SEPSIS CONFERENCE 2026

Kidney Injury in the Septic Patient

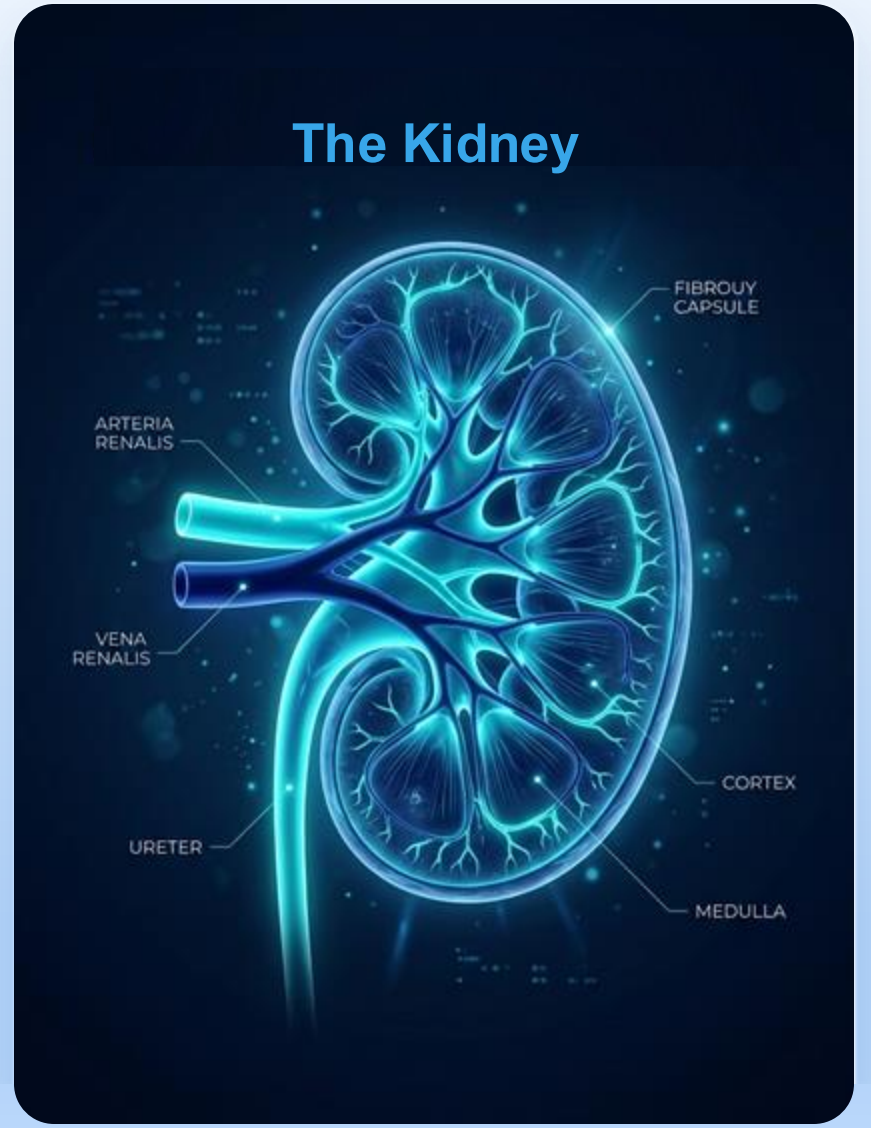
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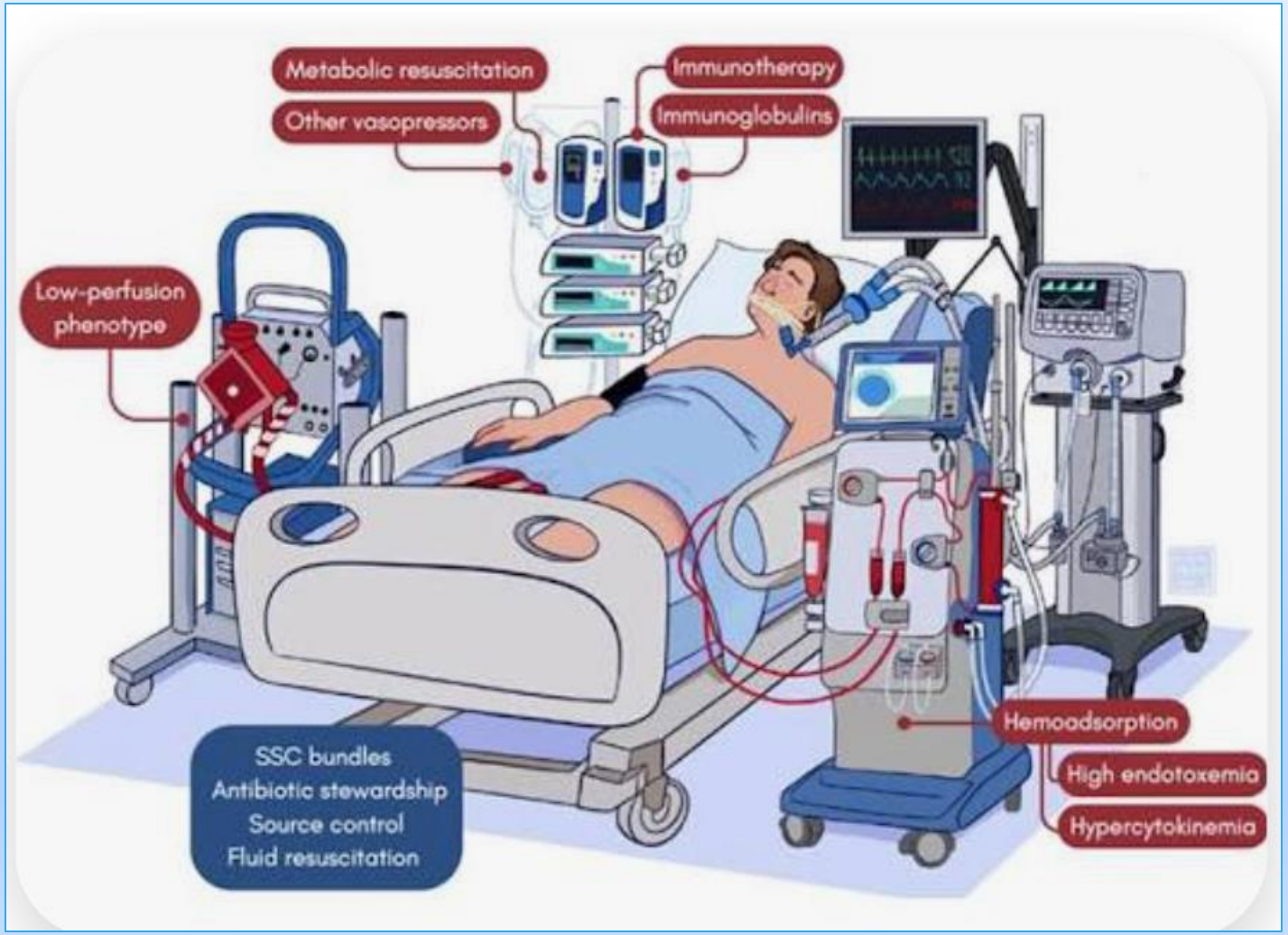
Vice President, Dallas Nephrology Associates

HURST CONVENTION CENTER • OCT 22, 2026



Disclosures

None relevant to this presentations



Objectives: AKI in Sepsis

01 Scope of the Problem

- **Incidence & Impact:** Effect on morbidity and mortality in septic patients.

02 Pathophysiologic Process

- **Vascular Alterations:** Macro- and microcirculatory dysfunction mechanisms.

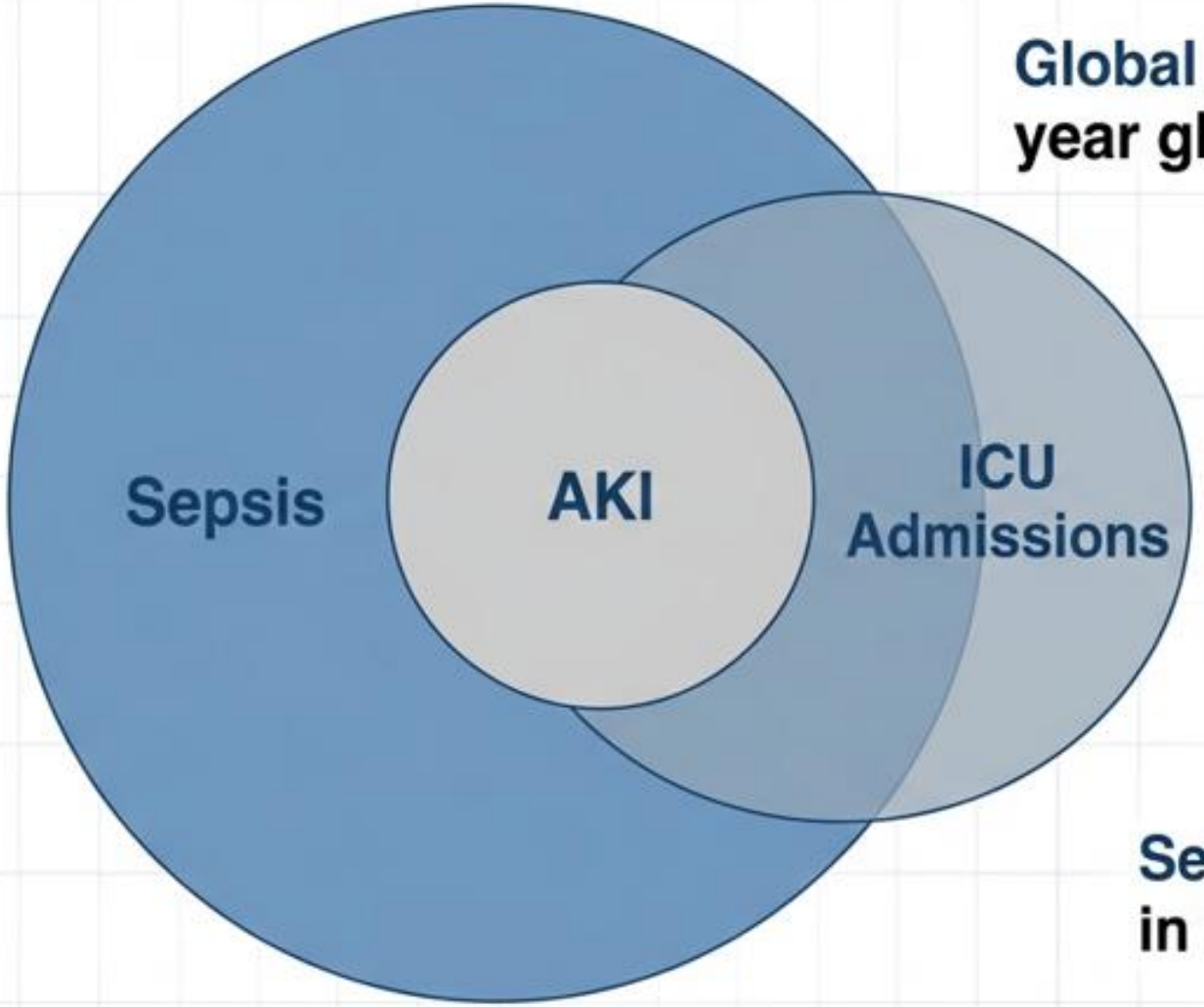
03 Supportive Therapies

- **Hemodynamics:** Vasopressors vs. fluid resuscitation
- **Fluid Selection:** Balanced solutions
- **Acid-Base:** Alkali therapy
- **Nutrition:** Metabolic & nutritional support

04 Renal Replacement Therapy (RRT)

- **Timing Strategy:** Early vs. late start evaluation
- **Modality Selection:** Choosing the optimal RRT modality

Scope of the Problem



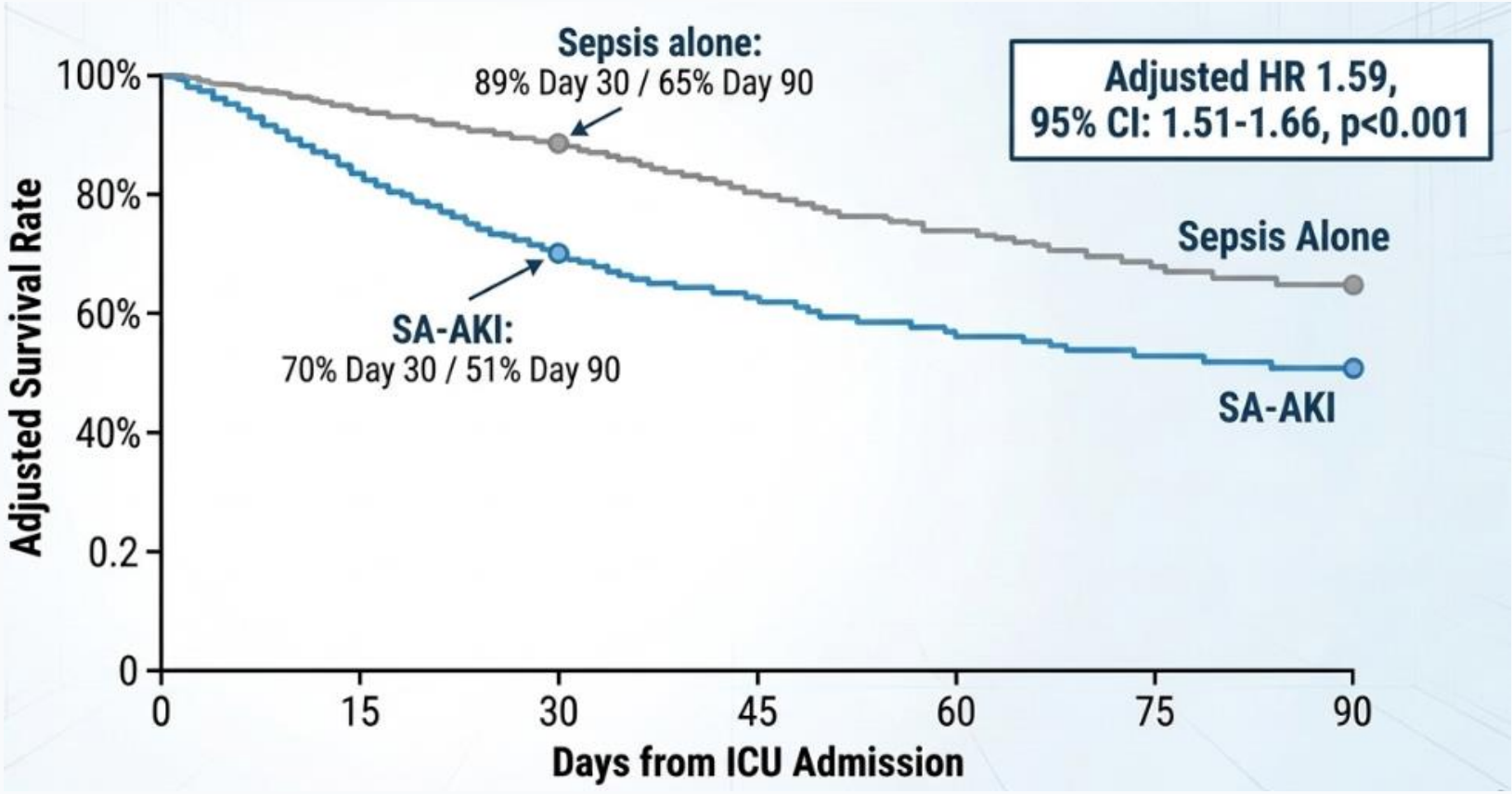
Global Burden: 6–10 Million cases per year globally

