

Acute Kidney Injury in Critical Care

Sepsis-AKI microcirculatory decoupling, KDIGO staging, Furosemide Stress Test (FST), urine microscopy, and the AEIOU dialysis threshold framework.

Last reviewed: 2026-09-07

Current against the final published KDIGO 2012 AKI guideline and major RRT-timing trials (AKIKI, IDEAL-ICU, STARRT-AKI). KDIGO released an AKI/AKD guideline draft for public review in 2026; it is tracked as a watchlist item and should not be represented as final guidance until formally published.

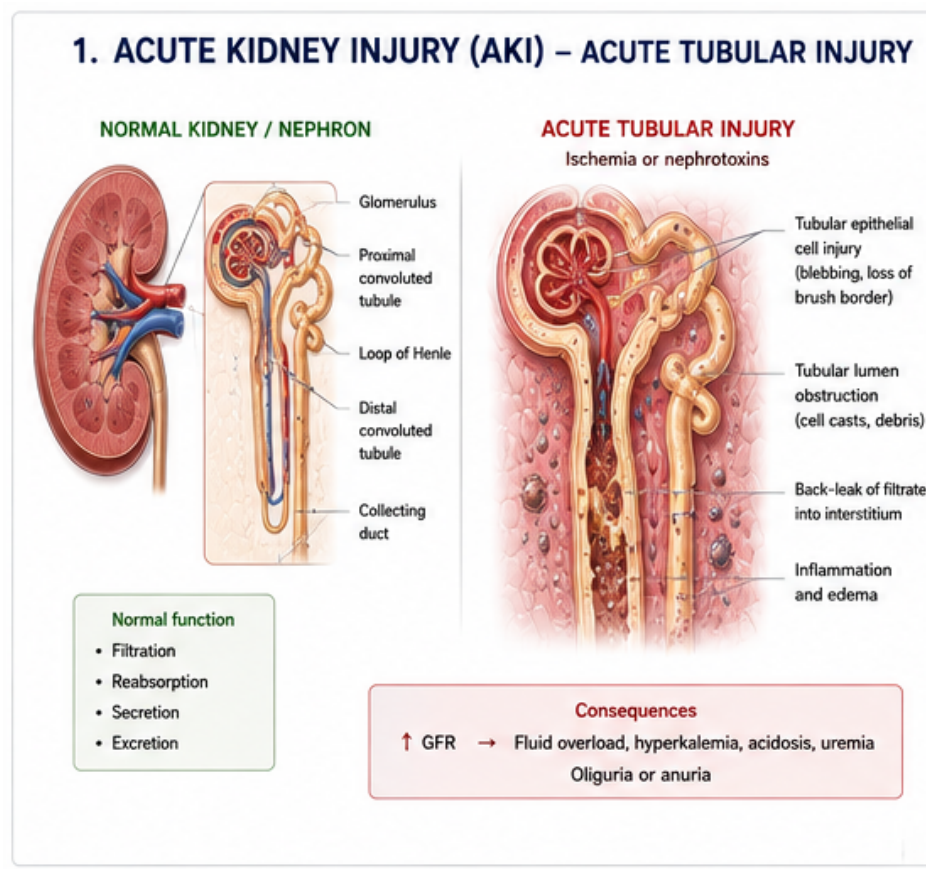
Developed by Fawaz Alanazi, MNGHA | iculearningplatform@gmail.com

GUIDELINE

Educational content only. Use this handout for structured review; verify patient-specific decisions against local protocols and current guidelines.

Overview

Acute Kidney Injury (AKI) is an abrupt decline in glomerular filtration and tubular function, staged by serum creatinine and urine output, carrying an ICU mortality of 30-50%.



aki tubular injury

Acute Kidney Injury (AKI) complicates up to 50% of all critically ill ICU patients and is an independent predictor of prolonged mechanical ventilation, multiorgan dysfunction, and hospital mortality. Sepsis is the single most common etiology (~50% of ICU AKI), followed by major surgery,

cardiogenic shock, and nephrotoxin exposure.

