Evidence-based Clinical Practice in *Critical Care* Nephrology

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The Persistent Challenge of Acute Kidney Injury

10-15%

Of all hospitalizations are complicated by AKI, rising to 50% in ICU admissions.

Ruinelli et al., Fu et al.

7% to 32%

In-hospital mortality, graded by severity (AKI to AKD), compared to 2% for patients without renal dysfunction.

Ruinelli et al.

35%

Of AKI cases based on laboratory data were appropriately coded at discharge, highlighting significant under-recognition.

Ruinelli et al.

Ruinelli L et al. PLoS One. 2025 Jul 1;20(7):e0326124.

Issues Addressed

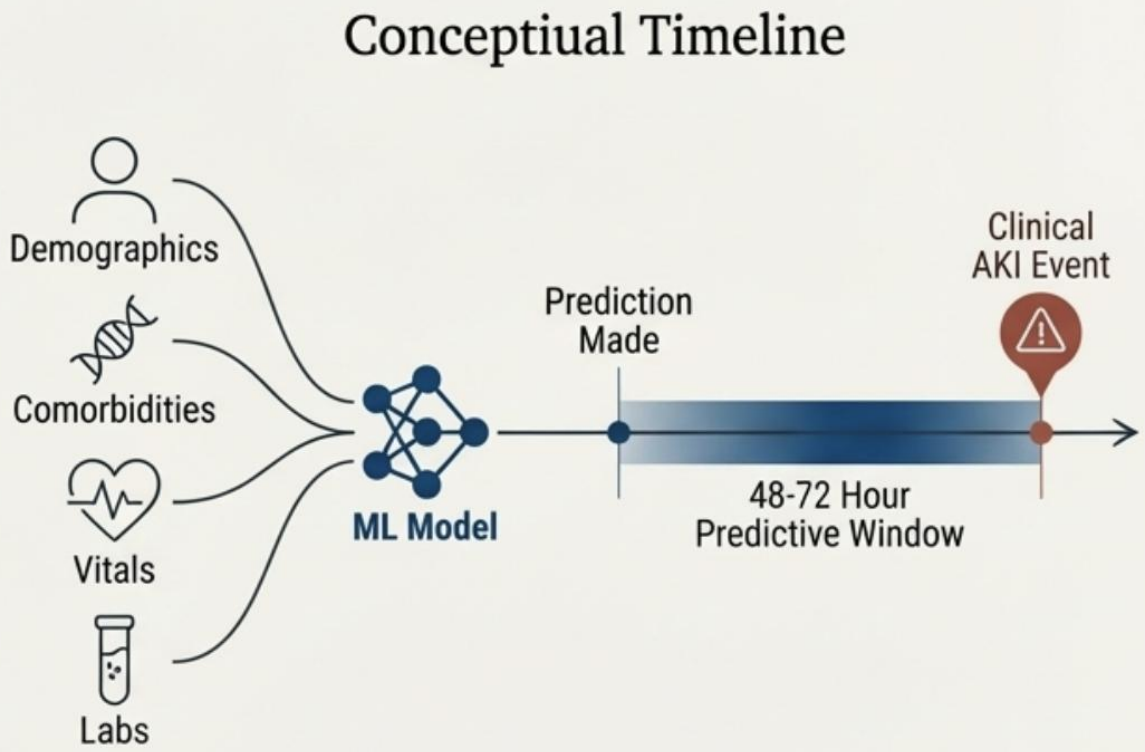
- From Prediction, Alert, to Action
- Updated Roles of AKI Biomarkers
- VeXUS and Fluid Management
- Could We Liberate from KRT More Efficiently?

The Promise of Machine Learning: Early and Accurate Prediction

Machine Learning models, leveraging rich Electronic Health Record (EHR) data, offer the potential to overcome the limitations of delayed clinical indicators. This provides a crucial window for proactive, preventative intervention.

- **The Primary Goal:** To achieve real-time, personalized risk stratification, identifying patients *before* irreversible injury occurs.
- **The Mechanism:** ML algorithms integrate dozens of variables—demographics, comorbidities, vital signs, and laboratory trajectories—to detect subtle patterns that precede clinical AKI manifestation.
- **Proven Potential:** Multiple models demonstrate high discriminative power in predicting AKI development, often 48-72 hours in advance. (Yang et al., 2025; Ma et al., 2024)

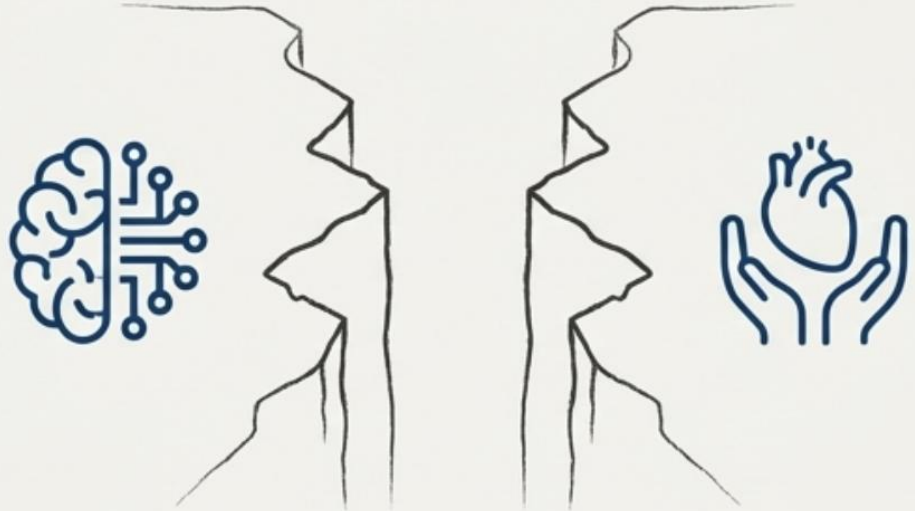
This capability has positioned ML as a cornerstone of next-generation strategies for AKI prevention and management.



Identifying the Critical Gaps: From Code to Bedside

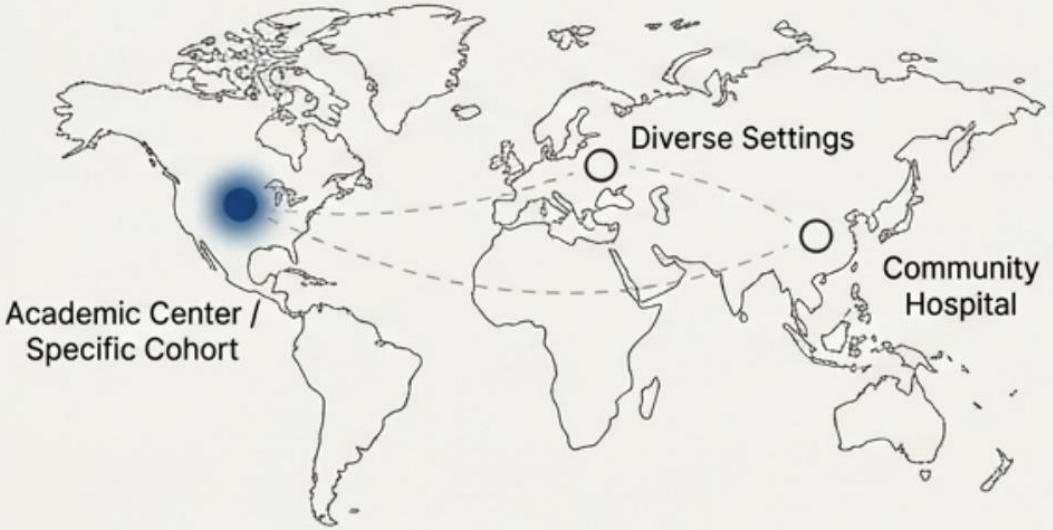
Despite the proliferation of accurate predictive models, their translation into tangible clinical benefit is not guaranteed. Two critical gaps have emerged, shifting the focus from algorithm development to implementation science.

Gap 1: The "Prediction-to-Action" Gap



- Does early risk identification, by itself, improve patient outcomes?
- Simply alerting clinicians to a high risk of AKI may not be sufficient to change the disease trajectory. The crucial question is what *action*, if any, is taken based on the prediction.

Gap 2: The "Generalizability and Implementation" Gap



- Do models developed in specific settings (e.g., academic centers, specific disease cohorts like CAP) perform reliably in diverse, real-world environments (e.g., community hospitals, different countries)?
- Are models simple and robust enough for seamless EHR integration and broad adoption?

Closing Gap #1: Enhancing Prediction Accuracy and Generalizability

Recent studies have successfully developed robust models for both broad and specific patient populations, demonstrating high performance and transportability.

Study	Population	Key Finding & Performance Metric
Yang et al., 2025	General hospitalized patients (China, 5 diverse hospitals)	Developed a simple, 20-variable model with high transportability. **Refitted AUC for AKI within 48h: 0.81 - 0.90.** Predicts AKI a median of 72h in advance.
Ma et al., 2024	Community-Acquired Pneumonia (CAP)	Deep Forest model accurately predicts CAP-associated AKI. **External Validation AUC: 0.87.** Identified 11 key predictors (e.g., BUN, neutrophils).
Ruinelli et al., 2025	General hospitalized patients (Switzerland)	ML accurately predicts progression from AKI to AKD, with performance improving as more data accumulates. **AUC for AKD prediction: 0.76 (Day 1) → 0.88 (Day 4).**

Conclusion: The technical feasibility of creating accurate, generalizable, and specialized AKI prediction models is well-established.

Li T et al. JAMA Netw Open. 2024 Jan 19;7(1):e2351710.

Prediction is Powerful, But Does Acting on it Improve Patient Outcomes?

