

Net Ultrafiltration During Continuous Kidney Replacement Therapy for Acute Kidney Injury: From Fixed Rates to Precision Fluid Removal

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Fluid overload is common among critically ill patients with acute kidney injury (AKI), particularly those requiring continuous kidney replacement therapy (CKRT), and is consistently associated with adverse clinical outcomes. Net ultrafiltration (UFNET), defined as the extracorporeal removal of fluid from the patient to reduce extracellular volume, is therefore a fundamental component of CKRT. However, unlike solute clearance, UFNET has historically been prescribed without well-established dosing principles. Insufficient fluid removal may prolong exposure to pulmonary, systemic, and organ edema, whereas overly rapid fluid removal may exceed vascular refill, reduce effective circulating volume, provoke hemodynamic instability, and potentially impair organ perfusion and kidney recovery. Observational studies have suggested a J- or U-shaped relationship between UFNET rate and mortality, with intermediate rates potentially indicating a favorable outcome with lower mortality.

More recent evidence challenges the interpretation of these observational thresholds as causal treatment targets. A recent multicenter analysis using hourly CKRT and fluid-balance found that the association between UFNET and mortality was substantially mediated by achieved fluid balance. Furthermore, the RELIEVE-AKI feasibility randomized trial demonstrated that maintaining targeted restrictive and liberal UFNET was challenging, as clinicians repeatedly adjusted the prescribed regimen. These findings suggest that UFNET should not be conceptualized as a fixed dose analogous to small-solute clearance. Rather, UFNET is a dynamic intervention whose appropriate intensity depends on the competing objectives of relieving congestion and preserving circulatory and organ perfusion.

This review examines the terminology, physiology, observational and interventional evidence, challenges in causal inference, bedside assessment, clinical phenotypes, kidney recovery, and future research priorities related to UFNET during CKRT. We propose a conceptual framework in which fluid-removal need and fluid-removal tolerance could determine individualized UFNET prescription, with repeated reassessment based on achieved fluid balance and physiologic response.

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INTRODUCTION

Acute kidney injury is among the most frequent forms of organ dysfunction encountered in the ICU.^{1,2} In the most severely ill patients, kidney replacement therapy is required to control metabolic abnormalities and volume status. CKRT is particularly useful in patients with hemodynamic instability because it enables continuous removal of solutes and fluids over prolonged periods.³ Despite advances in CKRT technology and substantial investigation into modality, solute-clearance dose, anticoagulation, and timing of treatment initiation, mortality among patients with severe AKI requiring kidney replacement therapy remains high.³ Tehranian and colleagues noted mortality of approximately 50% in this population, illustrating that optimization of conventional CKRT solute dosing alone has not resolved the substantial residual risk associated with critical illness and severe AKI.⁴

Fluid accumulation is particularly relevant to this risk.⁵⁻⁷ Approximately two-thirds of critically ill patients with AKI requiring kidney replacement therapy develop clinically relevant fluid overload, as fluid accumulation is associated with mortality, impaired kidney recovery, prolonged mechanical ventilation, and other organ dysfunction. More recent literature has adopted the broader concept of fluid accumulation syndrome, commonly characterized by cumulative positive fluid balance exceeding approximately 5 to 10% of the admission body weight.⁸ This syndrome has been highlighted as an important determinant of prolonged ventilation, ICU resource use, and mortality.⁸⁻¹⁰

Once diuretic therapy and fluid restriction are insufficient, extracorporeal fluid removal becomes an important therapeutic function of CKRT.¹¹⁻³ The objective, however, is not simply to remove as much fluid as technically possible. Inadequate removal may perpetuate interstitial and organ edema, whereas removal faster than the circulatory tolerance may reduce intravascular volume, compromise cardiac output, and impair tissue perfusion.^{11,14} The UFNET prescription, therefore, represents a balance between two competing hazards.¹¹

Despite its clinical importance, UFNET remains less standardized than almost every other

component of CKRT prescription. A European survey of 485 practitioners across 31 countries demonstrated marked variation in practice. The median initial UFNET prescription in hemodynamically stable patients was 149 mL/h, the maximum prescription was 300 mL/h, and the typical rate in hemodynamically unstable patients was 98 mL/h, with substantial between-country variation.¹⁵

Over the past decade, UFNET has increasingly been viewed as a potentially modifiable CKRT exposure. Initial observational studies suggested that greater fluid removal could improve survival among markedly fluid-overloaded patients.^{4,16} Subsequent analyses, however, associated high weight-normalized UFNET rates with increased mortality, prompting the hypothesis that both extremes might be harmful.^{11,17,18} More recent analyses have further complicated this paradigm by suggesting that achieved fluid balance, not UFNET rate itself, may be the more clinically meaningful exposure.⁹

The objectives of this review are therefore to define UFNET terminology, examine the physiologic rationale for fluid removal and potential mechanisms of harm, critically evaluate the observational and interventional evidence, examine causal inference challenges, describe an individualized bedside approach, and identify priorities for future research. The central premise is that UFNET should be considered a dynamic, titratable treatment embedded within overall fluid management, rather than an isolated machine setting with a universally applicable target rate.^{9,14,19}

TERMINOLOGY AND CONCEPTUAL FRAMEWORK

Ultrafiltration Versus Net Ultrafiltration

Terminological inconsistency has complicated the interpretation of the UFNET literature. “Ultrafiltration” may refer technically to water movement across the hemofilter membrane, total machine effluent, or clinically intended fluid removal from the patient. These quantities are not interchangeable.¹¹ For CKRT fluid-management research, net ultrafiltration (UFNET or NUF) is the most clinically relevant concept. The most common definition of UFNET is the “net extracellular

volume of fluid removed from the patient using an extracorporeal device with the intention of reducing fluid overload".^{11,19} This definition focuses appropriately on the patient-level therapeutic exposure rather than total extracorporeal effluent.

In continuous venovenous hemodiafiltration, for example, net ultrafiltration can be expressed as total effluent volume minus dialysate and replacement fluid volumes. The RENAL-derived heterogeneity analysis used this formulation and subsequently calculated weight-normalized UFNET rate as cumulative UFNET volume divided by body weight and actual treatment duration.¹⁷

Machine Fluid Removal Versus Patient Fluid Balance

A crucial distinction exists between extracorporeal fluid removal and whole-patient net fluid balance. A patient receiving UFNET of 150 mL/h while simultaneously receiving 200 mL/h of intravenous medications, nutrition, blood products, and other fluids remains in positive fluid balance despite active ultrafiltration. Conversely, an identical UFNET rate in a patient receiving minimal fluid intake may result in a substantial negative balance.⁹

Thus, patient fluid balance is equivalent to all fluid inputs minus all fluid outputs, where outputs include urine, gastrointestinal losses, drains, blood loss, and extracorporeal net fluid removal. Identical UFNET rates can produce substantially different net fluid balances depending on concurrent fluid administration, and the apparent mortality association of UFNET is largely mediated through its effect on fluid balance.⁹