Diagnostic evaluation requires rapid KDIGO staging, medication/hemodynamic review, urinalysis and urine microscopy, assessment for obstruction, and selective use of functional indices or the Furosemide Stress Test when they answer a specific question. FeNa/FeUrea and FST refine probability or prognosis; none independently distinguishes every prerenal versus intrinsic-AKI phenotype or mandates dialysis.

Differential Diagnosis of Acute Oliguria & Azotemia in Critical Care

Differentiate pre-renal hemodynamic azotemia, acute tubular necrosis (ATN), acute interstitial nephritis (AIN), and post-renal obstruction.

- Hemodynamic / pre-renal physiology vs tubular injury: traditional low FeNa (<1%) or low FeUrea (<35%) patterns can support sodium/urea avidity, while muddy-brown granular casts and renal tubular epithelial cells support tubular injury. These indices are not diagnostic cutoffs: sepsis, CKD, diuretics, glomerular disease, pigment injury and mixed shock frequently blur the classic pattern; integrate urine sediment, hemodynamics, obstruction assessment and the clinical trajectory.
- Abdominal Compartment Syndrome (ACS): High intra-abdominal pressure (IAP > 20 mmHg) compressing renal veins and parenchyma, causing sudden oliguria with elevated CVP; confirmed by bladder pressure measurement.
- Acute Interstitial Nephritis (AIN): Allergic drug reaction (antibiotics, PPIs, NSAIDs) presenting with sterile pyuria, WBC casts, eosinophiluria, and rash.
- Cardiorenal Syndrome Type 1: High central venous congestion (CVP > 15-20 mmHg) causing backward venous hypertension and drop in net renal perfusion pressure.

Definition & KDIGO Staging Matrix

The 2012 KDIGO consensus staging system across Stage 1, Stage 2, and Stage 3 based on serum creatinine rise and duration of oliguria.

AKI is diagnosed when any ONE of the following three criteria is met:

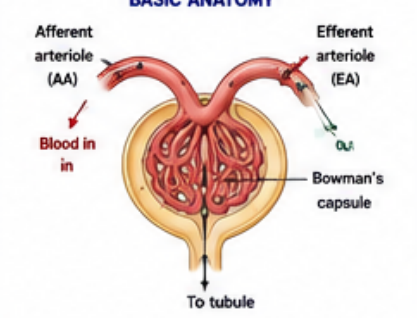
Diagnostic Criteria	1. Serum creatinine increase by ≥ 0.3 mg/dL (≥ 26.5 $\mu\text{mol/L}$) within 48 hours; OR 2. Serum creatinine increase to ≥ 1.5 times baseline within the prior 7 days; OR 3. Urine volume < 0.5 mL/kg/hour for ≥ 6 consecutive hours.
Stage 1	Serum creatinine 1.5-1.9 times baseline OR increase ≥ 0.3 mg/dL; OR urine output < 0.5 mL/kg/hr for 6-12 hours.
Stage 2	Serum creatinine 2.0-2.9 times baseline; OR urine output < 0.5 mL/kg/hr for ≥ 12 hours.
Stage 3	Serum creatinine ≥ 3.0 times baseline OR increase to ≥ 4.0 mg/dL (≥ 353.6 $\mu\text{mol/L}$) OR initiation of Renal Replacement Therapy; OR urine output < 0.3 mL/kg/hr for ≥ 24 hours OR anuria for ≥ 12 hours.

Pathophysiology: Sepsis-AKI, Autoregulation, & Nephrotoxins

The sepsis-AKI microcirculatory paradigm, renal perfusion pressure (MAP - CVP), tubular mitochondrial hibernation, and nephrotoxicity mechanisms.

