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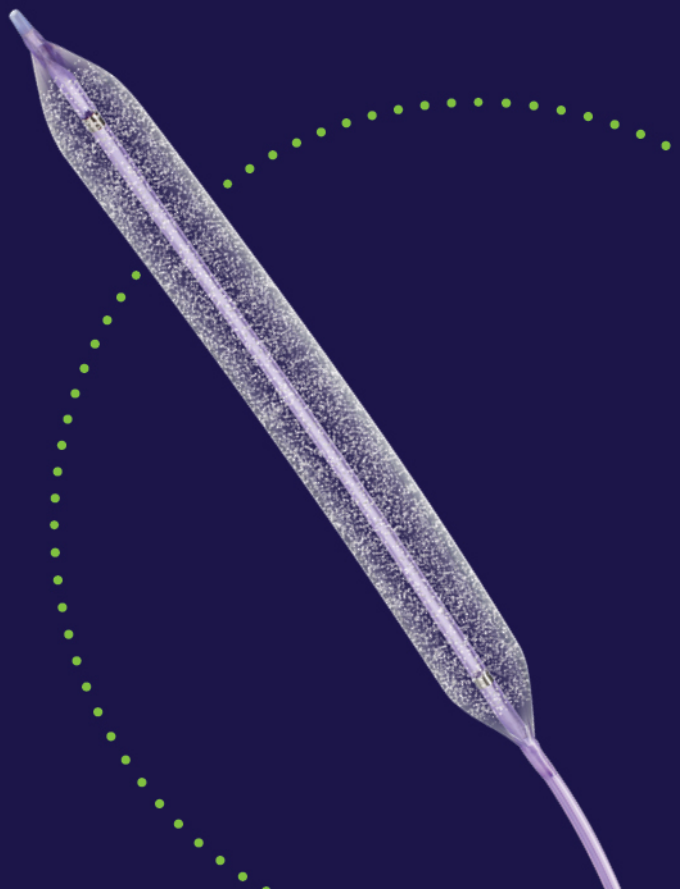

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Fluid balance management during continuous renal replacement therapy

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Abstract

In critically ill patients, particularly in the setting of shock and sepsis volume management frequently results in a fluid overloaded state, requiring diuresis or intervention with renal replacement therapy. Achieving appropriate volume management requires knowledge of the underlying cardiovascular pathophysiology and careful evaluation of intravascular and extravascular volume status. In the presence of a failing kidney, fluid removal is often a challenge. Continuous renal replacement therapy (CRRT) techniques offer a significant advantage over intermittent dialysis for fluid control, however, any form of RRT in the critically ill patient requires careful attention to prescription and monitoring to avoid complications. In order to utilize these therapies for their maximum potential it is necessary to understand which factors influence fluid balance and have an understanding of the principles and kinetics of fluid removal with extra-corporeal techniques.

1 | INTRODUCTION

Fluid management is an integral component of continuous therapies to achieve fluid balance.[1] The prescription of ultrafiltration (UF), and management of fluid balance during continuous renal replacement therapy (CRRT) therefore remains an area of prime clinical importance however there is considerable clinical practice variation.[2] Such variation is understandable as fluid balance is not confined to the treatment of kidney dysfunction but has to be seen within the context of the patient as a whole, most importantly their hemodynamic status and their respiratory function. Nevertheless, while fluid balance management during CRRT requires a significant degree of individualization, often this aspect or prescription is not given adequate clinical attention and is similarly neglected in therapeutic guidelines.[3] In this review, we consider the physiology of extra-corporeal fluid removal and its relationship to the prescription and delivery of UF in critically ill patients.

2 | UF IN THE EXTRA-CORPOREAL CIRCUIT

One of the most important functions of the failing kidney that needs to be replaced by renal replacement therapies (RRT) is homeostasis of body fluid volume and composition. The ability to control the rate and amount of UF is an essential feature of all modern RRT devices. As negative pressure is applied across a rigid dialysis membrane, plasma water and its dissolved solutes are removed from the circulation in proportion to the pressure applied and the water permeability of the membrane, the process we know of as UF. This enables control of plasma volume and indirectly extracellular and intracellular volume. In conventional hemodialysis UF is limited to meet the fluid balance requirement of the patient, with convection contributing only a small degree of solute clearance, with majority of solute removal is dependent on diffusive clearance through the application of dialysate. Conversely, in continuous hemofiltration convective clearance is relied on for solute removal as well as volume control. This necessitates a continuous UF rate in excess of fluid removal requirements and a replacement fluid is then required to prevent a volume deficit and to provide electrolytes and buffer, enabling appropriate regulation of plasma composition. However, in all these techniques and hybrid therapies such as diafiltration, extracorporeal fluid removal will be determined by the difference between the total UF and any replacement rate, termed the *net ultrafiltration volume* (NetUF).[4]