ICU Impact: Sepsis is the underlying cause for 45–70% of all ICU AKI cases

Patient Risk: 40–50% of all sepsis patients develop AKI

Severity Escalation: >90% of patients in septic shock develop AKI

The Immediate Stakes: In-Hospital Mortality

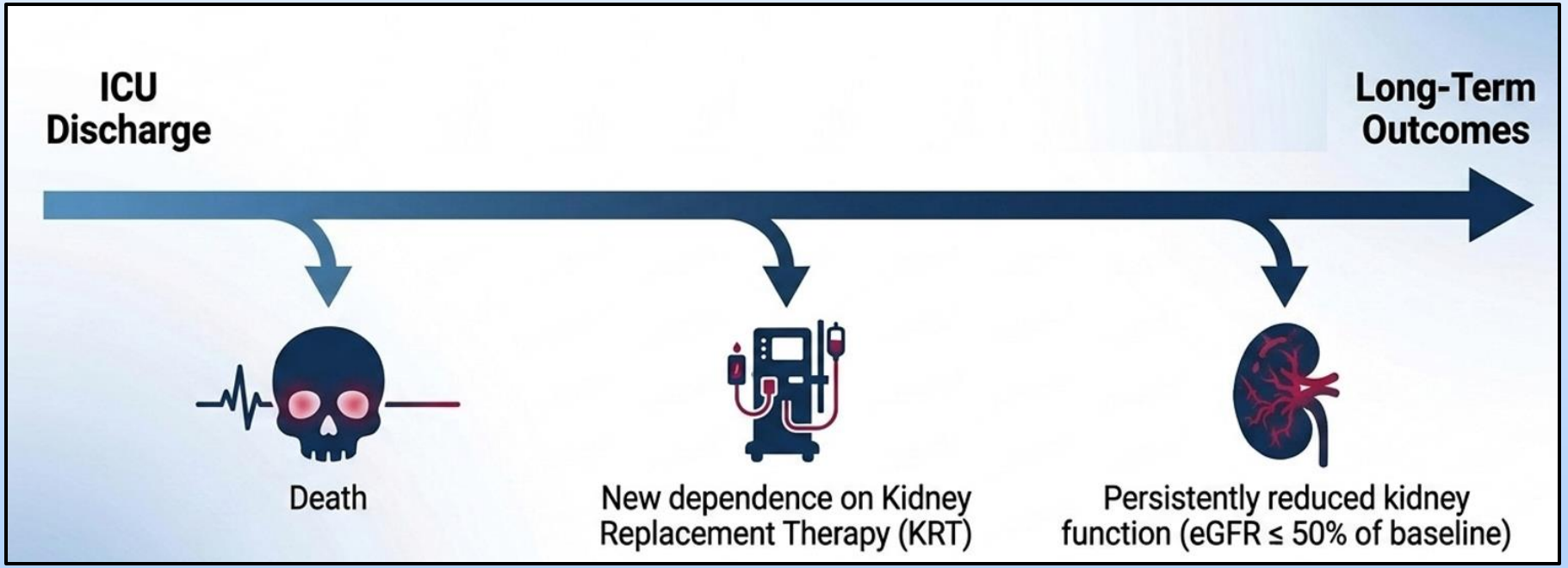


Systemic Failure Impact

Mortality is not explained solely by loss of kidney function; it **amplifies systemic failure**.

Long-Term Impact: Major Adverse Kidney Events

38% of SA-AKI survivors experience long-term sequelae



Even a single episode of SA-AKI significantly increases the subsequent risk of CKD or even ESRD

SA-AKI vs. Non-Septic AKI

Non-Septic AKI



Phenotype
Usually isolated organ failure

Severity
Usually KDIGO AKI Stages 1 and 2

Duration
Typically of short duration

Complexity
Usually low and transient

Sepsis-Associated AKI



Distinct Phenotype
Unique pathophysiology

Severity
Usually KDIGO AKI Stages 2 and 3 (severe)

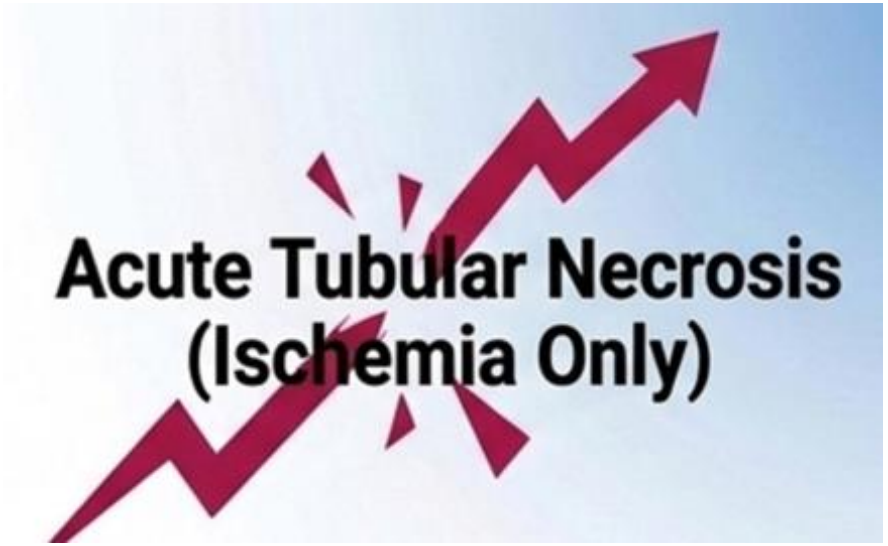
Duration
Significantly longer duration

Complexity
Concurrent with multi-organ failure, drastically **complicating the clinical trajectory**.

SA-AKI Pathophysiology: A Paradigm Shift

Re-evaluating sepsis-associated acute kidney injury mechanisms

THE OLD MODEL | ISCHEMIC ATN ONLY



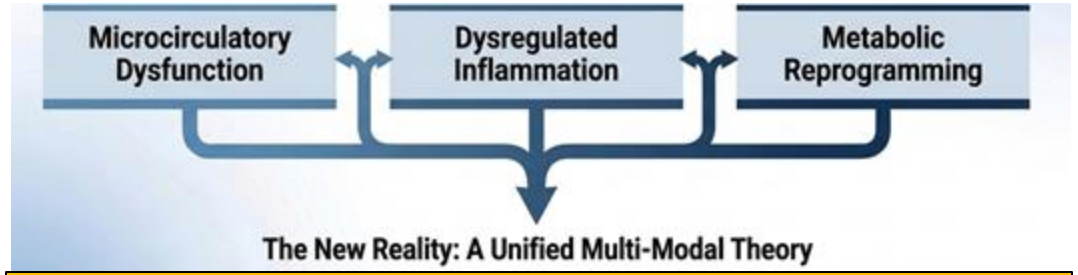
Historical Assumption

Ischemic injury due to systemic hypotension leading to Acute Tubular Necrosis (ischemia only).

The Flaw in the Old Model

Global renal blood flow is typically preserved or even increased in early sepsis

THE NEW REALITY | UNIFIED MULTI-MODAL THEORY



Complex cascade extending beyond hypoperfusion, driven by three synergistic pathways:

1. Microcirculatory Dysfunction

Intra-renal blood flow redistribution, localized capillary shunting, and patchy perfusion loss.

2. Dysregulated Inflammation

Systemic inflammatory cascade, cytokine storm, and immune-cell-mediated microvascular damage.

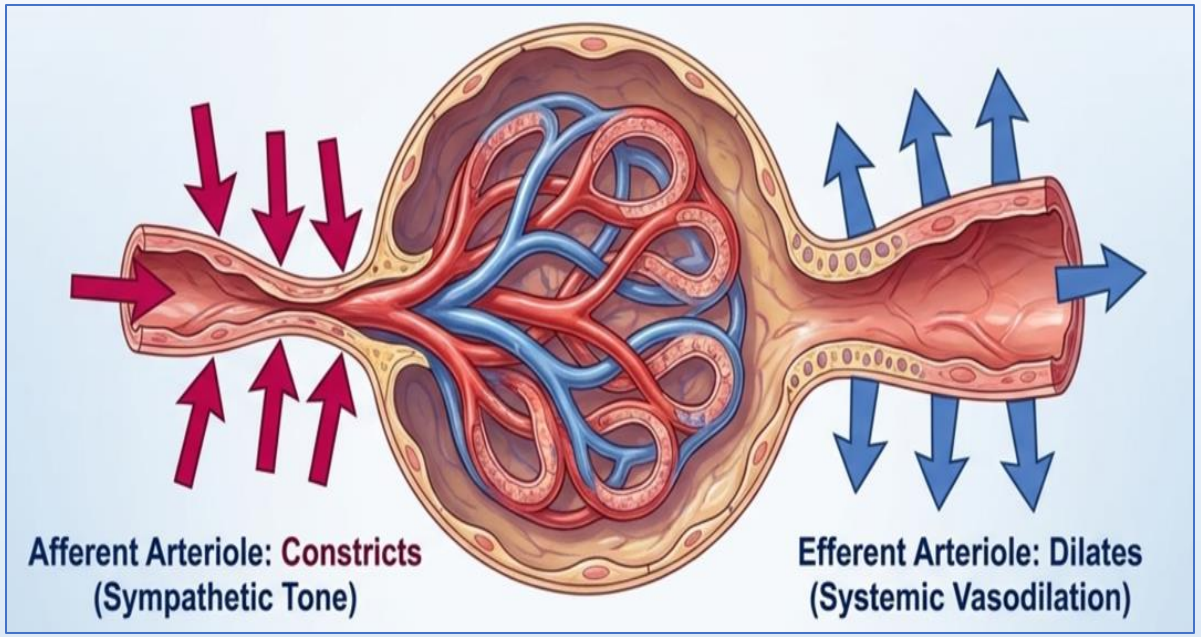
3. Metabolic Reprogramming

Adaptive down-regulation of oxidative metabolism preserving tubular cell viability under stress.

Microcirculatory Mismatch

Renal hemodynamic alterations and localized capillary perfusion breakdown

GLOMERULAR HEMODYNAMICS & FILTRATION GRADIENT



01 | MACRO VS. MICRO CIRCULATION

Decoupled Circulation

Macro-circulation (systemic) and micro-circulation (renal) decouple entirely.

Result: Loss of glomerular filtration despite preserved or elevated total organ blood flow.

02 | CAPILLARY OBSTRUCTION

Microthrombi Formation

Inflammatory cascades promote localized microvascular thrombosis within the renal capillaries.

Impact: Blocks localized capillary perfusion, inducing patchy focal ischemia and cell stress.

GLOMERULAR PRESSURE ↓

Afferent Arteriole: Constricts via sympathetic tone.

Efferent Arteriole: Dilates due to systemic vasodilation.

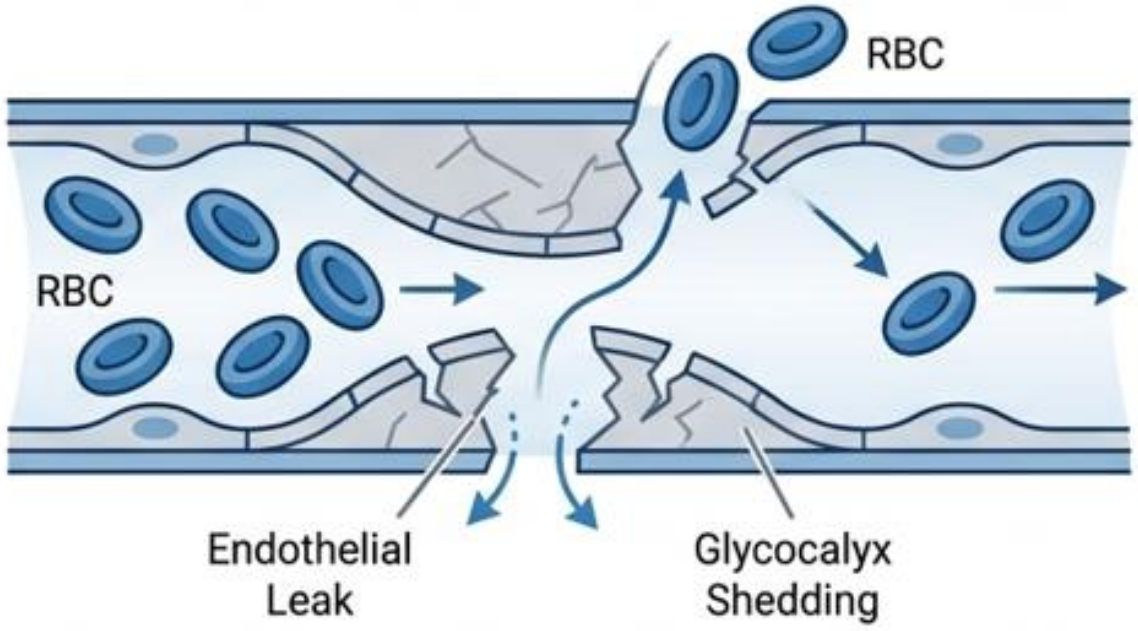
→ **Loss of intraglomerular driving pressure drops GFR.**

Functional loss, w/o systemic hypoperfusion

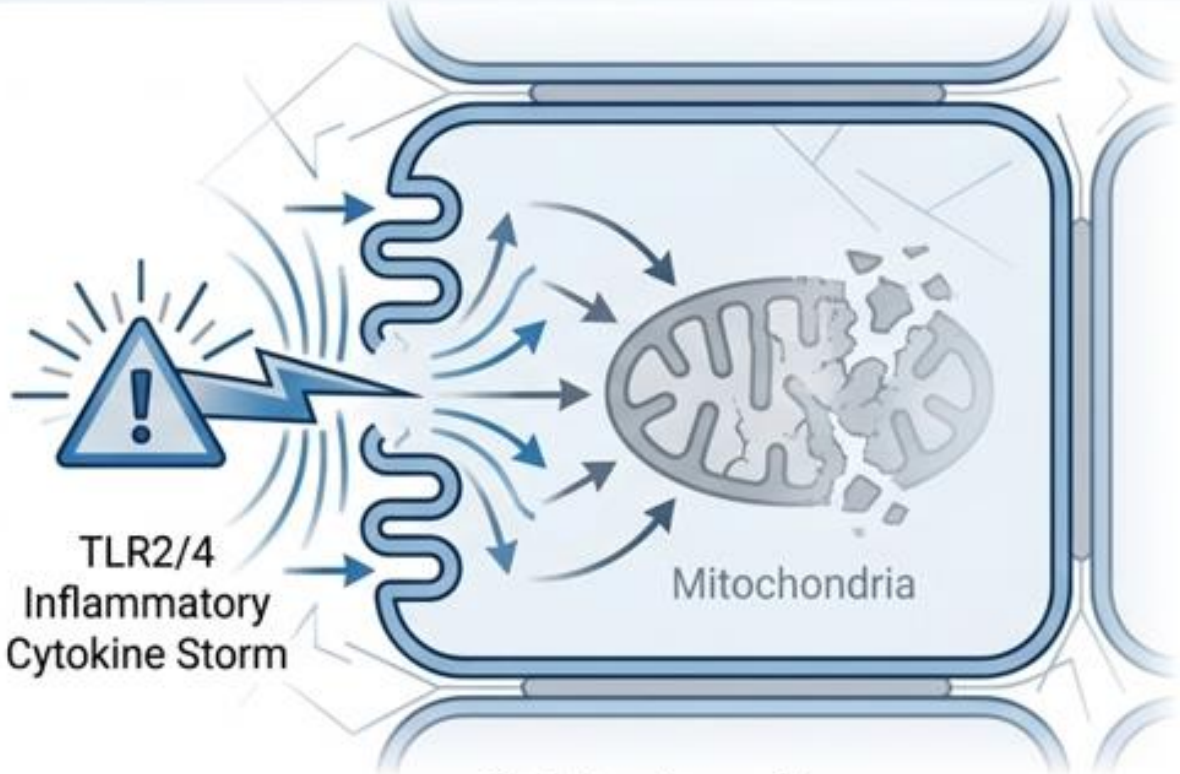
Unlike classic ischemic ATN, acute GFR failure in sepsis is driven by altered intra-renal vascular resistance and microthrombi rather than global renal ischemia.

The Mechanism of Injury: A Two-Front War

- **Vascular Disruption:** Breakdown of the endothelial barrier and shedding of the protective glycocalyx leads to profound microvascular perfusion heterogeneity.
- **Cellular Assault:** Toll-like receptors (TLR2/4) trigger a massive inflammatory cascade directly impacting tubular cells.