High-Fidelity Prediction

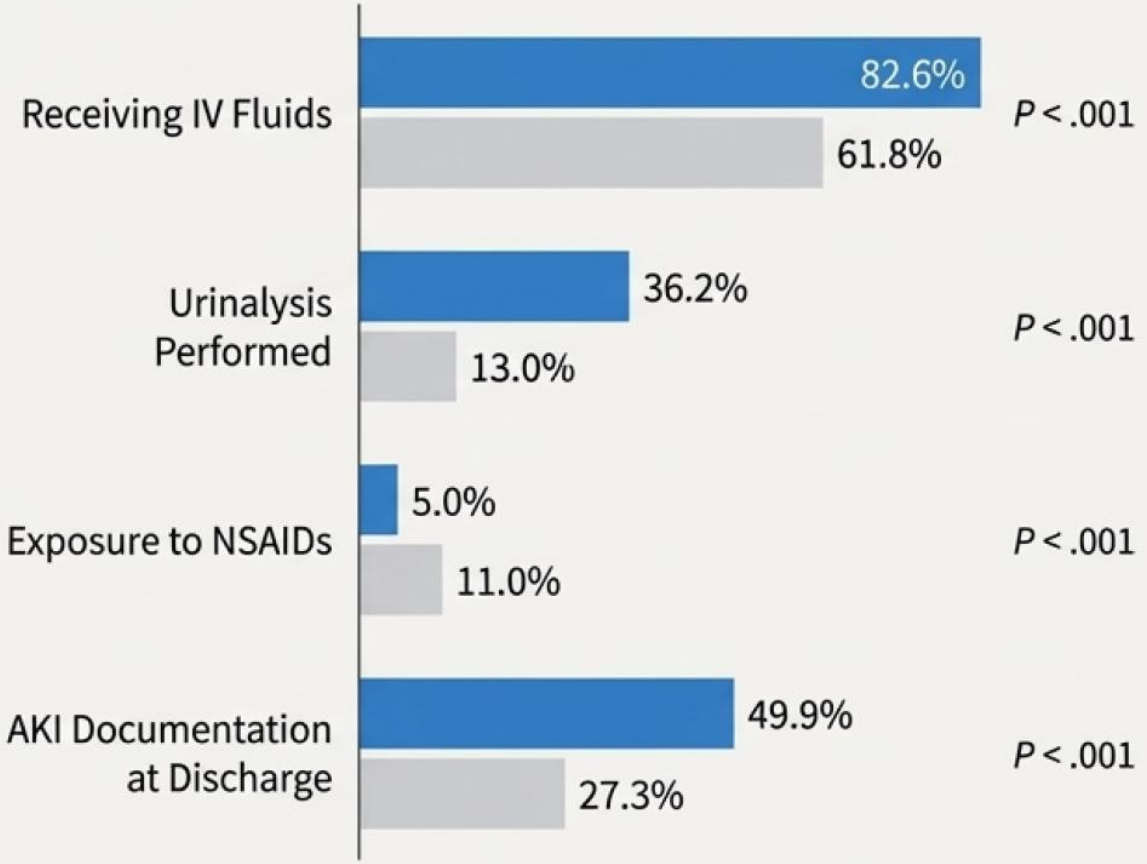
Improved Patient Outcome

- **The Critical Question:** The ability to predict an event is only clinically valuable if the subsequent intervention improves the patient's course.
- **The Next Step:** We now examine the evidence from Randomized Controlled Trials (RCTs) and meta-analyses that tested the impact of acting on these predictions, primarily through electronic alerts and associated care bundles.

Reality Check 1: A Major RCT Reveals a Stark Disconnect

Li et al. (2024), single-center, double-blind RCT of 2,208 adults with hospital-acquired AKI.

Alerts Successfully Changed Clinician Behavior



But These Changes Did Not Improve Kidney Function

Maximum change in eGFR within 7 days.

Alert Group: 3.7 mL/min/1.73 m^2

Usual Care Group: 2.9 mL/min/1.73 m^2

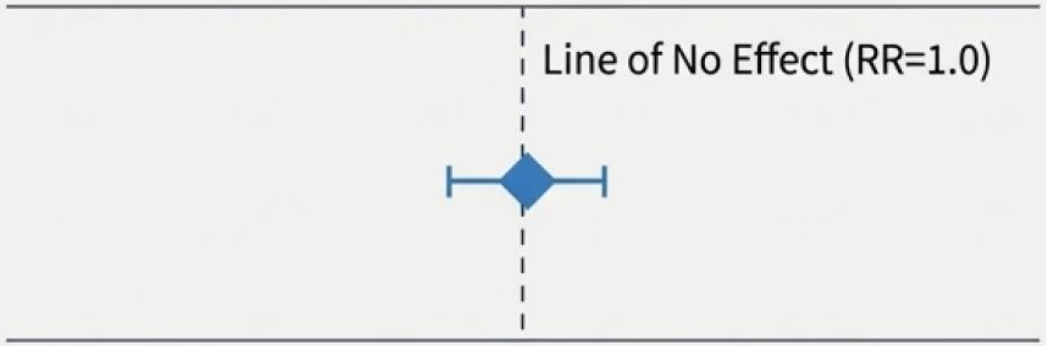
$P = .24$

No significant difference in the primary outcome or other patient-centered secondary outcomes like death or dialysis.

The Meta-Analysis Confirms: Alerts Do Not Improve Patient-Centered Outcomes

Fu et al. (2024), meta-analysis of 6 RCTs including 40,146 patients.

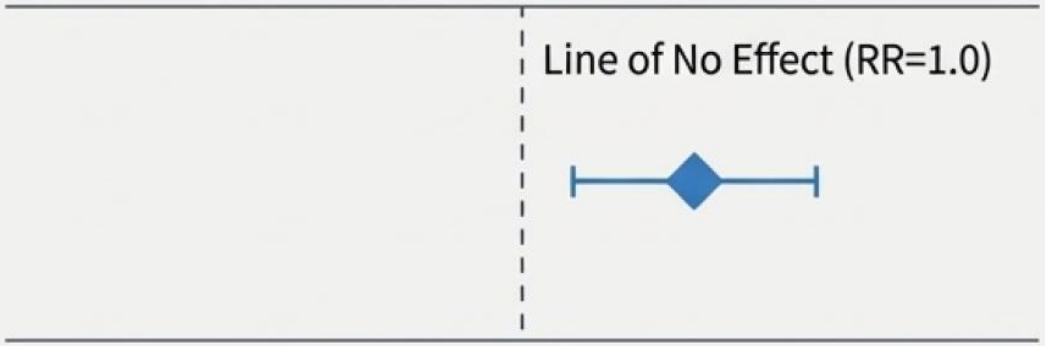
Mortality



Relative Risk (RR) = **1.02**
95% CI = 0.97–1.08
P = 0.44

Interpretation: No effect on survival.

Receipt of Dialysis



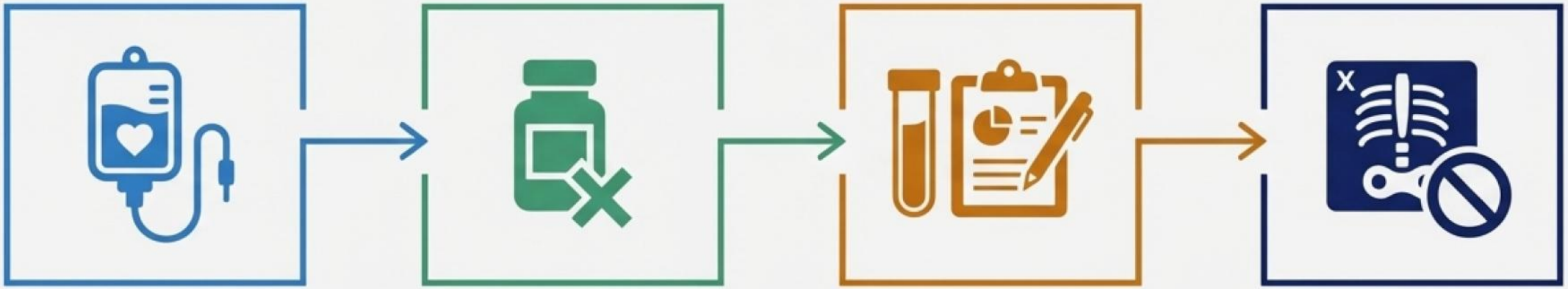
Relative Risk (RR) = **1.14**
95% CI = 1.05–1.25
P = 0.002

Interpretation: Alerts were associated with a statistically significant *increase* in dialysis initiation, likely reflecting improved recognition without a corresponding survival benefit.

If Not the Alert, What About the Intervention? Assessing the AKI Care Bundle

The KDIGO guidelines recommend a “care bundle” of supportive measures. Is this bundle, on its own, effective at improving patient outcomes?

Evidence: Huang et al. (2025), a systematic review and meta-analysis of 12 studies involving 30,152 participants.



1. Optimize volume status and perfusion.
2. Avoid nephrotoxic agents.
3. Monitor serum creatinine and urine output.
4. Consider alternatives to radiocontrast agents.

Huang Y et al. BMC Nephrol. 2025;26:519.

The Solution: Proven Efficacy of Structured Care Bundles

If alerts alone are insufficient, the key lies in the intervention that follows. A meta-analysis focused on the AKI care bundle provides the answer: a structured, evidence-based response is critical to improving outcomes.