A key principle of all CRRT techniques is that solute clearance is defined by $E/P \times V$ where E = concentration of the solute in the effluent and P is the concentration in the plasma, and V is the effluent volume over a given period (e.g. an hour). Consequently, if the concentration of the solute in effluent and plasma is equivalent $E/p = 1$ then solute clearance will be dependent on the effluent volume V.[5] Depending on the CRRT technique, the effluent volume is derived from UF in continuous veno-venous hemofiltration (CVVH), dialysate (D) in continuous veno-venous hemodialysis (CVVHD) and both UF and dialysate in continuous veno-venous hemodiafiltration (CVVHDF). Thus, the amount of UF needed is dependent on how much is needed for solute removal and how much for volume control. In CVVH convective clearance is the sole mechanism that can be varied to achieve solute control, whereas in CVVHD and CVVHDF diffusive clearance adds another element to adjust solute clearance independent of the UF. These differences between modalities reliant on dialysis, and those using convection to achieve solute control (continuous hemofiltration), do result in some confusion in terminology as in the latter circumstances total UF rate is a measure of dose, whereas UF rate in continuous hemodialysis (and hemodiafiltration), is only one contribution to total dose, which is then approximated by total effluent flow rate. However, in both instances the NetUF represents the fluid removed per unit time across the machine, ie the machine fluid balance. It is important to recognize that NetUF generally represents the net fluid removal within the extracorporeal circuit irrespective of modality, but does not reflect the overall patient fluid balance as patients will have intakes (oral and IV) and outputs (urine, drains etc) that are not captured by the machine.[6]

In fact, from the point of view of fluid management with CRRT the most important aspect of fluid removal is not the modality of solute clearance, but the time over which fluid removal occurs. The rate and amount of fluid removal can be adjusted continuously during any modality of CRRT, more intermittently during a therapy provided over a proportion of the day, or over just a few hours on a daily or alternative daily basis during conventional hemodialysis sessions. Clearly in order to achieve the same fluid removal during a shorter period of time a much higher rate of UF is required. This is a key aspect when considering the tolerability of fluid removal and ability to maintain continuous homeostasis of body fluid volume in the critically patient.[7]

3 | RATIONALE FOR PRO-ACTIVE FLUID BALANCE MANAGEMENT IN CRITICAL ILLNESS

The key rationale for the importance of fluid balance management of the critically ill patient is the prevention and/or treatment of fluid overload.[8] Across a large number of observational studies, positive fluid balances have been associated with the adverse outcomes in a broad variety of patient contexts, in particular in those with advanced AKI requiring RRT.[9-11] Furthermore, evidence suggests that patients achieving a negative fluid balance in the ICU have an increased survival in septic shock[12] and in AKI[13]; and have a shorter duration of mechanical ventilation and ICU stay.[14,15] Of course, as positive fluid balances are also a marker of severity critical illness, both as a reflection of the degree of physiologic instability and its treatment, not all of this association represents direct causation.[16] However, many plausible mechanisms do exist to mediate a direct association between fluid overload the development of interstitial edema and the development of progressive organ dysfunction.[17] These include impaired oxygen and metabolite diffusion, distorted tissue architecture, obstruction of organ perfusion, venous outflow, and lymphatic drainage, and disturbed cell-cell interactions. There are thus strong biological arguments, supported by substantial observational and experimental evidence, that fluid overload worsens organ function and, therefore, that limitation and resolution of fluid accumulation are a central component to approaches to improving patient outcomes.

4 | FORMATION AND PERSISTENCE OF INTERSTITIAL EDEMA

In individual organs, interstitial edema impedes capillary and lymphatic flow, especially in encapsulated organs, the kidneys and liver, where additional volume results in steep increase in interstitial pressure, causing further impairment of organ perfusion and function.[18,19] Importantly, in recent years, our understanding of the vascular biology of edema formation has progressed from the classic Starling model, to a revised model incorporating knowledge of the structure and function of the endothelial glycocalyx.[20,21] The glycocalyx is a complex network of cell-bound proteoglycans, glycosaminoglycans, and sialo-proteins that coats the luminal side of the intact endothelium and the endothelial clefts.[22] In this model, a local oncotic gradient that remains fairly constant along length of the capillary opposes and attenuates pressure-mediated plasma water efflux without ever causing actual reabsorption of fluid from the interstitium, except in specialized vascular beds in the renal tubules and the intestines.[20] This construct then has several important implications; firstly, increased capillary permeability in inflammatory states is caused by disruption of the glycocalyx, which is not rapidly reversible once established and, secondly that transcapillary fluxes are predominantly unidirectional so almost all vascular refilling from the interstitium occurs via lymphatic channels (Figure 1). A further mechanism formation and persistence of edema is alteration of structure and function of the extracellular matrix in systemic inflammation and critical illness (Figure 1).[23] Normally, fluid loss from capillaries leads to increased interstitial pressure, opposing further fluid accumulation and promoting lymphatic drainage. However, after local tissue injury or exposure to inflammatory mediators, interstitial pressure decreases, despite rapid fluid influx. Decreased interstitial pressure is thought to arise because loss of extra-cellular matrix mechanical integrity and the resultant exposure of glycosaminoglycans which expand and takes up fluid. Finally, low interstitial pressure in combination with