Prescribed Versus Delivered UFNET

Another important distinction is between the ultrafiltration rate clinicians intend to deliver and the rate actually delivered. Delivered UFNET may diverge from the prescription due to hemodynamic instability, circuit downtime or clotting, procedures and transport, interruptions for diagnostic testing, changes in fluid intake, clinician or nursing adjustments, rescue fluid administration, changes in urine output and deliberate physician override.^{19,20} In the RELIEVE-AKI trial, substantial separation existed between intended treatment strategies, yet the delivered rates converged because liberal

UFNET was frequently reduced, and restrictive UFNET was frequently required to escalate or rescue.^{19,21}

Absolute Versus Weight-normalized UFNET

UFNET can be expressed as an absolute rate, usually mL/h, or normalized to body weight as mL/kg/h or mL/kg/d.¹¹ Absolute rates are intuitive at the bedside but yield markedly different physiologic exposures across patients of different sizes. Weight normalization potentially improves comparability, but the appropriate denominator is unresolved. Published studies have variously used admission weight, weight at CKRT initiation, enrollment weight, or predicted body weight.^{4,16,17,19} Fluid accumulation itself alters measured body weight, making it possible that the denominator is partly determined by the exposure being treated.^{16,17} For example, in the RENAL trial analyses, investigators used weight at enrollment. The investigators acknowledged that this weight could already have been affected by fluid overload, introducing uncertainty into the normalized exposure.¹⁷ RELIEVE-AKI instead used predicted body weight within its automated dosing strategy.^{19,22}

Cumulative Fluid Balance and Percentage Fluid Overload

Fluid accumulation is commonly quantified using cumulative balance or percentage fluid overload. Percentage fluid overload is roughly estimated as cumulative fluid balance divided by the reference body weight multiplied by 100. Thresholds of 5 and 10% have frequently been used to identify clinically important fluid accumulation.⁵⁻⁷ Importantly, these cutoffs describe accumulated volume burden rather than the rate at which fluid is subsequently removed.

UFNET Intensity, Cumulative Removal, and Duration

The literature has sometimes used the term "UFNET intensity" to refer to a time-averaged rate.¹⁶ These measures should be separated conceptually as: 1) UFNET rate: fluid removed per unit time, often mL/kg/h; 2) Cumulative UFNET: total extracorporeal volume removed; 3) UFNET

exposure duration: duration over which active removal occurs; 4) UFNET trajectory: how the rate changes over time; and 5) Achieved fluid balance: overall result after accounting for all inputs and outputs. Two patients can therefore have the same average UFNET rate but substantially different peak rates, cumulative removal, treatment duration, fluid inputs, and resulting fluid balance.^{9,17}

Proposed Terminology

For clarity, the terminology for this review is outlined in Table 1. This terminology reinforces an essential distinction that UFNET is an intervention and fluid balance is an outcome of that intervention, combined with all other fluid inputs and outputs.⁹

WHY REMOVE FLUID DURING CKRT?

Fluid accumulation during critical illness results from both disease biology and treatment. Sepsis, systemic inflammation, surgery, shock, and ischemia increase endothelial permeability and promote the movement of fluid from the vascular to the interstitial compartment.⁸ At the same time, patients commonly receive substantial quantities of resuscitation fluids, maintenance solutions, medication carriers, nutrition, and blood products. When AKI reduces urine output, the ability to excrete this volume is impaired.^{10,13} Fluid accumulation is therefore not merely an increase in total body water. It represents the redistribution of sodium and water across vascular and interstitial compartments in a patient whose endothelial permeability, vascular tone, cardiac function, and renal function may all be abnormal.^{8,14}

Pulmonary Consequences

Pulmonary interstitial and alveolar edema impair lung compliance and gas exchange, increase ventilatory requirements, and may prolong the need for mechanical ventilation.²³ Consistent with this

biological rationale, fluid accumulation syndrome is associated with prolonged mechanical ventilation and longer ICU stays.^{7,24}

Renal Congestion

The kidney is particularly vulnerable to venous congestion. Increased central and renal venous pressure raises renal interstitial pressure, potentially reducing the effective transrenal perfusion gradient.^{23,25} Intra-abdominal hypertension may amplify this process. Tehranian and colleagues summarized evidence linking cumulative fluid balance, intra-abdominal hypertension, venous congestion, and AKI, suggesting that fluid accumulation can be both a consequence and a potential contributor to persistent renal dysfunction.^{23,25}

Cardiac and Systemic Consequences

Interstitial edema may adversely influence myocardial function, hepatic congestion, gastrointestinal wall integrity and absorption, tissue oxygen diffusion, and wound healing.¹³ Congestion is particularly important in cardiorenal syndrome, where elevated venous pressure, sodium retention, neurohormonal activation, and reduced cardiac performance form a reinforcing cycle.^{23,25} The cardiorenal review in the uploaded literature describes systemic congestion and “nephrosarca” as clinically relevant manifestations of this interaction.

FLUID ACCUMULATION AS MARKER OF MEDIATOR

Fluid accumulation is also strongly confounded by illness severity. Patients with profound shock receive more fluid, develop more severe AKI, require more vasopressors, and are simultaneously more likely to die. A positive balance can therefore be a marker of disease severity.^{10,26} Nevertheless, the consistency of associations between persistent

Table 1. Terminology

Concept	Definition
UFNET rate	delivered net extracorporeal fluid removal normalized to weight and time
UFNET volume	cumulative net extracorporeal fluid removal
Fluid balance	whole-patient inputs minus outputs
Fluid accumulation/fluid overload	accumulated positive balance relative to a reference body weight
UFNET prescription	intended rate or range
Delivered UFNET	fluid-removal exposure actually received

positive balance and adverse outcomes, the biologic mechanisms underlying organ edema and venous congestion, and the improvement associated with successful decongestion support the possibility that fluid accumulation is also a mediator of injury.^{5,6,10}

This distinction has major implications for UFNET research. If fluid accumulation is purely a marker, increasing extracorporeal removal would not necessarily improve the outcome. If it is partly mediated, timely decongestion may represent an important modifiable treatment target.^{9,16}

PHYSIOLOGY OF NET ULTRAFILTRATION

The physiologic effect of UFNET is determined not by extracorporeal removal alone but by the interaction between fluid removal and redistribution of fluid among extracellular compartments.¹⁴

Plasma Volume and Interstitial Fluid

UFNET directly removes plasma volume from the vascular compartment. Maintenance of effective circulating volume, therefore, depends on the movement of fluid from the interstitial space into the intravascular compartment, commonly referred to as plasma refill.¹⁴ When vascular refill approximately matches extracorporeal removal, substantial total-body decongestion may occur without major circulatory compromise. When UFNET exceeds refill, intravascular volume falls.^{11,14}

Plasma refill depends on hydrostatic and oncotic gradients, vascular permeability, venous pressures, interstitial fluid availability, cardiac function, and the underlying inflammatory state. In critical illness, these determinants may change over hours in the course of critical illness.¹⁴ A patient with severe peripheral edema may appear to have abundant removable fluid but simultaneously have limited effective intravascular reserve. Conversely, patients with venous congestion and relatively preserved vascular refill may tolerate substantial removal. Patients with severe illness, vasopressor requirements, and ongoing capillary leak, refill may be too limited to compensate for high UFNET rates.²⁷

