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REVIEW ARTICLE

VExUS: The Holy Grail or Achilles Heel of fluid management?

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Declaration:
The authors declare the use of AI (leonardo.ai) to generate a part of one of the images (Figure 1) to better depict the probe positioning in relation to the human body. However, the image generated with AI did not include the ultrasound images or any of its parts.

ABSTRACT

Excessive use of intravenous fluids is becoming less favored in most critical case scenarios due to increased identification of adverse effects associated with fluid overload. Venous Excess Ultrasound (VExUS) is a recent point of care ultrasound (POCUS) tool in critical care. It has a promising utility to identify end point of resuscitation, onset of fluid congestion and to facilitate initiation of de-resuscitation. Whether or not significant association or causation exists between congestion as identified by VExUS and clinically relevant outcomes is yet to be observed as newer evidences surface and establish the place of VExUS in clinical practice. This narrative review aims to describe the current need to have a tool to accurately identify fluid overload, give a brief description of the physiology behind along with techniques of performing VExUS. We have also summarized the available evidences so far for and against VExUS and the limitations of this technique.

Keywords: *fluid overload, point of care ultrasound (POCUS), Venous Excess Ultrasound (VExUS)*

INTRODUCTION

Derangement of physiology is at the heart of any pathophysiological mechanism. Understanding physiology and its derangement during pathology leads to development of newer modalities for diagnosis, monitoring and possibly identify the key moments at which to intervene. Fluids are one of the most prescribed drugs in critical care medicine. But they are not without side effects. Until recently, all the focus was on assessment of fluid status for identifying fluid responsiveness, mainly to guide the initiation or continuation of fluid therapy. Debate still persists on when, how and what fluids need to be administered.[1] A few studies have unveiled adverse effects of specific types of fluids. Some have shown that certain types of fluids are potentially hazardous to use and strongly recommended against use.[2] But in recent years, it has been shown that any type of intravenous fluid is capable of causing side effects when prescribed in excessive quantities without careful monotoring.[3]

These side effects are often seen in patients with heart failure who are in a decompensated state and show all the features of fluid overload which may include hydrostatic pulmonary oedema, pleural effusions, congestive gastro/hepatopathy, cardio-renal syndrome etc.[4] Not only in patients with heart failure, but also in critically ill patients in general, excessive cumulative fluid balance has shown to increase morbidity and mortality. A post-operative patient who has undergone intestinal resection anastomosis may have decreased peristalsis or even leakage of the anastomotic site following excessive fluid administration. This has led to the development of Enhanced Recovery after Abdominal Surgery (ERAS) protocol, primarily aimed to improve perioperative recovery, to emphasize on the importance of managing fluids peri-operatively as an important component.[5] Similarly, a positive cumulative fluid balance in patients with ARDS may lead to worsening P/F ratio and various guidelines of ARDS treatment recommend targeting negative fluid balances.[6] In patients with acute severe pancreatitis, fluid management is among the main pillars in managing acute pancreatitis besides pain management. In these patients, the total positive fluid balance at the end of 48 hours is a predictor of mortality with higher chances of death with higher degrees of fluid sequestration.[7] Recently the trend is moving even towards managing patients will very less fluids.[8] Even in patients with septic shock where timely fluid resuscitation with at least 30ml/kg of crystalloids was considered a key factor determining survival, excessive cumulative fluid balance is associated with worsened outcomes.[2,9–11]

Cordemans et al in 2012 coined the term global increased permeability syndrome which describes the pathophysiology behind organ system effects of increased cumulative fluid balance.[12] The famous "fluid overload man" from Malbrain et al describes the effects in all the organs in the body and the four phases of de-resuscitation have been described in the ROSE model to counteract these. Attainment of euvolemia by day 3 is the standard target to achieve for most patients.[13,14] No modality had been devised to reliably assess the fluid overload for stopping fluid therapy or starting fluid removal for that matter.[15]

Venous Excess Ultrasound (VExUS)

