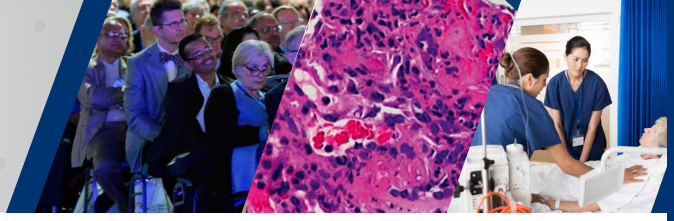

Ultrafiltration Tolerance and Improving Outcomes with Continuous Renal Replacement Therapies

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Introduction

Fluid overload (FO) occurs frequently in critically ill patients with AKI and is one of the indications for continuous KRT (CKRT). FO is associated with increased morbidity and mortality.[1,2] For those receiving KRT, net fluid balance represents the balance of all fluid inputs minus all fluid outputs. For critical care patients who often have low urine outputs, outputs generally represent extracorporeal fluid removal. The prescription of net ultrafiltration (UF_{NET}) requires careful consideration of fluid balance and overload, the resuscitation phase in which the patient is, the total amount of fluid to be removed, and the appropriate removal rate to achieve euvolemia while avoiding cardiovascular complications and intradialytic hypotension (IDH)—events that contribute to decreasing organ perfusion and slower or incomplete recovery of kidney function.[3]

Clinical Case

A 64-year-old male patient was admitted to the intensive care unit with septic shock secondary to community-acquired pneumonia. He was admitted with a positive fluid balance of 7 L due to resuscitation in the emergency department and with vasoactive drug requirements (NE 0.7 μg/kg per minute), mechanical ventilation, and antibiotic therapy. In the intensive care unit, he improved, with decreased inflammatory activity and better oxygenation. He was noted to be fluid overloaded (12 L positive). In addition, the patient developed anuric AKI Kidney Disease Improving Global Outcomes stage 3 that required the start of CKRT 48 hours ago. Attempts at fluid removal at a rate of 1.5 ml/kg per hour of UF_{NET} were unsuccessful because of hemodynamic instability (Figure 1).

Discussion

Evaluation of Ultrafiltration Tolerance

IDH occurs in 17%–70% of acute hemodialysis treatments. The main goal is to remove excess fluid by evaluating the severity of congestion, cardiac dysfunction, vascular tone, and impaired hemodynamic compensatory responses. These evaluations predict and identify the point at which the patient is most tolerant to ultrafiltration (UF),[3,4] without hemodynamic effect, hypoperfusion, episodes of hypotension, and/or compromised cardiac output. Several tools are available to guide clinicians.

Clinical Assessment

Resolution of the triggering event that led to critical illness is a key step that allows for safe UF_{NET}. Variables that indicate an inadequate sympathetic response to the relative hypovolemia generated during UF_{NET} (autonomic dysfunction) can be monitored, including the evaluation of peripheral vasomotor tone. In this context, heart rate variability and peripheral perfusion index (the latter being defined as the ratio of pulsatile blood flow to the nonpulsatile blood flow and measured using pulse cooximetry technology) have been shown to be predictors of IDH during dialytic therapies.[3,5] Another tool that allows prediction of IDH is the relative blood volume monitor measurement, predicting the vascular refilling rate in real time. Integrating this technology into CKRT machine circuits before the administration of fluids (*e.g.*, prefilter replacement fluid) could help in the detection of a change in blood volume greater than −6.5% per hour, reducing the episodes of IDH and maintaining the balance between UF_{NET} and vascular refilling.[3,6] Artificial intelligence algorithms that integrate BMV and other parameters may lead to a next generation of smart CKRT machines that automatically halt UF in response to key parameters. Nevertheless, this innovative approach still requires additional research. In addition, the system proposed by Bellomo *et al.*[6] would enable its use in various types of CKRT machines.

Several methods have been suggested to noninvasively assess fluid responsiveness by examining heart–lung

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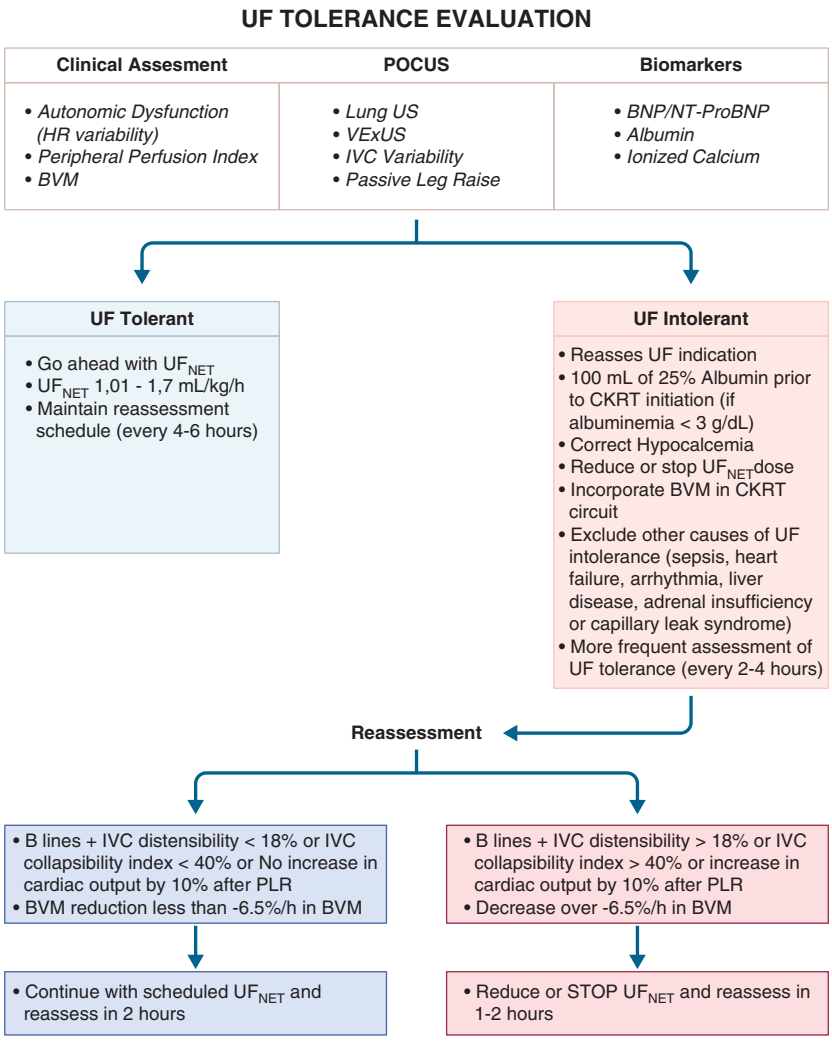