5. GFR & RENAL AUTOREGULATION

BASIC ANATOMY



EFFECT OF ARTERIOLE TONE ON GFR

	1. AA Constriction	2. AA Dilation	3. EA Constriction	4. EA Dilation
Glomerular Pressure	↓ Decrease	↑ Increase	↑ Increase	↓ Decrease
GFR	↓ Decrease	↑ Increase	↑ Increase (moderate)	↓ Decrease (marked)

INTRINSIC AUTOREGULATION MECHANISMS

1. Myogenic Response

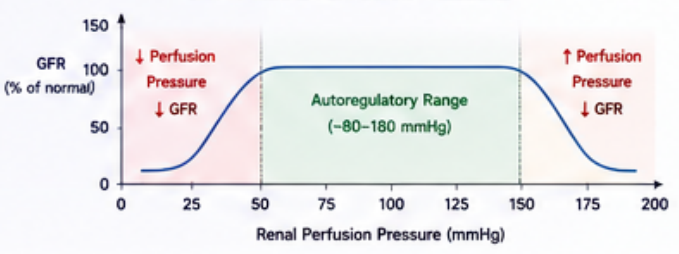
↑ Renal perfusion pressure
→ AA stretches
→ Vasoconstriction
→ ↓ GFR toward normal

2. Tubuloglomerular Feedback (TGF)

↑ NaCl delivery to macula densa
→ AA constriction
→ ↓ GFR



GFR vs RENAL PERFUSION PRESSURE



KEY MESSAGE

GFR is maintained constant over a wide range of perfusion pressures by myogenic response and TGF. Outside this range, GFR becomes pressure-dependent (↓ in hypotension, ↓ in severe hypertension).

gfr renal autoregulation

ICU Learning Platform | Educational use - verify local protocols

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5. FILTRATION / GLOMERULAR FORCES

Determinants of glomerular filtration rate (GFR)

STARLING FORCES IN THE GLOMERULUS

1 **Glomerular hydrostatic pressure (P_{GC})**
Pushes fluid out of capillary (filtration) ~ 50–60 mmHg

2 **Bowman space hydrostatic pressure (P_{BS})**
Opposes filtration ~ 10–20 mmHg

3 **Plasma oncotic pressure (π_{GC})**
Opposes filtration ~ 25–30 mmHg

4 **Net Filtration Pressure (NFP) =**
 $P_{GC} - P_{BS} - \pi_{GC}$
Normal NFP ~ 10 mmHg

GFR EQUATION

$GFR = K_f \times NFP$

Where:
 K_f = Filtration coefficient
(surface area $\times$ permeability)
NFP = Net filtration pressure