Venous Capacitance, Preload, and Cardiac Output

The circulation contains both stressed and

unstressed blood volume. A reduction in stressed volume can reduce mean systemic filling pressure and thus venous return. Whether this translates into lower cardiac output depends on ventricular function and preload responsiveness.¹⁴ Consequently, the same absolute volume removal can produce very different hemodynamic consequences. A preload-independent patient with venous congestion may tolerate removal well. A preload-responsive patient with distributive shock may experience a fall in stroke volume.¹⁴

Neurohormonal and Microcirculatory Effects

Rapid intravascular volume contraction can stimulate sympathetic and neurohormonal responses and may impair microvascular perfusion despite apparently acceptable systemic blood pressure. Evidence from maintenance hemodialysis demonstrates an association between rapid ultrafiltration and myocardial hypoperfusion or stunning. This is while chronic hemodialysis differs substantially from CKRT-treated critical illness, these observations provide biologic plausibility for cardiovascular injury when fluid removal exceeds circulatory tolerance.^{11,28-30}

The implication is fundamental, which is that UFNET cannot be interpreted as a dose with a uniform biological effect. A rate of 1.5 mL/kg/h may be well tolerated in one patient and excessive in another.^{11,14}

FLUID TOLERANCE

Fluid management is often framed in terms of fluid responsiveness, meaning cardiac output increases after fluid administration. Fluid responsiveness, however, does not determine whether additional fluid is desirable.¹⁴ A patient may be fluid responsive while simultaneously experiencing pulmonary or venous congestion. This distinction motivates the complementary concept of fluid tolerance. Fluid tolerance is the patient's ability to receive or retain additional fluid without clinically significant organ consequences.¹⁴

The corresponding concept during de-resuscitation is fluid-removal tolerance. This is the ability to remove fluid without compromising effective circulation, tissue perfusion, or organ function.¹⁴ Fluid-removal tolerance depends on

the degree and distribution of congestion, vascular refill, cardiac reserve, vasoplegia, vasopressor dependence, capillary permeability, mechanical ventilation, right ventricular function, ongoing fluid inputs, and trajectory of kidney recovery.¹⁴

This framework helps reconcile seemingly contradictory observations. A patient may have a strong need for fluid removal because of pulmonary or systemic congestion, but poor tolerance because of severe vasoplegia or right ventricular preload dependence.¹⁴ Thus, the clinically meaningful question is not the optimal UFNET rate, but it is about the rate and trajectory of fluid removal that will achieve the desired fluid-balance goal while remaining within each patient's current physiologic tolerance. This leads to the conceptual framework that fluid-removal need and fluid-removal tolerance could determine individualized UFNET prescription. Notably, both of these variables change over time.^{9,14}

FLUID STEWARDSHIP, ROSE, AND TIMING OF UFNET

Fluid therapy in critical illness can be conceptualized using the ROSE framework, i.e., resuscitation, optimization, stabilization, and evacuation.⁸ During resuscitation, the immediate priority is restoration of perfusion. Active net fluid removal may be inappropriate when uncontrolled shock and true intravascular depletion dominate.⁸ During optimization, clinicians repeatedly assess whether additional fluid, vasopressors, inotropes, or other therapies can improve circulation while avoiding unnecessary accumulation.⁸ During stabilization, ongoing fluid input should be minimized, and cumulative fluid balance should be reassessed. The presence of persistent oliguria or fluid accumulation may become increasingly important.⁸ Finally, during evacuation or de-resuscitation, accumulated fluid becomes an active therapeutic target. Diuretics are generally preferred when effective, but CKRT-based UFNET becomes important when kidney failure, oliguria, diuretic resistance, or other CKRT indications coexist.^{8,13}

The transition between these phases is rarely discrete. Fluid removal may begin while low-dose vasopressors are still required, particularly when pulmonary edema or severe venous congestion is

itself contributing to organ dysfunction.^{8,14} The European practice survey illustrates this variability. Persistent oliguria or anuria was the most frequently reported criterion for UF initiation, followed by pulmonary edema.¹⁵

Active fluid removal should generally be reconsidered when evidence emerges that UFNET is exceeding physiologic tolerance. However, hypotension alone should not automatically trigger complete cessation. CKRT-associated hypotension may arise from vasoplegia, impaired myocardial performance, or other processes unrelated to fluid removal.^{14,15} The survey authors specifically cautioned that reducing or stopping UFNET may not always be appropriate in a persistently congested patient.¹⁵ The endpoint of de-resuscitation is also dynamic. As congestion resolves, urine output returns, or effective circulating volume becomes increasingly limiting, the treatment objective should shift from negative balance toward neutrality and, eventually, CKRT liberation.¹⁴

PRESCRIBED AND DELIVERED UFNET DURING CKRT

UFNET prescription requires translation of a clinical fluid-balance goal into an extracorporeal fluid-removal rate. One simple approach is to define the desired 24-hour net balance and estimate expected inputs and non-CKRT outputs. The resulting extracorporeal requirement can then be distributed across treatment hours.^{11,19} Yet this apparently straightforward calculation becomes complex because ICU fluid inputs and outputs change continuously.⁹ Relevant inputs include maintenance and resuscitation fluids, vasopressor and sedative carriers, antibiotics, nutrition, blood products, and other medication infusions.³¹ Outputs include urine, gastrointestinal losses, drains, blood loss, insensible loss, and UFNET.⁹

Daily fluid-balance goals provide clinical direction, but hourly titration allows adaptation to physiologic changes. Both levels are necessary.^{9,12} An hourly rate without a daily goal risk treating the machine rather than the patient. Conversely, a daily goal without frequent reassessment risks continuing at an inappropriate rate.⁹

Real-world practice frequently diverges from prescription. In the European survey, only

about one-quarter of practitioners reported hourly monitoring of net fluid balance, and substantial discrepancies between prescribed and delivered balance were recognized.^{12,15} Frequent UFNET assessment and management is unusual among ICU therapies because bedside nurses may need to make frequent adjustments while simultaneously managing numerous competing clinical demands.^{20,22}

RELIEVE-AKI provides valuable implementation data. In a survey of 90 nurses, 59% believed weight-based UFNET reduced severe fluid overload, and 50% believed it reduced intradialytic hypotension; however, increased workload, time requirements, and reduced perceived flexibility were common concerns.²² These observations emphasize that a theoretically optimal UFNET protocol will fail if it cannot be reliably implemented within the bedside workflow.^{20,22}

RELIEVE-AKI used a web-based calculator incorporating predicted body weight, treatment assignment, and concurrent intravenous fluid infusion to generate an hourly UFNET range.^{19,22} Automated decision support could eventually integrate fluid inputs, urine output, CKRT interruptions, vasopressor trajectory, blood pressure, congestion measures, current UFNET exposure, and cumulative fluid balance. However, nursing feedback emphasized that automation should augment rather than replace bedside clinical judgment.²²