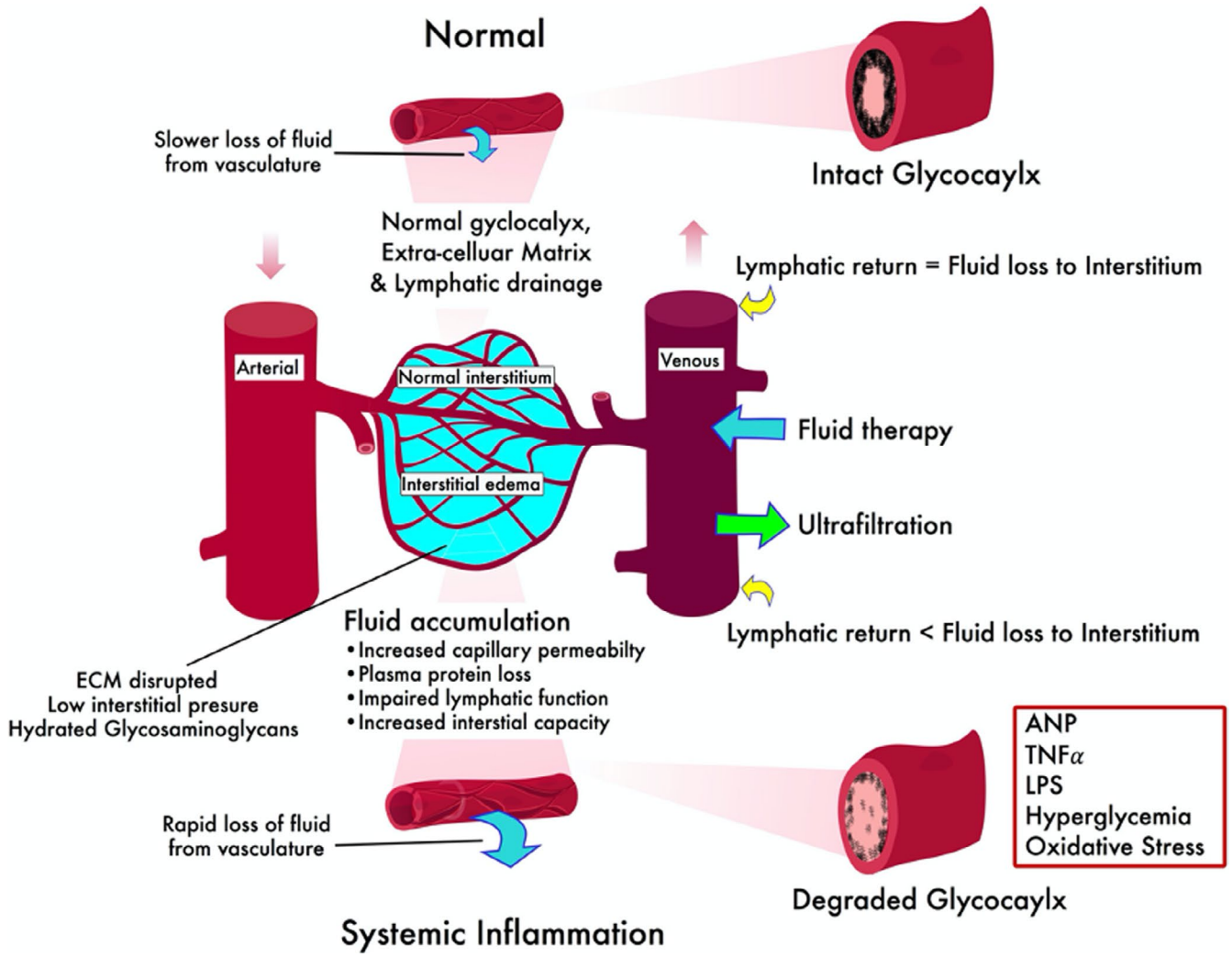

FIGURE 1 Systemic inflammation results in disruption of endothelial glycocalyx and changes in the extra-cellular matrix (ECM) and lymphatic drainage that promote loss of plasma fluid to the extra-cellular space and its retention in the interstitial compartment. These processes have implications for the magnitude and duration of response to fluid therapy and ability to resolve fluid overload once it has arisen. Reproduced from ref. 8

disruption of local lymphatic architecture and the direct effect of inflammatory mediators and patent immobility on lymphatic function result in impaired lymphatic drainage of accumulated tissue fluid.[24] All of these feature suggest that once established interstitial edema will be difficult to resolve with speed of fluid removal limited by slow rates of vascular refilling.

