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How to Determine Fluid Management Goals during Continuous Kidney Replacement Therapy in Patients with AKI: Focus on POCUS

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Key Points:

Abstract:
The utilization of kidney replacement therapies (KRT) for fluid management of critically ill patients has significantly increased over the last years. Clinical studies have suggested that both fluid accumulation and high fluid removal rates are associated with adverse outcomes in the critically ill population receiving KRT. Importantly, it is not known what are the ideal indications and/or fluid management strategies that could favorably impact these patients; however, differentiating clinical scenarios in which effective fluid removal may provide benefit to the patient by avoiding congestive organ injury compared to other settings in which this intervention may result in harm is direly needed in the critical care nephrology field. In this review, we describe observational data related to fluid management with KRT, and examine the role of point-of-care ultrasonography as a potential tool that could provide physiological insights to better individualize decisions related to fluid management through KRT.

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How to Determine Fluid Management Goals during Continuous Kidney Replacement Therapy in Patients with AKI: Focus on POCUS

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Abbreviation

AKI: Acute kidney injury; ARDS: Acute respiratory distress syndrome; KRT: Kidney replacement therapy; ICU: Intensive care unit; IVC: Inferior vena cava; POCUS: Point-Of-Care Ultrasound; RAP: Right atrial pressure; VTI: Velocity-time integral

Abstract

The utilization of kidney replacement therapies (KRT) for fluid management of critically ill patients has significantly increased over the last years. Clinical studies have suggested that both fluid accumulation and high fluid removal rates are associated with adverse outcomes in the critically ill population receiving KRT. Importantly, it is not known what are the ideal indications and/or fluid management strategies that could favorably impact these patients; however, differentiating clinical scenarios in which effective fluid removal may provide benefit to the patient by avoiding congestive organ injury compared to other settings in which this intervention may result in harm is direly needed in the critical care nephrology field. In this review, we describe observational data related to fluid management with KRT, and examine the role of point-of-care ultrasonography as a potential tool that could provide physiological insights to better individualize decisions related to fluid management through KRT.

1- Introduction

Acute kidney injury (AKI) is a frequent complication of critical illness affecting up to 50% of ICU populations, with 5 to 15% of patients requiring kidney replacement therapy (AKI-KRT) (1, 2). Importantly, AKI-KRT is associated with a higher risk of mortality and significant burden of morbidity in survivors (1-4). KRT is commonly needed in the ICU for managing patients with AKI and concomitant electrolyte or acid-base derangements and fluid overload (FO). Continuous kidney replacement therapy (CKRT) modalities are commonly utilized to support hemodynamically unstable patients as these modalities provide better hemodynamic stability and the ability to manage FO more effectively (5-7). Nonetheless, significant practice heterogeneity has been demonstrated in relation to fluid management with KRT through different survey studies (8, 9). Further, the COVID-19 pandemic has reinforced the importance of KRT in the comprehensive management of critically ill patients with multiorgan failure and FO (10).

Multiple observational studies have shown a dose-response relationship between FO and mortality as well as multiorgan dysfunction during AKI and critical illness (11, 12). Therefore, fluid management during KRT (through net ultrafiltration rate) is an important goal of extracorporeal support. Despite the observation that higher FO at the time of CKRT initiation has been associated with higher risk of 90-day major adverse kidney events, including mortality and decreased kidney recovery, there is a paucity of interventional data to guide optimal rates of fluid removal during KRT (13). Recent observational studies have highlighted a potential U-shape relationship between net ultrafiltration rate and mortality, which highlights the concept of patient tolerance to fluid removal (14-16). It is also important to recognize that fluid balance targets are not always achieved not only due to patients' inability to tolerate fluid removal but also due to logistical factors specific to KRT delivery such as treatment interruptions or inadequate prescription, among others.

In this review, we describe observational data related to net ultrafiltration during CKRT, and examine the role of point-of-care ultrasonography as a potential tool that could assist the evaluation and fluid management of critically ill patients with AKI requiring KRT.

2- Impact of Net Ultrafiltration Rate on mortality

The term net ultrafiltration rate (UF_{NET} or NUF) refers to the net fluid removal rate from the patient or the hourly difference between patient and CKRT machine fluid balances. It should be differentiated from the machine set fluid removal rate. UF_{NET} is a critical CKRT parameter because it refers to the actual volume of extracellular fluid being removed from the patient by the CKRT machine. Importantly, one should note that UF_{NET} is closely linked to the overall fluid balance target of the patient and that the same UF_{NET} may have a different impact on a different patient according to the clinical context.

Murugan and colleagues were among the first to comprehensively examine the relationship of UF_{NET} with mortality in critically ill patients with AKI on KRT. In an observational cohort study of 1075 patients with FO ≥5% prior to KRT initiation, they found that UF_{NET} intensity >25 ml/kg/day vs. ≤ 20 ml/kg/day was associated with lower 1-year risk-adjusted mortality. In this study, the authors determined UF_{NET} as the net volume of fluid ultrafiltered per day from initiation of KRT until the end of ICU stay adjusted for patient hospital admission body weight (14). A subsequent study by the same group of investigators used data from 1434 patients enrolled in the Randomized Evaluation of Normal vs. Augmented Level (RENAL) of Renal Replacement Therapy trial. UF_{NET} was defined as the volume of fluid removed per hour adjusted for patient body weight. They found that when not restricting the cohort to patients with a specific cutoff of FO, UF_{NET} rates greater than 1.75 mL/kg/h (highest tertile) vs. less than 1.01 mL/kg/h (lowest tertile) were associated with lower 90-day survival. One important observation in this study was that patients in the highest tertile of UF_{NET} had more hypophosphatemia and cardiac arrhythmias when compared to the lower tertiles (17). Subsequent analysis evaluated these UF_{NET} thresholds according to time on treatment (i.e. early UF_{NET} withing the first 48 h) and showed concordant results (18). One additional study addressed the indication bias inherent to UF_{NET} observational data by mediation analysis to further examine the association of UF_{NET} with mortality and its interaction with possible mediators such as fluid balance, hemodynamic status, and/or electrolyte abnormalities. The investigators concluded that UF_{NET} >1.75 ml/kg/hr was independently associated with increased hospital mortality, and this effect was not mediated by fluid balance, low blood pressure, vasopressor use, hypokalemia, or hypophosphatemia (19). In another study, the investigators evaluated the heterogeneity of effect of UF_{NET} in critically ill patients receiving CKRT and found that both high and low UF_{NET} rates may be harmful, especially in those with edema, sepsis, and greater acuity of illness severity (20). When evaluating kidney recovery, one study found that UF_{NET} >1.75 ml/kg/hr was independently associated with lower kidney recovery rates (21). A summary **Table 1** is provided to highlight the aforementioned studies.