UFNET RATE AND OUTCOMES

The central challenge in the UFNET literature is that observational studies have produced apparently discordant associations. Chronologically, however, these studies describe an evolving understanding rather than necessarily contradictory biology. Murugan and colleagues studied 1,075 critically ill patients with at least 5% fluid overload before kidney replacement therapy. UFNET intensity was classified as ≤ 20 , > 20 to 25, or > 25 mL/kg/d. One-year mortality was 69.7, 60.2, and 59.4%; respectively. After multivariable adjustment, UFNET > 25 mL/kg/d was associated with lower mortality than UFNET ≤ 20 mL/kg/d (adjusted odds ratio = 0.61; 95% CI: 0.41 to 0.93). Propensity-matched analyses produced similar findings.¹⁶

The study therefore suggested that insufficient extracorporeal removal in substantially fluid-overloaded patients might be harmful. However, the authors appropriately questioned whether the capacity to tolerate higher UFNET represented a treatment effect or simply a marker of recovery.¹⁶

A separate retrospective Mayo Clinic cohort included 1,398 patients with AKI receiving CRRT. UFNET was classified as < 35 versus ≥ 35 mL/kg/d. Thirty-day mortality was 60% in the lower-intensity group and 48% in the higher-intensity group. After adjustment, ≥ 35 mL/kg/d was associated with lower 30-day mortality (adjusted OR = 0.47, 95% CI: 0.37 to 0.59).⁴ Again, the data appeared to favor more aggressive net removal, but the retrospective design prevented the determination of causality.⁴

The above-drawn picture was updated by the secondary analysis of the RENAL trial.^{11,17} Among 1,434 patients receiving continuous venovenous hemodiafiltration, Murugan and colleagues categorized UFNET as: 1) low < 1.01 , 2) middle: 1.01 to 1.75, and high > 1.75 mL/kg/h. Median rates were 0.52, 1.38, and 2.21 mL/kg/h; respectively.¹⁷ When adjusted for risk factors, including fluid balance, the high-rate group demonstrated lower survival than the low-rate group after the first week of treatment, with adjusted hazard ratios of 1.51 from days 7 to 12, 1.52 from days 13 to 26, and 1.66 from days 27 to 90.¹⁷ Importantly, high UFNET was also associated with longer mechanical ventilation, ICU, and hospital stays.^{17,27} Dialysis dependence at day 28 was 21.9% among survivors in the high-rate group, compared with 11.7 and 6.6% in the middle- and low-rate groups, although the difference was no longer significant at day 90.¹⁷ These findings raised concern that excessive removal might impair organ recovery even while achieving a more negative fluid balance.¹⁷

Naorungroj and colleagues then focused specifically on the first 48 hours of CKRT, using actual hourly fluid data in a contemporary single-center cohort of 347 patients.¹⁸ The same categories as post-hoc RENAL trial analysis were used, i.e., < 1.01 , 1.01 to 1.75, and 1.75 mL/kg/h. In comparison of different UFNET rates during the earlier phases of CKRT, 1.75 mL/kg/h was associated with increased 28-day mortality across

multiple time periods, with adjusted hazard ratios rising from 1.27 (days 0 to 5) to 4.18 (days 27 to 28).¹⁸ This analysis strengthened concerns about high UFNET because the investigators used directly recorded early-hour data rather than averaging exposure over the duration of treatment.¹⁸ The putative effect on mortality was direct and not mediated by a causal pathway that included fluid balance, low blood pressure, vasopressor use, hypokalemia, or hypophosphatemia. However, the investigators themselves recognized the difficulty of time-varying confounding and competing mortality in UFNET studies.³²

Serpa Neto and colleagues subsequently reanalyzed the RENAL data to determine whether the effect of UFNET differed across clinical phenotypes.^{27,33} Two broad clusters emerged. The first contained patients with greater acute illness severity, more sepsis, edema, and vasopressor use. In these patients, high UFNET was particularly associated with harm, and an increase in the cardiovascular SOFA score amplified this relationship.^{27,33} Consistent with this, in the primary RENAL secondary analysis, a UFNET > 1.75 mL/kg/h was associated with mortality among patients with cardiovascular SOFA scores of 3 or greater (adjusted HR = 1.89; 95% CI: 1.27 to 2.81).¹⁷ The presence of edema complicated the picture. Among congested patients (cluster 1 and those with baseline edema), both high and low rates, relative to the middle rate, increased mortality risk, whereas the intermediate group consistently showed more favorable associations. This analysis provides one of the strongest arguments against a universal threshold: a rate associated with benefit in one phenotype may be poorly tolerated in another.

In summary, the earlier studies supported a biologically plausible nonlinear relationship that a low UFNET could lead to persistent fluid overload and organ edema, while an intermediate UFNET could result in effective decongestion with acceptable hemodynamic tolerance, and a high UFNET causes circulatory stress, hypoperfusion, and organ injury.^{9,17,27} This is better conceptualized as a hypothesis than an established therapeutic curve. The boundaries of < 1.01 and > 1.75 mL/kg/h were largely data-derived categories rather than prospectively validated safety thresholds.^{9,17}

Recently, Monai and colleagues provided a major challenge to a simple UFNET-rate paradigm.⁹ The study included 973 critically ill adults and 6,914 CKRT treatment-days from two European ICUs. UFNET was classified as none, < 1.01, 1.01 to 1.75, or > 1.75 mL/kg/h, while the daily fluid-balance change was classified separately.⁹ When the UFNET was modeled without accounting for fluid balance, it was associated with mortality. Once fluid balance was incorporated, however, the independent association with UFNET was substantially attenuated. Causal mediation analysis suggested that the apparent effect of higher UFNET was largely mediated by achieving a more negative balance. Positive fluid balance remained consistently associated with adverse outcomes.⁹ This observation changes the interpretation of the prior literature. Therefore, the relevant therapeutic exposure may not be the amount of (mL/kg/h) fluid removed, but rather the fluid-balance trajectory and its related physiologic cost.⁹ Table 2 summarizes the major studies in this field.