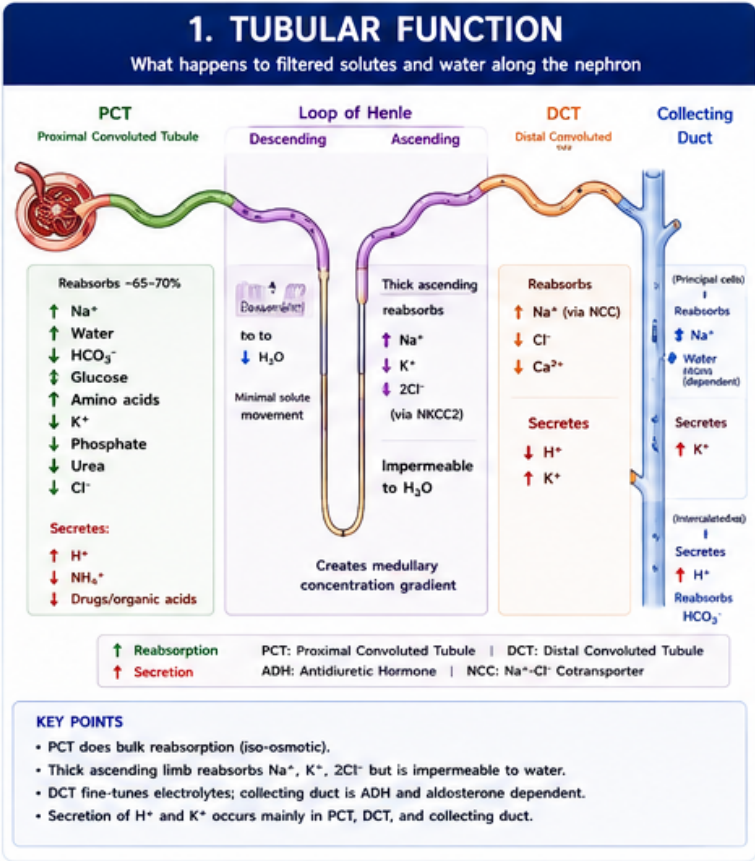
HOW ARTERIOLAR TONE AFFECTS GFR

Change	Effect on Pressure	Effect on GFR
AFFERENT ARTERIOLE		
Constriction	$\downarrow P_{GC}$	$\downarrow$ GFR
Dilation	$\uparrow P_{GC}$	$\uparrow$ GFR
EFFECTOR ARTERIOLE		
Constriction (mild-mod)	$\uparrow P_{GC}$	$\uparrow$ or $\leftrightarrow$ GFR
Constriction (severe)	$\downarrow RBF, \downarrow P_{GC}$	$\downarrow$ GFR
Dilation	$\downarrow P_{GC}$	$\downarrow$ GFR

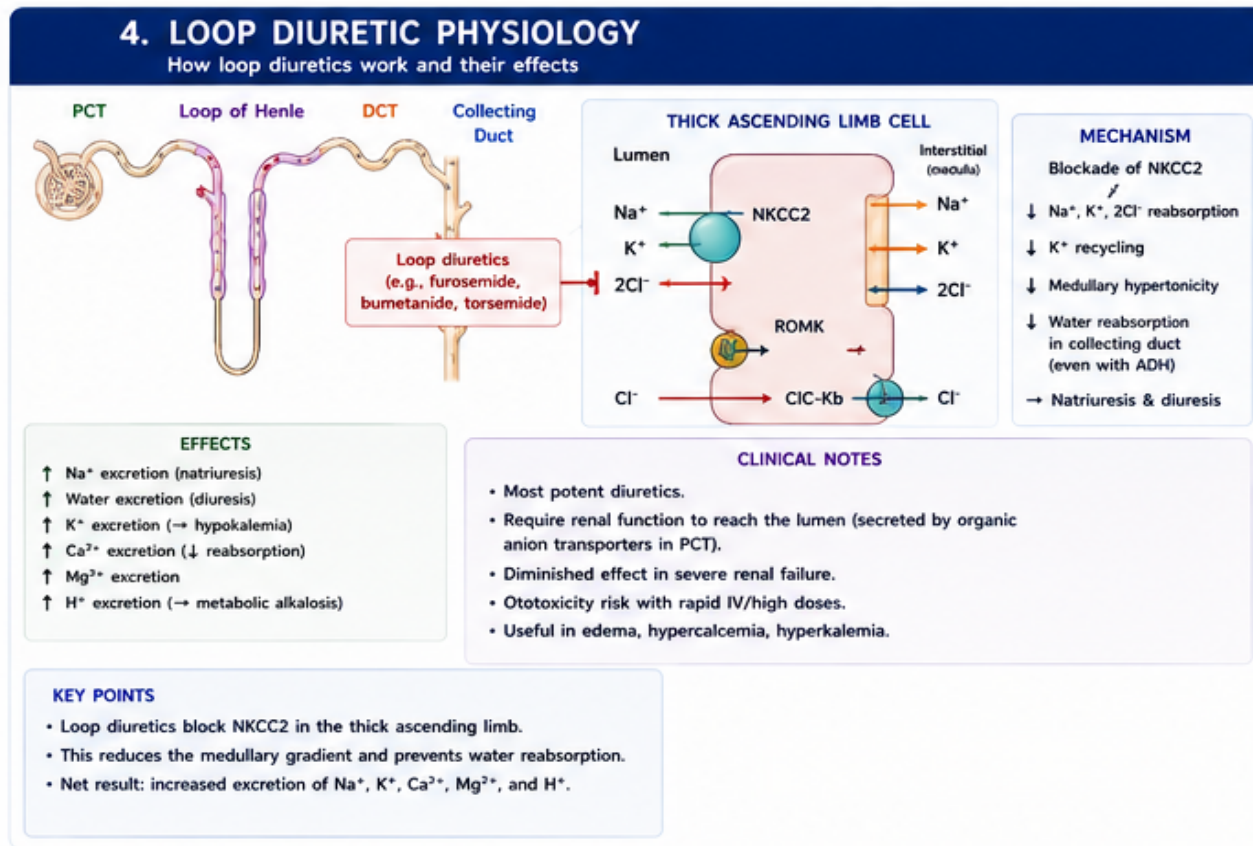
KEY POINTS

- GFR depends on balance of pressures and K_f .
- Afferent constriction lowers GFR; efferent dilation lowers GFR.
- Autoregulation keeps GFR stable within MAP 80–180 mmHg.