One should note thus far that there is a dire need for interventional studies testing different UF_{NET} approaches and/or comprehensive strategies for fluid management (i.e. de-resuscitation) in critically ill patients with AKI on CKRT. Further, standardization of terminology, implementation of logistics for dynamic monitoring of CKRT fluid management parameters, and the feasibility of these clinical trials need to be first achieved and/or determined.

3- Role of Point-of-Care Ultrasonography (POCUS)

Despite the epidemiological association between cumulative fluid balance and outcomes in the setting of AKI, it is evident that this parameter alone is insufficient to guide decisions related to mechanical fluid removal through KRT. Indeed, cumulative fluid balance can be unrepresentative of fluid status in many clinical situations in which fluid overload was already present before ICU admission such as congestive heart failure, or when fluid input or output cannot be reliably quantified. Therefore, clinicians must rely on the integration of multiple clinical parameters to orient fluid management including physical examination at the bedside.

Beyond careful evaluation of peripheral edema and measured hemodynamic parameters, Point-Of-Care ultrasound (POCUS) has emerged as a potential adjunct to refine the evaluation and decision-making process of clinicians related to the prescription of fluid removal.

Lung ultrasound

Air impedes the transmission of ultrasound and renders the aerated lung impossible to image using 2D ultrasound. Nevertheless, lung ultrasonography has been used to assess the presence of lung pathologies as it enables the detection of pleural and parenchymal anomalies (22). The presence of increased density from water-thickened interlobular septa in the first millimeters of lung parenchyma produces a verticle line artifact commonly referred to as “b-line” which arises from the pleura as shown in **Figure 1** (23). The presence of diffuse pulmonary b-lines indicates interstitial-alveolar syndrome which may indicate the presence of cardiogenic pulmonary edema. This was previously well-documented in end-stage kidney disease patients. In this population, lung congestion as detected by the presence of b-lines is associated with adverse outcomes (24). B-lines disappear in real-time with ultrafiltration in this population enabling this bedside technique to monitor lung decongestion(25). Lung ultrasound has been shown to perform better than auscultation(26) or chest X-ray(27) for the early detection of lung congestion. Lung ultrasound can be easily learned and rapidly performed at the bedside in a matter of minutes (28, 29).

Identifying lung congestion at the bedside of critically ill patients on KRT could identify patients for which fluid removal is most likely to lead to an improvement in respiratory status. B-lines artefacts decrease rapidly in the context of fluid removal during hemodialysis (25, 30). Therefore, repeated assessments could be useful to determine when net fluid removal could be tapered down or stopped to avoid complications.

However, in the setting of critical illness, many other etiologies can produce an interstitial-alveolar syndrome resulting in the diffuse bilateral presence of b-line artifacts. This includes acute respiratory distress syndrome (ARDS)(31), viral pneumonia(32), and other interstitial lung diseases. Some features may enable the ultrasonographer to differentiate pulmonary edema from ARDS. Common findings in ARDS or pneumonia that are rare in cardiogenic edema include reduced pleural motion, the presence of sub-pleural consolidations, a patchy pattern with spared areas, and pleural line abnormalities (33, 34). The identification of these features may be challenging for a novice ultrasonographer. Furthermore, their sensitivity to differentiate cardiogenic pulmonary edema and ARDS is not well reported. Consequently, while lung ultrasound is a sensitive modality to identify interstitial-alveolar syndrome, additional information related to the clinical context of the patient is important to determine the main physiopathological drivers and whether hydrostatic pressure is the main culprit. Nevertheless, the presence of ARDS may also be an indication to treat and prevent fluid accumulation. Although not focused on fluid removal on KRT, the FACCT trial showed that a conservative fluid management strategy resulting in a near-neutral cumulative fluid balance in patients with ARDS was associated with an increased number of ventilator-free days compared to a liberal strategy in which fluid accumulation occurred in most patients (35). Finally, pre-existing interstitial lung pathologies or pleural disease may also generate artefacts akin to B-lines that may be mistaken for increased extra-vascular lung water.

Inferior vena cava

The inferior vena cava (IVC) is readily accessible through the liver using POCUS. Its assessment has been proposed to help differentiate phenotypes of shock, and predict fluid responsiveness as well as fluid tolerance. The IVC is a highly compliant structure that is affected by variations in intra-thoracic and intra-abdominal pressure. In spontaneous breathing, inspiration decreases intra-thoracic pressure which leads to increased venous return and a transient decrease in IVC diameter. However, an elevation of right atrial pressure (RAP) leads to a plethoric IVC with an absence of respiratory variations **(Figure 2)**. During positive pressure ventilation, this relationship is reversed since the positive pressure during ventilation tends to increase venous pressure resulting in distention, and therefore an increase in diameter, instead of a collapse. Assessments performed before and after intubation or changes in positive end expiratory pressure may reveal the impact of mechanical ventilation on the appearance of the IVC.

Right atrial pressure can be roughly estimated by measuring the maximal and minimal diameters of the IVC in the longitudinal view, as proposed by the American Society of Echocardiography guidelines presented in **Table 2** (36). This classification offers a coarse estimation with a broad range of RAP values for each category in non-mechanically ventilated patients. An IVC assessment suggesting a normal/low RAP may still be present despite an increased total body water content if a redistribution phenomenon is present such as third spacing, vasoplegia, and vascular leak syndrome. Consequently, fluid removal may still be warranted. However, an IVC assessment suggesting a normal/low RAP might be useful to identify patients unlikely to have venous hypertension who may benefit from a slower rate of fluid removal in order to avoid the occurrence of intradialytic hypotension(37).