CAUSAL INFERENCE

The observational UFNET literature is exceptionally vulnerable to causal inference problems, including: 1) Confounding by indication: Clinicians do not assign UFNET randomly. A hemodynamically unstable patient may receive low or zero UFNET because clinicians believe the patient cannot tolerate removal. Such patients already have a high mortality risk. Therefore, even a low UFNET could be associated with death. This may actually represent the fact that in severe shock, fluid removal is challenging, and it is associated with high mortality rates. This phenomenon likely contributes to the high mortality observed among patients receiving no UFNET in the Monai cohort.⁹ The authors specifically noted that a zero UFNET may identify patients with hemodynamic instability and persistent fluid overload who are clinically unable to tolerate removal.^{9,34} Conversely, high UFNET may be prescribed because fluid accumulation is severe. Thus, a high UFNET could be associated with high mortality, which may partly reflect that severe fluid overload would require a higher UFNET and is associated with a higher risk of death;^{9,16} 2) Tolerance bias:

Table 2. Summary of Major Studies

Study	Population	UFNET exposure	Principal finding	Key interpretation
Murugan 2018 ¹⁶	1,075 critically ill patients with $\geq 5\%$ fluid overload receiving RRT	≤ 20 , > 20 to 25 , > 25 mL/kg/d	> 25 mL/kg/d associated with lower 1-year mortality	Low removal may prolong harmful fluid overload
Tehrani 2019 ⁴	1,398 AKI patients receiving CRRT	< 35 vs. ≥ 35 mL/kg/d	≥ 35 mL/kg/d associated with lower 30-day mortality	Higher cumulative removal associated with survival
Murugan 2019, RENAL ¹⁷	1,434 patients receiving CVVHDF	< 1.01 , 1.01 to 1.75 , > 1.75 mL/kg/h	> 1.75 associated with lower 90-day survival	High rates may be harmful
Naorungroj 2021 ^{18,32}	347 CRRT patients	first-48-h rate using the same categories	> 1.75 associated with greater 28-day mortality	Early high-rate exposure may matter
Serpa Neto 2021 ³³	RENAL secondary phenotype analysis	same tertiles	Harm from extremes varied by severity, edema, and cardiovascular SOFA	The UFNET effect is heterogeneous
Monai 2026 ⁹	973 patients, 6,914 CRRT days	none, < 1.01 , 1.01 to 1.75 , > 1.75	UFNET was not independently associated after accounting for fluid balance	Achieved fluid balance may be more important than rate
RELIEVE-AKI 2026 ¹⁹	97 patients in 10 ICUs	restrictive 0.5 to 1.5 vs. liberal 2 to 5 mL/kg/h	Poor separation of delivered exposure	Dynamic physiology limits fixed-rate strategies

The ability to sustain high UFNET may itself be a prognostic marker. Patients recovering from shock can tolerate greater removal.¹⁶ Therefore, an association between higher delivered UFNET and improved outcome does not prove that increasing UFNET caused the improvement. The 2018 study by Murugan *et al.*, using the University of Pittsburgh Medical Center ICU cohort, explicitly acknowledged this problem;¹⁶ 3) Time-varying confounding: UFNET, vasopressors, fluid intake, urine output, cardiac function, and illness severity all change over time.^{27,32,33} A patient may receive low UFNET during shock, higher UFNET after stabilization, and low UFNET again as euvolemia approaches. Averaging these rates over several days obscures the clinical trajectory. At the same time, prior UFNET affects subsequent fluid balance and hemodynamics, which themselves influence future UFNET prescription. Conventional regression cannot fully resolve this feedback loop;^{9,27,33} 4) Survivor bias: Patients must survive long enough to accumulate substantial UFNET exposure. Conversely, early death truncates treatment exposure. Monai and colleagues therefore performed landmark analyses at 48 and 72 hours and showed that early UFNET remained a poor predictor of subsequent mortality after accounting for fluid balance, whereas positive early fluid balance remained associated with worse outcomes;⁹ 5) Selection bias: Clinical trials and observational cohorts exclude different types of patients. RELIEVE-AKI, for example, excluded

patients requiring emergent fluid removal for pulmonary edema because clinical equipoise between restrictive and liberal strategies did not exist.^{19,21} Thus, trial populations may not represent patients in whom the clinical consequences of fluid removal are greatest; and finally 6) measurement error: Exposure classification depends on the weight denominator, actual treatment time, accurate documentation of replacement and dialysate fluids, machine data, interruptions, distinction between prescription and delivery, and concurrent fluid intake. These factors differ across studies.^{17,19} The central implication is that observational categories should not be converted into therapeutic thresholds without randomized evidence.^{14,17}

HARMS OF EXCESSIVELY RAPID UFNET

The principal concern with aggressive UFNET is that extracorporeal removal may exceed vascular refill (Figure 1).^{14,34} The immediate consequence is contraction of the effective circulating volume. Depending on cardiovascular reserve, this may produce hypotension, increased vasopressor requirement, reduction in venous return, decreased stroke volume and cardiac output, arrhythmia, myocardial ischemia, tissue hypoperfusion, and organ dysfunction.^{14,34}

Rapid fluid removal during maintenance hemodialysis has been associated with coronary hypoperfusion and myocardial stunning, providing a mechanistic precedent for cardiovascular injury

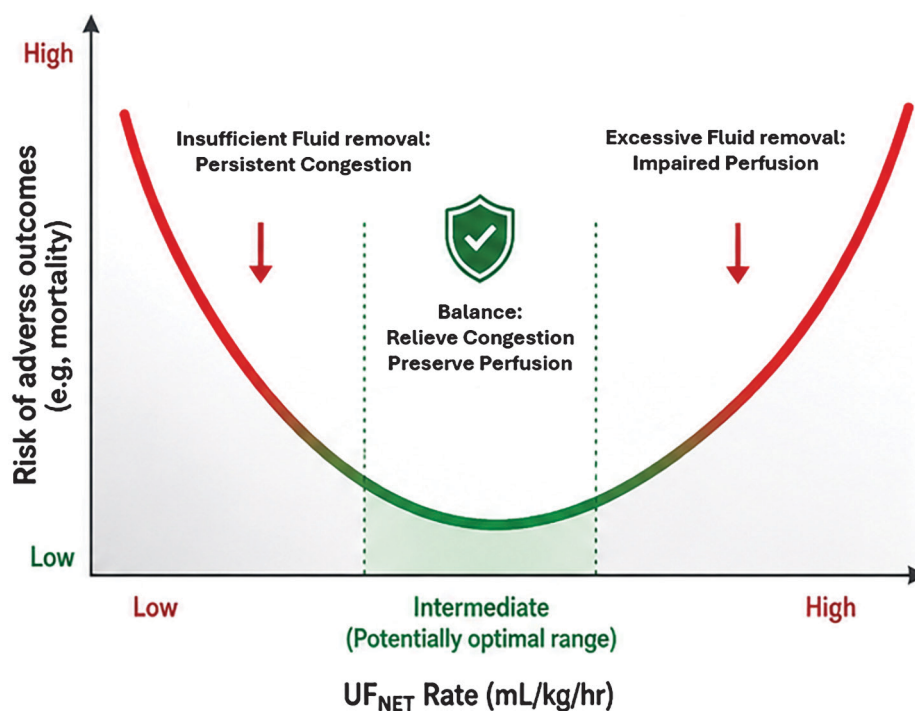


Figure 1.

from excessive ultrafiltration.^{29,30,35} In critically ill patients, the vulnerability may be greater because vasoplegia, mechanical ventilation, myocardial dysfunction, and impaired vascular refill frequently coexist.^{14,34} Renal recovery may also be vulnerable. High UFNET was associated with greater dialysis dependence on day 28 in the RENAL analysis, although the difference disappeared by day 90.¹⁷ This association cannot establish direct ischemic renal injury, but it raises an important mechanistic concern.¹⁷ Critically, a numerical rate does not become “excessive” solely because it crosses a universal threshold. Excess is better defined physiologically as fluid removal exceeding the patient’s refill and circulatory tolerance.¹⁴