Microvascular Perfusion Heterogeneity



Cellular Assault

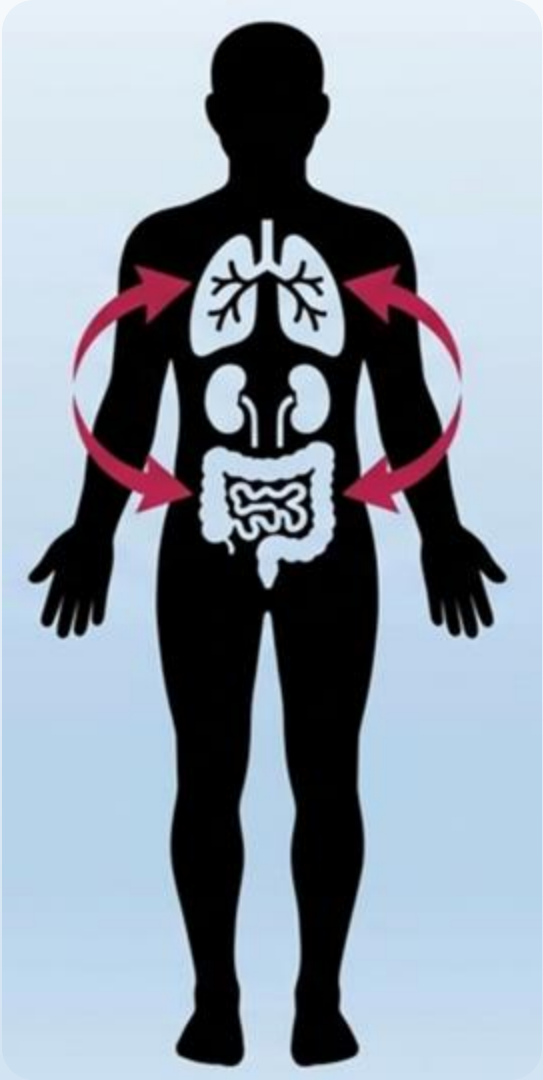
Pathophysiology: Organ Crosstalk

Heart-Kidney Axis

Right heart strain with congestion and increased intra-thoracic pressure impede renal venous outflow → AKI

Lung-Kidney Axis

Ventilator-induced lung injury releases systemic inflammatory cytokines → AKI



Gut-Kidney Axis

Systemic inflammation erodes intestinal barrier → allowing bacterial translocation → AKI

A Vicious Cycle

Loss of renal function leads to fluid accumulation → lung and gut edema.

Summary of Core Principles

1. **Massive Burden:** SA-AKI occurs in half of all sepsis patients, radically amplifying morbidity in the ICU.
2. **Multi-Modal Injury:** Pathophysiology extends far beyond ischemia, driven by microvascular mismatch, inflammation, and metabolic shutdown.
3. **Severe Stakes:** The addition of AKI to sepsis dramatically increases acute mortality and long-term risk of ESRD (MAKE).

MAKE: **M**ajor **A**dverse **K**idney **E**vents

4. **Watch and Wait:** Clinical trial evidence strongly favors **delayed RRT initiation** unless absolute, life-threatening indications emerge. **(There are exceptions)**
5. **Tailored Modality:** CRRT and IHD offer equivalent survival; the choice is dictated entirely by patient hemodynamics and clinical urgency. **(? - new data)**

Treatment Paradigm: Four Pillars of Renal Support



PILLAR 1

Hemodynamics

Vasopressor strategies & perfusion targets



PILLAR 2

Fluid Stewardship

Balanced crystalloids, active de-resuscitation



PILLAR 3

Acid-Base

Targeted sodium bicarbonate therapy

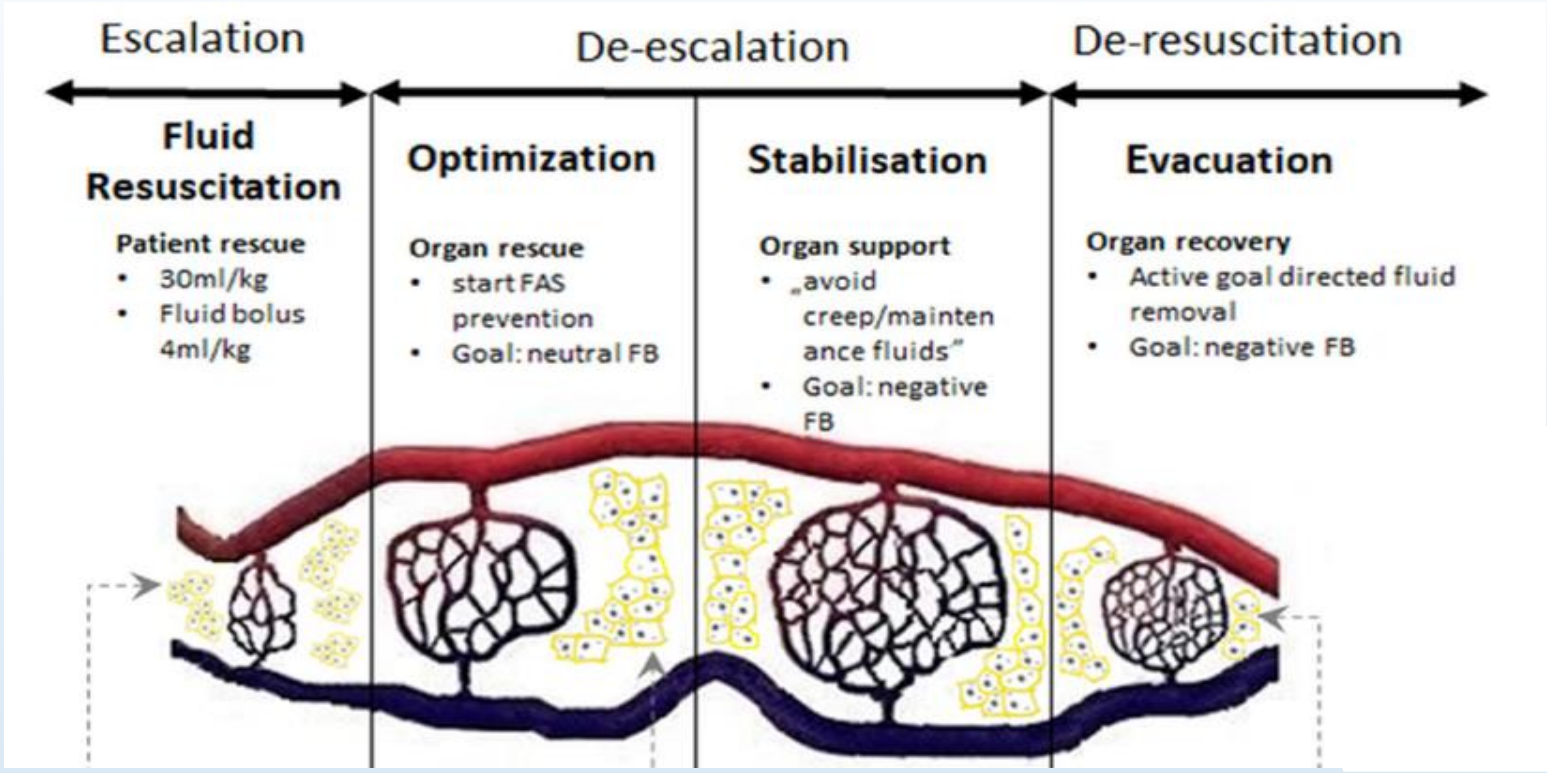


PILLAR 4

Metabolic Support

Protein dosing, and fluid minimization

Pillar 1: Hemodynamic Targets & First-Line Support



- **Early NE initiation is preferred over excessive fluid loading if fluid-unresponsive**
- **Protocoled early peripheral vasopressor reduces cardiogenic pulmonary edema**
- **Goal is to restore adequate organ perfusion without precipitating venous congestion**

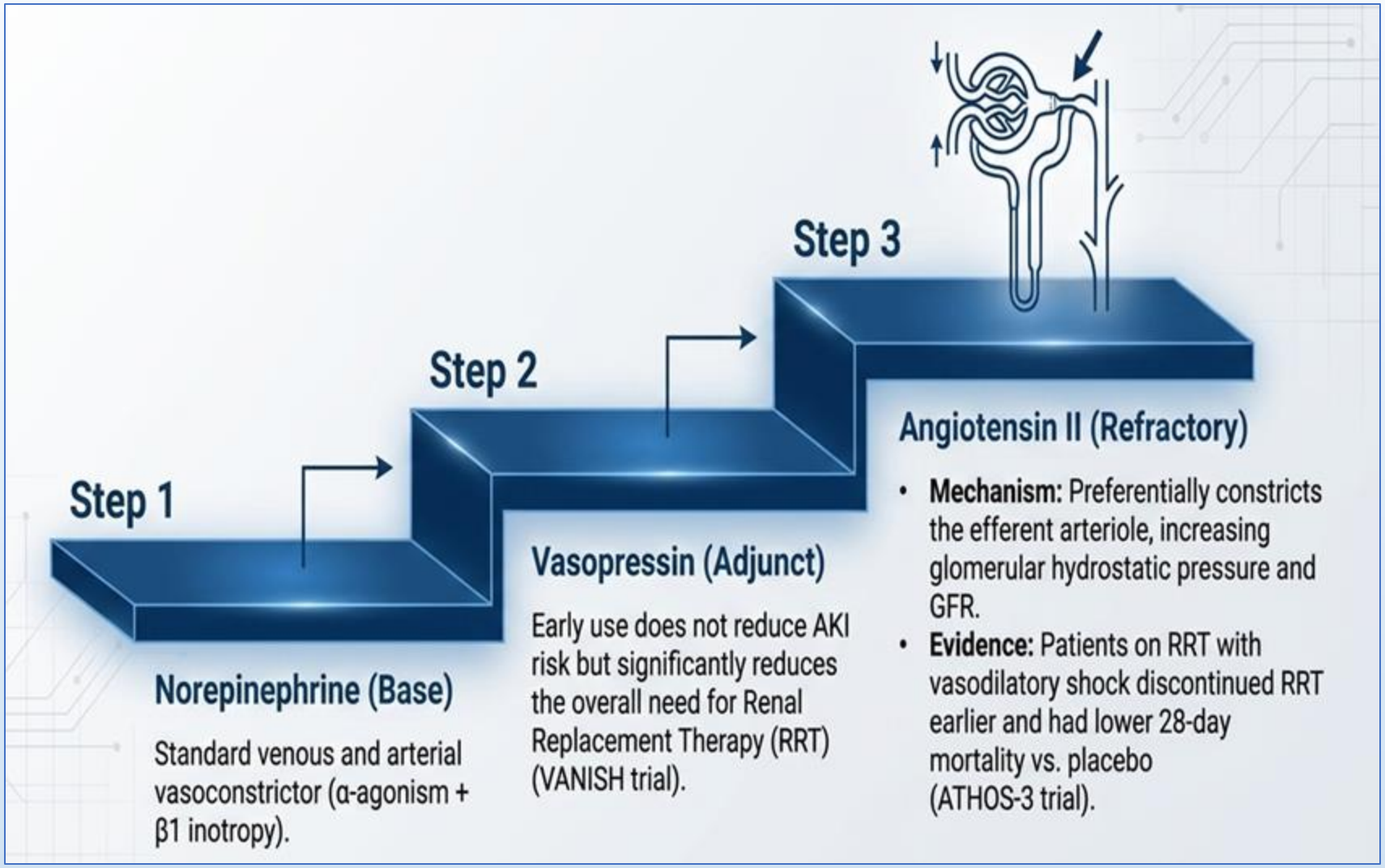
Pillar 1: Vasopressor Escalation

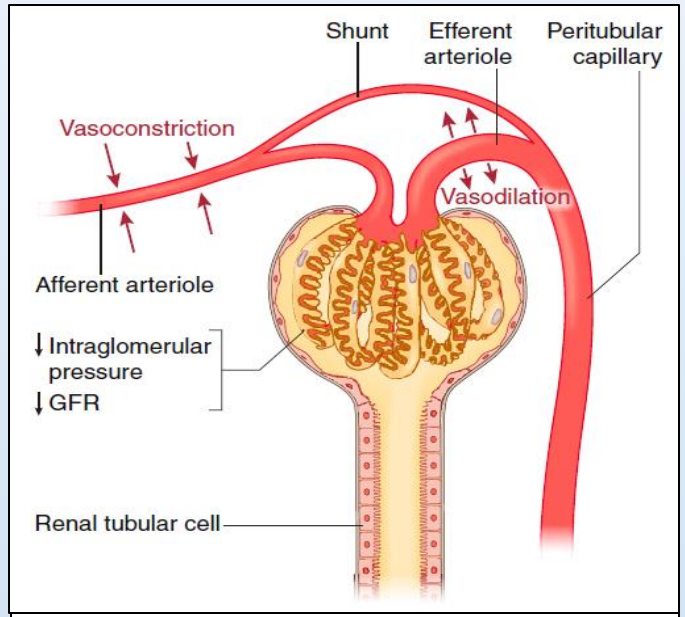
Target Dashboard

MAP Target: >65 mmHg

(Note: Targeting >85 mmHg in pre-existing hypertension reduces RRT but does not improve survival).

First-Line Agent: Norepinephrine (NE)





Renal Perfusion in Sepsis

Fluid Resuscitation vs Vasopressors: Key Clinical Trials

	CLASSIC (2022)	CLOVERS (2023)	ARISE FLUIDS (2026)
SETTING & POPULATION	ICU (N=1,554)	Emergency Department (N=1,563)	Emergency Department (N=1,000)
THE BASELINE	Septic shock already receiving >1L IV fluids.	Sepsis-induced hypotension after 1-3L initial IV fluids.	Early septic shock after ≥1L initial IV fluids.
RESTRICTIVE STRATEGY	Fluids ONLY for severe hypoperfusion/losses. Median 24h volume: 1,798 mL	Vasopressor-dominant with rescue fluids. Median 24h volume: 1,267 mL	Immediate vasopressors; 250mL boluses if indicated. Median 24h volume: 1,140 mL
LIBERAL STRATEGY	Standard Surviving Sepsis guidelines. Median 24h volume: 3,811 mL	2L initial infusion + clinical triggers for more. Median 24h volume: 3,400 mL	Up to 1L initial bolus + 500mL boluses for hypoperfusion. Median 24h volume: 2,248 mL

CLINICAL SYNTHESIS & SAFETY SIGNALS

Early Vasopressors / Restrictive Fluids

Liberal Fluids / Rescue Vasopressors



Zero significant difference in 90-day mortality, renal replacement therapy, or days alive and out of hospital.

SAFETY SIGNAL: PULMONARY EDEMA



Aggressive fluid resuscitation carries a documented, heavier weight of adverse safety signals.

THE VERDICT: Both strategies yield equivalent primary outcomes. Tailor resuscitation to individual patient hemodynamics while guarding against fluid-induced pulmonary edema.