5 | CONTROL AND RESOLUTION OF FLUID OVERLOAD BY EXTRA-CORPOREAL UF

A key aspect of both normal renal function and forms of RRT in controlling fluid balance is that fluid removal occurs only from the plasma volume, whereas the majority of fluid within the body lies within the intracellular space and the interstitial space (Figure 1). In particular, in states of salt and water overload common in critical illness and AKI, it is the interstitial space that is predominantly expanded in the context of a normal or even somewhat reduced plasma volume. Thus, when fluid is removed from the plasma water in order to achieve a total body fluid balance goal, there is the inevitable risk of intravascular hypovolemia if rates of fluid removal exceed the rates of intravascular refilling from the interstitial space. Thus, when considering the prescription of UF in RRT one must always consider the whole organism's response to the prescribed fluid removal physiological limits of vascular refilling. According to the glycocalyx model, the majority of vascular refilling occurs via lymphatic return of interstitial fluid and this lymphatic inflow will be relatively fixed during acute application of UF. Total thoracic duct lymph flow in man is around 4–5 L/day (around 200–250 ml/h), but can escalate several-fold in exercise and a similar volume of fluid may return directly to the circulation in lymph nodes.[25] However, as indicated above, lymphatic drainage is likely to be impaired and in fluid overload arising in the context

TABLE 1 Recent studies considering UF rate and fluid removal during CRRT for AKI in the ICU

Citation	Population	Comparator	Conclusion
Murugan 2018[28]	1075 patients with fluid overload ≥5% of body weight prior to initiation of RRT from a large academic medical center ICU dataset	Net UF >25 ml/kg/day compared with ≤20 ml/kg/day	Among critically ill patients with ≥5% fluid overload and receiving RRT high net UF was associated with lower 1-year risk-adjusted mortality
Tehranian S 2019[37]	1398 patients with AKI who received CRRT between December 2006 and November 2015 at the Mayo Clinic, Rochester, MN	Net UF was categorized into low- and high-intensity groups (<35 and ≥35 ml/kg/day)	More intensive fluid removal, UF NET ≥35 ml/kg/day was associated with lower mortality
Murugan 2019[29]	1434 patients recruited to the Randomized Evaluation of Normal versus Augmented Level (RENAL) of Renal Replacement Therapy trial	Three terciles of Net UF defined: high, rate greater than 1.75 ml/kg/h; middle, from 1.01 to 1.75 ml/kg/h; and low, less than 1.01 ml/kg/h	Net UF rates greater than 1.75 ml/kg/h compared with less than 1.01 ml/kg/h were associated with lower survival
Serpa 2020[31]	1434 patients recruited to the Randomized Evaluation of Normal versus Augmented Level (RENAL) of Renal Replacement Therapy trial (secondary reanalysis of Murugan[29])	Three terciles of Net UF defined: high, rate greater than 1.75 ml/kg/h; middle, from 1.01 to 1.75 ml/kg/h; and low, less than 1.01 ml/kg/h Heterogeneity of effect was assessed according to patient groups, baseline edema and related to the additional impact of baseline cardiovascular Sequential Organ Failure Assessment (SOFA) score	In a group of more severely ill patients, with more sepsis, more edema, and more vasopressor therapy (n = 941) the probability of harm was greater with the high tertile of Net UF rate in patients in cluster 1 and in patients with baseline edema Higher baseline cardiovascular SOFA score also increased mortality risk with both high and low compared to middle NUF rates in cluster 1 patients and in patients with edema
Naorungroj, 2020[30]	Retrospective, observational study of all patients treated with CRRT within 14 days of intensive care unit admission in a single teaching hospital ICU	Net UF rate as the volume of fluid removed per hour adjusted for patient body weight and analysed as a categorical variable (>1.75, 1.01–1.75 and <1.01 ml/kg/h) in first 48 h of CRRT	Net UF rate >1.75 ml/kg/h in the first 48 h was independently associated with increased 28-day mortality longer duration of CRRT and increased ICU length of stay compared with a NUF rate <1.01 ml/kg/h
Hall 2020[38]	820 patients admitted to the multidisciplinary adult ICU who received CRRT for acute kidney injury for at least 24 h	Hospital survivors versus non-survivors	In the 7 days after CRRT initiation, hospital survivors had a significant decline in cumulative FB whilst there was no significant change in cumulative FB in non-survivors. Higher severity of illness at CRRT initiation, shorter duration of CRRT, the number of days without a prescribed FB target and need for higher doses of noradrenaline were independent risk factors for not reaching a FB nadir during CRRT

Abbreviation: AKI, Acute Kidney Injury; CRRT, continuous renal replacement therapy.

of acute critical illness. It is true that during UF decrease in capillary pressure tends to reduce fluid losses to the interstitial space while reduction in elevated central venous pressure may encourage lymphatic return, however, importantly, both of these mechanisms imply the occurrence of hemodynamic consequences of fluid removal that have the potential to acutely impair tissue perfusion. Similarly, during acute fluid removal physiological responses such as tachycardia, contraction of central venous reservoirs and peripheral vasoconstriction may 'defend' the cardiovascular system, however, all these mechanisms imply a physiological response to hypovolemia and, may in any case be maximally recruited in the context of shock and critical illness.