HARMS OF INADEQUATE UFNET

At the opposite extreme, insufficient fluid removal prolongs exposure to positive fluid balance (Figure 1).^{9,16} Consequences may include persistent pulmonary edema, impaired oxygenation, prolonged mechanical ventilation, systemic tissue edema, venous congestion, renal interstitial congestion, delayed mobilization, impaired wound healing, and persistent organ dysfunction.⁹

The 2018 Murugan cohort provides the clearest observational signal supporting this concern that patients with fluid overload receiving ≤ 20 mL/kg/d had substantially higher mortality than those receiving > 25 mL/kg/d.¹⁶ Importantly, low UFNET may also fail simply because ongoing fluid administration exceeds extracorporeal removal. Thus, the response to a persistent positive balance should not always be to increase UFNET; reducing unnecessary fluid intake may achieve the same balance objective with less circulatory stress.⁹ This reinforces a broader principle that fluid stewardship requires management of both sides of the balance equation.⁹

HEMODYNAMIC INSTABILITY RELATED TO CKRT

Hemodynamic instability during CKRT is common but difficult to attribute specifically to UFNET.³⁴ The European survey defined new hemodynamic instability as new or worsening tachycardia, hypotension, or need to initiate or increase vasopressors. Practitioners estimated that it occurred in approximately 20% of patients. When instability developed, 70.1% reduced fluid removal

and 51.3% initiated or increased vasopressors. Not all hypotension during CKRT is caused by fluid removal. Potential contributors include progressive septic vasoplegia, myocardial dysfunction, arrhythmia, bleeding, sedation, positive-pressure ventilation, changes in temperature, extracorporeal circuit effects, and worsening underlying illness.³⁴

Consequently, reflexively setting UFNET to zero may be inappropriate in a patient with severe pulmonary or systemic congestion.³⁴ The appropriate response requires determining whether removal is contributing to the reduction in effective circulation. Relevant questions include whether blood pressure fell shortly after increasing UFNET; whether vasopressor requirement changed; whether there is evidence of reduced stroke volume; whether passive leg raising suggests preload responsiveness; whether congestion is still substantial; whether lactate is increasing; whether urine output has changed; and whether another cause of shock is emerging.^{14,34} A temporary reduction, rather than complete cessation, may maintain decongestion while improving tolerance.³⁴

DETERMINING THE APPROPRIATE UFNET RATE AT THE BEDSIDE

Because no validated universal UFNET target exists, the prescription should begin with two parallel assessments, i.e., how urgently the patient needs fluid removal, and how much fluid removal the patient can currently tolerate (Figure 2).¹⁴

Assessing Fluid-removal Need

Assessment should integrate cumulative balance, percentage fluid overload, weight trajectory, pulmonary edema, peripheral edema, oxygenation, mechanical ventilation, intra-abdominal pressure when clinically relevant, central and systemic venous congestion, urine output, and ongoing fluid

input.¹⁴ Physical examination remains useful, but should not be considered definitive.¹⁴

Hemodynamics

Blood pressure alone is insufficient. Trends in mean arterial pressure, vasopressor and inotrope dose, heart rate, capillary refill, lactate, mental status, skin temperature, urine output, and other markers of tissue perfusion provide a more complete assessment.^{14,34}

Echocardiography and Point-of-Care Ultrasound

Cardiac ultrasound may identify left ventricular systolic dysfunction, right ventricular failure, major preload dependence, pericardial pathology, and changes in filling patterns. Lung ultrasound can quantify pulmonary congestion using B-lines and pleural findings. Venous Doppler approaches, including the Venous Excess Ultrasound grading system (VexUS)-type assessment,³⁶ may help characterize systemic venous congestion.¹⁴ The cardiorenal review specifically identifies lung and cardiac ultrasound, VExUS, natriuretic peptides, hemoconcentration markers, and related measures as potential tools for monitoring decongestion. Their role in specifically titrating CKRT UFNET, however, remains insufficiently validated.¹⁴

Initiation and Titration

A conservative strategy is to begin at a relatively low rate and progressively titrate according to congestion and tolerance rather than immediately pursuing a maximal negative balance.¹⁴ RELIEVE-AKI used this principle operationally, when both study groups began at 0.5 mL/kg/h and increased in increments of 0.5 mL/kg/h as tolerated.^{19,21} This should not be interpreted as validation of 0.5 mL/kg/h as a universal starting dose; rather, it illustrates a clinically adaptable titration strategy.^{19,21}

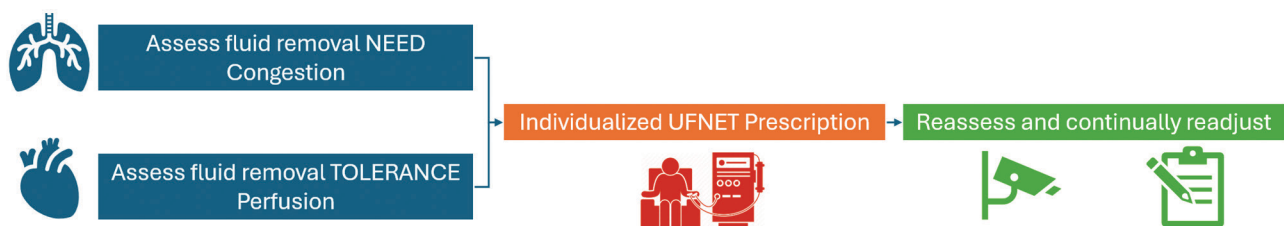


Figure 2.

To define the goal of fluid balance before ordering UFNET, a useful sequence is to define the desired fluid-balance trajectory, estimate fluid input and other outputs, prescribe UFNET, reassess actual balance and physiologic response, and then adjust.^{9,14} This is preferable to selecting a rate first and observing where the patient ends up.

UFNET should be reassessed with new or worsening hypotension temporally related to removal, rapidly escalating vasopressors, evidence of reduced cardiac output, increasing lactate or impaired peripheral perfusion, new arrhythmia, evidence of myocardial ischemia, resolution of congestion, spontaneous diuresis, or signs suggesting intravascular depletion.^{14,34} The goal should be the lowest rate sufficient to achieve the desired fluid-balance trajectory without exceeding physiologic tolerance, rather than maximal fluid removal.¹⁴