Rather than estimating a static RAP, a collapsibility index (CI) has been proposed to predict fluid responsiveness (**Table 2**). This is measured 2-4 cm from the cavoatrial junction and calculated as: CI = (IVC max – IVC min) / IVC max with maximum and minimum values measured through the respiratory cycle. Studies have various thresholds for predicting fluid responsiveness and range from a CI of 12 to 42% (38). Overall, the CI has moderate predictive utility of fluid responsiveness in mechanically ventilated patients but only fair predictive utility (poor sensitivity) in patients with spontaneous breathing, in part due to irregular or large swings in intrathoracic pressure (39).

There are several limitations to consider when using this technique. While a plethoric IVC is suggestive of a high RAP, it is unlikely that this parameter alone will be sufficient to differentiate between moderate or severe elevation of venous pressures. While moderate elevations of RAP are ubiquitous in critically ill patients due to the use of positive pressure ventilation, severe elevations of RAP may mediate congestive organ injury and might therefore represent an urgent indication for decongestive treatment with diuretics and/or KRT. This level of nuance is likely necessary to identify patients who are most likely to benefit from directed fluid removal.

While IVC ultrasound is generally presented as an easy technique, there are several technical factors to consider. Firstly, the IVC is an oval-shaped cylinder, and measuring it off-axis can easily under or overestimate its diameter**.** Experienced ultrasonographers often suggest also obtaining a transverse view to assess the shape of the IVC to avoid these issues. Secondly, the movement of the diaphragm can extend into the line of measurement or provide a false impression of collapse near the junction with the right atria. Hence, respiratory variations should be assessed in the intra-hepatic portion of the IVC. Furthermore, multiple physiological factors can affect IVC diameter and lead to misinterpretation. Patient positioning, respiratory status, and effort can modify the degree of collapsibility. Special consideration should be given to any factors affecting intra-abdominal or intra-thoracic pressure. These factors could modify IVC dimensions and may mislead interpretations if used as a single-tool for the purpose of informing KRT fluid removal decisions. Similarly, patients with severe congestive heart failure or pulmonary hypertension may remain with a distended non-collapsible IVC since they may depend on elevated cardiac filling pressure to generate a viable cardiac output. Therefore, some patients exhibiting a plethoric IVC may still experience episodes of hypotension in response to fluid removal (40).

Echocardiographic assessment of preload dependance

An additional way to anticipate tolerance to fluid removal is by assessing pre-load dependence before the initiation of fluid removal (41, 42). By applying a pre-load modifying maneuver, we can infer the position on the Frank-Starling relationship by measuring changes in left ventricular stroke volume. Multiple types of technology have been developed for this purpose. However, they are costly or invasive. Stroke volume can also be assessed non-invasively by utilizing the aortic velocity-time integral (VTI) in conjunction with the diameter of the aortic outflow tract as shown in **Figure 3** (43) The value can be compared before and after an intervention, such as the passive leg raising test, fluid bolus or inotropic support(44). In this context, an absolute increase of 12-15% or more is considered to indicate preload dependence. Additionally, respirophasic variation of the VTI with breathing greater than 12% is also considered a sign to be pre-load responsive in mechanically ventilated patients (45). Even by experienced operators, adequate cardiac views may not be possible in up to 15% of critically ill patients. Alternatively, changes in stroke volume could be measured indirectly with Doppler examination of the common carotid artery (46, 47).

Assessing preload dependence may be useful to predict reduced tolerance to fluid removal in critically ill patients with AKI on KRT (45, 48). In an exploratory study in 39 critically ill patients on intermittent KRT, Monnet et al showed that the change in cardiac output induced by passive leg raise and measured by invasive pulse contour analysis predicted KRT-related hypotension (49). However, larger studies are needed to validate these findings.

As when it is used to assess fluid responsiveness, these methods may produce misleading results in some particular contexts. The risk of intolerance to fluid removal may be underestimated in patients with right ventricular failure, increased intra-adbominal pressure, and cardiac arrythmias, while the technique may overestimate the risk in the setting of reduced lung compliance, increased respiratory rate, or open chest (50).

Venous Doppler Ultrasound

By assessing blood velocity during the cardiac cycle in the systemic venous circulation, Doppler ultrasound enables the operator to appreciate the pattern of venous return during the cardiac cycle and determine whether RAP variations are transmitted backward through a non-compliant venous circulation.

In the individual with normal right atrial pressure, venous return predominates in systole, when the right atrium dilates and the tricuspid annulus moves downward during right ventricular contraction. When right atrial pressure is high, the already dilated right atria cannot accommodate as well for venous return and this may be aggravated by systolic right ventricular dysfunction which limits tricuspid valve systolic excursion. In these circumstances, venous return occurs predominantly in diastole, when the tricuspid valve opens. With very high right atrial pressure, and particularly when significant tricuspid regurgitation is present, venous return during systole is absent and retrograde flow (away from the heart) is observed.

To assess this using POCUS, the hepatic veins represent a window of this physiologic principle. The identification of a dominant diastolic component can reliably identify elevated right atrial pressure (51-53) while a retrograde systolic component is suggestive of, but not synonymous with, hemodynamically significant tricuspid regurgitation (54, 55). While the reproducibility of the assessment has been reported to be excellent (56), the use of concurrent ECG tracing to ensure the proper identification of the systolic and diastolic phases remains critical for accurate interpretation.

In the normal individual, the pattern observed in the hepatic veins is attenuated, or blunted, progressively in the venous circulation as we move upstream away from the heart. This is due to the high compliance of the venous system which impairs the transmission of rapid pressure variations observed in the right atrium during the cardiac cycle. Venous flow in the splanchnic circulation and within distal organs such as the kidney is therefore usually devoid of important cardiophasic velocity variations (pulsatility), resulting in a continuous waveform on pulse-wave Doppler. The distension of the venous circulation in pathological states of high venous pressure renders it non-compliant resulting in the distal transmission of cardiophasic pressure variations. This results in a pulsatile pattern that can be observed at multiple sites including in the main portal vein of the liver and interlobar veins of the kidney using pulse-wave Doppler.