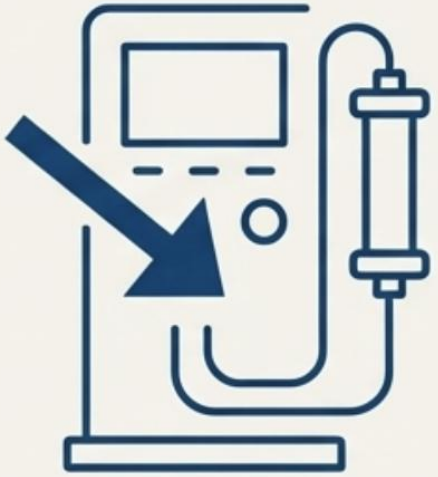
****Huang et al., 2025 (Meta-Analysis, 12 Studies, n=30,152)**
The implementation of AKI care bundles was associated with significant improvements in key renal outcomes.

Reduced AKI Progression

Care bundles significantly lowered the risk of progressing to more severe AKI.

RR 0.77

(95% CI 0.60–0.98)



Reduced Need for Renal Replacement Therapy (RRT)

A structured approach led to a one-third reduction in the need for dialysis.

RR 0.66

(95% CI 0.46–0.94)

Conclusion: Clinical benefit is derived not from the alert itself, but from the reliable execution of a high-quality, evidence-based care process that the alert facilitates.

The Nuanced Impact of Care Bundles: Kidney-Specific Gains, But No Survival Benefit

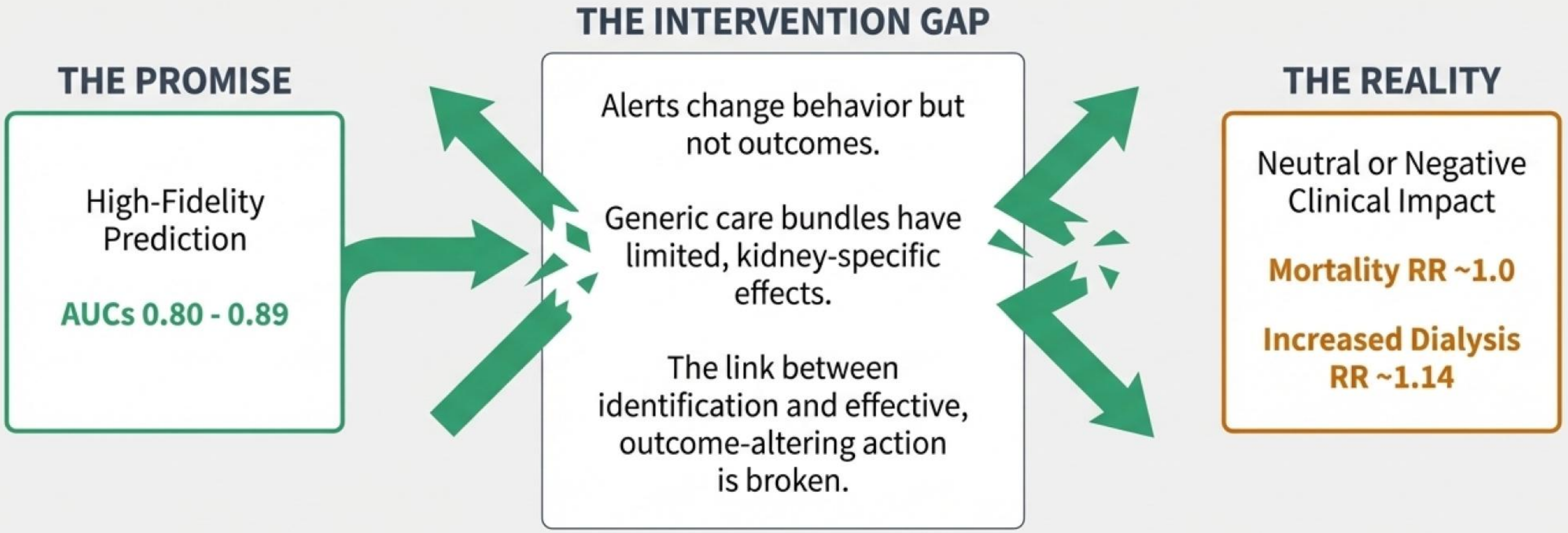
Key Findings from Huang et al. (2025) Meta-Analysis

Areas of Improvement (Statistically Significant)		
Reduced AKI Severity	Risk of progressing to moderate-to-severe AKI was significantly lower.	RR: **0.77** (95% CI: 0.60–0.98)
Reduced Need for Renal Replacement Therapy (RRT)	Implementation of bundles was associated with less need for dialysis.	RR: **0.66** (95% CI: 0.46–0.94)

Areas with No Improvement (Not Statistically Significant)	
AKI Incidence	RR: **0.95** (95% CI: 0.81–1.13)
In-Hospital Mortality	RR: **0.93** (95% CI: 0.81–1.07)
Length of Hospital Stay	MD: **–0.16** days (95% CI: –0.80 to 0.47)

AKI care bundles appear to mitigate the progression of kidney damage but do not change the ultimate outcome of in-hospital survival.

The Central Disconnect: Why Doesn't Better Prediction Lead to Better Outcomes?



An Evidence-Based Assessment of Current AKI Strategies

Strategy	Evidence Level	Key Finding & Conclusion	Status
ML-Based Prediction	**Moderate**	High discriminative power (AUC 0.80-0.89) shown in retrospective studies.	**Promising** requires prospective validation.
Electronic Alerts	**High**	Multiple RCTs and a meta-analysis confirm no mortality benefit (RR 1.02) and a potential for increased interventions.	**Ineffective** in its current form.
Care Bundles	**Moderate**	Meta-analysis shows reduced AKI severity/RRT need but no mortality benefit. High heterogeneity & compliance issues.	**Needs Refinement** and better implementation.

Ruinelli L et al. PLoS One. 2025 Jul 1;20(7):e0326124.
Ma M et al. J Med Internet Res. 2024;26:e51255.
Li T et al. JAMA Netw Open. 2024 Jan 19;7(1):e2351710.
Fu Z et al. BMC Med. 2024;22:408.
Huang Y et al. BMC Nephrol. 2025;26:519.
Zhang Y et al. Nat Commun. 2024. doi: 10.1038/s41467-024-55629-5.

The Next Frontier: Translating Prediction into Meaningful Action

1. The technology to accurately **predict** acute kidney injury has outpaced our ability to effectively **intervene**.
2. Automated alerts and generic care bundles have been rigorously tested and, while they can change process measures, they **do not improve patient-centered outcomes** like survival.
3. Future progress depends not on building slightly better prediction models, but on designing and validating **smarter, targeted, and high-compliance interventions** that are directly linked to the risk identified by those models.

Issues Addressed

- From Prediction, Alert, to Action
- Updated Roles of AKI Biomarkers
- VeXUS and Fluid Management
- Could We Liberate from KRT More Efficiently?

Gap 1: Accurately Predicting Successful KRT Liberation

The central challenge is the lack of validated, objective methods to assess a patient's capacity for renal recovery while on KRT. Clinicians currently face two opposing risks:

1. Premature Discontinuation

- Leading to fluid overload, metabolic derangements, and the need to re-initiate KRT, which is associated with increased morbidity.

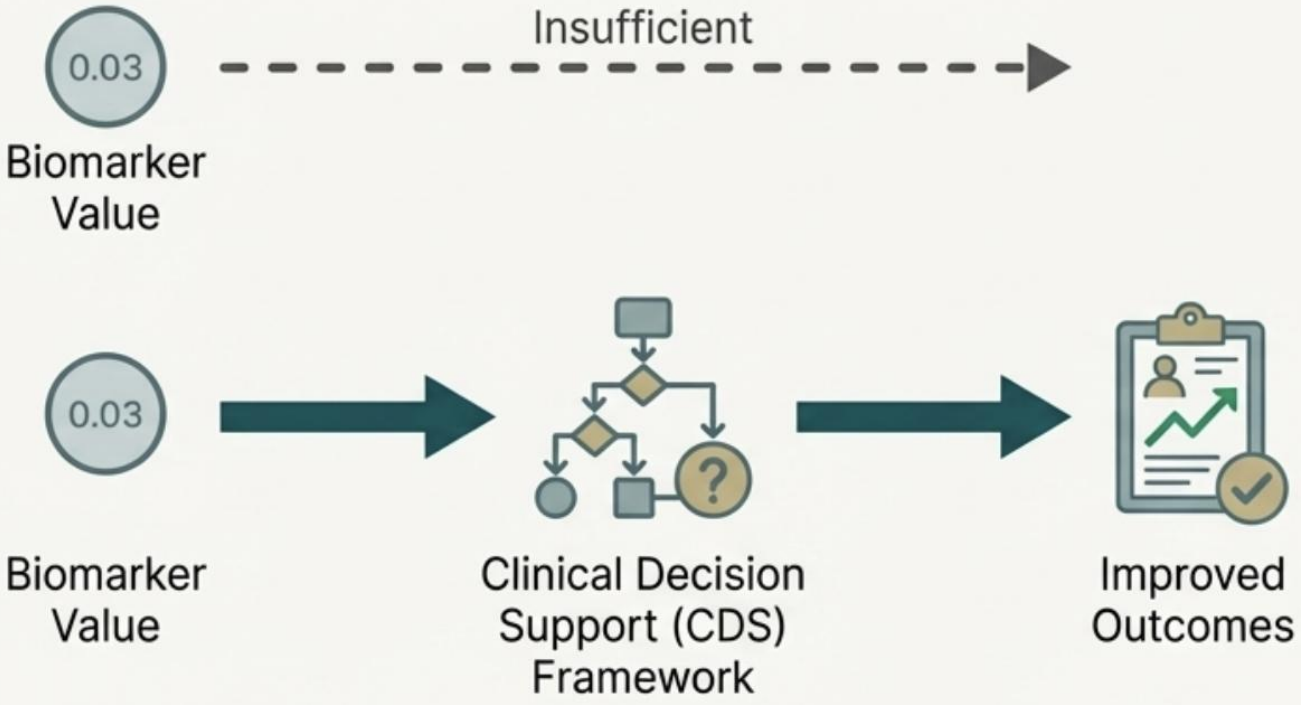
2. Delayed Discontinuation

- Exposing patients to unnecessary risks of KRT, including catheter-related infections, bleeding from anticoagulation, nutrient loss, and prolonged immobility.