UFNET IN SPECIFIC CLINICAL PHENOTYPES

A phenotype-based framework is more defensible than a single numerical rate.¹⁴ Among patients with septic/distributive shock, when a combination of capillary leak, vasodilation, and variable myocardial dysfunction is present, severe edema may coexist with limited effective circulating volume. High vasopressor requirements and ongoing capillary leak may reduce tolerance for rapid removal. The RENAL heterogeneity analysis raised particular concern about high UFNET among patients with greater illness severity and cardiovascular dysfunction.²⁷ Fluid removal may still be needed, but titration should be especially responsive to perfusion and vasopressor trajectory.^{14,37} This is because among patients with cardiogenic shock and acute heart failure, venous congestion may derive substantial physiologic benefit from decongestion, particularly when elevated venous pressure contributes to renal dysfunction. However, severe biventricular failure may also make cardiac output highly preload dependent. Ultrasound and hemodynamic assessment are therefore particularly valuable.¹⁴ For example, right ventricular failure is a paradigmatic example of why “volume overloaded” does not necessarily mean “tolerates rapid removal.” Reduction in venous congestion may improve organ function, but excessive reduction in preload can

reduce right ventricular output and consequently left ventricular filling.¹⁴

Among patients with acute respiratory distress syndrome (ARDS), persistent positive balance contributes to pulmonary edema and may prolong mechanical ventilation. Fluid removal is therefore an important objective once resuscitation is complete, but removal must remain compatible with systemic perfusion.^{14,23}

During the postoperative time, rapidly changing fluid inputs, bleeding, vasoplegia, and ventricular dysfunction complicate prescription. The practical experience from RELIEVE-AKI demonstrated specific protocol challenges in cardiovascular surgical ICUs due to complex CKRT plans and procedures, as well as rapidly changing clinical requirements.^{19,20} Patients with liver failure have a marked third spacing that can coexist with reduced effective circulating volume and profound vasodilation. Edema alone, therefore, cannot determine the appropriate UFNET rate.¹⁴ During treatment with extracorporeal membrane oxygenation (ECMO), additional extracorporeal circuitry, an increased inflammatory burden, and complex volume targets make volume management very challenging. Evidence specifically defining UFNET rates for this phenotype remains limited in the uploaded source set.¹⁴

When patients are experiencing severe capillary leak, interstitial accumulation is accompanied by poor vascular refill and ongoing vasoplegia. Aggressive removal may cause hypotension before substantial tissue decongestion occurs.¹⁴ This is while among patients with a recovery phenotype, as spontaneous urine output increases, the extracorporeal UFNET requirements should generally decrease. Failure to account for the recovery of kidney output can lead to an excessive net negative balance.⁹

UFNET AND KIDNEY RECOVERY

The relationship between decongestion and kidney recovery is bidirectional.^{14,23} Persistent venous congestion can impair renal perfusion gradients and contribute to interstitial edema. Therefore, relieving congestion may improve renal function. Conversely, excessive intravascular contraction may reduce renal blood flow and

potentially delay recovery.^{14,23,34} Observational evidence reflects both possibilities. Fluid overload has been associated with reduced kidney recovery; therefore, patients with > 10% fluid accumulation were less likely to recover renal function.^{5,7} In the RENAL UFNET analysis, high rates were associated with greater dialysis dependence among survivors at day 28,¹⁷ and, in a separate analysis after accounting for the competing risk of death, high UFnet was independently associated with longer time to renal recovery.³⁸ RELIEVE-AKI similarly showed no significant difference in dependence on kidney replacement therapy at discharge, but the study was designed for feasibility and was not powered to assess clinical outcomes.¹⁷

During kidney recovery, clinicians should incorporate spontaneous urine output into the total fluid-removal equation. A CKRT setting that was appropriate during anuria may rapidly become excessive once native diuresis begins.⁹ Kidney recovery should trigger active reevaluation of UFNET rather than continuation of an established machine rate.

PRECISION AND DYNAMIC UFNET

The concept of a single optimal UFNET rate is increasingly difficult to reconcile with available evidence.^{9,14,19} The traditional model treats UFNET as a static exposure, in which a specific rate can be delivered consistently. A precision model instead treats it as a continuously updated intervention. In this model, frequent assessment is needed to provide an appropriate prescription. This also needs to be followed by observing responses and updating the prescription continuously.¹⁴

The relevant variables to be monitored include congestion phenotype, hemodynamic phenotype, cumulative fluid burden, rate of ongoing fluid input, vasopressor trajectory, kidney function and urine output, mechanical ventilation, cardiac function, plasma refill capacity, and prior response to fluid removal.

Future research should move beyond the mean rate. Potentially important features include starting rate, rate of escalation, peak rate, duration at high rates, cumulative dose, variability, time spent with no UFNET, time spent outside a target range, and the relation between rate and concurrent fluid

balance.⁹ Monai and colleagues examined upper-quartile exposure, early exposure, and first-48-hour measures, illustrating how different rate summaries can capture different treatment dimensions.⁹

Automated systems could continuously integrate EHR and CKRT machine data, estimate projected fluid balance, and suggest adjustments. The practical literature from RELIEVE-AKI proposes automation and even AI-assisted approaches to reduce the burden of manual calculations and nursing documentation.²⁰ Any such system should support, not replace, clinician assessment because the most important variables, including bleeding, changing shock states, procedures, and emerging organ dysfunction, cannot be reduced reliably to a single rate calculation.²⁰

CLINICAL TRIALS AND INTERVENTIONAL EVIDENCE

For many years, almost all UFNET evidence was observational. The RELIEVE-AKI trial represents an important transition toward prospective testing.¹⁹ This trial was a stepped-wedge cluster-randomized feasibility study conducted in 10 ICUs across two US healthcare systems, assigning patients to restrictive UFNET (0.5 to 1.5 mL/kg/h) or liberal UFNET (2.0 to 5.0 mL/kg/h).^{19,21} Ninety-seven patients (55 liberal, 42 restrictive) were enrolled. Despite substantial intended separation in UFNET dosage, mean delivered rates were 2.05 versus 1.81 mL/kg/h and did not differ significantly in the primary analysis. Meanwhile, the investigators reported that the rescue UFNET was substantially more frequent in the restrictive group (66.7 vs. 14.5%).²¹

The result is important not because it attempted to establish an optimal rate, but because it demonstrates that fixed UFNET strategies are difficult to sustain amid changing physiology. The UFNET in liberal arm was frequently reduced due to hemodynamic instability or physician override, whereas restrictive patients frequently required rescue removal.^{19,21} Clinical outcomes, including mechanical ventilation duration, ICU stay, hospital mortality, dependence on kidney replacement therapy, intradialytic hypotension, and arrhythmia, did not differ significantly, but the trial was not powered to assess these endpoints.