During intermittent maintenance hemodialysis, it is well-recognized that even when there is significant pre-dialysis fluid overload, vascular refilling lags behind rate of fluid removal when UF is performed over a 3–4 h session. Ample evidence exists that, in maintenance hemodialysis, UF rates in excess of 10–13 ml/kg/h are associated with significant risk of cardiovascular and all-cause mortality,[26] representing UF rates at which vascular refilling and compensatory mechanisms are exceeded. Similarly, plasma refilling rates during intermittent dialysis (IHD) for end stage kidney disease have been assessed as around 70% of the applied UF rate and are relatively independent of prior degree of fluid overload.[27] Crucially, the context of the critically ill patient and the stable end stage kidney disease patient are very different. During

critical illness, despite baseline fluid overload lymphatic return is likely to be more impaired as is ability to increase augment refiling during fluid removal. Similarly, as vascular integrity is compromised, loss of fluid from the circulation to the interstitial space is more likely to persist despite removal of fluids from the circulation. Finally, as vasoplegia and impaired cardiac contractility and both likely to be present, ability to withstand transient hypovolaemia during fluid removal will be substantially impaired, while the potential for secondary organ injury from transient impaired tissue perfusion will be magnified. Thus, the maximally tolerated rate of fluid removal during critical illness is likely to be substantially lower than that associated with harm during IHD for ESKD.[7]

Recently evidence has accrued that while resolution of fluid overload during CRRT in critical illness is beneficial, net UF rates in excess of a threshold level are associated with worse outcomes. Interpreting this evidence is complex due to the competing influences of the benefits from resolution of fluid overload, the potential harm from excessively rapid UF and confounding indication bias of the baseline degree of fluid overload affecting both therapeutic choices and outcomes. Recent studies examining this area are summarized in Table 1. Overall, larger overall achieved UF and more negative fluid balances are associated with improved outcomes,[28] however, this benefit is likely to represents a combination of ability to tolerate fluid removal (as an indicator of physiological stability) and the actual benefits of resolution of fluid overload. However, evidence also suggests that higher net weight-adjusted UF rates (greater than 1.75 ml/kg/h net UF) on an hourly basis are independently associated with adverse outcomes - potentially by exceeding rates of vascular refilling during fluid removal.[29-31] Thus, it seems likely that, UF prescription needs to balance the long-term benefits against short-term harm of fluid removal. Importantly, for each individual patient's circumstances, the optimal UF rate and goal are likely to differ and this is further likely to change dynamically during the course of critical illness.[7] Furthermore, while net UF rate is routinely documented and easily studied, this does not take into account other direct and indirect fluid gains and losses from the patient, while physiologically, the combined hourly patient fluid balance would be the best reflection of potential for transient intra-vascular underfilling. However, these additional data are often poorly recorded and difficult to assess.

6 | COMPONENTS OF THE FLUID BALANCE DURING CKRT

Before consideration of the prescription of UF during renal replacement therapy we need to formally consider how we fit the machine prescription of UF within the overall patient balance and the frequency with which these are monitored (Figure 2). During a continuous therapy, it is the net UF that determines the machine balance, that is, the difference between the total UF and replacement volume. The net UF then forms one component of the overall patient fluid balance which is a sum of fluid gains from drugs, feed, intravenous fluids and blood products and metabolism and losses from the urine (if any), the GI tract and from the lung and body surface as well as the extra-corporeal circuit. On a daily basis this sum determines the daily balance of the whole patient. On a continuous basis the balance of net UF and rate of any intravenous infusions reflect direct changes in the plasma volume which is also then affected by loss of fluid to the interstitial space and vascular refilling, as well as any residual glomerular filtration and renal tubular reabsorption. Other gains and losses from the body including enteral intake and insensible losses and gains act indirectly on the circulation and may have delayed effect of vascular volume. Thus, while the daily patient balance is relatively easily appreciated, the minute-by-minute vascular volume is to a degree inherently unpredictable.