A reliable predictor of liberation success is needed to navigate this clinical tightrope.

Gap 2: Translating Prediction into Improved Clinical Outcomes

Even with a promising predictive biomarker, a second gap exists: **how to systematically integrate it into clinical practice to demonstrably improve patient outcomes.**



The availability of a biomarker value alone is insufficient. Its true value is realized only through a structured clinical decision support (CDS) framework that guides clinicians toward specific, timely interventions.

Evidence is needed to show that a biomarker-guided strategy leads to better outcomes than standard care, such as reduced length of stay, lower mortality, and decreased healthcare costs.

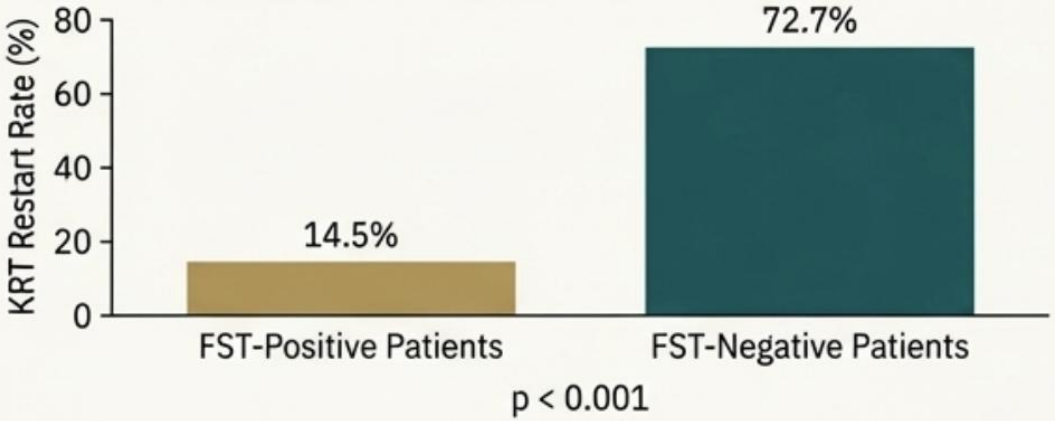
Solution A: The Furosemide Stress Test as a Functional Assessment of Tubular Reserve

Key Study: Weidhase et al., *Critical Care* (2025) - A prospective observational study (n=98) in ICU patients on KRT who had resumed spontaneous diuresis (SD) of >400 ml/24h.

Primary Findings:

A positive FST (>200 ml urine output in 2h) was a strong predictor of successful KRT liberation.

KRT Restart Rate (within 7 days):

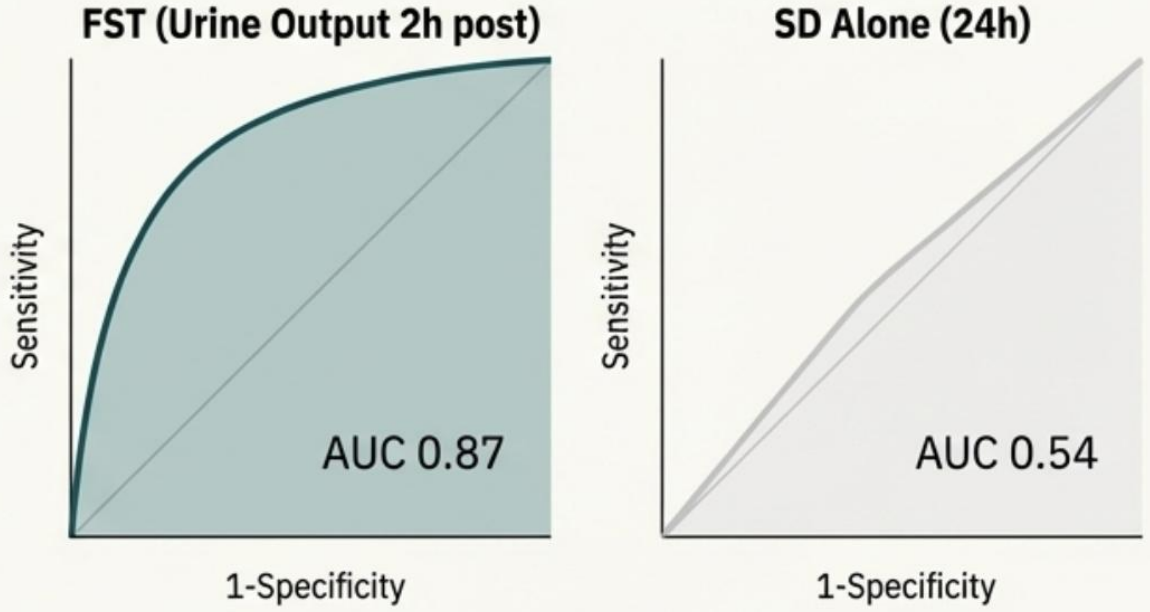


Weidhase L et al. Crit Care. 2025;29:214

Predictive Power (AUC):

Urine output 2h post-FST: **0.87** (p < 0.001)

24h Spontaneous Diuresis alone: **0.54** (p = 0.531)



Conclusion:

In patients regaining urine output, the FST provides a robust functional assessment to identify those with sufficient renal reserve for successful liberation.

Solution B: Proenkephalin A (penKid) to Monitor GFR Recovery

Key Study: von Groote et al., *Critical Care* (2023) – A post-hoc analysis of the multicenter RICH trial, measuring penKid at CRRT initiation and on Day 3.

Primary Findings: While baseline penKid was not predictive, a low penKid level *during* CRRT signaled a higher likelihood of recovery.

Landmark Analysis (Day 3 of CRRT)

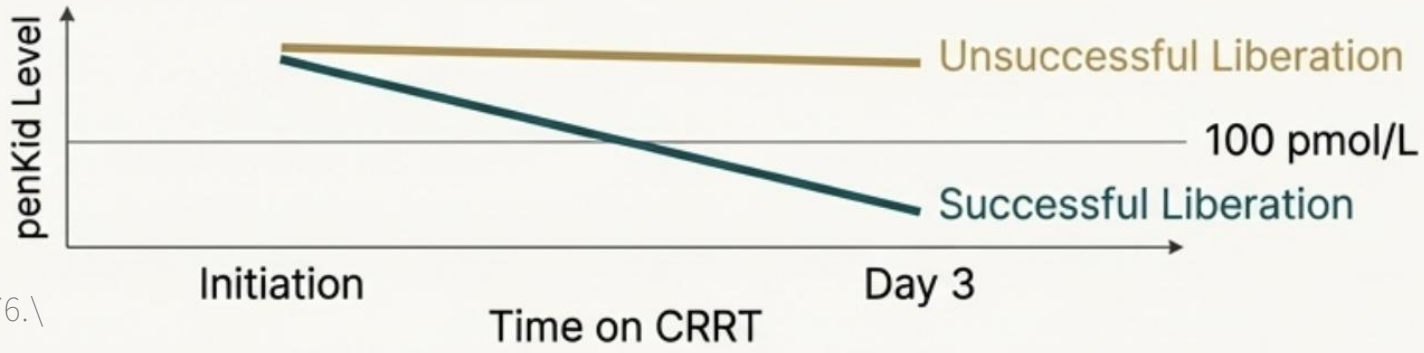
Low penKid (≤100 pmol/L) was significantly associated with successful liberation.

Subdistribution Hazard Ratio (sHR): **2.35** (95% CI 1.45–3.81, p < 0.001)

Clinical Context

High daily urine output (>436 ml/d) remained an even stronger predictor in this cohort.

sHR **2.91** (p < 0.001)



von Groote T et al. Crit Care. 2023;27:276.\

Conclusion: Serial penKid measurement during KRT may help identify an improving GFR trajectory but should be interpreted alongside clinical parameters like urine output.

Solution C: Cell-Cycle Arrest Biomarkers for Early Prognosis and Risk Stratification

Biomarker: Urinary [TIMP-2]*[IGFBP7] (NephroCheck)

Key Study: Wang et al., *Renal Failure* (2023) - A systematic review and meta-analysis of 10 studies (1,559 patients) on the value of [TIMP-2]*[IGFBP7] for predicting poor prognosis (Stage 3 AKI, KRT, non-recovery, or death).

Pooled Performance Metrics

Key Caveats from Source:

Significant heterogeneity was observed, driven by different outcome endpoints and cutoff values. The modest specificity suggests a risk of false positives.