Pillar 1: Hemodynamic Timing & Renal Protection





Avoid: Fluid-Driven Resuscitation

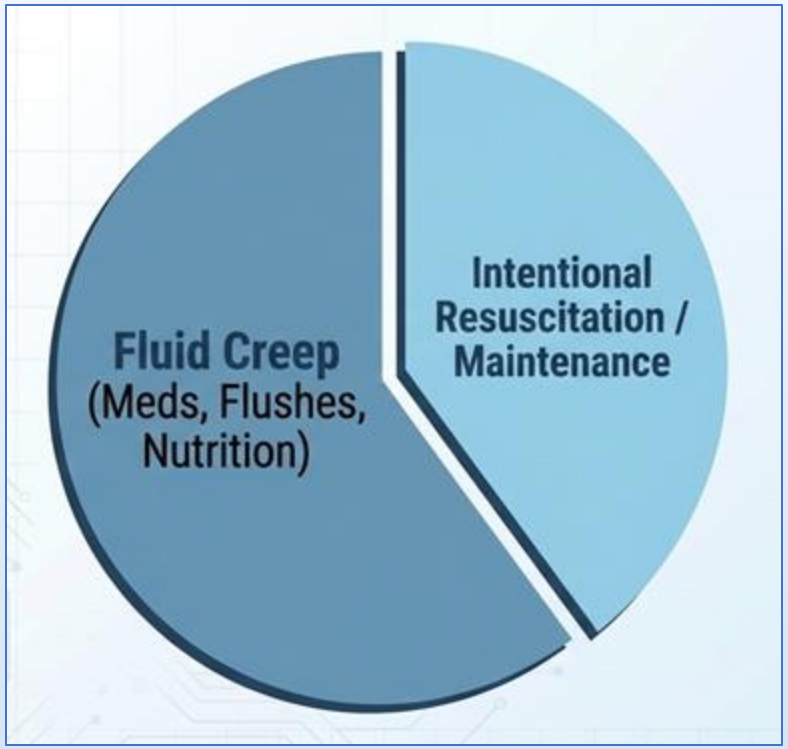
- Risk of capsular organ edema (kidneys).
- Renal venous congestion and intra-abdominal pressure (drop in GFR)

Adopt: Early Vasopressor Strategy

- Helps restore perfusion pressure.
- Allows for a more fluid-restrictive approach.
- Prevents transcapillary fluid leak

Individualize Approach – Patient-driven Decision Making

Mitigate “Fluid Creep”



The Problem:

- **Fluids given with medications and flushes, nutrition, account for > 60% of total fluid input.**
- **Nutrition alone accounts for 25–33% of daily fluid intake.**

The Solution:

- **Mandate high-density enteral formulas (e.g., 2 kcal/mL)**
- **Concentrated medication administration**

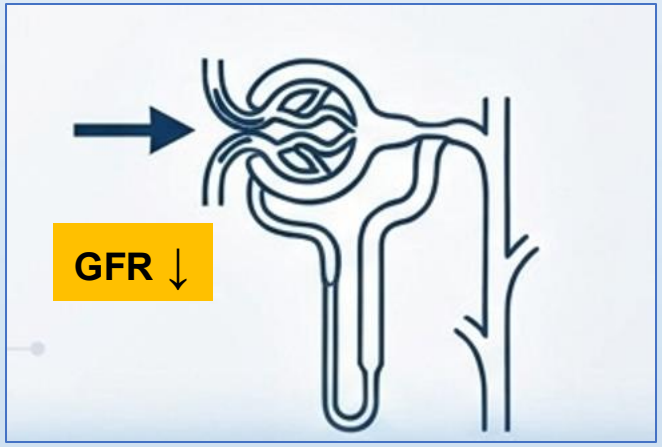
Pillar 2: Fluid Selection Matrix

0.9% Normal Saline

- High chloride concentration.
- Induces afferent arteriole vasoconstriction.
- Reduces renal blood flow and GFR.

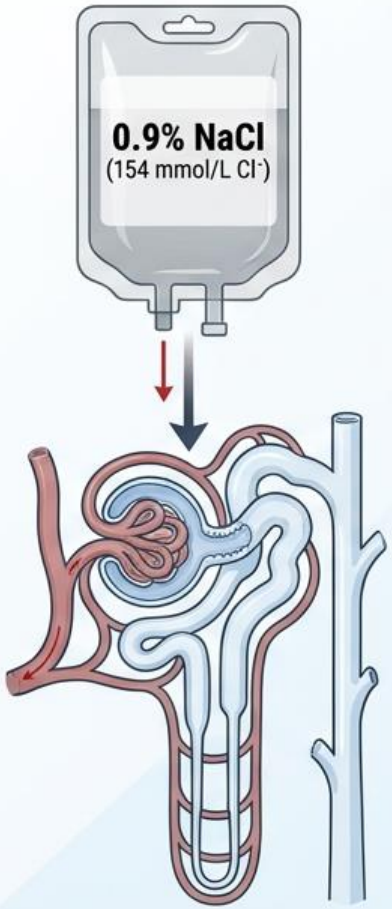
Balanced Crystalloids

- Physiological chloride levels.
- Reduces hyperchloremic metabolic acidosis.
- Benefits on kidney function and MAKE, mortality?



The Physiologic Rationale

0.9% Normal Saline



Supraphysiologic Chloride Load

↓

Increased Macula Densa Sensing (NKCC2 channel uptake)

↓

Tubuloglomerular Feedback Activation

↓

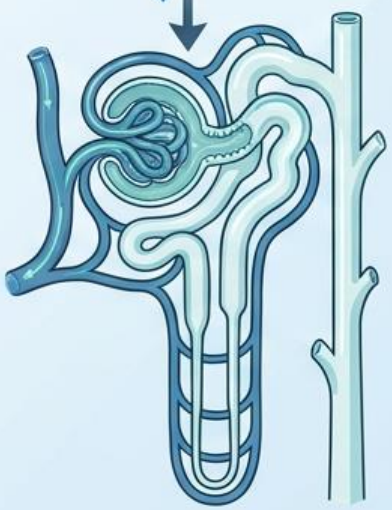
Afferent Arteriolar Vasoconstriction

↓

Result: Reduced GFR & Renal Blood Flow

Balanced Crystalloids





Plasma-like Chloride Concentration

↓

Normal Macula Densa Signaling

↓

Avoidance of Hyperchloremic Metabolic Acidosis

↓

Result: Maintained GFR & Renal Perfusion

The Evidence Base: >100,000 Patients Analyzed

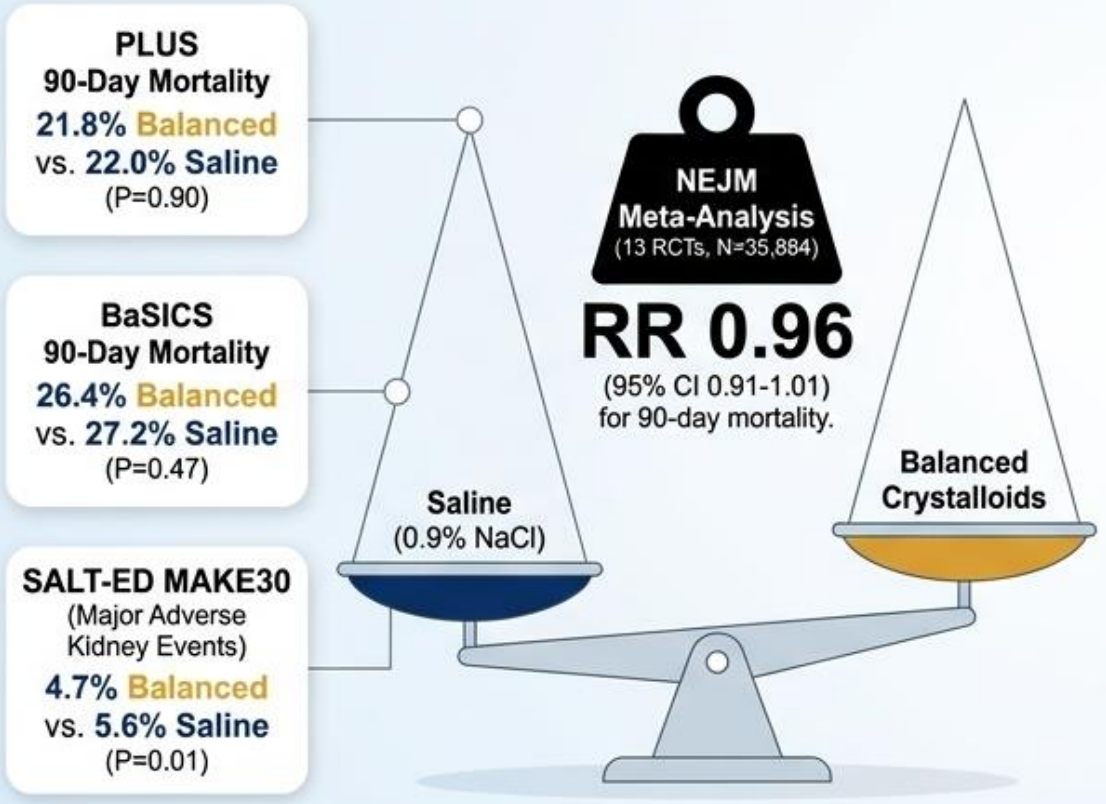
Global Cohort Matrix

Critical Care (ICU)	**BaSICS** N=11,052 Factorial, Double-blind	**PLUS** N=5,037 Double-blind RCT	**SMART** N=15,802 Multiple-crossover	**SPLIT** N=2,278 Double-blind, Crossover
Emergency & Ward	**SALT-ED** N=13,347 Multiple-crossover	**FLUID** Hospital-wide Cluster-crossover		
Pediatrics	**PRoMPT BOLUS** N=9,041 Pragmatic RCT			
Specialty (Transplant)	**BEST** N=807 Double-blind RCT			

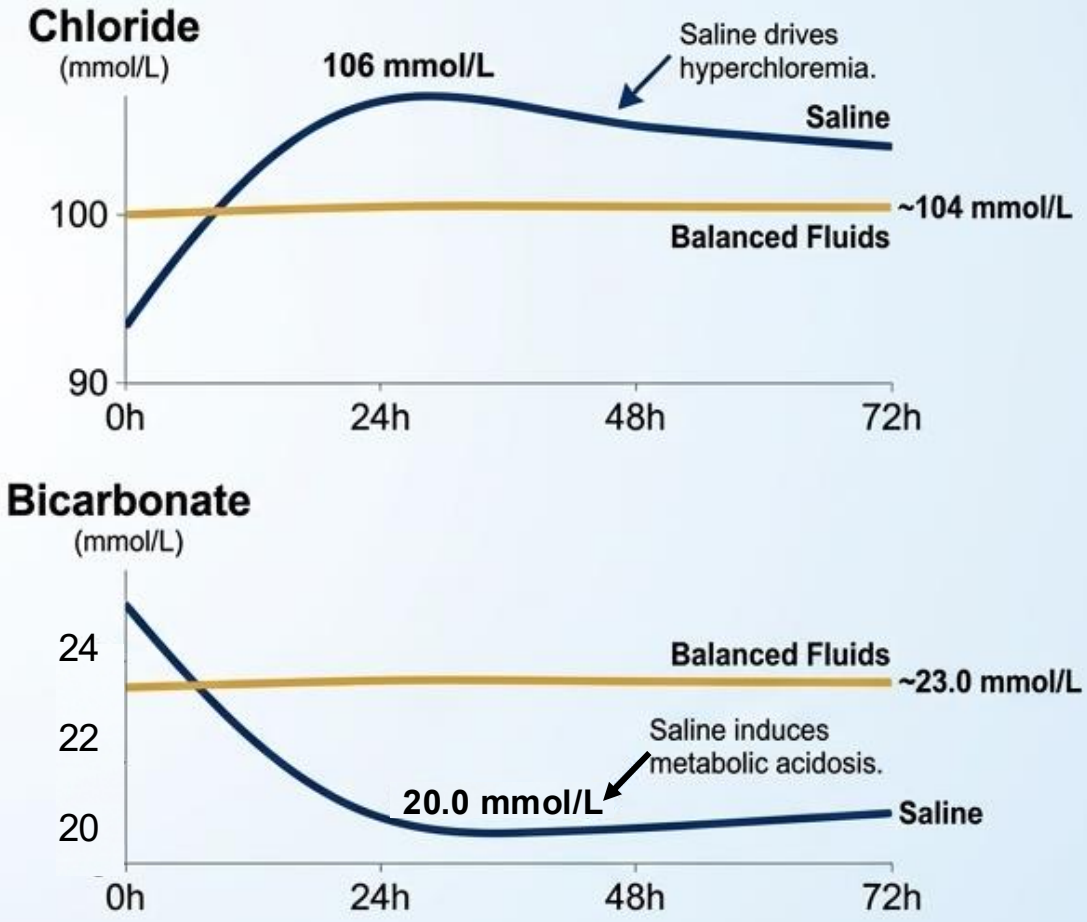
= Double-blind
= Crossover design
= Cluster-randomized

