephrotoxicity

	Mechanism of Nephrotoxicity	Examples
	Vasculitis of renal vessels	Penicillamine
		Allopurinol Anti–TNF-α Cocaine-containing levamisole Hydralazine
	Atheroembolism	Anticoagulants
Glomerular damage	Minimal change disease	NSAIDs Lithium Quinolones Penicillins Interferon Pamidronate Gold
	Focal segmental glomerulosclerosis	Lithium Bisphosphonates Heroin IFNs

OTHER CAUSES OF AKI

- Rhabdomyolysis
- Contrast-Associated Acute Kidney Injury
- Obstructive Acute Kidney Injury
- Primary Kidney Diseases (Rare)
- Hepatorenal Syndrome

RECOVERY FROM ACUTE KIDNEY INJURY

- There is no consensus on the definition of recovery from AKI.

Return to previous baseline S.Cr

- Discharge time S.Cr may not be representative of kidney function because muscle loss that overestimation of kidney function.

S.Cr at 3 months after discharge may be more representative.

CONCLUSIONS

AKI represents a multifactorial syndrome involving a variety of :

- Etiologies
- pathophysiologic mechanisms
- clinical manifestations.

The definition of AKI is currently based on functional criteria only

In the future, given the expanding information about the dynamic course, pathophysiology, and the discovery of new kidney biomakers