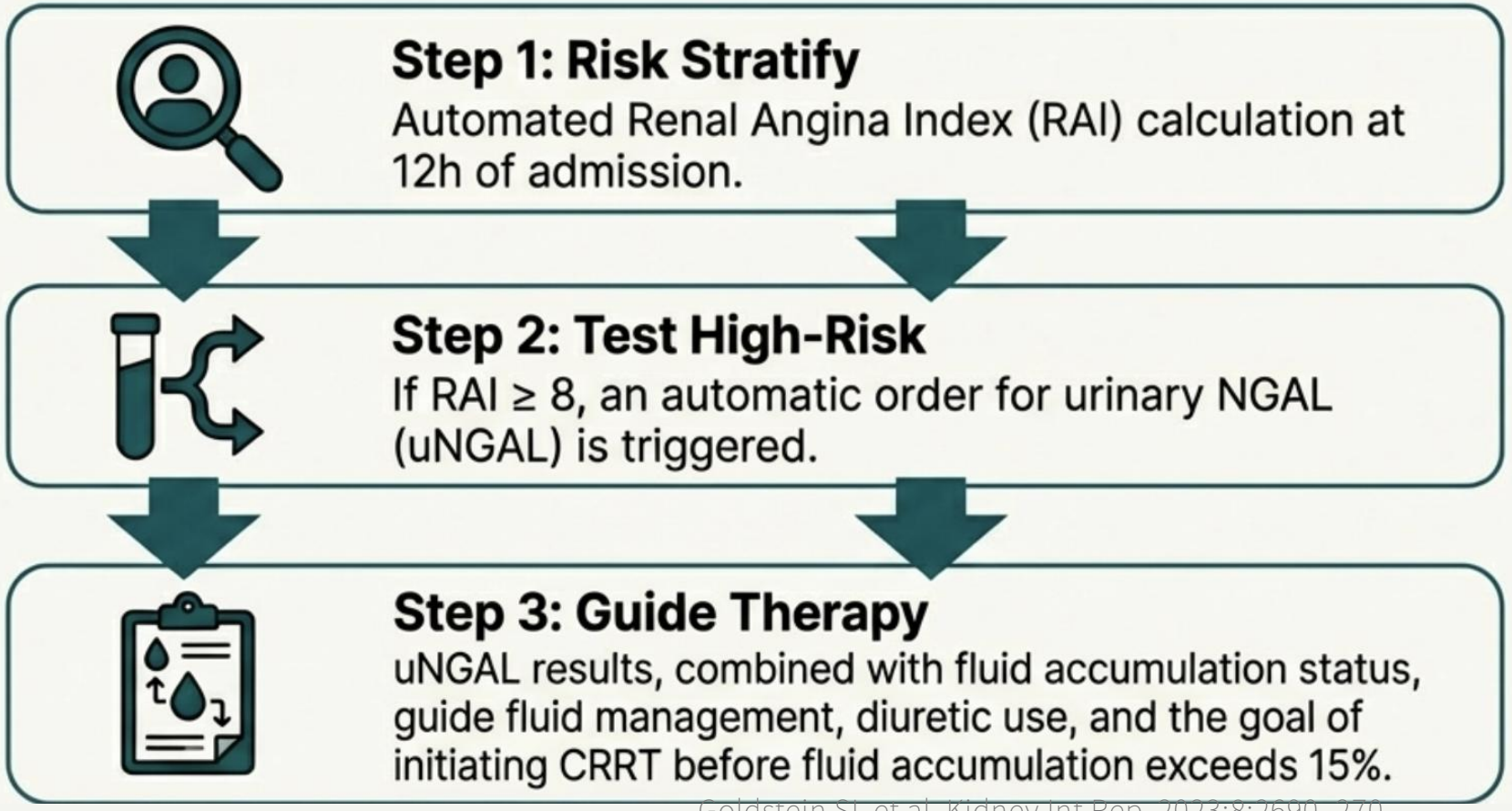
Conclusion: [TIMP-2]*[IGFBP7] is a useful tool for identifying patients at high risk for adverse AKI outcomes but should be integrated with other clinical risk factors.

Wang W et al. Ren Fail. 2023;45(2):2253933

Solution D: An Integrated System for Actionable Intelligence

Key Study: Goldstein et al., *Kidney Int Rep* (2023) - A prospective study implementing a Clinical Decision Support (CDS) pathway in a pediatric/young adult ICU.

The TAKING FOCUS 2 (TF2) Pathway



This approach moves beyond passive prediction to demonstrate how a biomarker-guided protocol can be systematically implemented to change practice and improve outcomes.

The Impact of a Biomarker-Guided CDS Pathway

Implementation of the TF2 pathway was associated with significant, durable improvements in both process of care and patient-centered outcomes for patients requiring CRRT.

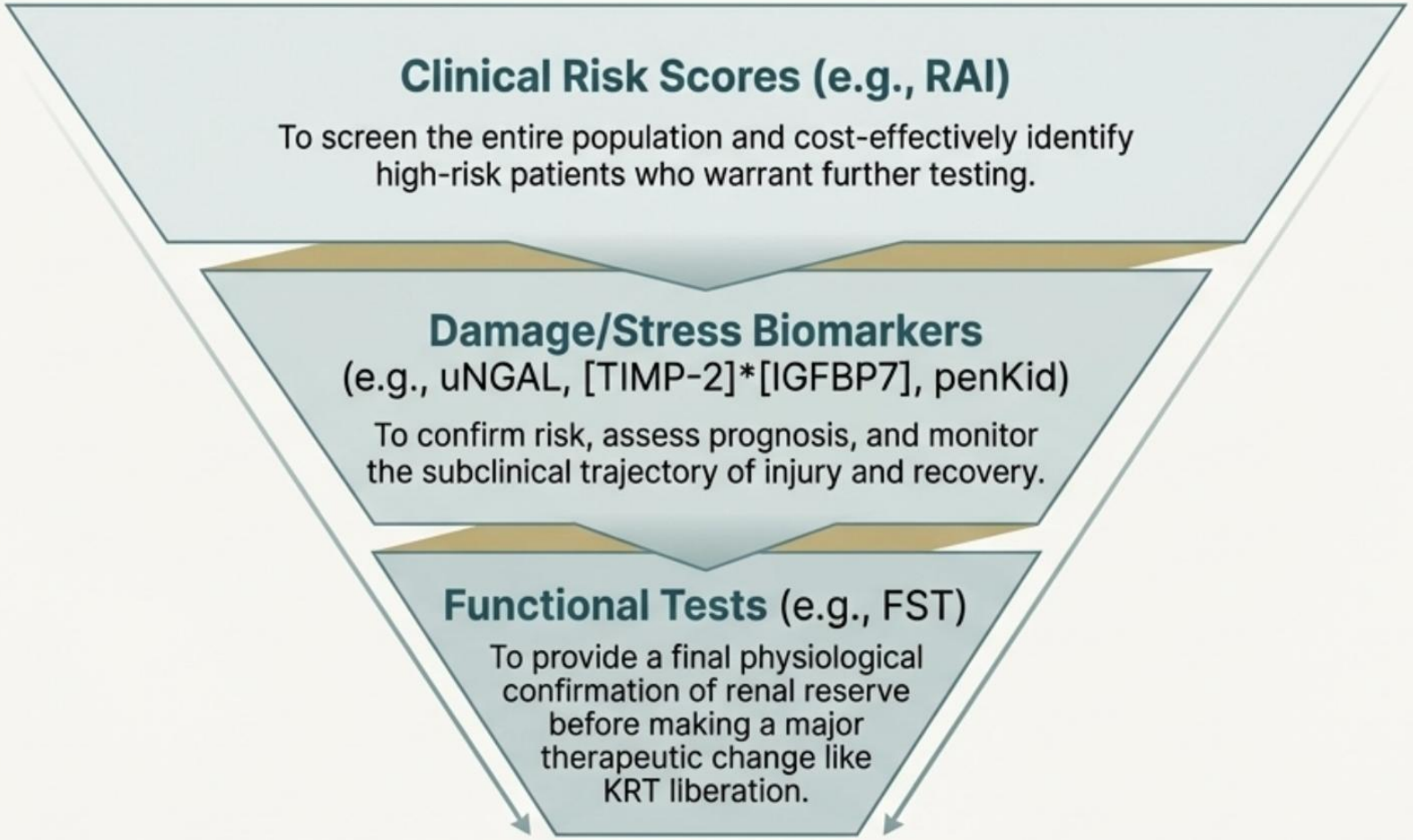
Metric (CRRT Patients)	Pre-TF2 Era	Post-TF2 Era	p-value
Time to CRRT Initiation (days)	4.5	**2.3**	0.002
Rate of >15% Fluid Accumulation	36.6%	**20.6%**	0.02
Survival to ICU Discharge	46.5%	**65.4%**	0.02
Total ICU LOS (days, Survivors)	24	**13**	0.02

Conclusion: A systematic, biomarker-informed CDS pathway can translate risk stratification into meaningful clinical action, leading to earlier CRRT initiation at lower fluid overload, shorter ICU stays, and improved survival.

Goldstein SL et al. Kidney Int Rep. 2023;8:2690–270

Synthesis: A Multi-Modal Approach to AKI Management

The evidence does not point to a single “magic bullet” biomarker. Instead, a more sophisticated, multi-modal strategy is emerging, combining different tools at different points in the patient’s course.



Wang W et al. Ren Fail. 2023;45(2):2253933.
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Goldstein SL et al. Kidney Int Rep. 2023;8:2690–2700.

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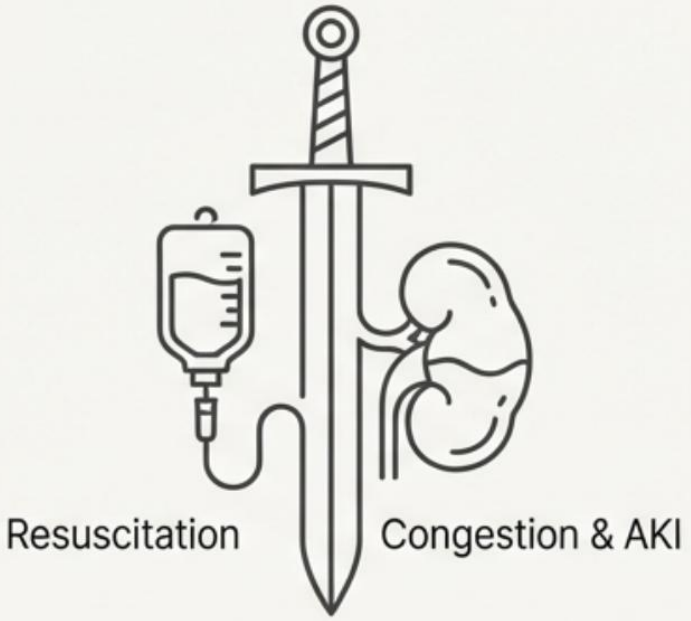
The Double-Edged Sword of Fluid Management in the Critically Ill



Fluid resuscitation is a cornerstone of sepsis management, yet it carries a substantial risk of iatrogenic harm. The transition from necessary resuscitation to harmful fluid overload is a critical challenge.