glomerular starling forces gfr



nephron tubular function



loop diuretic physiology nkcc2

Renal hemodynamic and cellular injury in the ICU is governed by complex microvascular and cellular mechanisms:

1. Renal Perfusion Pressure (RPP)	RPP = Mean Arterial Pressure (MAP) - Central Venous Pressure (CVP). In circulatory shock or venous congestion (VExUS grade 3), falling MAP and rising CVP drastically narrow net transglomerular filtration pressure, triggering oliguria.
2. The Modern Sepsis-AKI Paradigm	Sepsis-AKI is NOT purely ischemic tubular necrosis. Human and experimental data show that sepsis causes profound renal microvascular flow heterogeneity, efferent arteriolar vasodilation (causing GFR collapse despite preserved global renal blood flow), pathogen-associated molecular pattern (PAMP) activation of TLR-4 receptors on tubular cells, and tubular cell mitochondrial shutdown (metabolic hibernation) to protect against apoptosis.
3. Common ICU Nephrotoxin Mechanisms	Vancomycin: Direct proximal tubular oxidative stress and cast formation. Aminoglycosides: Megalin-receptor-mediated endocytosis into proximal tubule lysosomes causing phospholipidosis. IV Iodinated Contrast: Medullary hypoxia from intense vasoconstriction + direct tubular cytotoxicity. NSAIDs: Block vasodilatory prostaglandins → afferent arteriolar vasoconstriction. ACEi / ARBs: Block angiotensin II → efferent arteriolar vasodilation. Rhabdomyolysis: Free myoglobin precipitation with Tamm-Horsfall protein + heme-mediated lipid peroxidation.

Diagnostic Protocol: FeNa, FeUrea, & Urine Microscopy

Fractional excretion formulas, distinguishing prerenal azotemia from intrinsic ATN, and sediment microscopy findings.

Fractional Excretion of Sodium (FeNa)	FeNa (%) = $[(\text{Urine Na} \times \text{Serum Cr}) / (\text{Serum Na} \times \text{Urine Cr})] \times 100$. Low or high values can support a physiology in the right context, but the classic <1% and >2% cutoffs are not diagnostic: sepsis, CKD, glomerular disease, pigment injury, contrast exposure, diuretics and mixed shock can all break the rule.
Fractional Excretion of Urea (FeUrea)	FeUrea (%) = $[(\text{Urine Urea} \times \text{Serum Cr}) / (\text{Serum BUN} \times \text{Urine Cr})] \times 100$. FeUrea may be less affected by loop diuretics than FeNa in some settings, but its diagnostic performance is also imperfect; <35% or >50% should not be used as stand-alone proof of prerenal azotemia or ATN.
Urine Sediment Microscopy ('Liquid Kidney Biopsy')	Muddy brown granular casts and renal tubular epithelial (RTE) cells: strongly support acute tubular injury/ATN in the appropriate clinical context, but urine microscopy is not perfectly diagnostic in isolation. White Blood Cell (WBC) Casts + Eosinophiluria: Suggests Acute Interstitial Nephritis (AIN). Dysmorphic Red Blood Cells + RBC Casts: Indicates Acute Glomerulonephritis / Vasculitis. Broad Waxy Casts: Reflects Chronic Kidney Disease / tubular dilation.

GUIDELINE

Interactive calculator available on the ICU Knowledge Map: fena

GUIDELINE

Interactive calculator available on the ICU Knowledge Map: feurea

Risk Stratification: The Furosemide Stress Test (FST)

Chawla et al. FST protocol for predicting progression to severe Stage 3 AKI and need for renal replacement therapy.