7 | PRESCRIPTION OF FLUID REMOVAL

Prescription of net UF during CRRT requires a consideration of the overall goal and the speed with which fluid removal can be achieved (Figure 3). In a newly admitted, appropriately resuscitated ICU patient, the goal is often to prevent fluid overload by matching obligate fluid inputs and allowing for other measured and estimated fluid losses during the so-called "stabilization phase" of fluid resuscitation. Conversely, in a patient with established fluid overload, the goal may be to resolve this at an appropriate rate. Rate of removal might need to be initially rapid, such as in the context of severe adverse effects of fluid overload (pulmonary edema, abdominal compartment syndrome). However, in most cases the initial targeted rate of net fluid removal, and thus the speed at which the fluid balance goal is achieved, will be slow, determined by the hemodynamic status of the patient. This reflects a desire to avoid overly rapid and potentially injurious rates of UF given the sequestration of the majority of fluid accumulation outside the vascular compartment. Furthermore, because the overall fluid balance goal and circulatory balance on an hour-by-hour basis are not directly set in the machine, these are affected by unpredictable fluid gains and losses outside of CRRT, and are subject to change in the context of altering hemodynamic status, dynamic serial re-evaluation is required for effective and safe control of fluid balance.[32] We therefore recommend the following steps in UF prescription for CRRT in the ICU. Firstly, that a total fluid balance goal for the patient accounting for all gains and losses should be set each day but be subject to revision during regular clinical review. Secondly, the overall desired patient fluid balance is calculated on an hourly basis and rate of net UF set on the machine is adjusted in the context of the other inputs and outputs to achieve the daily goal smoothly and without large swings between net fluid accumulation and net fluid removal. To achieve this second step, two approaches can be used.[33] In the traditional approach the overall goal for fluid balance over is met by adjusting the UF rate periodically. In this approach, which is the standard for most CRRT devices, adjustments in UF rates contribute to alterations in the delivered dose as the effluent volume changes with