The core clinical dilemma remains: How do we balance necessary resuscitation with the prevention of harmful venous congestion?

The Pathophysiology of Venous Congestion:

- Excessive fluid administration can lead to **systemic venous congestion**, a primary driver of organ dysfunction.
- The encapsulated kidney is particularly vulnerable. Elevated central venous pressure (CVP) increases renal venous pressure, leading to interstitial edema and a "renal compartment syndrome."
- This impairs the glomerular filtration pressure gradient, promoting Acute Kidney Injury (AKI).

Clinical Impact:

- Multiple studies link positive fluid balance to an **increased incidence of AKI** and **mortality** in septic patients.
- The incidence of AKI in the critically ill ranges from **30% to 60%.**

The Challenge of Assessing Venous Congestion

Identifying the transition from euvolemia to harmful congestion at the bedside is notoriously difficult. Traditional methods have significant limitations.

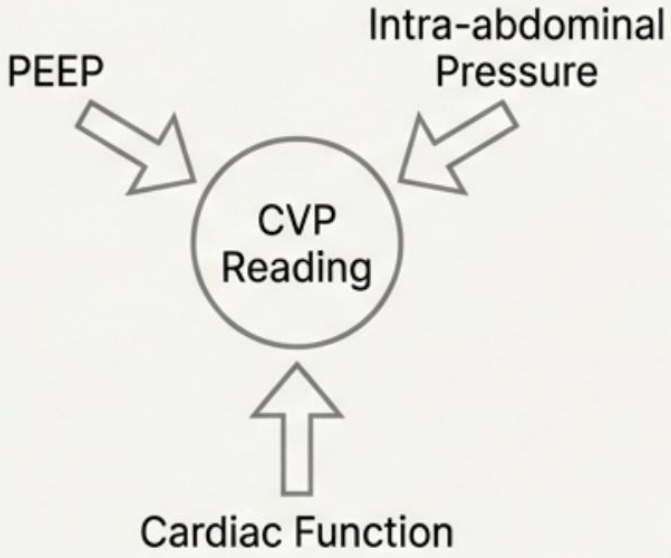
Central Venous Pressure (CVP): An Imperfect Standard

- **Invasive:** Requires a central venous catheter.
- **Unreliable:** CVP is influenced by numerous factors beyond intravascular volume, including ventilator settings (PEEP), intra-abdominal pressure, and cardiac function, complicating its interpretation.
- **Poor Correlation:** In a recent multicenter study of septic patients (Song et al., 2025), there was no significant correlation between CVP and VExUS grades.

Clinical Signs:

- Peripheral edema is a late and non-specific sign of systemic fluid overload and does not reliably correlate with organ-level congestion.

There is a critical need for a reliable, non-invasive method to quantify venous congestion and guide fluid management.

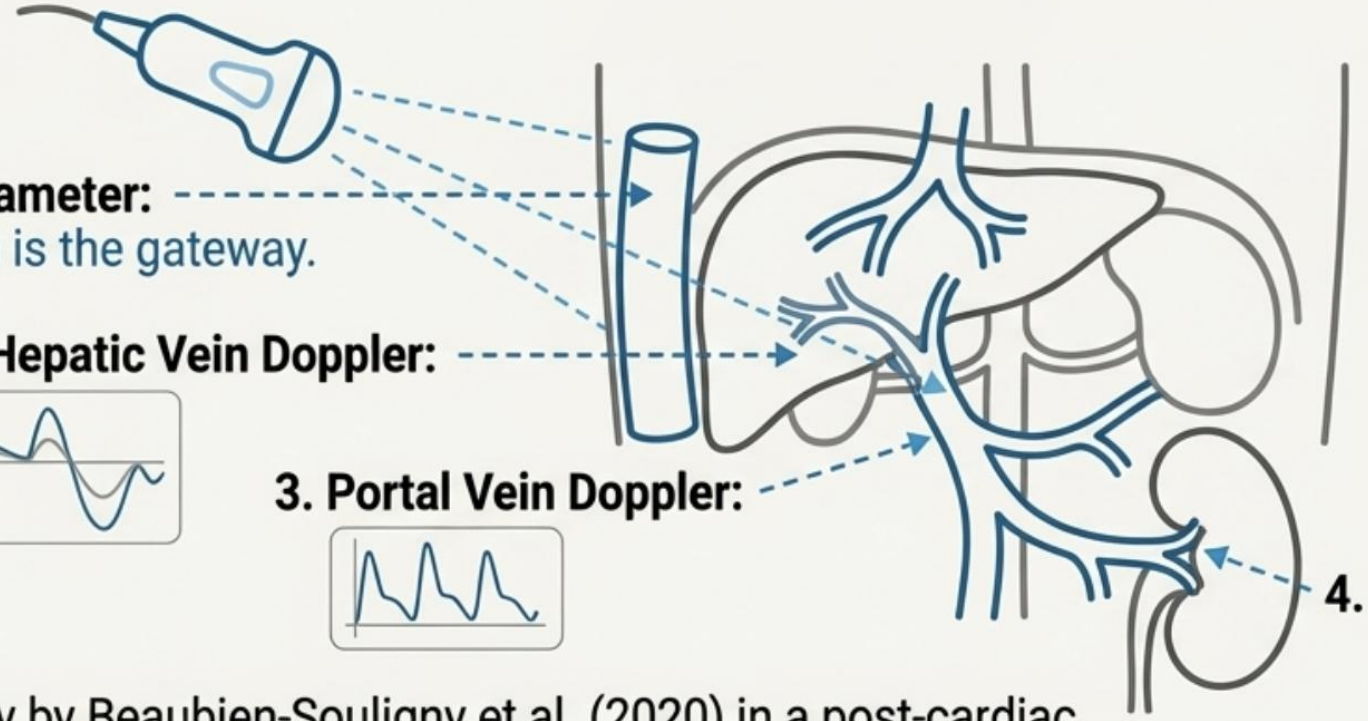


CVP vs. VExUS in Sepsis (Song et al., 2025)

Correlation Coefficient: **-0.019**
95% CI: -0.01 to 0.05
p-value: **0.204**

VExUS: A Non-Invasive Window into Systemic Congestion

The **Venous Excess Ultrasound (VExUS) score** was developed as a point-of-care tool to directly visualize and grade the severity of systemic venous congestion.



Initial Promise:

- The pioneering study by Beaubien-Souligny et al. (2020) in a post-cardiac surgery cohort demonstrated a strong association between a high VExUS score (≥2) and the development of severe AKI.
- This seminal work sparked widespread interest in its broader application across different critically ill populations.

The Generalizability Gap: From Cardiac Surgery to the General ICU

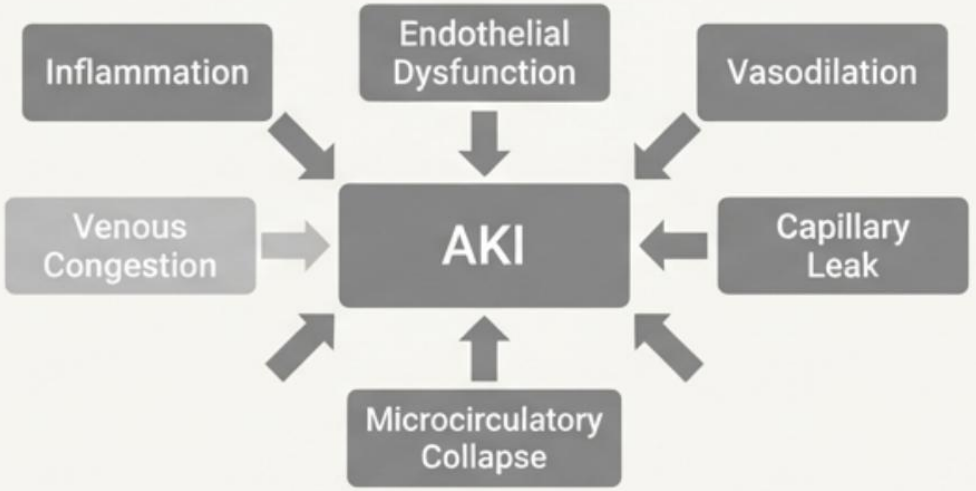
The initial success of VExUS was in a relatively homogenous post-cardiac surgery population, where cardiorenal syndrome and venous congestion are often primary drivers of AKI. The general ICU patient presents a far more complex picture.

Key Question 1: Does VExUS predict AKI in heterogeneous ICU populations like sepsis?

Cardiac Surgery

AKI is often driven by direct hemodynamic effects of venous congestion on the kidney.

Sepsis / General ICU



Sepsis-associated AKI involves a complex interplay of multiple factors. Venous congestion may be just one contributor.

The conflicting results in the literature highlight a critical need to validate VExUS in the diagnostically challenging environment of the general ICU before it can be widely adopted.

The Application Gap: Static Prediction vs. Dynamic Guidance

Even if an association exists, the optimal way to use VExUS in clinical practice remains undefined.

Key Question 2: Is a single VExUS measurement sufficient, or is its trajectory more informative?

Static Snapshot | Dynamic Trajectory

Most initial studies evaluated a single VExUS score at or near ICU admission. Critical illness, however, is a dynamic process. A single snapshot may not capture the evolving clinical picture of resuscitation, inflammation, and recovery.