The Furosemide Stress Test (FST) is a validated functional challenge assessing the integrity of the loop of Henle and collecting duct in early AKI (Chawla et al., Crit Care 2013):

FST Protocol	Patient must be euvolemic / adequately fluid resuscitated. Administer IV Furosemide: 1.0 mg/kg in loop-diuretic-naïve patients OR 1.5 mg/kg in patients with prior loop diuretic exposure. Measure hourly urine output.
FST Interpretation	Urine Output <200 mL in the 2 hours after furosemide is commonly used as a positive FST threshold. In the original derivation study, this threshold had about 87% sensitivity and 84% specificity for progression to KDIGO Stage 3 AKI. The FST is a risk-stratification tool: a response >200 mL/2 h suggests greater tubular functional reserve and a lower risk of severe AKI progression, but it does not guarantee renal recovery or by itself determine whether RRT will be required.

Indications for Renal Replacement Therapy: The AEIOU Framework

Absolute emergency indications versus watchful waiting in non-emergent AKI.

Medical visual available in the online topic: crrt-circuit-principles

A - Acidemia	Severe refractory metabolic acidemia (pH < 7.15-7.20) uncorrectable by medical therapy (see BICAR-ICU protocol).
E - Electrolyte Abnormalities	Severe hyperkalemia (K ⁺ > 6.5 mEq/L) with ECG changes or refractory to medical shifting/stabilization.
I - Ingestions / Toxins	Dialyzable toxic ingestions: Methanol, Ethylene Glycol, Lithium, Salicylates, Theophylline.
O - Overload	Refractory hypervolemia / flash pulmonary edema unresponsive to high-dose loop diuretics and vasodilators.
U - Uremia	Severe uremic complications: Uremic encephalopathy (asterixis, seizures, coma), uremic pericarditis (friction rub), uremic coagulopathy / bleeding.

Complications of Acute Kidney Injury

Hyperkalemia, uremic bleeding, fluid overload-induced organ crosstalk, and transition to chronic kidney disease.

- **Cardiopulmonary Crosstalk:** Fluid overload causing acute pulmonary edema, RV afterload increase, and failure to wean from mechanical ventilation.
- **Uremic Platelet Dysfunction:** Impaired platelet adhesion and aggregation from uremic toxins, predisposing to major gastrointestinal and surgical bleeding.
- **Altered Pharmacokinetics:** Severe accumulation of renally-cleared drugs (sedatives, opioids, enoxaparin, beta-lactams), causing toxic neuro-encephalopathy and bone marrow suppression.
- **Chronic Kidney Disease (CKD) Transition:** AKI survivors have a 9-fold higher risk of developing progressive CKD and end-stage renal disease (ESRD).

Common ICU Pitfalls

Critical diagnostic and therapeutic pitfalls in AKI management.

- **Relying on serum creatinine alone for acute detection:** Serum creatinine lags behind GFR loss by 24-48 hours; urine output is a vastly more rapid and sensitive marker of acute injury.
- **Giving reflexive IV fluid boluses for oliguria without assessing fluid responsiveness or venous congestion:** If the patient is fluid non-responsive or has high CVP, fluids exacerbate renal interstitial edema and worsen AKI.
- **Treating FeUrea as a magic replacement for FeNa in a patient receiving diuretics:** both fractional-excretion indices are context dependent and should be interpreted with hemodynamics, urine sediment and the clinical course.
- **Withholding urgent contrast-enhanced imaging solely because AKI is present:** contrast-associated kidney risk should be mitigated when possible, but a time-critical CTA/angiographic diagnosis may outweigh that risk. Document the tradeoff, optimize hemodynamics and avoid unnecessary nephrotoxins rather than claiming iodinated contrast is risk-free.

- Failing to dose-adjust antibiotics to actual dynamic GFR: Underdosing broad-spectrum beta-lactams in septic shock during initial hyperfiltration vs overdosing renally cleared toxins during anuric phases.

Controversies & Areas of Uncertainty

Timing of renal replacement therapy initiation (early vs delayed strategies).

Timing of RRT Initiation in AKI: Multiple massive multicenter RCTs (AKIKI, IDEAL-ICU, STARRT-AKI) compared an 'accelerated/early' strategy (starting RRT immediately upon reaching KDIGO Stage 3) versus a 'standard/delayed' strategy (watchful waiting until an absolute urgent AEIOU indication developed). STARRT-AKI (NEJM 2020, 3019 patients) demonstrated no mortality difference at 90 days, but early RRT significantly increased dialysis dependence at 90 days (10.4% vs 6.0%) and adverse vascular/hypotension events. Conclusion: Watchful waiting with supportive medical management is preferred in the absence of urgent AEIOU indications, avoiding unnecessary invasive dialysis in ~40% of patients whose kidneys recover spontaneously.