Macro Outcomes: Marginal Absolute Differences, Divergent Physiology

The Macro-Outcome Balance Scale



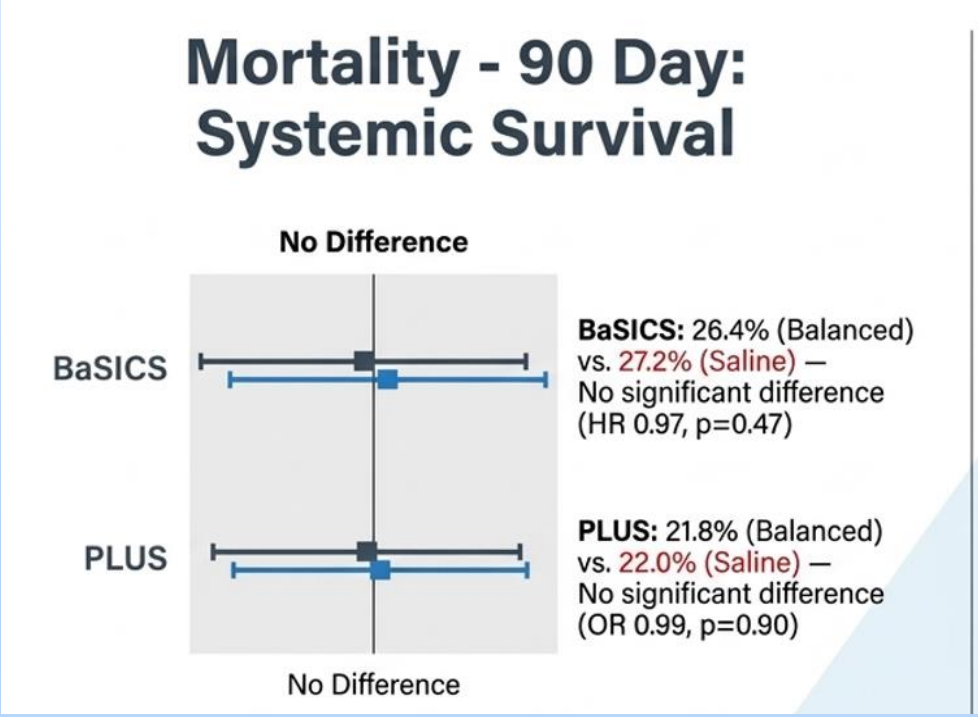
The Physiological Divergence

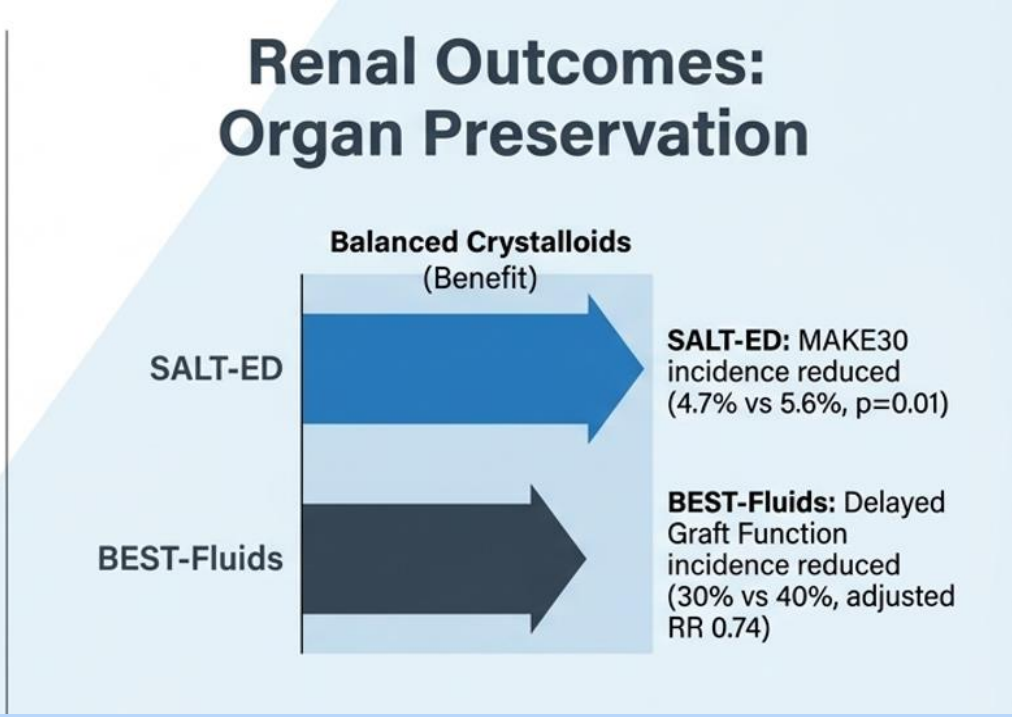


Mortality vs Renal Protection

No significant mortality benefit in general ICU populations

Kidney protection at 30 days and reduced RRT

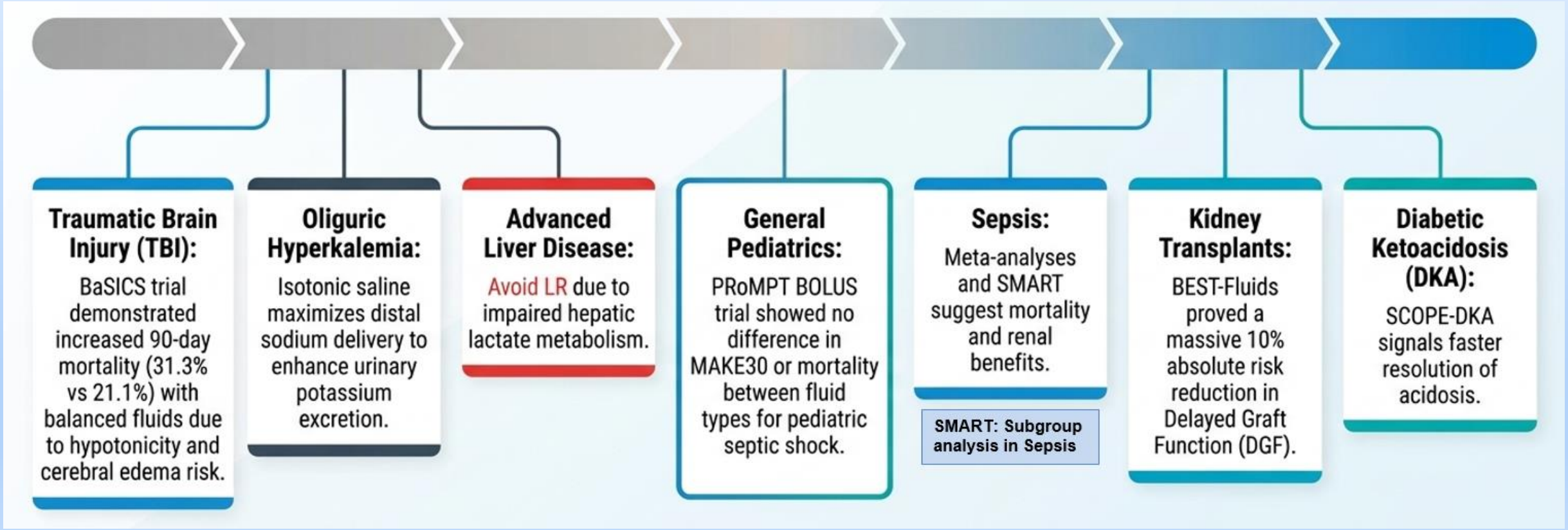




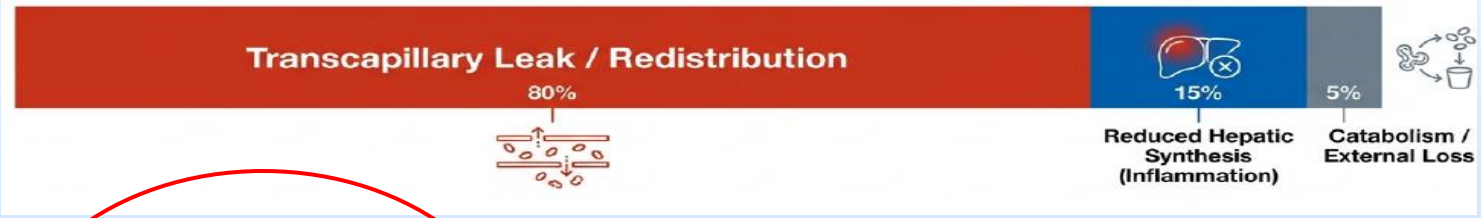
Sepsis subgroup in SMART: MAKE30 favored balanced fluids

FLUID CHOICE in clinical settings

Favors 0.9% Saline	Equipoise	Favors Balanced Fluids



Causes of Low Serum Albumin in Acute Illness



80%

Capillary leak

Albumin redistributes into the interstitium via VEGF-mediated permeability.

15%

Reduced hepatic synthesis

IL-6 and TNF-α down-regulate albumin gene transcription.

5%

Catabolism / loss

Renal, GI, or wound-bed losses; hyper-catabolism.

Causes of Low Serum Albumin in Chronic Illness

80%

Reduced hepatic synthesis

IL-6 and TNF-α down-regulate albumin gene transcription.

15%

Catabolism / loss

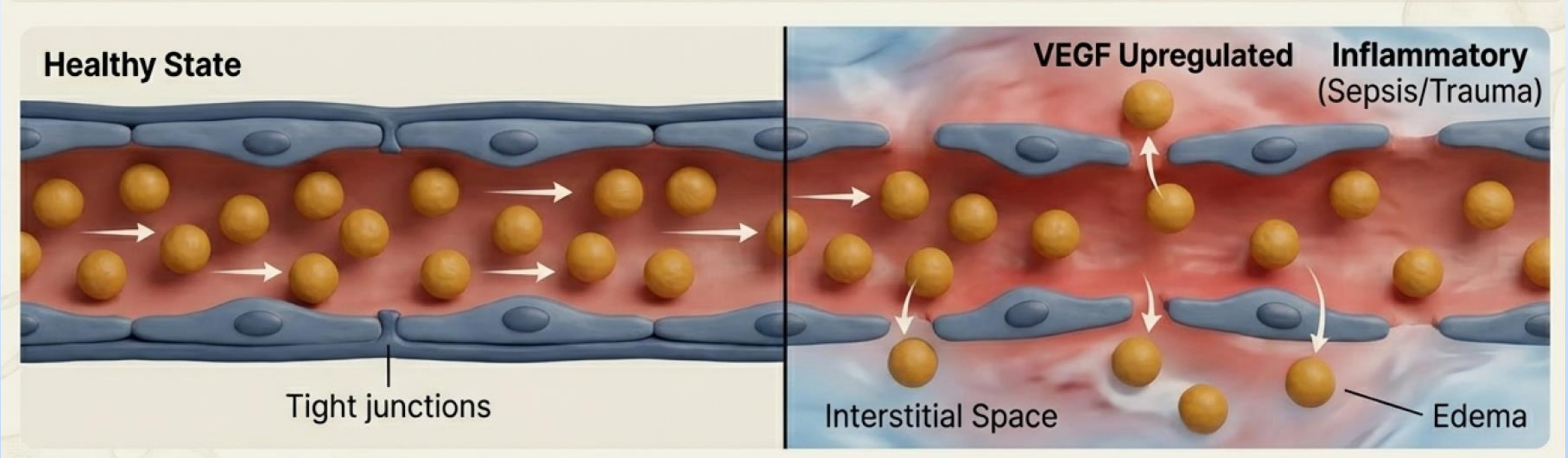
Renal, GI, or wound-bed losses; hyper-catabolism.

5%

Capillary leak

Albumin redistributes into the interstitium via VEGF-mediated permeability.

Capillary Leak of Serum Albumin



1 Trigger

Sepsis or surgery releases IL-6 and TNF-α.

2 Permeability

VEGF widens endothelial gaps; glycocalyx degrades.

3 Transcap. Escape

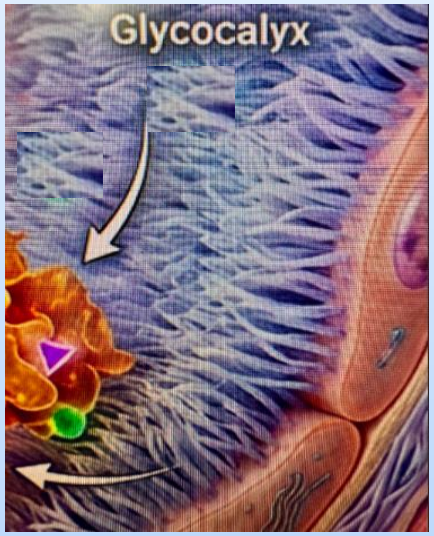
Albumin shifts from plasma into the interstitium.

4 Dilution

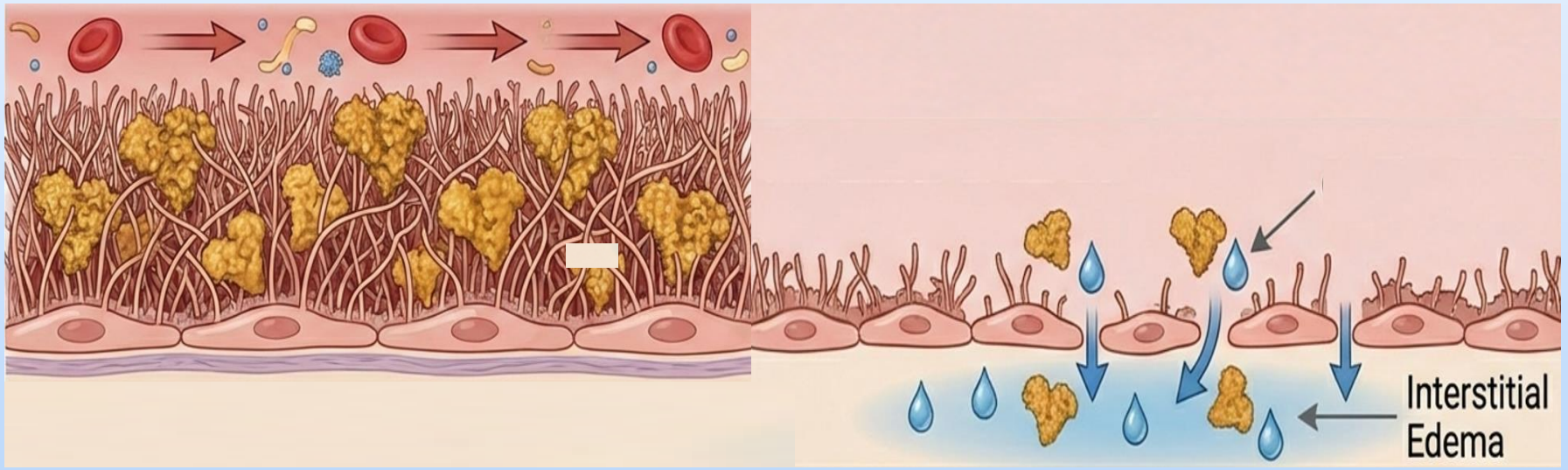
Interstitial volume expands, lowering serum concentration.

Loss of Endothelial Glycocalyx Barrier

Healthy State



Sepsis and Inflammation



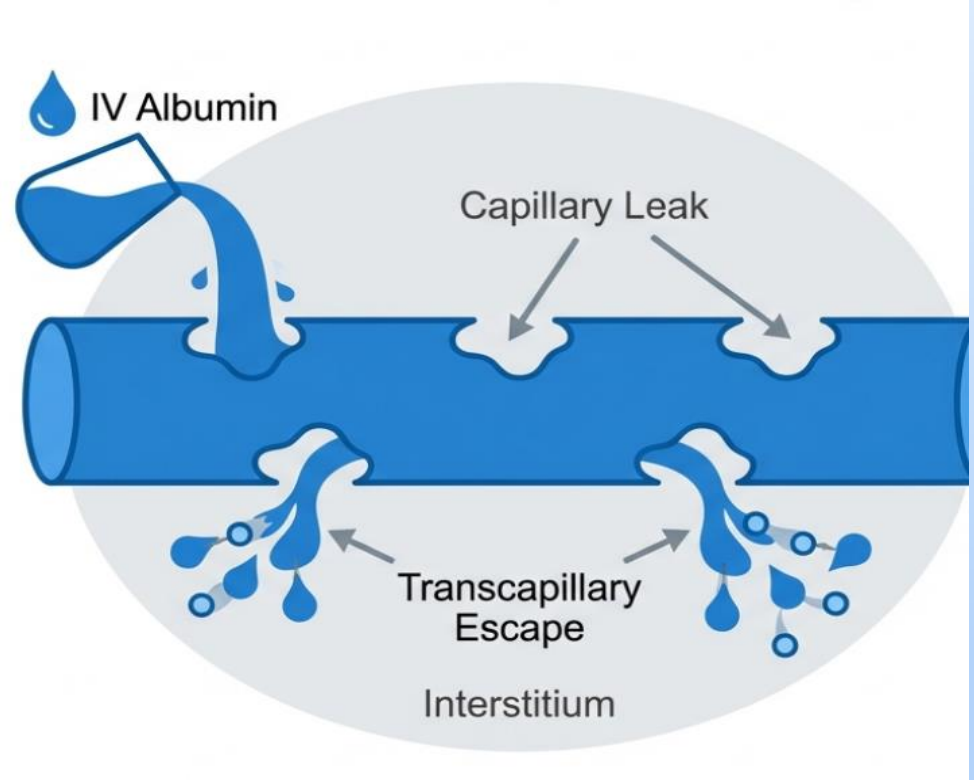
Albumin floats AND is structurally embedded in the glycocalyx barrier

"A microscopic, slippery web of hair-like sugars and proteins coating the endothelial layer like the ultimate non-stick Teflon coating and a physical shield"

Sepsis / Inflammation → Degradation of barrier → extravasation of albumin into interstitial space

Clinical Consequence: Why IV Albumin Doesn't Fix Edema

*The **leaking-bucket problem** in capillary disruption*
Edema does not reflect intravascular volume



Filling a Leaking Bucket

In inflammatory states, the endothelial barrier is compromised.

Transcapillary Escape

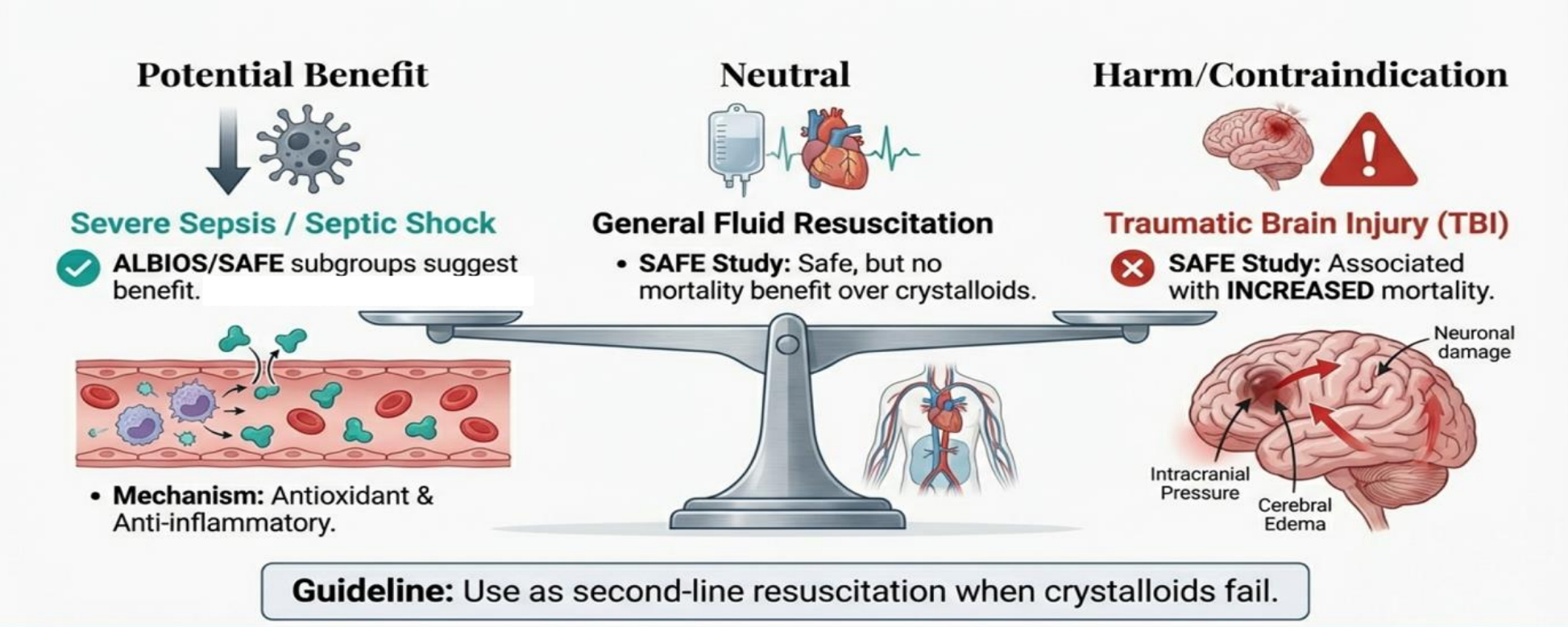
Infused albumin rapidly redistributes from the vascular space into the interstitium.