Key Question 3: Is the primary role of VExUS prediction or therapeutic guidance?

Prognostication | Intervention

- **Prognostication:** Does a high VExUS score simply identify patients at high risk of AKI?
- **Intervention:** Can VExUS be used as a therapeutic target? Does actively working to lower the VExUS score with decongestive therapy improve patient outcomes?

Answering these questions is essential to move VExUS from a novel research tool to a clinically useful instrument.

The Sepsis Cohort: Static VExUS Fails to Predict AKI

A recent prospective, multicenter study by Song et al. (2025) directly tested the prognostic value of VExUS in 108 critically ill patients with sepsis.

Study Finding: An elevated VExUS score (≥2) measured serially on days 1, 3, and 5 was **not associated** with the primary outcome of AKI.

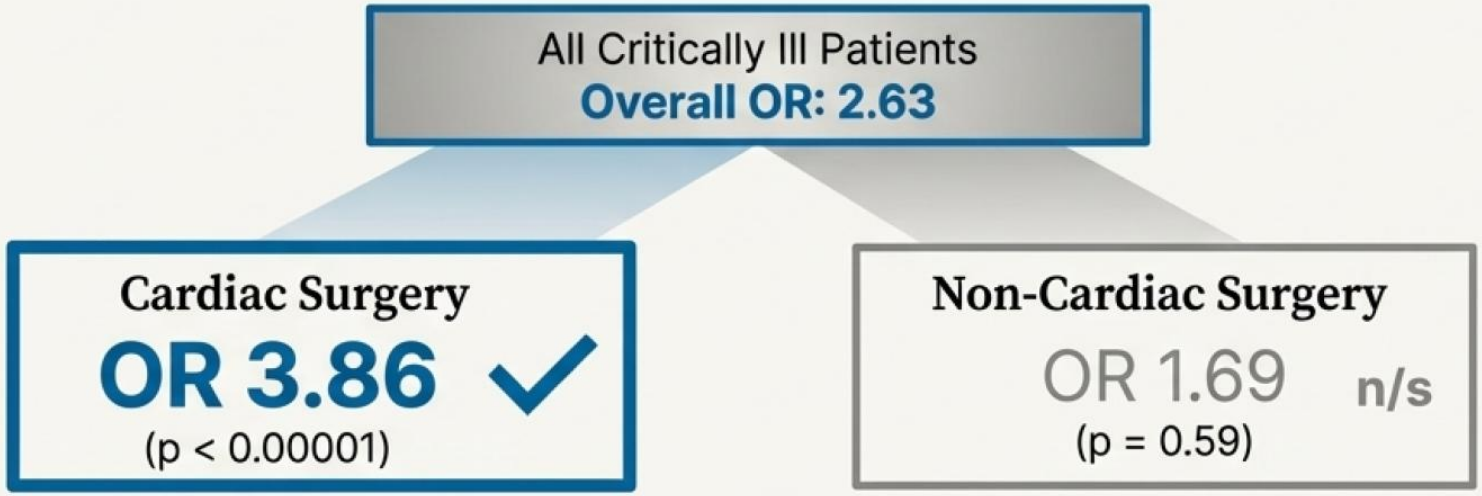
Outcome	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
AKI	**1.82**	**0.62 – 5.31**	0.274
30-day Mortality	0.82	0.28 – 2.40	0.711
Requirement for RRT	2.29	0.68 – 7.64	0.179

Key takeaway: This study suggests that in the complex pathophysiology of sepsis, a static VExUS score has limited utility for predicting AKI or mortality. The prevalence of significant congestion (VExUS ≥ 2) was also relatively low (18% on day 1).

The Meta-Analytic View: Association Is Highly Population-Dependent

A systematic review and meta-analysis by Melo et al. (2025) synthesized data from 9 observational studies (1036 patients) to clarify the overall association between VExUS and AKI.

- **Overall Finding:** Across all critically ill patients, a VExUS score ≥ 2 was significantly associated with AKI, with an overall Odds Ratio of 2.63 (95% CI 1.06–6.54; p = 0.04).



However, a crucial subgroup analysis reveals the source of this association:

Patient Population	Odds Ratio (OR) for AKI	95% Confidence Interval (CI)	p-value
Cardiac Surgery	**3.86**	**2.32 – 6.42**	**< 0.00001**
Non-Cardiac Surgery	1.69	0.25 – 11.53	0.59

Conclusion: The prognostic value of a static VExUS score for AKI is robust in cardiac surgery patients but is not statistically significant in the heterogeneous non-cardiac surgery/general ICU population. This largely reconciles the conflicting findings in the literature.

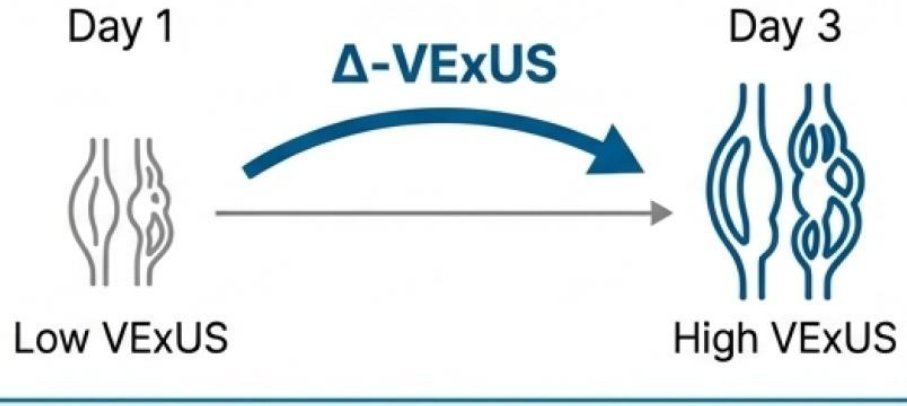
Trajectory Matters: The Shift from Static to Dynamic Assessment

A prospective study by Trigkidis et al. (2024) in 89 general ICU patients shifted the focus from single measurements to the change in congestion over time.

Study Findings:

- **Static Failure:** A single VExUS score on Day 1 or Day 3 was **not** associated with the primary outcome of Major Adverse Kidney Events at 30 days (MAKE30).
- **Dynamic Success:** The *change* in VExUS score from Day 1 to Day 3 (Δ-VExUS) **was** significantly associated with MAKE30, even after adjusting for confounders.

An increasing VExUS score over the first 3 days was an independent predictor of adverse renal outcomes.



Adjusted Hazard Ratio (HR) for MAKE30 per 1-point increase in VExUS:

HR: 2.07

(95% CI 1.17 – 3.66; p = 0.01)

Conclusion: The trajectory of venous congestion, rather than a single snapshot, holds significant prognostic value in the general ICU population. Worsening congestion is a key danger signal.

Trigkidis KK et al. Shock. 2024 Mar;61(3):400–405.

Beyond Prediction: VExUS as a Therapeutic Target for Decongestion

A quasi-experimental study by Rihl et al. (2023) investigated if VExUS could be used to guide therapy in 90 ICU patients with severe AKI.

Study Design & Findings:

- **Intervention:** The team suggested diuretic use for patients with a VExUS score >1. A repeat scan was performed after 48 hours.
- **Guidance was Followed:** Patients with VExUS >1 received significantly more diuretics (75.0% vs 38.9%, p=0.001).
- **Reduction was Associated with Better Outcomes:** Patients who successfully reduced their VExUS score in 48 hours had significantly more Renal Replacement Therapy (RRT)-free days.

	Outcome (RRT-free days at Day 28)	
VExUS Score Reduced	**28.0 (8.0–28.0)**	**0.012**
VExUS Score Not Reduced	15.0 (3.0–27.5)	

Conclusion: This study provides the first evidence that a VExUS-guided decongestion strategy may improve patient-centered renal outcomes. The role of VExUS may be more powerful as a guide to intervention than as a simple prognostic tool.

Rihl MF et al. J Ultrasound Med. 2023 Nov;42:2547–2556.

A New Paradigm: The Evolving Role of VExUS in the ICU

The latest evidence refines our understanding of VExUS, moving beyond its initial application. A comprehensive VExUS-based fluid strategy should incorporate three key principles:

1. Population Specificity

The predictive power of a single, static VExUS measurement for AKI is highest and most reliable in post-cardiac surgery patients. Its utility as a standalone prognostic marker in unselected sepsis or general ICU patients is patients is limited.

2. Emphasis on Trajectory

In the general ICU, serial VExUS assessments are critical. A worsening score (increasing congestion) over the first 48-72 hours is a stronger predictor of adverse outcomes than any single measurement. Dynamic assessment is superior to a static snapshot.