A definitive UFNET trial faces several challenges, including: 1) treatment contamination as clinicians alter rates for safety; 2) poor exposure separation as patient physiology drives convergence; 3) dynamic fluid inputs, so the same UFNET does not produce the same balance; 4) changing disease state, so an appropriate rate today may be inappropriate tomorrow; 5) marked heterogeneity in congestion and tolerance; 6) nursing burden from frequent calculations and titration; and 7) outcome selection, since mortality may be too distal to fluid-management biology.¹⁹⁻²¹ The investigators' experience suggests that future interventions should be adaptive rather than rigid.²⁰

A recent proof-of-concept trial has already shown that a hemodynamically guided UFNET strategy can safely achieve markedly more negative fluid balance than usual care in patients receiving vasopressors, supporting the feasibility of physiology-driven titration.³⁷ In future trials, candidate endpoints could include fluid-balance trajectory, organ failure-free days, ventilator-free days, duration of vasopressor support, kidney recovery, CKRT-free days, MAKE, ICU length of stay, and patient-centered functional outcomes.^{14,21}

PRACTICAL APPROACH TO UFNET PRESCRIPTION

A practical bedside strategy can be organized around a repeated decision cycle, to include assessing congestion and tolerance, defining fluid-balance goal, initiating UFNET, reassessing response, continued titration, and transition toward euvolemic status and recovery.^{9,14} In this regard, the following phenotypes (Table 3) could be recognized: 1) Phenotype 1: congested and hemodynamically stable (pulmonary / systemic edema, stable or decreasing vasopressor requirements, adequate perfusion, no strong evidence of preload dependence). Active fluid removal is appropriate; initiate or continue

UFNET and titrate toward the desired negative balance while monitoring tolerance;¹⁴ 2) Phenotype 2: congested and hemodynamically unstable (congestion remains important while vasopressors are required). Do not assume UFNET must be zero; determine whether hypotension is driven by fluid removal or the underlying shock state, and consider slower removal, treatment of the underlying circulatory disorder, and frequent reassessment;^{34,37} 3) Phenotype 3: uncertain congestion (physical findings and cumulative balance conflict). Avoid aggressive empiric removal; use multimodal assessment, including fluid history, ultrasound when available, oxygenation, venous congestion, hemodynamic response, and fluid-balance trajectory;¹⁴ 4) Phenotype 4: approaching euvolemia (congestion improved, rationale for persistent negative balance weakening). Reduce UFNET toward a neutral balance and avoid overshooting the decongestion target;^{9,14} and 5) phenotype 5: suspected intravascular depletion (worsening perfusion temporally associated with removal, escalating vasopressors, preload responsiveness, or spontaneous large-volume diuresis). Reduce or discontinue UFNET and reassess the overall fluid strategy.^{14,34} These categories intentionally indicate direction, not a universal numerical dose.¹⁴

KNOWLEDGE GAPS AND RESEARCH PRIORITIES

Several fundamental questions remain unresolved:¹⁴ 1) There is no standardized definition of UFNET. Studies should clearly report machine-derived net extracorporeal removal and distinguish it from whole-patient fluid balance;⁹ 2) Optimal exposure metrics are uncertain. The biologically relevant exposure may be hourly UFNET, time-weighted mean, peak rate, cumulative volume, duration above a threshold, trajectory, rate of escalation, or the interaction between UFNET and

Table 3. Volume Status Phenotypes

Clinical state	Fluid-removal need	Fluid-removal tolerance	General UFNET direction
Congested, stable ¹⁴	High	High	Increase or maintain
Congested, unstable ^{14,34,37}	High	Low / uncertain	Individualize; slower titration, frequent reassessment
Congestion uncertain ¹⁴	Uncertain	Variable	Avoid aggressive escalation until clarified
Near euvolemia ^{9,14}	Low	Maybe adequate	De-escalate toward neutral
Intravascular depletion ^{14,34}	Low	Low	Reduce or stop

achieved fluid balance, possibilities that require prospective evaluation.⁹ These possibilities require prospective evaluation; 3) Appropriate weight denominator is unclear. Admission weight, pre-illness weight, CKRT-start weight, and predicted body weight produce different normalized rates. Fluid accumulation can distort the measured weight;¹⁷ 4) Integration of fluid balance in UFNET prescription is infrequently done. Future studies should not examine UFNET without measuring concurrent fluid input and achieved balance. The Monai analysis demonstrates why doing so can fundamentally alter interpretation;⁹ 5) Definition of UFNET-related organ injury needs to be established. The potential intermediate endpoints should include cardiac injury, cerebral perfusion, hepatic and splanchnic perfusion, microcirculatory dysfunction, kidney recovery, and vasopressor requirement;¹⁴ 6) We need to develop and validate biomarkers of removal tolerance. No validated biomarker or physiologic test currently defines the maximum safe rate of fluid removal in critically ill patients; 7) Ultrasound-guided decongestion needs to be further studied and implemented in clinical practice. Lung ultrasound, echocardiography, and “venous Doppler / VE x US” are biologically attractive tools, but prospective trials must establish whether ultrasound-guided UFNET improves outcomes rather than merely improving measurement; 8) Phenotype-specific strategies need to be validated and implemented. Septic shock, right ventricular failure, cardiorenal syndrome, ARDS, postoperative vasoplegia, liver failure, and severe capillary leak almost certainly differ in both need and tolerance; 9) The safety and effectiveness of UFNET during vasopressor therapy should be tested. Vasopressor use is frequently treated as synonymous with inability to remove fluid, yet congested patients may benefit from continued decongestion despite low-dose support. Prospective studies are needed to determine the appropriate interaction between the vasopressor trajectory and UFNET; 10) Kidney recovery should be considered an important clinical outcome of safe UFNET prescription. Trials should incorporate the duration of kidney replacement therapy, CKRT-free days, dialysis dependence, and MAKE, rather than mortality alone;¹⁷ 11) Dynamic adaptive trials to accommodate the dynamic

nature of patients should be conducted. RELIEVE-AKI suggests that rigid target separation may be unrealistic. Future trials should test algorithms that permit physiologically defined adaptations rather than fixed rates; and 12) Automated, AI-enabled fluid management needs further development and validation. Continuous integration of machine, EHR, ultrasound, and hemodynamic data could permit personalized decision support. However, algorithms must be interpretable, clinically validated, and designed around workflow rather than adding documentation burden.

CONCLUSIONS

Net ultrafiltration is one of the most consequential yet least standardized components of CKRT for severe AKI. Fluid accumulation is associated with mortality, prolonged ventilation, organ edema, and impaired kidney recovery, providing a strong rationale for active decongestion when spontaneous or diuretic-mediated fluid removal is inadequate. At the same time, extracorporeal removal can reduce effective circulating volume when UFNET exceeds vascular refill and cardiovascular tolerance. Observational studies have produced conflicting results. The controversies arise from nonrandomized exposures that are strongly influenced by illness severity, clinician selection, fluid burden, treatment duration, and hemodynamic tolerance.

RELIEVE-AKI demonstrated that maintaining fixed restrictive and liberal UFNET strategies was challenging because changing patient physiology repeatedly compelled clinicians to deviate from protocolized targets. Therefore, there is a need to transition to a dynamic, tightly regulated model for fluid removal during CKRT. The clinical objective should not be to identify and universally apply a single “optimal UFNET rate.” Instead, UFNET should be viewed as a dynamic therapeutic lever used to achieve an individualized fluid-balance goal. The prescription should then be continuously revised according to congestion, fluid input, hemodynamics, organ perfusion, urine output, kidney recovery, and the achieved fluid-balance trajectory.

Accordingly, the future of UFNET research should move from static rate thresholds toward precision decongestion by identifying which patients require

fluid removal, determining how rapidly they can safely tolerate it, defining measurable physiologic responses, and developing adaptive strategies that can change as rapidly as the critically ill patients in whom they are applied.

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