Figure 1. Summary of UF tolerance evaluation and management intervention. IVC distensibility cutoff of 18% applies to ventilated patients only. BNP, brian natriuretic peptide; BVM, blood volume monitor; CKRT, continuous KRT; HR, heart rate; NT-proBNP, N-terminal pro-BNP; IVC, inferior vena cava; PLR, passive leg raise; UF, ultrafiltration; US, ultrasound; VExUS, venous excess ultrasound score.

interactions during mechanical ventilation. These methods include pulse pressure variation, stroke volume variation, end-expiratory occlusion test, and variation of end-tidal carbon dioxide. Detailed descriptions of these techniques to begin fluid removal can be found in various available reviews.

Point-of-Care Ultrasound

Point-of-care ultrasound (US) is a noninvasive tool that can be used to perform hemodynamic monitoring and congestion evaluation through lung US, measurement of inferior vena cava (IVC) diameter, venous excess US score protocol, and echocardiographic estimation of stroke volume. The use of provocative maneuvers, such as an increase in the cardiac index after a passive leg raising, can predict the risk of IDH, helping guide the prescription of UF$_{NET}$.[3,7] Although the study by Monnet *et al.*[7] was conducted with transpulmonary thermodilution and pulse contour analysis, other ways of measuring cardiac index, such as point-of-care US, would facilitate the reproducibility of these techniques in a noninvasive manner. In addition, lung US with IVC diameter variation allows for further risk assessment for IDH. Of importance is the serial measurement of these parameters during UF and temporarily pausing or reducing UF$_{NET}$ in response to changes that suggest vascular underfilling.[3,8] Serial measurements offer the opportunity to make proactive changes in UF that can avoid hypotensive episodes and organ hypoperfusion.

Biomarkers

Biomarkers can predict an IDH episode. Critically ill patients are prone to excessive fluid shift from the intravascular to extravascular space, generating intravascular hypovolemia. This phenomenon, called capillary leak syndrome, is often driven by systemic inflammation. Serum

angiopoietin 2 plays an important role in regulating the vascular barrier and is a marker of vascular permeability, inflammation, glycocalyx shedding, FO complications, and a higher chance of vasopressor requirement. Angiopoietin 2 and also TNF-α and IL-1β were predictors of capillary leak syndrome and IDH, respectively. Despite the interest in phenotyping our patients regarding the inflammatory profile, these markers are not widely available in daily practice.[3] Serum albumin is also a good predictor of IDH. Patients with albumin levels <3 g/dl may benefit from using exogenous albumin supplementation (single dose of 25 g albumin intravenously at the start of dialysis), reducing hypotension episode risk by 74.2%. Increased oncotic pressure may explain the benefits of intravenous albumin; nevertheless, other possible explanations are beyond the scope of this article.[3,9] B-type natriuretic peptide and N-terminal pro-brain natriuretic peptide elevations before dialysis have been associated with FO and less risk of IDH. The use of these biomarkers could help define the start of deresuscitation and beginning of fluid removal when they are elevated.[3,10] In addition, serum-ionized calcium <1.02 mmol/L was associated with IDH during CKRT, mainly because of its effects on systemic vasodilation and left ventricular function.[3]

Resolution of Clinical Case

The patient was evaluated with multiple methods. Ultrasonography showed a pulmonary B pattern, IVC of 2.0 cm, with a distensibility >18% (values >18% suggest volume depletion). In addition, the venous excess US score showed a pattern with moderate congestion, and portal vein Doppler demonstrated 60% of pulsatility index, and discontinuous biphasic flow in kidney vein Doppler. Passive leg raising test was performed, showing no increase over 10% in cardiac output. Laboratory tests showed hypoalbuminemia 2.5 g/dl, ionized calcium 1.2 mmol/L, and elevated B-type natriuretic peptide. A blood volume monitor sensor was introduced into the CKRT circuit to monitor and reduce the UF_{NET} rate in case it presented a plasma volume reduction greater than −6.5% per hour. In addition, therapy was started with 100 ml of 20% albumin before connection, scheduling a UF_{NET} rate of 1.3 ml/kg per hour and re-evaluating again after 4 hours with US to define whether to temporarily reduce or stop the UF_{NET} according to changes in intravascular congestion. Therapy was successfully completed with only temporarily reducing the UF rate.

Conclusion

The assessment of volume status in a critically ill patient is variable and complex. Available and emerging tools help predict and monitor volume status more actively and dynamically to best design UF strategies that avoid hypotension but alleviate congestion.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at http://links.lww.com/CJN/C138.

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Author Contributions

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