Doppler assessment of the portal vein in a normal individual will reveal minimal variations of velocities during the cardiac cycle. In the patient with venous systemic hypertension, the portal vein Doppler pattern becomes pulsatile with minimal velocity in systole and maximal velocity in late diastole. A pulsatility index ((Max velocity – Min velocity)/Max velocity) of >0.5 is considered abnormal (57, 58). Portal vein pulsatility has been described in the setting of heart failure where it correlates with disease severity (58-61) and outcomes(62), as well as in the settings of cardiac surgery (63, 64) and critical illness (65) where it was also associated with adverse outcomes including AKI. Most interestingly, some reports indicated that the portal pulsatility index correlates better with perfusion pressure (mean arterial pressure – central venous pressure) than with central venous pressure itself (64). As such, it may be a better marker of the overall hemodynamic impact of venous hypertension.

The Doppler assessment of interlobar veins of the kidney may further inform about the pattern of venous return and the presence of abnormal venous compliance. Contrary to the normal individual for which intra-renal venous velocities are continuous, or with a brief interruption during atrial contraction only, the Doppler pattern becomes interrupted with systolic and diastolic phases in individuals with reduced systemic venous compliance and progresses to severe alteration characterized by prolonged interruption with the venous signal typically present only during diastole, which testifies of the altered pattern of systemic venous return as previously described for the hepatic veins. As the alteration of intra-renal venous Doppler progresses, a detectable venous signal is seen for a shorter period of time in relation to the duration of the cardiac cycle. The intra-renal Doppler pattern has been shown to be highly predictive of death or re-hospitalization in patients with congestive heart failure (66) and is also associated with AKI after cardiac surgery (64). Nonetheless, its utility has not been evaluated in critically ill patients on KRT.

The typical continuum of venous Doppler waveforms is presented in **Figure 4**. Confounding factors related to the site of assessment might be present when performing venous Doppler (67-70). For this reason, assessing venous Doppler at multiple sites may be beneficial as verifying that the information is consistent across multiple sites may mitigate the impact of potential confounders. The Venous Excess UltraSound (VExUS) grading system is an attempt at proposing the integration of venous Doppler ultrasound assessment at multiple sites (71). Using data from a previously performed cohort study in cardiac surgery patients, it was observed that the presence of at least 2/3 severe Doppler anomalies on the hepatic, portal, and intra-renal Doppler assessment in conjunction with a dilated (≥2cm) IVC at ICU admission is very specific (96%) for the subsequent development of AKI presumed to be of congestive etiology.

4- Integrating POCUS to support decisions on mechanical fluid removal

The clinician prescribing mechanical fluid removal through KRT must balance the potential risk of congestive organ injury from persistent fluid accumulation with the probability of hemodyamic instability due to a high net ultrafiltration rate. Due to the underlying complexity of critically illness and its dynamic nature, it is unlikely that either a "one-size fits all" fluid management strategy, or that an approach based on a single clinical parameter will be optimal.

We propose that a multimodal evaluation integrating ultrasound features to support clinical decision-making may represent one of the components of an optimal fluid management strategy on KRT **(Figure 5)**. Two frequent clinical dilemma could be improved by the use of POCUS.

First, ultrasound features of congestion on lung ultrasound and venous Doppler may identify a sub-group of patients for which prompt decongestion should be prioritized. This may be particulary helpful when other source of clinical information such as cumulative fluid balance are likely erroneous. This can occur in the presence of pre-existing fluid accumulation before ICU admission (i.e. known heart failure), or when non-quantified fluid gains or losses limit the value of fluid balance estimation. A systematic documentation of features compatible with organ congestion may lead to the identification of patients for which fluid removal should be initiated or increased in order to prevent congestive organ injury. Repeated assesments may also yield valuable information that could be used to titrate fluid removal.

Second, tolerance to fluid removal is known to be highly variable and dynamic among critically ill patients. Intradialytic hypotension might in part mediate adverse outcomes seen with high UF_{NET} in observational studies but it is unlikely that a single maximal high UF_{NET} threshold could be generalized to all critically ill patients. Tolerance to fluid removal might be better predicted using dynamic markers rather than static parameters. A significant drawback is the need for cardiac output monitoring but LVOT VTI assessment might provide a useful adjunct in this setting to predict tolerance to fluid removal during KRT without requiring intensification of patient monitoring or additional costs.

The value of POCUS as a tool to support decision-making related to fluid removal prescription in the context of KRT is largely unexplored at the present time. While the available and evolving technology makes this avenue promising, it is still unknown in what proportion of patients the addition of POCUS to other source of clinical information will meaningfully change fluid management. With the recent increase in the adoption of POCUS training in critical care medicine and nephrology, we expect that future efforts will gradually fill the knowledge gaps in this field.

5- Summary of statement

On an epidemiological basis, both fluid accumulation and high net ultrafiltration rates are associated with adverse outcomes in critically ill patients with AKI receiving KRT. The ideal fluid management strategy may involve distinguishing clinical situations in which effective fluid removal may benefit the patient by avoiding congestive organ injury compared to other settings in which this intervention will result in harm. POCUS may provide physiological insights to better individualize decisions related to fluid removal through KRT.

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Table 1: Featured observational studies evaluating the association of UF_{NET} with clinical outcomes

Study	Sample	Independent variable	Outcomes	Results	Comments
Murugan 2018 (14)	1075 adult patients with FO ≥5% prior to KRT initiation	UF_{NET}	1-year mortality	UF_{NET} intensity >25 ml/kg/day vs. ≤ 20 ml/kg/day was associated with lower 1-year risk-adjusted mortality	UF_{NET} was calculated as the net volume of fluid ultrafiltered per day from initiation of KRT until the end of ICU stay adjusted for patient hospital admission body weight
Murugan 2019 (17)	1434 adult patients from RENAL trial	UF_{NET}	90-day mortality	UF_{NET} rates greater than 1.75 mL/kg/h (highest tertile) vs. less than 1.01 mL/kg/h (lowest tertile) were associated with lower survival	UF_{NET} was defined as the volume of fluid removed per hour adjusted for patient body weight
Naorungroj 2020 (18)	347 adult patients	Early UF_{NET} (first 48h of KRT)	28-day mortality	Early UF_{NET} rates >1.75mL/kg/h vs. <1.01mL/kg/h were associated with increased mortality	Early UF_{NET} was defined as the volume of fluid removed per hour adjusted for patient body weight in the first 48 h
Naorungroj 2020 (19)	347 adult patients	UF_{NET}	Hospital mortality	UF_{NET} >1.75 ml/kg/hr was independently associated with increased hospital mortality, and this effect was not mediated by fluid balance, low blood pressure, vasopressor use, hypokalemia or hypophosphatemia	Interaction evaluation of UF_{NET} with possible mediators (fluid balance, hemodynamic status, key electrolytes) through mediation analysis
Serpa Neto 2020 (20)	1434 adult patients from RENAL trial	UF_{NET} evaluated in clusters of patients according to baseline characteristics	90-day mortality	Both high and low UF_{NET} rates may be harmful, especially in those with edema, sepsis, and greater acuity of illness	Two clusters of patients were idenfied. Cardiovascular SOFA scores modulate the association of UF_{NET} with mortality.