Reverse Effect

Interstitial albumin raises tissue oncotic pressure – progressive edema without volume benefit.

Your critically ill patient with generalized edema will still need crystalloids to fill the intravascular space

CRYSTALLOIDS: Strongly recommended as first-line therapy



SAFE Trial N = 6,997

4% albumin vs. 0.9% saline : No difference in 28-day mortality

ALBIOS Trial N = 1,818

Target albumin >30 g/L in sepsis yielded no survival benefit.

JAMA Clinical Guideline Synopsis 2024:
Use of Intravenous Albumin

SUGGESTED USES
(CONDITIONAL RECOMMENDATIONS)



PATIENTS WITH CIRRHOSIS & ASCITES UNDERGOING LARGE-VOLUME PARACENTESIS (>5 L):
To prevent paracentesis-induced circulatory dysfunction (PICD)



PATIENTS WITH CIRRHOSIS & SPONTANEOUS BACTERIAL PERITONITIS (SBP):
To reduce mortality and kidney impairment

NOT SUGGESTED USES
(CONDITIONAL RECOMMENDATIONS)



HOSPITALIZED PATIENTS WITH DECOMPENSATED CIRRHOSIS & HYPOALBUMINEMIA (<3.0 g/dL):
Not for reducing infection, kidney dysfunction, or mortality by increasing albumin levels



CRITICALLY ILL ADULT PATIENTS
Not with diuretics for removal of extravascular fluid

EVIDENCE BASE: 47 studies (RCTs, systematic reviews)
SAFETY CONSIDERATIONS: Volume overload, anaphylaxis, hemodilution, peripheral gangrene

REFERENCE: Fuest S, Fischer C, Alexander JT. Use of Intravenous Albumin. *JAMA Clinical Guidelines Synopsis*. 2025;333(23):2104-2105

Pillar 3: Acid-Base Management

Sodium Bicarbonate in the ICU: A Comparative Analysis of Three Landmark Trials (BICAR-ICU, BICARICU-2, & SODa-BIC)

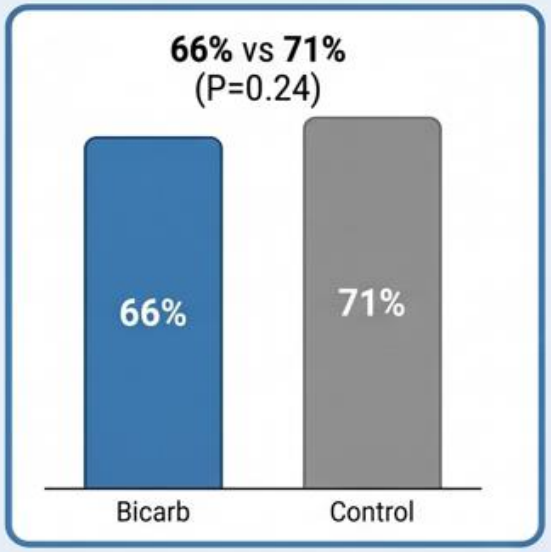
Summarizing clinical efficacy and outcome data of intravenous sodium bicarbonate for critically ill patients with metabolic acidemia.

Compares three major randomized controlled trials (2018-2026) evaluating sodium bicarbonate's impact on survival and renal outcomes across diverse ICU populations, ranging from general critical care to severe Acute Kidney Injury (AKI) or shock.

BICAR-ICU (2018)



Population Focus:
General ICU (pH ≤7.20)



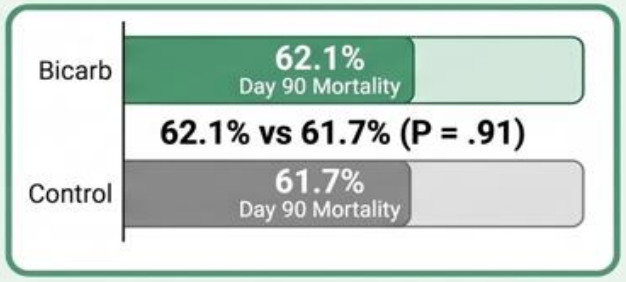
No Significant Mortality Benefit

All three trials failed to show a significant reduction in primary mortality endpoints.

BICARICU-2 (2025)



Population Focus:
AKI Stage 2-3 (pH ≤7.20)



No Significant Survival Difference

In patients with severe AKI, there was no survival difference.

Renal Impacts & Secondary Findings

15.5% Absolute Reduction in KRT Use

Bicarbonate significantly lowered the need for Kidney Replacement Therapy.

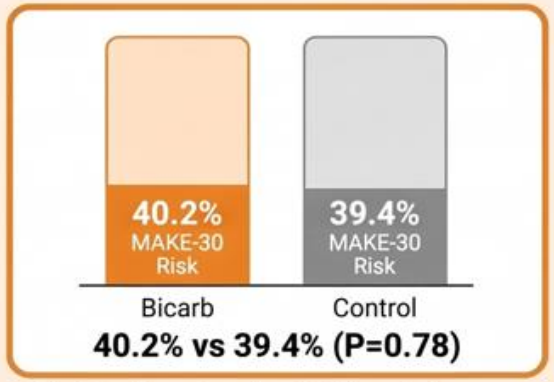
Delayed KRT Initiation

Bicarbonate therapy increased median time to KRT from 16 to 31 hours.

SODa-BIC (2026)



Population Focus:
Vasopressors (pH <7.30)



No Reduction in Major Adverse Kidney Events

Bicarbonate did not reduce MAKE-30 in patients on vasopressors.

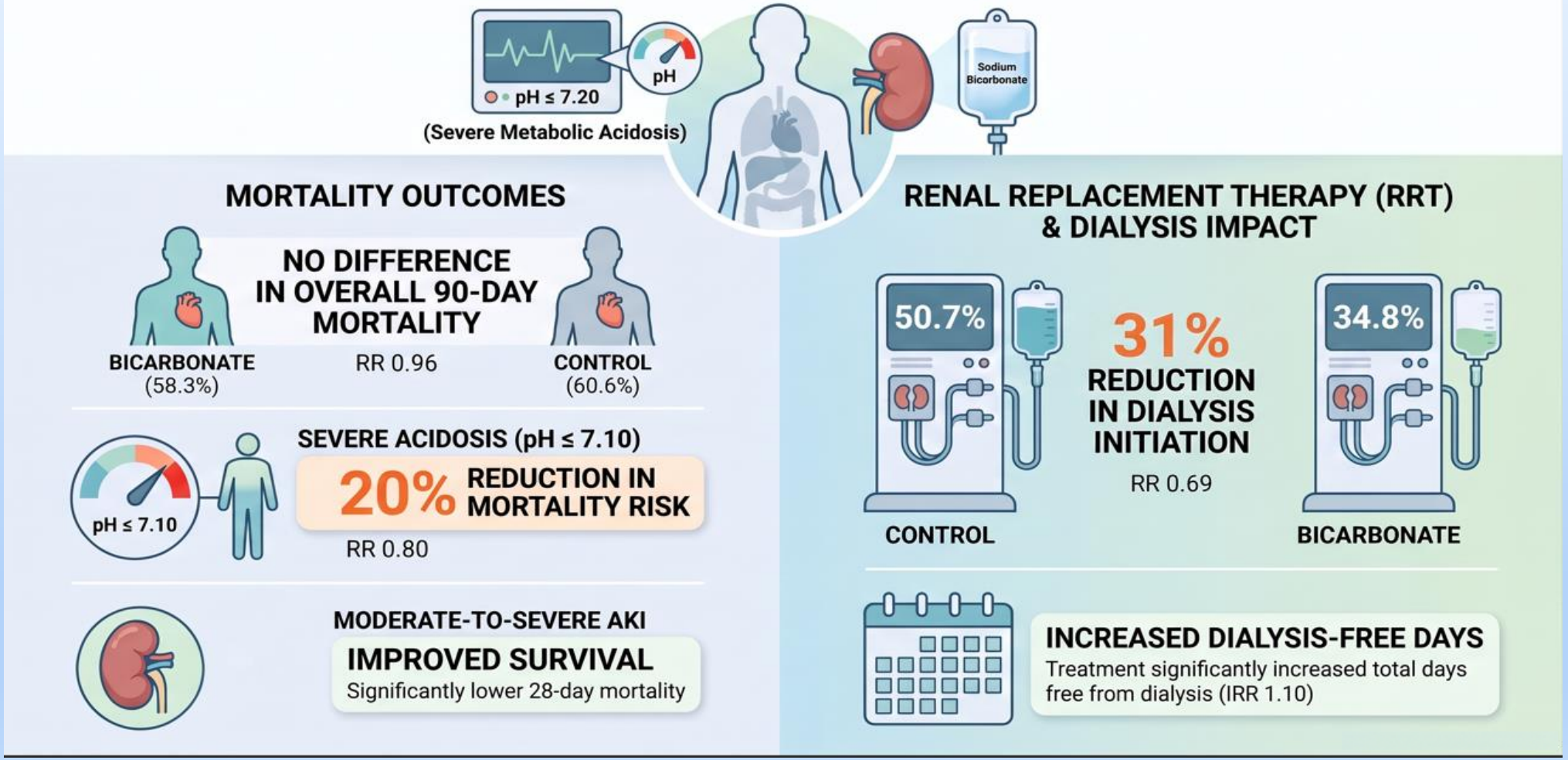
Physiological Correction

Rapid Physiological Correction

Faster pH and base excess normalization, despite lack of clinical benefit.

Subgroup Analysis: NaHCO3 in the ICU

Meta-analysis: 4 RCTs, total of 1,111 patients



Chen, J.J. et al: Acute Metabolic Acidosis in Critically Ill Adults: A Meta-Analysis of Randomized Clinical Trials. Critical Care Medicine, 54(8), 1870–1877, 2026



Norepinephrine remains first-line vasopressor over vasopressin or angiotensin II.

Crystalloid fluid bolus ≥ 30 mL/kg within 3 hours for sepsis-induced hypoperfusion/septic shock (but not for all patients – exceptions apply!). Crystalloids <u>alone</u> (without albumin)

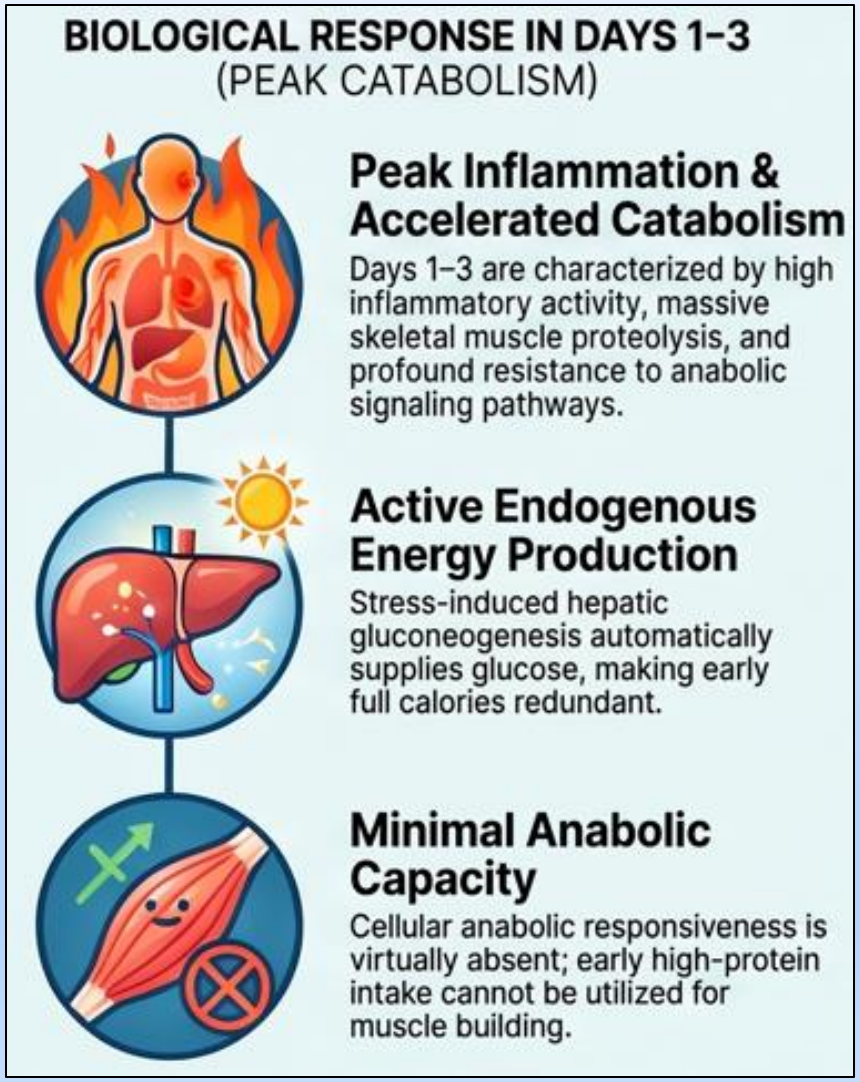
Active fluid removal following the acute resuscitation phase

Dynamic measures to guide fluid resuscitation over physical examination or static measures

May use Na-Bicarbonate in septic shock with severe acidosis (pH <7.2) and AKI

Pillar 4: Nutritional Strategies

- **Phase-specific approach:**
  - Shift from aggressive feeding to cautious nutrition for critically ill adults.
- **Early enteral nutrition (?supplemental parenteral)**
  - Preferred for gut health, short-term parenteral as a safe backup.
- **Avoid early full-doses:**
  - Early high-calorie or high-protein feeding offers no benefit (? measuring protein catabolic rate)
  - Potential for metabolic harm, especially in acute kidney injury.
- **Restrictive strategy:**
  - Manage energy delivery, control blood glucose, prevent refeeding syndrome.



Patel J et al : N Engl J Med 395:162-74, 2026

Acute Critical Care Nutrition: The "Less is More" Paradigm

Evidence-based guidelines for nutrition therapy in critically ill adults, emphasizing restrictive dosing in the early acute phase and proper monitoring safety.

Early Acute Phase (Days 1–3): Restrictive Dosing



Start Early Enteral Nutrition Within 24–36 Hours

Early enteral feeding supports gut barrier integrity and microbiome health better than parenteral feeding.

Apply Restrictive Caloric Intake (~25% Target)



Full-dose feeding during peak inflammation increases metabolic complications and gastrointestinal adverse events.

Avoid High-Dose Protein (>2.0 g/kg/day)



Standard protein (1.2–1.3 g/kg/day) is safer, as higher doses cause harm in acute kidney injury.

Late Acute to Recovery Phase: Progression & Safety



Advance Nutrition Dosing Gradually as Inflammation Resolves

Progressively scale energy delivery to 80–100% as catabolism subsides and gut function recovers.

Avoid Routine Gastric Residual Volume Monitoring

Residual checks cause unnecessary feeding interruptions without decreasing pneumonia or aspiration risks.

Target Glycemic Control Below 180 mg/dL



Manage stress hyperglycemia actively while advancing calories cautiously in patients at refeeding risk.

LANDMARK TRIAL EVIDENCE (EARLY ACUTE PHASE DOSING)

TRIAL & POPULATION	COMPARISON (RESTRICTIVE vs. FULL DOSE)	KEY FINDINGS / CLINICAL OUTCOMES
EDEN (2012) Acute Lung Injury	vs. Trophic (10 ml/hr) vs. Full Dose (25 kcal/kg/d)	No difference in ventilator-free days or mortality; significantly more GI complications in full-dose.
NUTRIREA-3 (2023) Shock & Mech. Vent.	vs. Low Dose (6 kcal/kg/d) vs. Full Dose (25 kcal/kg/d)	Shorter time to readiness for ICU discharge in low-dose; severe GI complications in full-dose.
REFEEDING (2015) Refeeding Hypophosphatemia	Caloric Restriction (20 kcal/hr ramp-up) vs. Standard Care	Higher 60-day survival (91% vs. 78%), shorter hospital stay, fewer infections in restricted group.