3. Application as a Therapeutic Guide

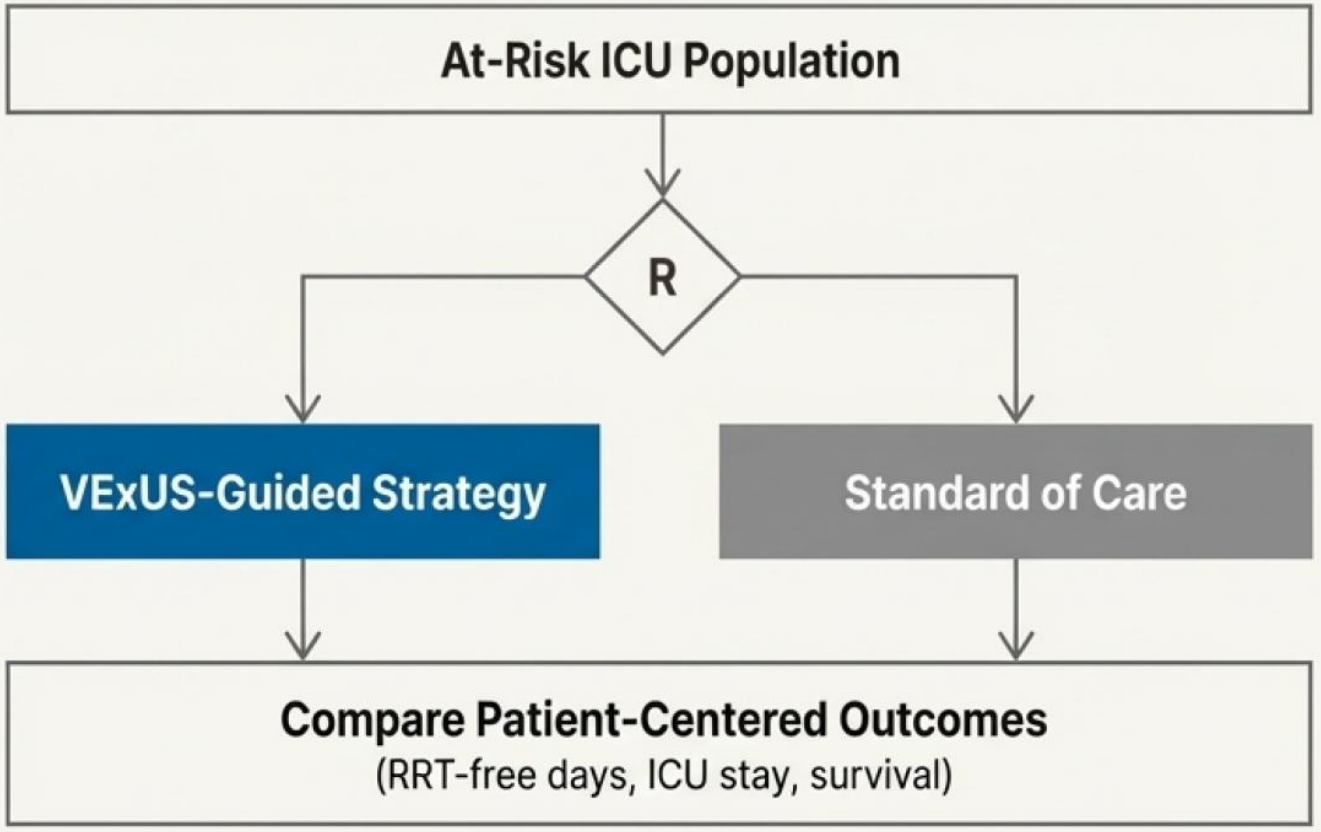
The most promising role for VExUS may be in guiding de-resuscitation. Identifying significant congestion can trigger and monitor the response to decongestive therapies (diuretics, ultrafiltration), with the goal of improving organ function and reducing the need for RRT.

Future Directions: From Observation to Intervention

While our understanding has grown, the evidence remains largely observational. The path forward requires a shift towards higher-level, interventional evidence to confirm clinical utility.

Key Research Priorities:

- **Large-Scale Validation of Trajectory:** Multi-center prospective studies are needed to confirm that Δ-VExUS is a robust predictor of outcomes across diverse ICU populations.
- **Defining Therapeutic Thresholds:** What VExUS score should trigger decongestion? What is the optimal target for reduction?
- **The Ultimate Test: Randomized Controlled Trials (RCTs):** The most critical next step is to conduct RCTs comparing a VExUS-guided fluid management and de-resuscitation strategy against standard of care.



Primary Question for RCTs: Does a protocolized approach to de-resuscitation based on serial VExUS assessments lead to improved patient-centered outcomes, such as more RRT-free days, shorter ICU stays, and improved survival?

Issues Addressed

- From Prediction, Alert, to Action
- Updated Roles of AKI Biomarkers
- VeXUS and Fluid Management
- Could We Liberate from KRT More Effi ciently?

Shifting Focus from Survival to Recovery

While mortality data is equivocal, a different signal has emerged from observational studies, pointing to a new and critical knowledge gap.

The Emerging Signal:

- Multiple large cohort studies and meta-analyses suggest that initial treatment with **CKRT is associated with a higher likelihood of kidney recovery and independence from dialysis** among survivors.
- A meta-analysis of 23 studies found patients starting on IHD had a nearly doubled risk of KRT dependence (**RR 1.99**; 95% CI, 1.53 to 2.59).
- Large cohort studies from France, Sweden, and Canada consistently show lower rates of dialysis dependence at hospital discharge with initial CKRT.

The New Knowledge Gap:

This raises a crucial question: If repetitive dialysis-induced hemodynamic stress can impede recovery, how should we manage KRT once a patient stabilizes?

Current practice lacks an **evidence-based approach for weaning and liberation from KRT**. Patients are often transitioned to a conventional thrice-weekly IHD schedule, but it is unknown if this standard of care actively hinders or masks recovery.

Liu KD et al. JAMA. 2025 Nov 7. doi: 10.1001/jama.2025.21530

Gap 1: The Lack of a Proven Strategy to Enhance Kidney Recovery **Solution:** The LIBERATE-D Randomized Clinical Trial

The LIBERATE-D trial was designed to test whether a less-intensive, indication-driven dialysis strategy could improve kidney function recovery in patients with established AKI-D.

Trial Element	Description
Population	220 hospitalized, hemodynamically stable adults with AKI-D who had already initiated KRT. Mean baseline eGFR was ~65 mL/min/1.73 m². Patients were a median of 9 days post-KRT initiation.
Intervention	**Conservative Dialysis Strategy:** Dialysis was performed *only* when specific clinical or metabolic indications were met (e.g., BUN >112 mg/dL, K+ >6 mmol/L, severe acidosis, or volume overload causing hypoxemia).
Comparison	**Conventional Dialysis Strategy:** Dialysis was performed thrice-weekly until clear evidence of recovery was present (e.g., urine creatinine clearance >20 mL/min).
Primary Outcome	Kidney function recovery at hospital discharge, defined as being alive and dialysis-free for at least 14 consecutive days.

This trial directly challenges the default 'thrice-weekly' paradigm by testing the hypothesis that less dialysis may lead to better outcomes.

Liu KD et al. JAMA. 2025 Nov 7. doi: 10.1001/jama.2025.21530

Gap 2: Does Reducing Dialysis Intensity Improve Recovery Rates?
Solution: A Conservative Strategy Leads to More Frequent Recovery

The LIBERATE-D trial demonstrated that dialyzing based on clinical need rather than a fixed schedule significantly increased the likelihood of kidney recovery.

Conservative Group:
64.2% (70 of 109) achieved recovery

Conventional Group:
50.5% (55 of 109) achieved recovery

Effect Size (Unadjusted):
Absolute Difference: **13.8%** (95% CI, 0.8% to 26.8%; p=0.04)
Odds Ratio: **1.76** (95% CI, 1.02 to 3.03; p=0.04)

These results provide strong evidence that the conventional thrice-weekly approach may actively delay or prevent recovery in this patient population.

Liu KD et al. JAMA. 2025 Nov 7. doi: 10.1001/jama.2025.21530

Gap 3: What is the Impact of Dialysis Intensity on Treatment Burden and Safety?
Solution: A Conservative Strategy Safely Reduces Dialysis Burden

The conservative strategy not only improved recovery but also significantly reduced the burden of treatment and was associated with fewer adverse hemodynamic events.

Secondary outcomes:

Outcome	Conservative Group	Conventional Group	Difference (95% CI)
Dialysis Sessions per Week	Median **1.8**	Median **3.1**	**-1.4** (-1.8 to -1.0)
Dialysis-Free Days to Day 28	Median **21 days**	Median **5 days**	**16 days** (5 to 27)
Time to Recovery (to Day 90)	Median **2 days**	Median **8.5 days**	**-6.5 days** (-10.2 to -2.8)

Key Safety Finding:

- **Dialysis-Associated Hypotension**: The conservative group experienced fewer total hypotensive events (**69 events**) compared to the conventional group (**97 events**), despite higher ultrafiltration rates when dialysis was performed.
- There was no increase in other serious adverse events, including hyperkalemia or severe acidosis.

This demonstrates that a less-intensive approach is not only more effective but also safer, likely by reducing the cumulative hemodynamic stress on recovering kidneys.

Synthesizing the Evidence: A Paradigm Shift in AKI-KRT

The LIBERATE-D results, viewed in the context of prior research, prompt a fundamental shift in our approach to KRT for acute kidney injury.

1. **The Question Has Evolved:** The most critical decision may not be **CKRT vs. IHD** at initiation, but rather **how much vs. how little** dialysis during the recovery phase.

2. **Dialysis is Not Benign:** The trial provides strong RCT evidence for the long-held hypothesis that **intermittent hemodialysis itself can be injurious**. By minimizing exposure through an indication-driven strategy, we can mitigate this harm and **facilitate intrinsic kidney recovery**.

3. **Rethinking 'Standard of Care':** **Routine thrice-weekly dialysis** for stable AKI-D patients is a convention inherited from end-stage kidney disease practice. LIBERATE-D suggests this is suboptimal and that a more **personalized, de-escalation approach** is superior.

The focus should move from a dogmatic debate on modality to a pragmatic, patient-centered strategy of applying the right intensity of therapy at the right time.

Liu KD et al. JAMA. 2025 Nov 7. doi: 10.1001/jama.2025.21530

Summary

- Prediction models exist; impact needs actionable interventions.
- E-alerts change behavior; don’t improve outcomes; may increase dialysis.
- AKI bundles reduce progression/RRT; mortality benefit unproven.
- Integrate scores + biomarkers + congestion tools into CDS pathways.
- VeXUS, Useful in certain groups, yet need to be validated vigorously
- Liberate from KRT in subacute patients, find the patients, closely monitor and then success.