Murugan 2021 (21)	1433 adult patients from RENAL trial	UF_{NET}	Kidney recovery (alive and independent of KRT)	UF_{NET} rates >1.75 mL/kg/h compared with rates 1.01-1.75 and <1.01 mL/kg/h were associated with a longer duration of dependence on KRT	Competing risk multivariable regression models were used

Table 2: Estimation of right atrial pressure (RAP) using echocardiography as suggested by the American Society of Echocardiography(36).

<table>
<tr><th>Diameter of the inferior vena cava</th><th>Percent collapsibility</th><th>Estimated RAP</th></tr>
<tr><td>≤2.1 cm</td><td>>50% collapse</td><td>3 mmHg (Range: 0 to 5)</td></tr>
<tr><td>≤2.1 cm</td><td><50% collapse</td><td rowspan="2">8 mmHg (Range: 5-10)</td></tr>
<tr><td>>2.1 cm</td><td>>50% collapse</td></tr>
<tr><td>>2.1 cm</td><td><50% collapse</td><td>15 mmHg (Range: 10-20)</td></tr>
</table>

Figure Legends

Figure 1: Lung ultrasound using a linear (A) and curvilinear (B) probe. The normal appearance included the rib shadow, the pleural interface with the pleural sliding motion, and horizontal a-line artifacts. The presence of interstitial-alveolar syndrome is associated with the appearance of vertical b-line artifacts that arise from the pleura and move with respiration (C and D).

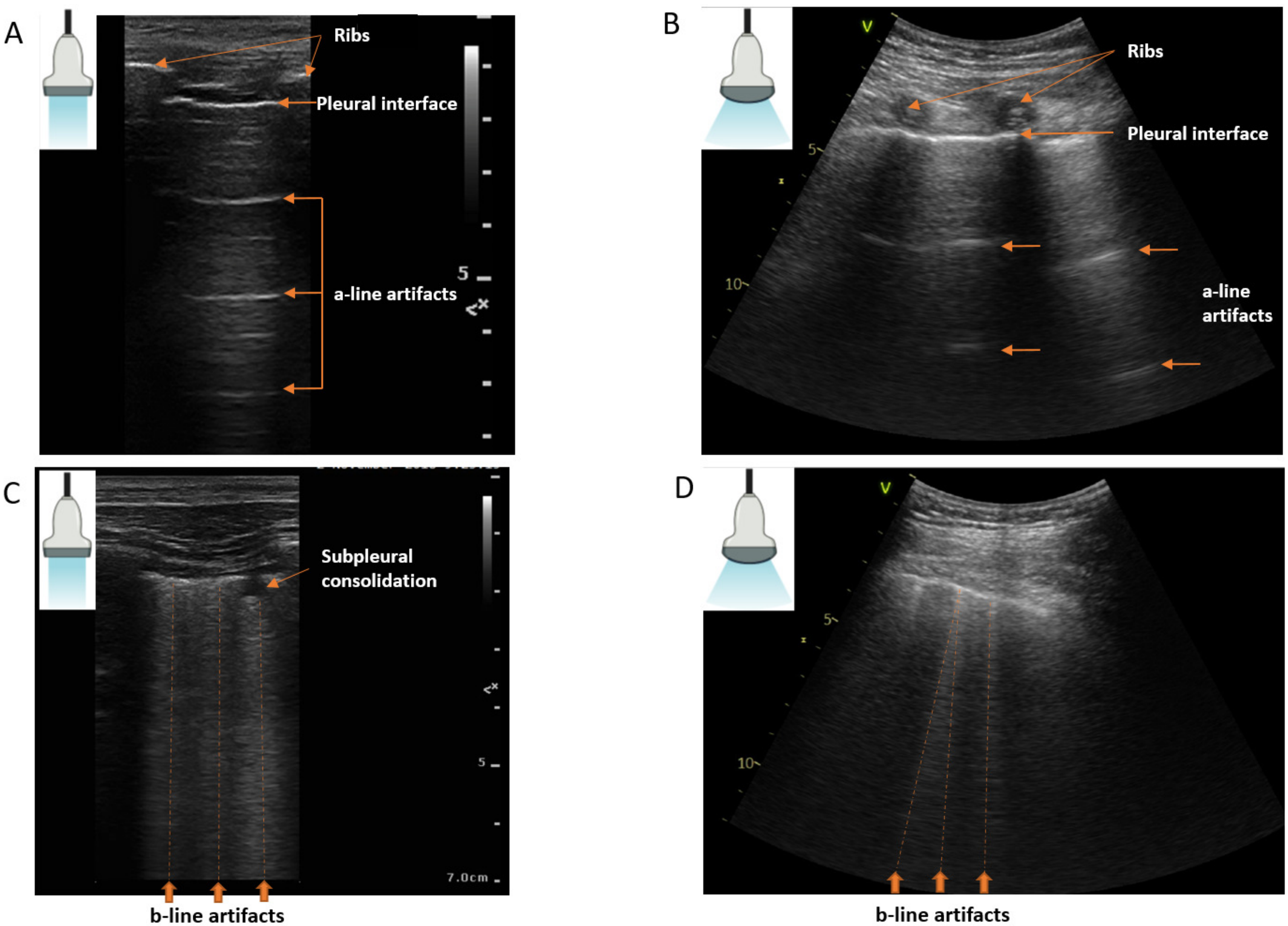
Figure 2: Inferior vena cava (IVC) assessment in the context of a normal/low (0-5 mmHg) right atrial pressure (RAP) (Pannel A, B, and C) compared to a high RAP (>10 mmHg). In the context of a normal/low RAP, the IVC will typically have a maximal diameter inferior to 2.1 cm (A), an oval appearance in transverse view (B), and respiratory variations >50% (C). In the setting of a high RAP, the IVC will be distended (D), with a round appearance (E), and an absence of respiratory variations (F). (Anatomic representations obtained using the Vimedix simulator (CAE Healthcare))