Other Support

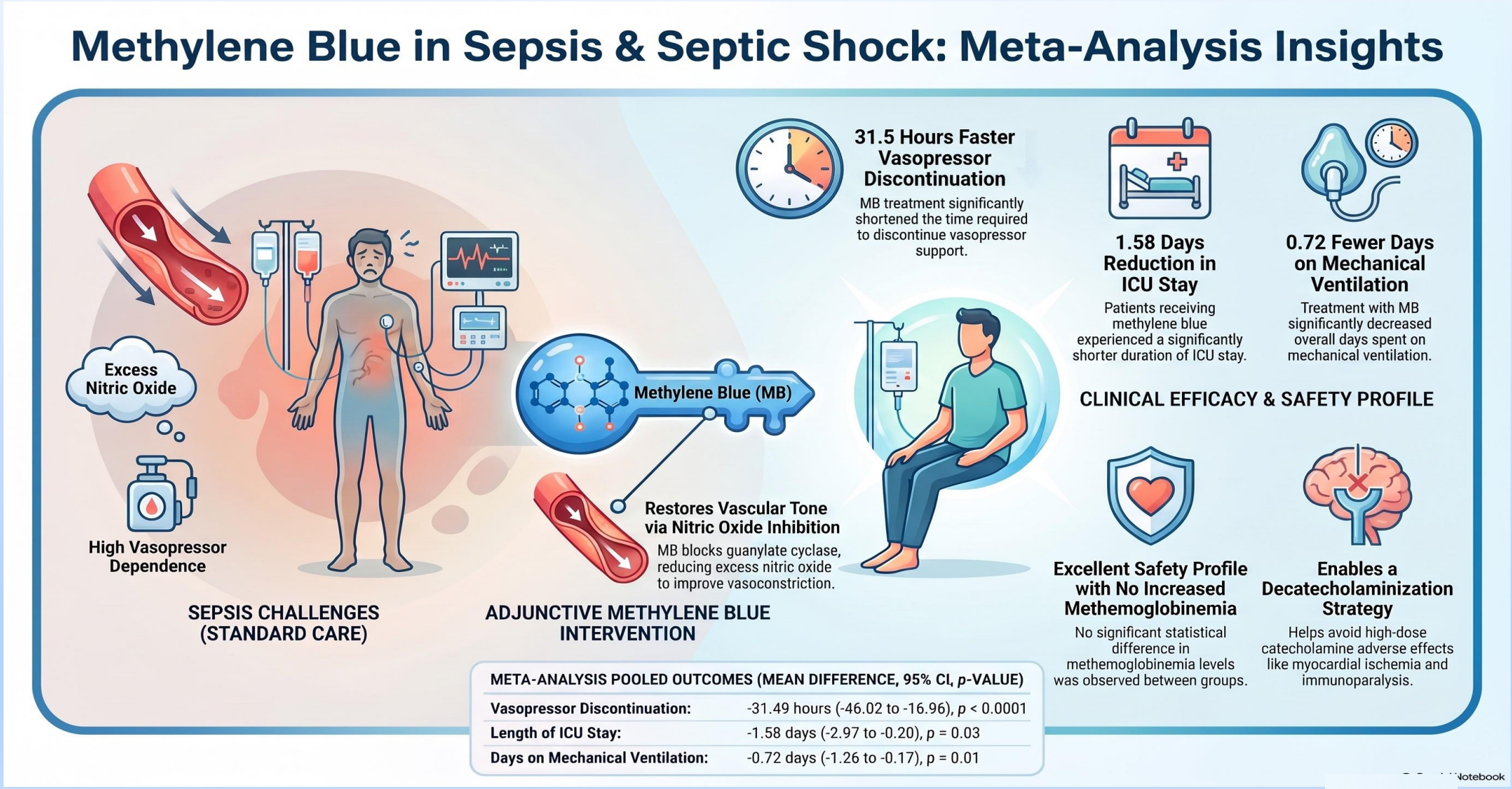


A Quiz: Green Urine

- 42 year old AA woman
  - SLE with baseline CKD
  - Chronic immunosuppression
  - Admitted with fever and abdominal pain
- Progressed to septic shock
  - Renal failure
  - Hypotension
  - On 3 pressors

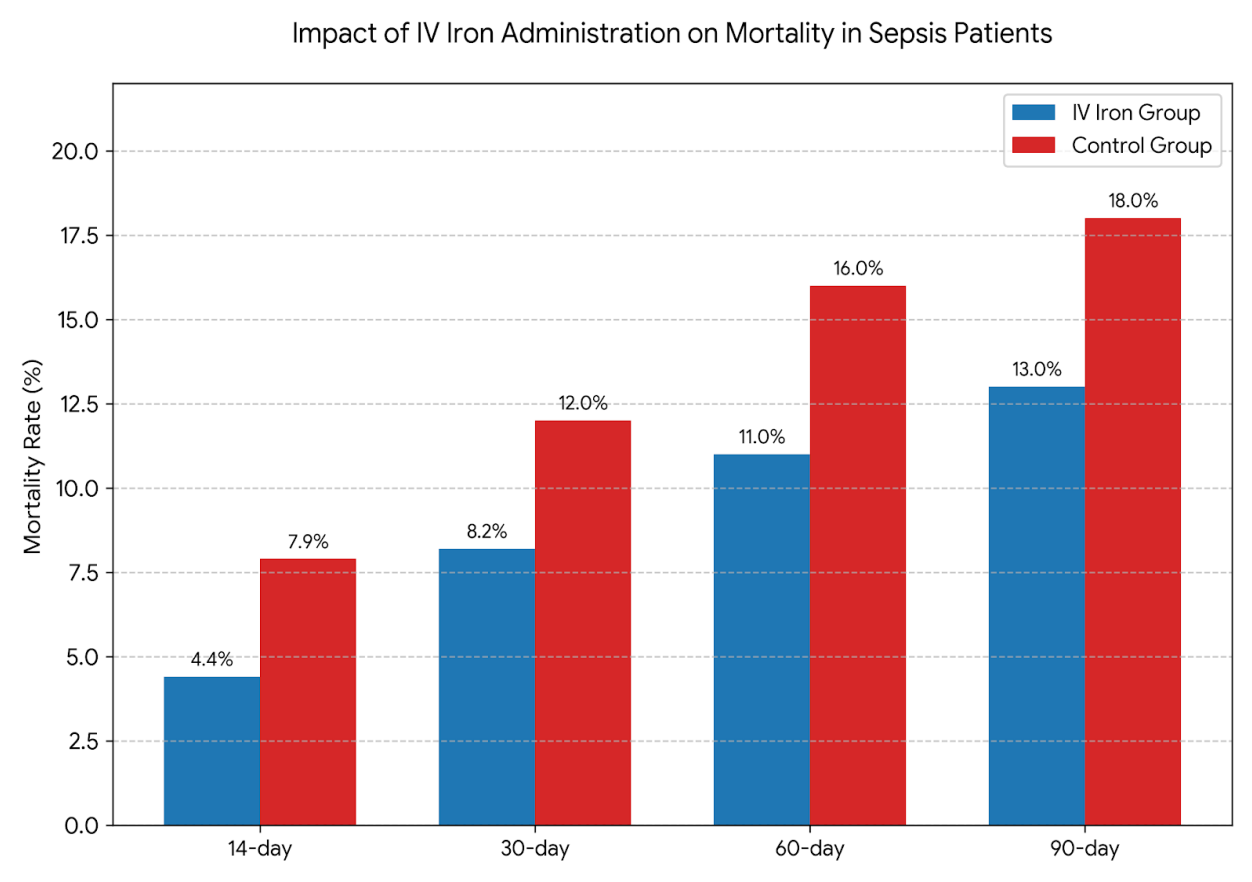
The answer?

Methylene Blue in Sepsis (?)



Ballarin, R et al: Frontiers in Medicine, 11, 2024

IV iron in Sepsis (?)



- **Pneumonia:** **HR 0.46** 95% CI, 0.43-0.5
- **UTI:** **HR 0.47** 95% CI, 0.43-0.52
- **Colitis:** **HR 0.60** 95% CI, 0.51-0.71
- **Cellulitis:** **HR 0.55** 95% CI, 0.46-0.65

- **Historical Concerns:** IV iron during sepsis has historically been viewed as risky due to fears that it could fuel microbial growth and impair immune function.
- This large retrospective cohort study of patients with sepsis and iron deficiency anemia, **early IV iron administration significantly reduced mortality at 14, 30, 60, and 90 days**
- **Prospective studies are still required** but this study **challenges longstanding assumptions**

Blood 146; 1129: The 67th ASH Annual Meeting Abstracts POSTER, 2025

Clinical Dashboard Summary:

	**Pillar 1:** Initiate norepinephrine early (MAP > 65); consider angiotensin II / vasopressin to spare fluids.
	**Pillar 2:** Preference for balanced crystalloids; actively de-resuscitate (furosemide/UF) once stable to avoid fluid accumulation
	**Pillar 3:** Administer IV sodium bicarbonate for severe metabolic acidosis (pH < 7.20) with acute kidney injury (AKI)
	**Pillar 4:** Utilize early trophic enteral feeds; restrict protein to ≤ 1.2 g/kg/day; use 2 kcal/mL formulas to stop fluid creep.

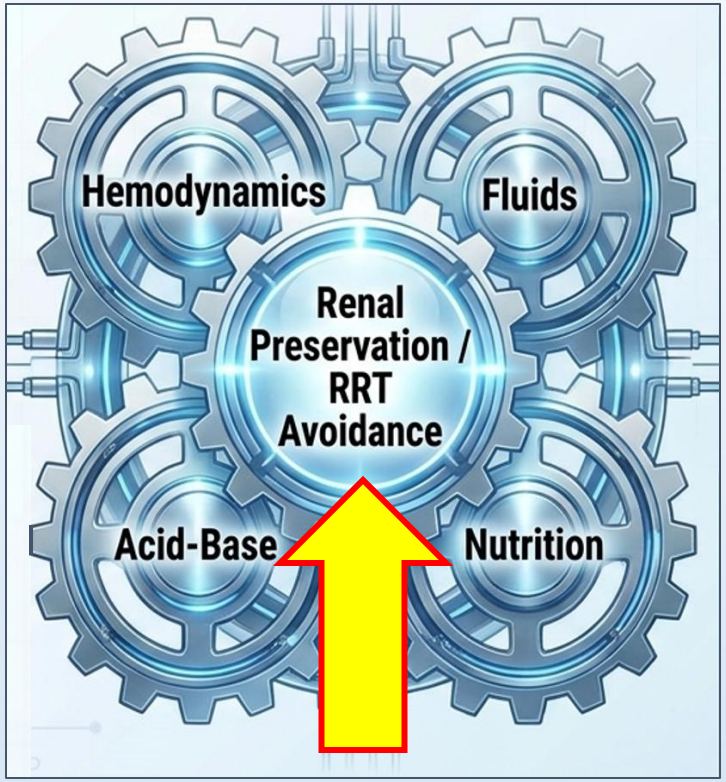
Renal Preservation – Avoiding RRT

Hemodynamics:

Early vasopressors allow for restrictive fluid use, preventing renal congestion.

Acid-Base

Targeted bicarbonate improves catecholamine (vasopressor) responsiveness in severe acidemia.



Fluids

Balanced Fluids vs crystalloids.

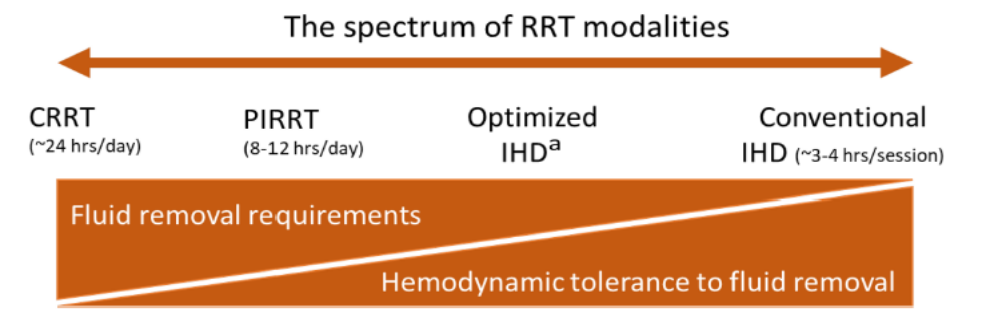
Nutrition:

Concentrated nutrition limits fluid creep, enabling successful de-resuscitation.

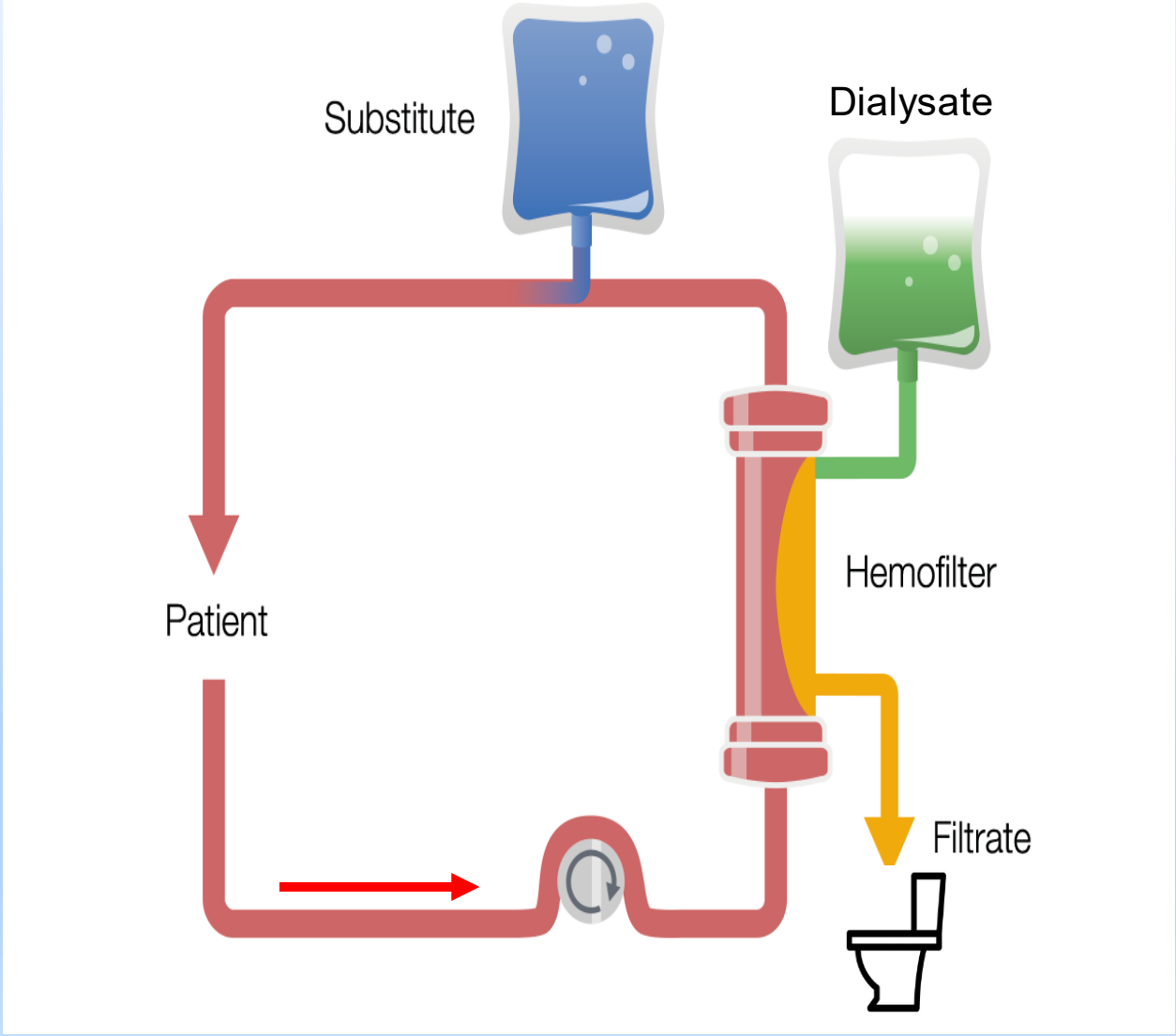
Core Outcome:

Synergistic approach to stabilize endothelial glycocalyx, restore GFR, prevent progression to dialysis.

RENAL REPLACEMENT: iHD – PRRT - CRRT







RRT Initiation: The Timing Dilemma

The Clinical Question: Start RRT early upon AKI diagnosis or wait until life-threatening indications arise (Late/Delayed)?