First-Hour AKI Phenotyping

Stage the injury, identify reversible threats, and distinguish perfusion, congestion, obstruction and intrinsic renal injury without relying on one urine index.

1. Confirm creatinine and urine-output trajectory, baseline kidney function and whether oliguria is real (catheter obstruction, retention, collection errors).
2. Review MAP/perfusion, venous congestion, fluid balance, sepsis, surgery, nephrotoxins, contrast, pigment injury and medications that alter creatinine or renal autoregulation.
3. Obtain urinalysis and urine sediment when intrinsic disease is plausible; use renal ultrasound promptly when obstruction is possible.
4. Escalate immediately for life-threatening hyperkalemia, severe acid-base disturbance, pulmonary edema/oxygenation failure, toxin clearance indications or uremic complications rather than waiting for a creatinine threshold.

Fluids, Diuretics & Venous Congestion

Oliguria is not synonymous with volume depletion; repeated fluid loading can worsen renal and extrarenal organ dysfunction.

- Give fluid when there is a plausible fluid-responsive perfusion deficit, then reassess the response; do not use urine output alone as the endpoint for repeated boluses.
- Look for venous congestion/RV failure and cumulative positive balance. In a congested patient, decongestion with diuretics or extracorporeal fluid removal may improve organ function even when creatinine transiently rises.
- Loop diuretics do not reverse intrinsic AKI or improve kidney recovery by themselves; use them to manage volume and electrolyte goals when the patient can respond.
- Dose vasoactive and antihypertensive therapy to the overall perfusion phenotype rather than a universal renal-perfusion-pressure number.

Recovery, AKD & Post-ICU Kidney Follow-Up

Kidney injury can persist after the ICU even when dialysis stops or creatinine partially improves.

- Track creatinine, urine output, electrolyte/acid-base stability and medication clearance during recovery; falling creatinine can lag behind improving filtration and is affected by muscle loss and dilution.
- Persistent kidney dysfunction after the acute phase should be recognized as an AKI-to-AKD/CKD continuum rather than assumed to be complete recovery at hospital discharge.
- Reconcile renally cleared drugs, RAAS/SGLT2/diuretic therapy and nephrotoxins as physiology stabilizes; restart beneficial chronic therapies when clinically appropriate rather than leaving them stopped indefinitely.
- Arrange follow-up kidney function and albuminuria/proteinuria assessment after significant AKI, especially after KDIGO stage 2-3 injury or kidney-replacement therapy.

FOUNDATION SOURCES

1. Irwin & Rippe's Intensive Care Medicine, 9th Edition, 2023 - Chapters on Acute Kidney Injury in the ICU, Pathophysiology and Prevention of AKI, and Drug Dosing in Renal Dysfunction
2. KDIGO Clinical Practice Guideline for Acute Kidney Injury, Kidney Int Suppl 2012;2(1):1-138 (with 2026 update framework notes)

LINKED EVIDENCE

1. Kidney Disease: Improving Global Outcomes KDIGO 2012 (2012). KDIGO Clinical Practice Guideline for Acute Kidney Injury. Status: current.
2. Kidney Disease: Improving Global Outcomes KDIGO 2026 (draft) (2026). KDIGO 2026 AKI/AKD Guideline - Public Review Draft. Status: public-review-draft.
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4. STARRT-AKI (2020). Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury. New England Journal of Medicine. DOI: 10.1056/NEJMoa2000741.
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OTHER REFERENCES

1. Chawla LS, et al. Development and standardization of a furosemide stress test to predict the severity of acute kidney injury. Crit Care. 2013;17(5):R207.
2. Bellomo R, et al. Acute kidney injury. Lancet. 2012;380(9843):756-766.
3. Perazella MA. The urine sediment as a biomarker of kidney disease. Am J Kidney Dis. 2015;66(5):748-755.