Figure 3: Stroke volume assessment using left ventricular outflow tract (LVOT) Doppler ultrasound. A) 3D representation of the left ventricular outflow tract. B) Schematic representation of the measurements to estimate the stroke volume as a column of blood as it exits the left ventricle (LV) through the aortic valve (AV). C) Measurement of the LVOT diameter at the level of the AV through a parasternal long-axis view. D) Pulse wave Doppler of the LVOT obtained using an apical 5 chamber view resulting in the measurement of a velocity-time integral VTI. E) Change over repeated assessments following a preload modifying manoeuver can inform whether preload dependence is present. MV: Mitral valve, LA: Left atrium (Anatomic representations obtained using the Vimedix simulator (CAE Healthcare))

Figure 4: Venous Doppler patterns with worsening venous congestion. Portal vein Doppler exhibits increased pulsatility as venous pressure increases. In the hepatic vein, the systolic component of venous return decrease and disappear or become retrograde with severe elevation in right atrial pressure. In the interlobar veins of the kidney, interruptions in the venous Doppler signal become prolonged as the venous systolic component disappear.

Figure 5: Evaluating the risk and benefit of fluid removal involves a multimodal assessment combining multiple sources of clinical information which can be supported by the identification of Point-Of-Care ultrasound features suggestive of organ congestion or preload dependance. CVP: central venous pressure,IVC: Inferior vena cava, PAP: pulmonary artery pressure, UF: Ultrafiltration.

Figure 1



A
Ribs
Pleural interface
a-line artifacts
B
Ribs
Pleural interface
a-line
artifacts
C
Subpleural
consolidation
b-line artifacts
D
b-line artifacts