Early Initiation (Preventative)

- Aims to proactively control volume.
- Attempts to clear detrimental inflammatory mediators early in the cascade
- Goal is to prevent severe, downstream complications.

Late / Delayed Initiation (Watchful Waiting)

- Avoids the risks of an invasive extracorporeal circuit (bleeding, hemodynamic instability).
- Allows time for patients who might recover renal function spontaneously.
- Reserves intervention for absolute necessity.

Criteria for RRT Initiation in Sepsis

Primary indications for urgent renal replacement therapy

Azotemia

BUN > 100 mg/dL

Or > 40 mmol/L (BUN 112 mg/dL)

Hyperkalemia

K > 6.0 mmol/L

Or > 5.5 mmol/L after max medical Rx

Severe Acidemia

pH < 7.15

Pure Metabolic
pCO2 < 35 mmHg

Mixed Acidosis
pCO2 > 50 mmHg (max vent)

Pulmonary Edema

Diuretic-resistant fluid overload requiring:

- **O2 flow > 5 L/min (to keep SpO2 > 95%)**
- **FiO2 > 50% (mechanically ventilated)**

STARRT–AKI: Does early initiation of kidney replacement therapy (KRT) decrease mortality?

#NephJC

Methods

Multinational open-label RCT
168 hospitals
15 countries

October 2015 - September 2019

Critically ill patients
+
Kidney dysfunction
+
Severe AKI
(KDIGO Stage 2 or 3)
N=3019

Standard strategy
Standard of care
n=1462

Accelerated Strategy
KRT within 12 hours of meeting eligibility criteria
n=1465

Findings

	Mortality at 90 days	KRT Dependence	Any Adverse Event
Standard strategy	43.7%	6%	17%
Accelerated Strategy	43.9%	10%	23%
	RR 1 p=0.92	RR 1.7 95% CI (1.2-2.4)	p < 0.001

Conclusion Among critically ill patients with acute kidney injury, an accelerated renal replacement strategy was not associated with a lower risk of death at 90 days than a standard strategy.

Reference: Sean Bagshaw MD, Ron Wald MD, CM, MPH., Neill Adhikari, MD, CM, et al. **Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury.** NEJM 2020 doi: 10.1056/ NEJMoa2000741

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NEPHROLOGY EST 2015 SOCIAL MEDIA COLLECTIVE

Evidence on RRT Timing: Trial Synthesis

The Data (AKIKI, IDEAL-ICU, STARRT-AKI):

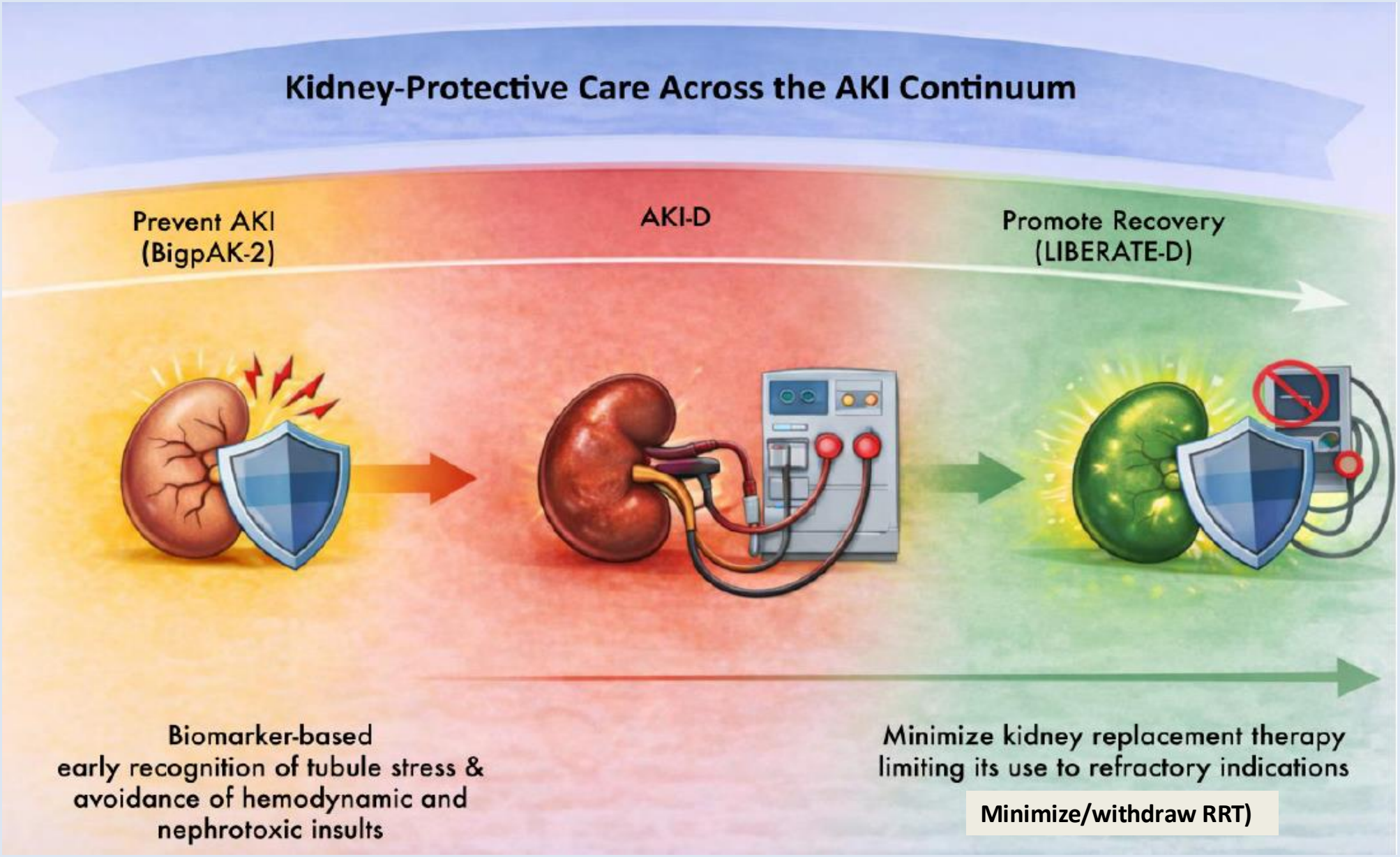
Large-scale randomized trials show NO survival benefit to early initiation.

- **Spontaneous Recovery:** A significant percentage of patients in the delayed groups recovered renal function without ever needing RRT.
- **Adverse Events:** Early initiation is consistently associated with higher rates of circuit-related adverse events and worsened hypotension.
- **No Mortality Benefit:** Proactive initiation does not alter the underlying disease trajectory.

The Consensus Verdict:

A “watch and wait” (delayed) strategy is preferred, reserving RRT for absolute, life-threatening indications (e.g., severe hyperkalemia, profound academia, pulmonary edema).

But often a less dogmatic approach – there are exceptions to the rule!



Saritas T et al: Protecting the stressed kidney: Prevention, dialysis and recovery in AKI. Nephrol Dial Transplant 0:1-4, 2026

ICRAKI: INTERMITTENT VS CONTINUOUS DIALYSIS

ORIGINAL ARTICLE

Intermittent or Continuous Renal-Replacement Therapy in Acute Kidney Injury

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The authors' full names, academic degrees, and affiliations are listed at the end of the article. Stéphane Gaudry can be contacted at stephanegaudry@gmail.com or at the Intensive Care Unit, Hôpital Avicenne, 125 Rue de Stalingrad, 93000 Bobigny, France.

*A list of the members of the ICRAKI Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Lucie Biard and Coralie Bloch contributed equally to this article.

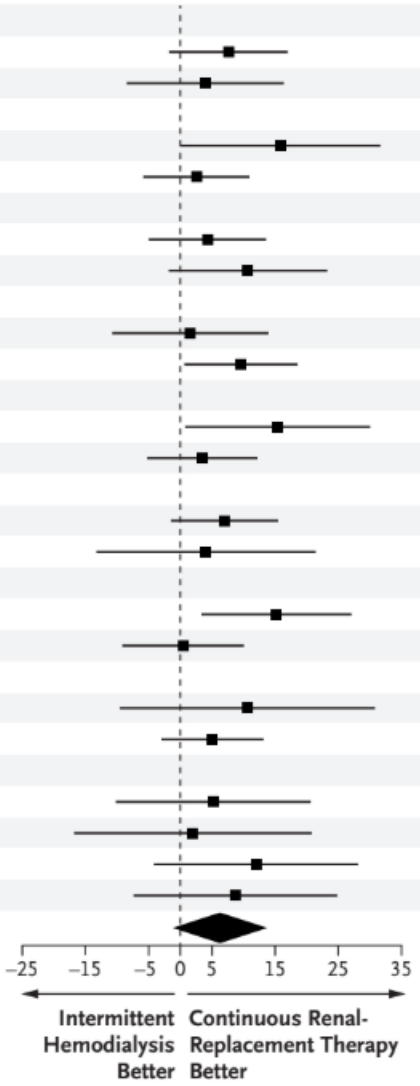
This article was published on October 14, 2026, at NEJM.org.

DOI: 10.1056/NEJMoa2608397

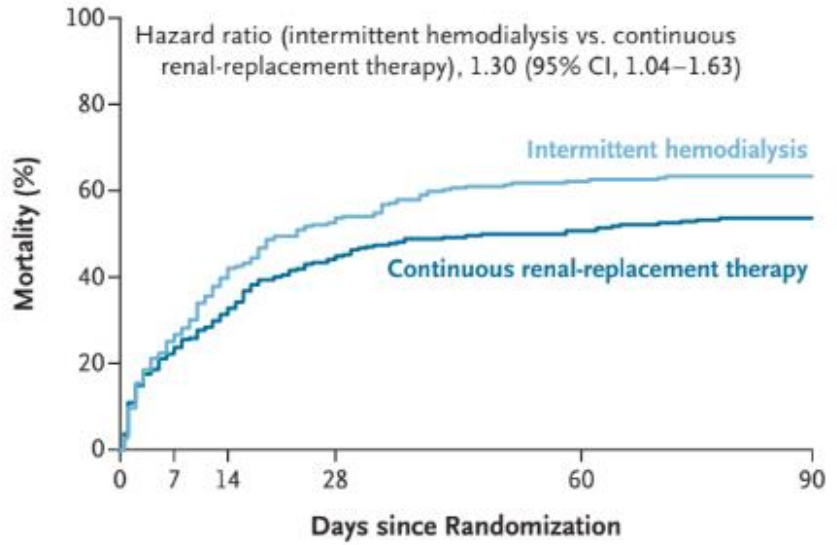
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iHD vs CRRT

Subgroup	Intermittent Hemodialysis	Continuous Renal-Replacement Therapy
	no. of patients with event/total no. (%)	
Cumulative fluid balance		
<6 liters	132/168 (78.6)	123/173 (71.1)
≥6 liters	71/92 (77.2)	75/102 (73.5)
Catecholamine support		
No	49/65 (75.4)	43/74 (58.1)
Yes	155/195 (79.5)	154/201 (76.6)
Catecholamine dose		
≤0.5 μg/kg/min	132/176 (75.0)	137/193 (71.0)
>0.5 μg/kg/min	71/84 (84.5)	61/82 (74.4)
Age		
<65 yr	74/111 (66.7)	82/125 (65.6)
≥65 yr	129/149 (86.6)	115/150 (76.7)
Sex		
Female	56/66 (84.8)	46/66 (69.7)
Male	147/194 (75.8)	151/209 (72.2)
Chronic kidney disease		
No	156/203 (76.8)	162/231 (70.1)
Yes	47/57 (82.5)	34/42 (81.0)
Sepsis		
No	77/93 (82.8)	75/112 (67.0)
Yes	125/166 (75.3)	122/163 (74.8)
Mechanical ventilation		
No	29/40 (72.5)	28/45 (62.2)
Yes	173/219 (79.0)	169/230 (73.5)
SOFA score at RRT initiation		
Q1	48/68 (70.6)	58/90 (64.4)
Q2	43/62 (69.4)	36/53 (67.9)
Q3	53/63 (84.1)	39/54 (72.2)
Q4	40/48 (83.3)	44/59 (74.6)
Overall	203/260 (78.1)	197/275 (71.6)



Forest Plot Analysis of Primary Outcome



No. at Risk

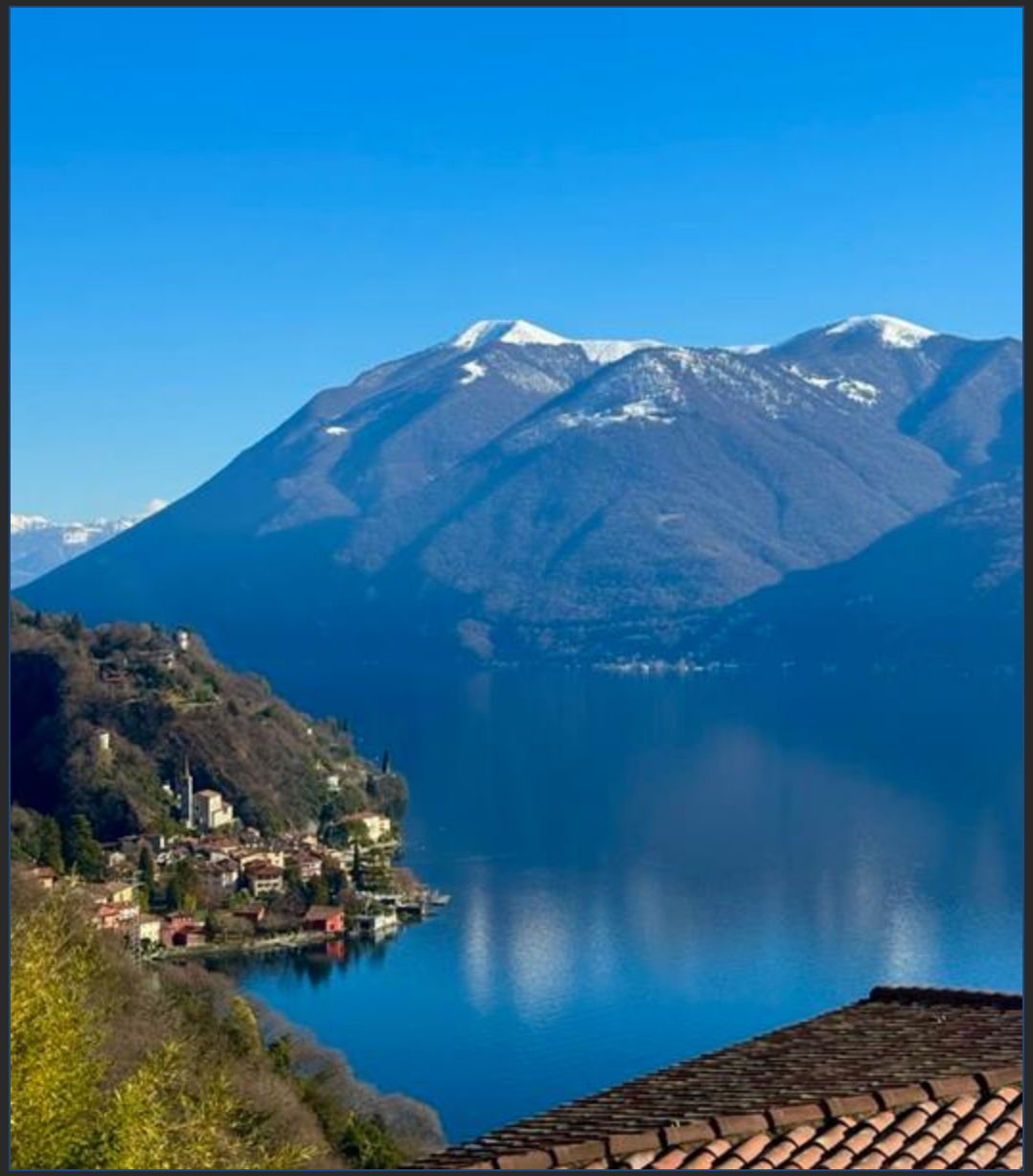
Intermittent hemodialysis	260	194	156	123	97	83
Continuous renal-replacement therapy	275	214	188	153	134	104

Figure 1. Kaplan–Meier Curves of the Probability of Death from Randomization to Day 90.

The gang







Lake Lugano, Switzerland/Italy, Jan 2026

Questions