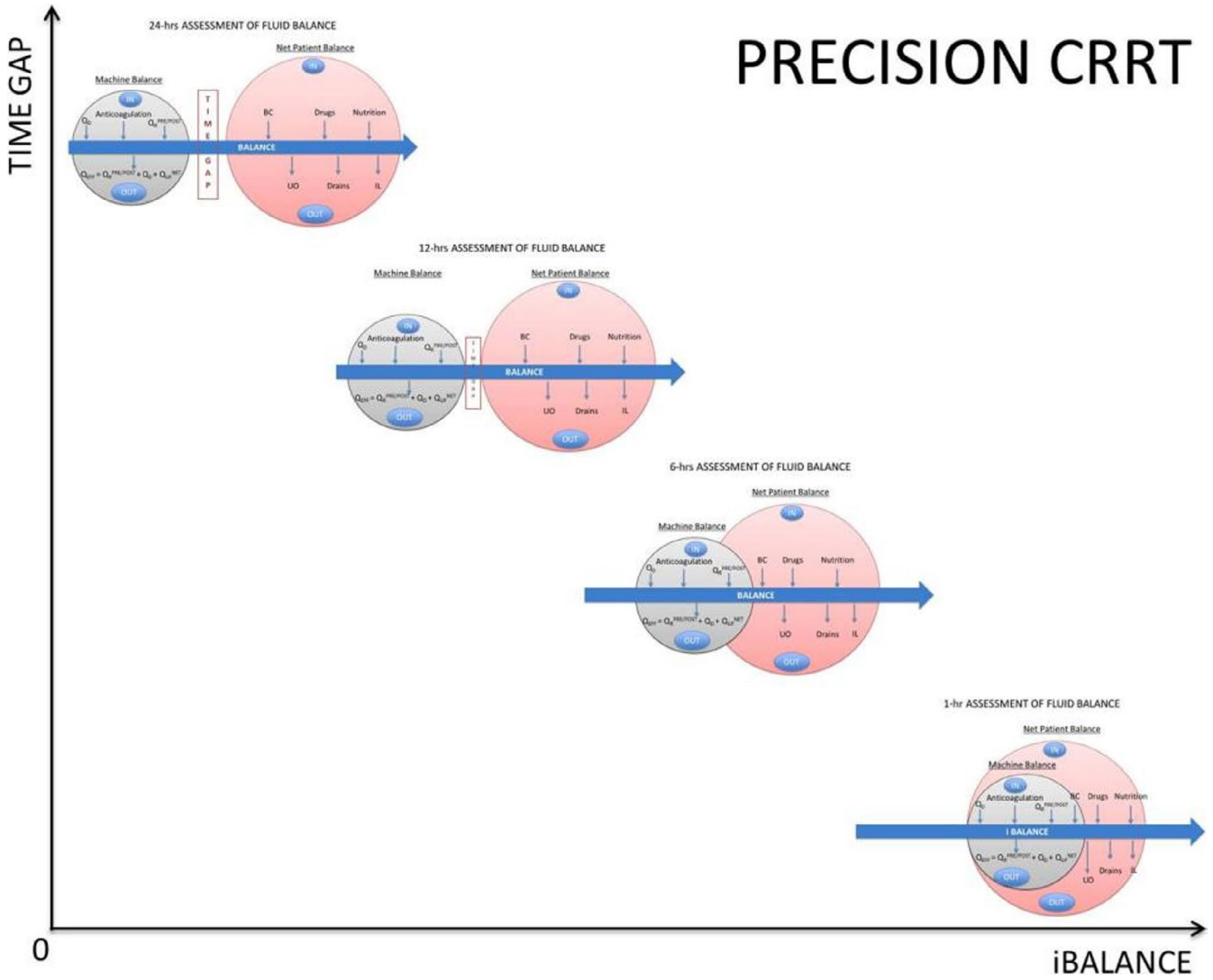

FIGURE 2 Integrated Balance (ibalance). The machine fluid balance (gray circle) depends on ultrafiltration, replacement fluid rates and anticoagulation. The net patient fluid balance (red circle) is calculated as the algebraic sum of patient inputs (e.g., blood compounds, drugs, nutrition) and outputs (e.g., urine output, drains, insensible losses). The machine-patient integrated fluid balance (ibalance) (blue arrow), which derives from the combination of the machine and the net patient fluid balance, is achievable only when frequent assessment of fluid inputs and outputs and CRRT fluid balance machine parameters are performed (e.g., every 1–2 h). The more frequent the assessment, the shorter is the time gap (vertical axis) and more precise the ibalance (horizontal axis). Reproduced with permission from Acute Dialysis Quality Initiative 17 www.adqi.org

each change in UF rate. An alternate approach sets a constant UF rate and adjust the amount of replacement fluid to achieve the desired fluid balance. The advantages and disadvantages of these approaches are shown in Table 2. In either approach it is essential to link the NetUF from the machine balance to the overall patient fluid balance in order to achieve clinical goals.

8 | ADJUSTING AND MONITORING FLUID REMOVAL

To achieve beneficial fluid removal for the prevention or resolution of fluid overload, without at the same time exceeding a rate of net UF that has potential for harm, requires continuous monitoring of fluid balance and hemodynamic status to enable real-time, dynamic adjustment of the CRRT prescription. As we have illustrated assessment of the appropriate quantity and rate of fluid is challenging. In the authors' opinion hourly assessment of total fluid balance and titration of net UF to achieve targets is the cornerstone to effective treatment. Within this framework, both the overall goal for the day or shift and the hourly net fluid removal set should avoid hourly UF rates exceeding 1.75 ml/kg/h unless there is a strong emergent indication for rapid removal of fluid. Importantly, if assessment of fluid balances occurs only a few times in every 12-h period, rather than on an hourly basis, the need for 'catch-up' rates of rapid fluid removal easily arises, abrogating the advantage of continuous therapy in maintaining a smooth fluid balance profile and potentially precipitating hemodynamic instability. Obligate requirement for large volume fluid infusions may

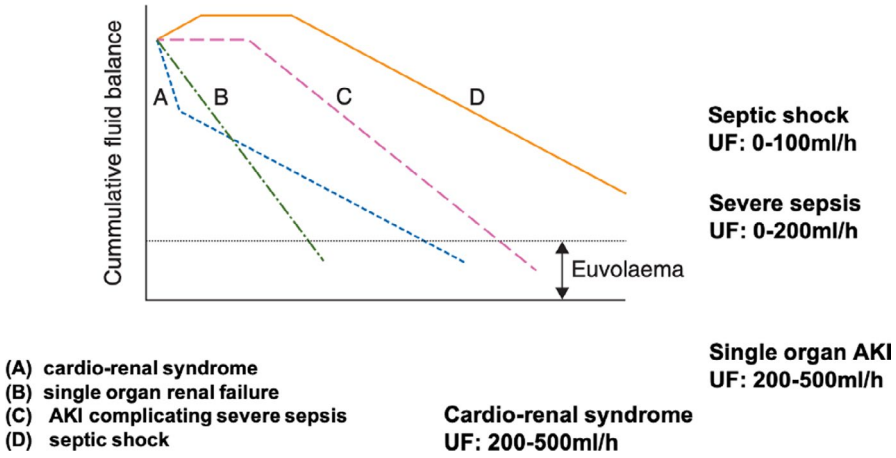

FIGURE 3 Rate of mechanical fluid removal. Examples of patients with fluid overload as a result of disease or fluid resuscitation requiring mechanical fluid management to illustrate how different rates of fluid removal are appropriate to different clinical settings. Rapid early fluid removal may be indicated in cardio-renal syndrome (A), but a slower removal than required for hemodynamic tolerability after resolution of pulmonary edema. Patients with single organ renal failure (B) may tolerate more rapid fluid removal than patients with acute kidney injury complicating severe sepsis (C) or septic shock (D). In septic shock mechanical fluid removal may at first be targeted to limit the accumulation of further fluid until clinical stabilization allows slow resolution of accumulated fluid excess. Modified with permission from Acute Dialysis Quality Initiative 12 www.adqi.org

TABLE 2 Approaches to achieving net ultrafiltration[33]