Figure 2

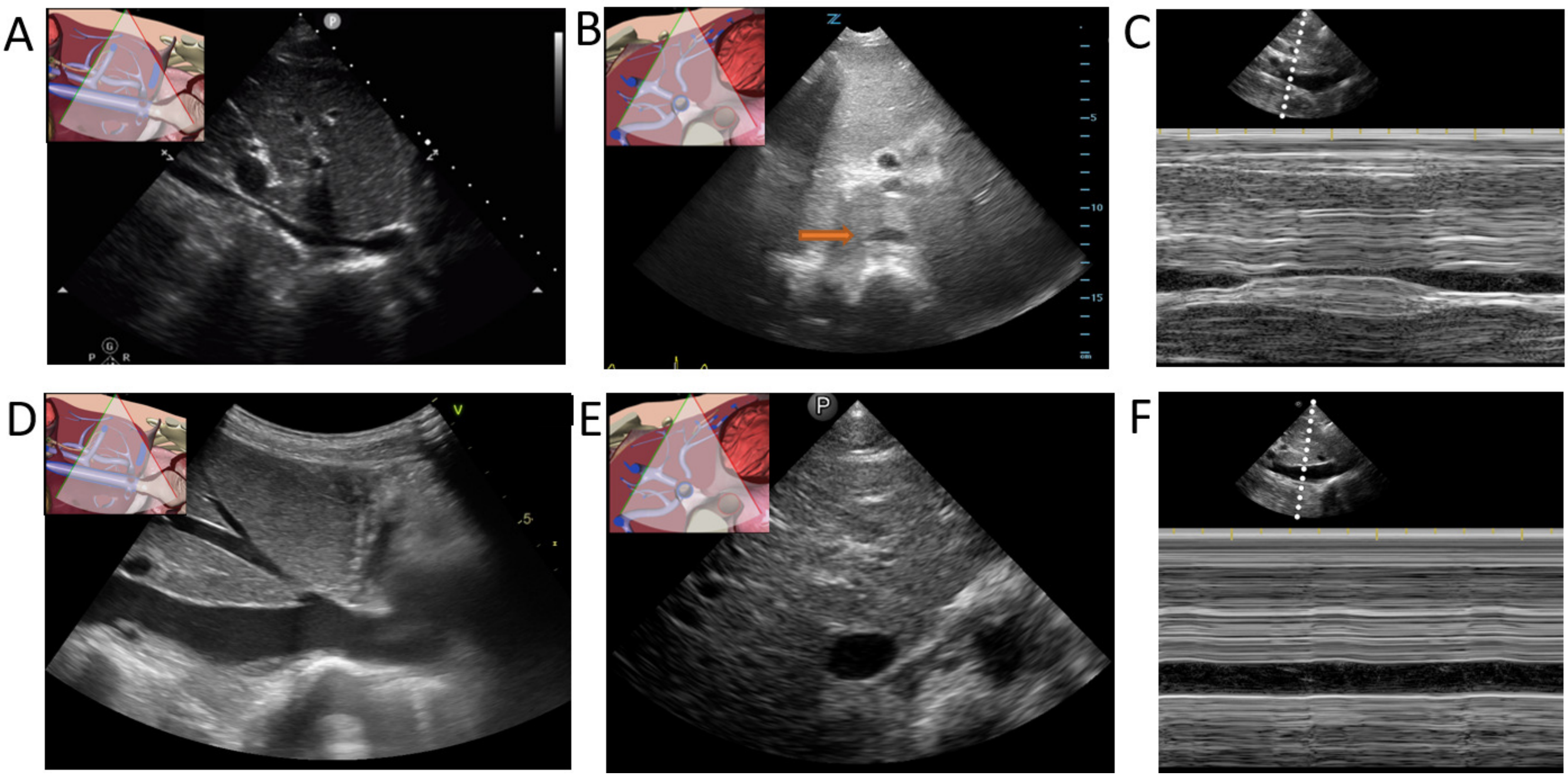


Figure 3

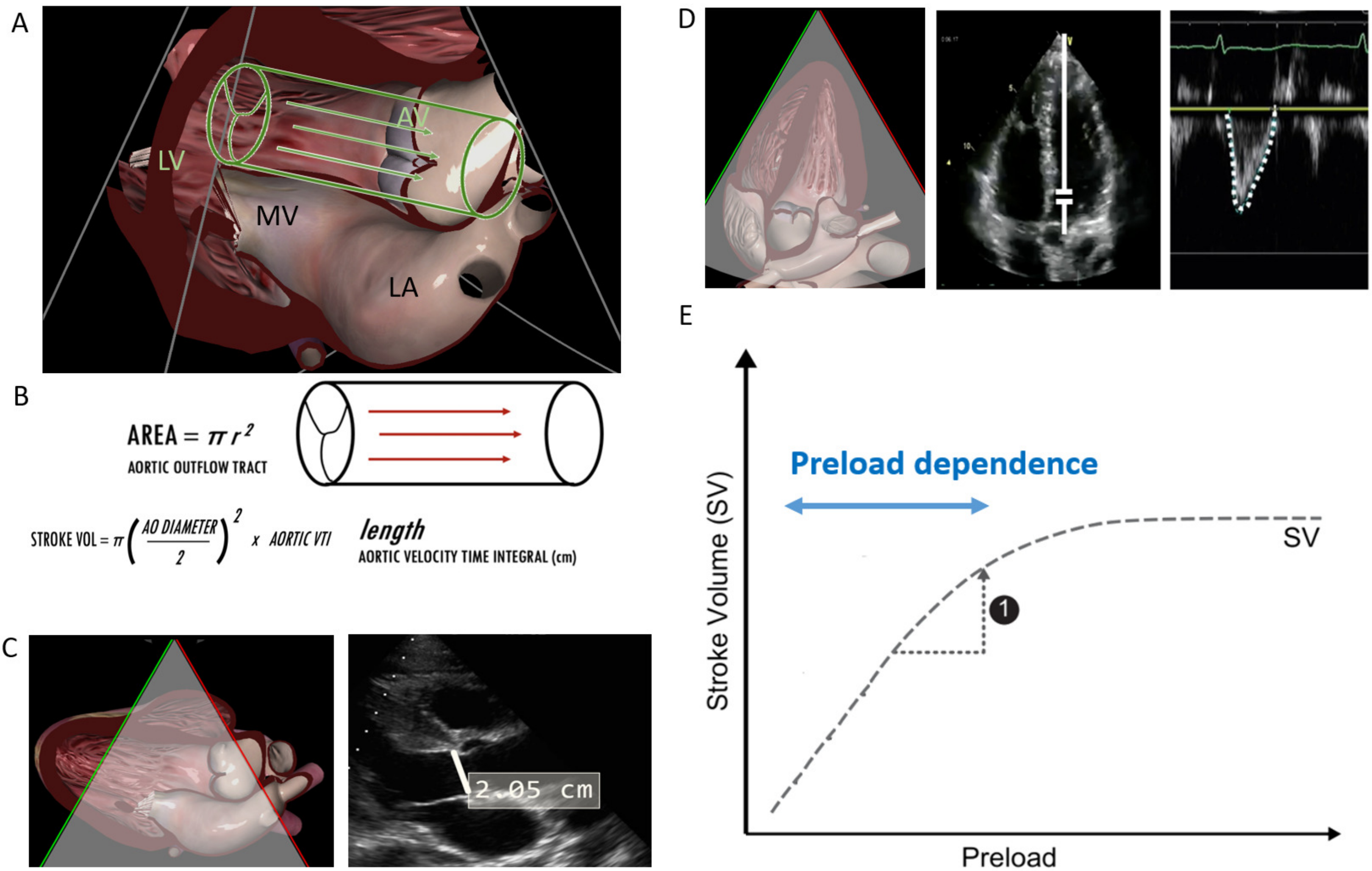
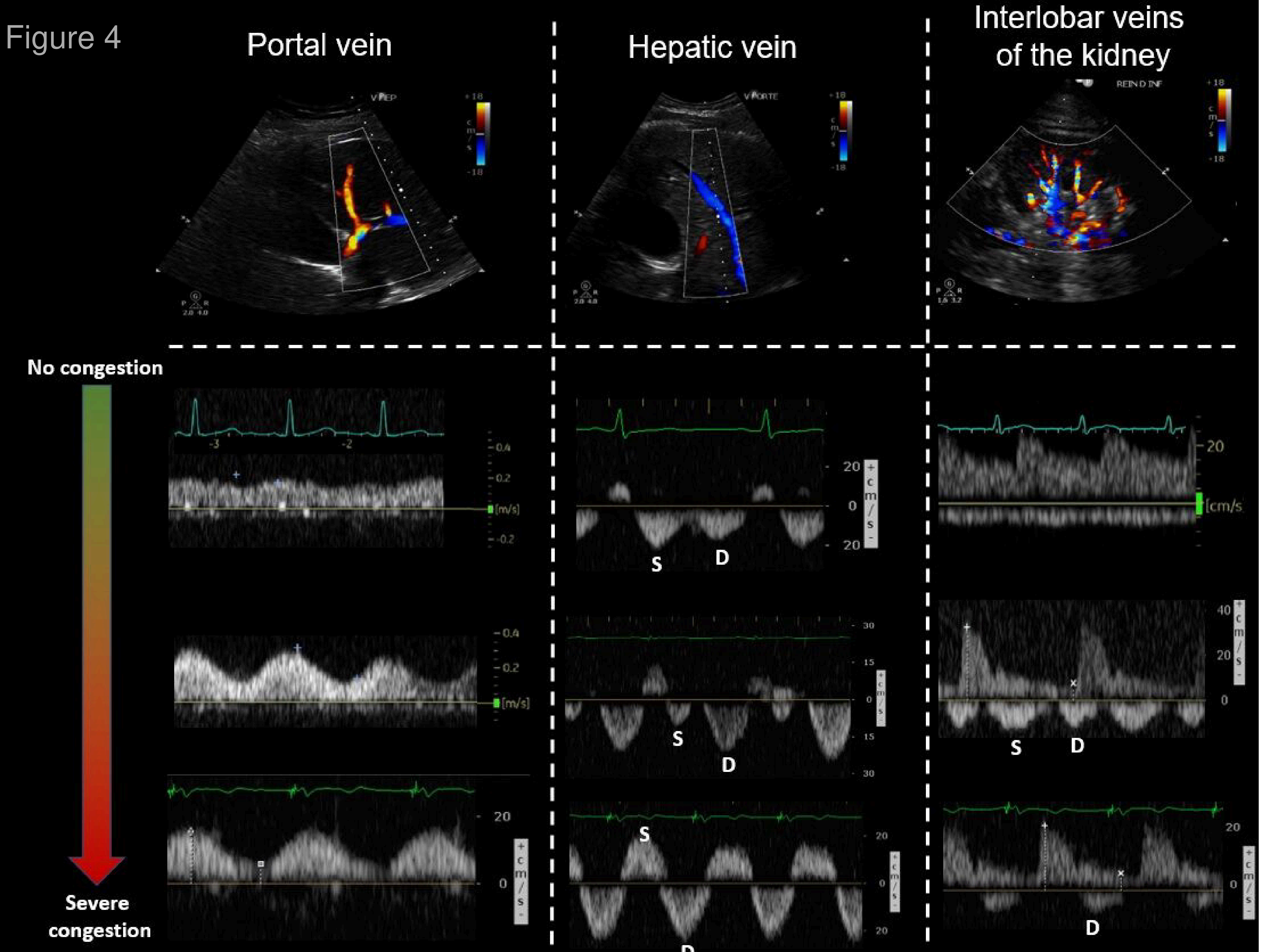
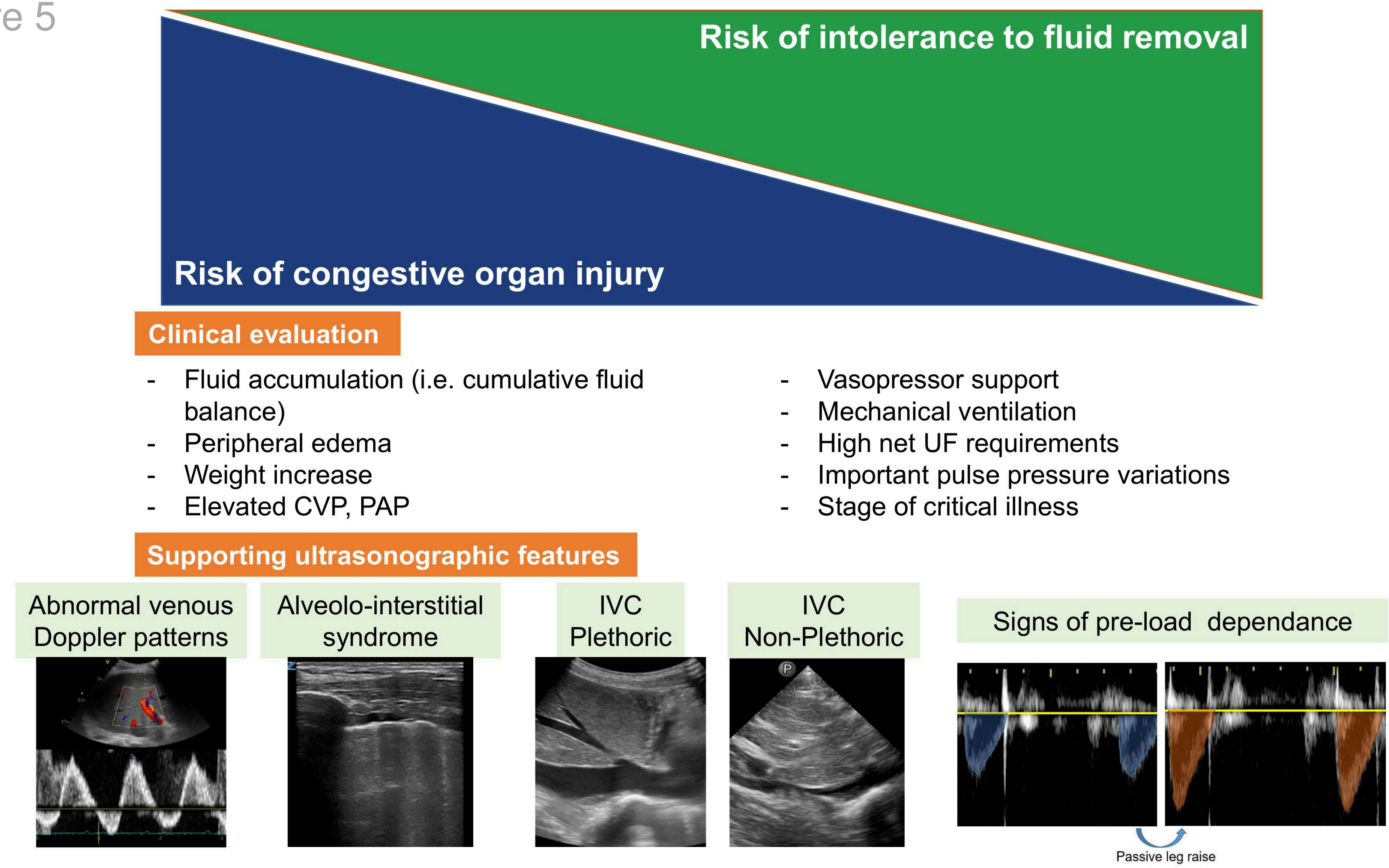

A
LV
AV
MV
LA
B
AREA = πr²
AORTIC OUTFLOW TRACT
STROKE VOL = π (AO DIAMETER / 2)² x AORTIC VTI
length
AORTIC VELOCITY TIME INTEGRAL (cm)
C
2.05 cm
D
E
Preload dependence
Stroke Volume (SV)
SV
1
Preload

Figure 4



Portal vein
Hepatic vein
Interlobar veins of the kidney
No congestion
Severe congestion
S
D
S
D
S
D
S
D
D

Figure 5



Risk of intolerance to fluid removal
Risk of congestive organ injury
Clinical evaluation
- Fluid accumulation (i.e. cumulative fluid balance)
- Peripheral edema
- Weight increase
- Elevated CVP, PAP
- Vasopressor support
- Mechanical ventilation
- High net UF requirements
- Important pulse pressure variations
- Stage of critical illness
Supporting ultrasonographic features
Abnormal venous Doppler patterns
Alveolo-interstitial syndrome
IVC Plethoric
IVC Non-Plethoric
Signs of pre-load dependance
Passive leg raise