Variable	Ultrafiltration technique	Replacement fluid technique
Fluid balance	Achieved by varying UF rate	Achieved by adjusting amount of replacement fluid
Differences	Output is varied to accommodate changes in intake and output to reach a fluid removal goal	Output is fixed to achieve solute clearance goal and replacement fluid rates are changed to allow flexibility in reaching net fluid balance goals
Advantages	Familiar strategy from IHD Can allow for fluid balance calculations over an extended period with calculation of a rate per unit time	Allows for constant solute clearance Dissociates clearance parameters form fluid balance
Disadvantages	Solute clearance may fluctuate Require frequent interactions with CRRT machine to adjust UF rate to meet patient needs	Requires hourly calculation of amount of replacement fluid to be given with risk for fluid imbalance if rate not calculated with correct appreciation of all patient fluid inputs and outputs. Not accommodated by software on most integrated CRRT platforms

Abbreviations: IHD, intermittent dialysis; UF, ultrafiltration.

occasionally require higher machine net UF to maintain even a neutral fluid balance, this is best recognized by hourly monitoring so that either need for the intake can be reviewed, fluid balance goal revised (such as in the context of new hemodynamic instability) or so that large fluid intakes can be slowly but effectively accounted for over time rather than only becoming apparent when final daily patient balance is reckoned. This practice should be embedded within the overall hemodynamic monitoring of the patient, which also forms a part of the boundaries of tolerance of fluid removal prescription, which occasionally may form an additional target in its own right. For instance, in specific circumstances, fluid removal might be additionally titrated to maintenance of a stroke volume target or to achieve a reduction in very elevated venous or intra-abdominal pressure.

In addition to this baseline approach to fluid balance management a number of adjunctive methods may be considered to quantify fluid overload and tolerance of fluid removal. Fluid overload and

thus fluid removal targets informed by change in patient weight and/or cumulative fluid balance and its impact informed by clinical examination, physiological parameters such as oxygenation and imaging including chest X-ray, focused ultrasound examination of lung or abdomen and clinical judgments are usually formed by integration of these various, individually unreliable, parameters. In addition, extracellular and intracellular volume expansion can be quantified using a bioimpedance analysis (BIA) techniques. By quantifying intracellular and extracellular volume, BIA can reveal the extent of interstitial fluid overload which may be masked by loss of intracellular volume related to loss of muscle mass when assessing fluid overload by body weight during critical illness.[34] However, while this technology has shown some benefit in the maintenance hemodialysis population[35] as yet, it has not been established that these measurements are sufficiently reliable or reproducible to inform the management of the critically ill AKI patient and they provide no information on the patient's ability to tolerate remove of the measured fluid overload.

In term of initiating fluid removal in potentially unstable patients, this may be considered as a form of 'reverse fluid challenge' and hemodynamic monitoring used as appropriate to a patients' hemodynamic status as it might be during initial resuscitation. Such hemodynamic monitoring may involve simply continuous monitoring of blood pressure via an arterial line or extend to use of cardiac output monitoring incorporating dynamic measurement of 'volume responsiveness' such as stroke volume variation that may detect development of intravascular hypovolemia. Serial echocardiography may also be employed in selected patients to assess ventricular filling inferior vena cava caliber and collapse to assess tolerance of fluid removal, much in the same way as assessing need for resuscitation. In the chronic dialysis setting, real time monitoring of plasma refilling during UF has been employed using continuous monitoring of blood hematocrit, so-called relative blood volume monitoring,[36] again, while conceptually attractive, this technology has not yet been shown to be sufficiently precise to guide fluid removal during RRT in critical illness.

9 | CONCLUSION

Critically ill patient developing AKI needing RRT are amongst the sickest patients treated in the ICU with very high risk of death. They are frequently both hemodynamically unstable and fluid overloaded. While fluid overload is strongly associated with adverse outcomes including persistence and non-recovery of AKI, the power of the extracorporeal circuit to remove fluid from the circulation irrespective of physiological tolerance risks secondary injury from over-rapid removal. There is now increasing evidence that requirement for high net UF rate during CRRT is associated with adverse outcomes and that this association persists after accounting for fluid balance at commencements of therapy. Overall, this evidence suggests that serial re-evaluation of both long-term fluid balance goal and short-term rates of fluid removal are required to safely deliver beneficial therapy. During critical illness and multi-organ failure this is likely to require hourly accounting of total patient fluid balance and continuous hemodynamic monitoring.

CONFLICT OF INTEREST

JRP has received grant and/or research support from bioMérieux, consulting fees from Quark Pharmaceutical and Medibeacon Inc., and speaker's honoraria from Nikkiso Europe GmbH, Baxter, Braun Medical Ltd, Fresenius Medical Care and Fresenius-Kabi UK. RLM has received grant and/or research support from Fresenius and Fresenius-Kabi and consulting fees from AM-Pharma, Sphingotec, Akebia, GE healthcare, Indalo, bioMérieux, Intercept, Baxter, Medtronic and Mallinckrodt.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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