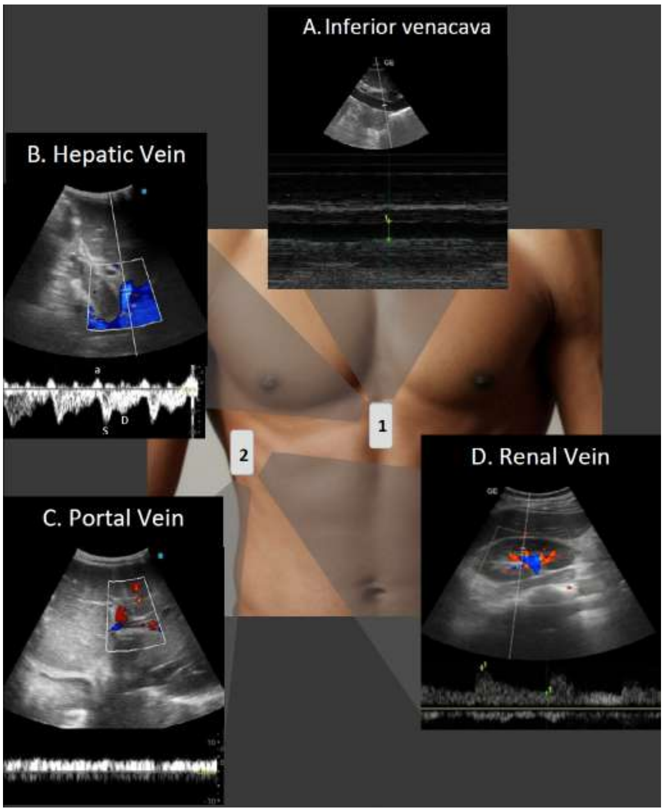

Figure 1. Probe positions and normal waveforms. The figure summarizes the scanning technique for VExUS. Either of the positions subxiphoid **(1)** or anterior axillary line **(2)** can be used for scanning and either of the probes curvilinear or phased array can be used. **(A)** Inferior Venacava (IVC) is scanned in M mode at a point 2cm caudal to the venoatrial junction. **(B)** Hepatic veins can be identified as hypoechoic structures entering the IVC. The flow is seen blue in color Doppler scan. Anterograde (towards the heart) waves "S" and "D" and retrograde (away from the heart) "a" wave can be seen in the pulsed waved Doppler tracing. S waves are larger than D waves in normal conditions. **(C)** Portal vein can be identified as vascular structure within the liver parenchyma with hyperechoic walls. The flow can be either blue or red. Pulsed waved Doppler shows a continuous flow pattern. **(D)** While scanning the kidneys, interlobar vessels need to be scanned. Both arteries and veins usually travel together giving both red and blue color Doppler patterns beside each other. Pulsed wave Doppler shows two tracing in normal conditions. Pulsatile flow directed upwards from the baseline represents arterial blood flow while continuous flow directed downwards from the baseline represents venous flow.

Venous excess ultrasound (VExUS) score was validated and devised as a model which was attained by integration of the ultrasound assessment of the venous side of three organs namely hepatic vein for the liver, portal vein for the gut and renal vein for the kidneys along with the inferior venacava (IVC).[16] The physiological basis of the protocol relies on the assumption that in case of fluid overload in the organs, its effects will be seen in the venous ends of the organs which leads to changes in venous blood flow patterns. The normal flow patterns have been shown in Figure 1.

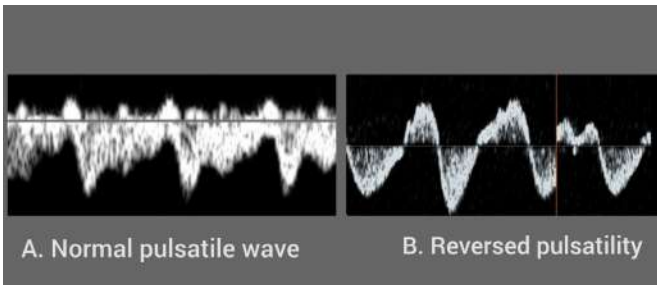

Figure 2. Change in the Doppler flow pattern of hepatic vein with increasing congestion. The normal anterograde pattern **(A)** has changed to retrograde reversal of S wave **(B)**.

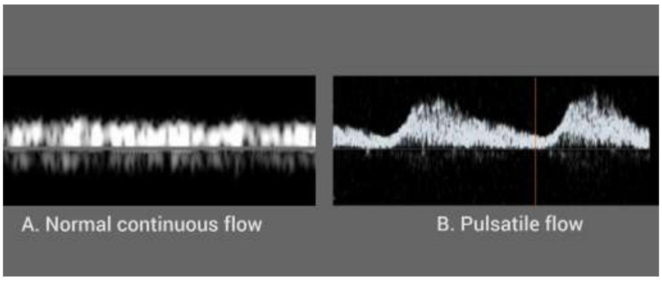

Figure 3. Change in the Doppler flow pattern of portal vein with increasing congestion. The normal continuous flow pattern **(A)** has changed to pulsatile flow **(B)**.

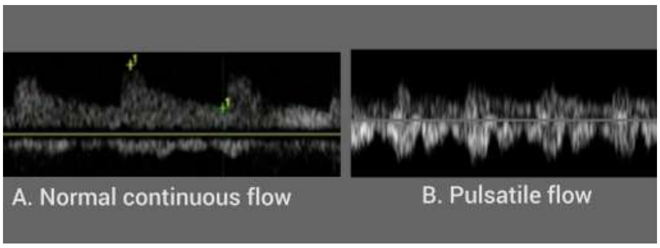

Figure 4. Renal flow pattern: Flow above the baseline represents arterial flow and below represents venous flow. With increasing congestion, the normal continuous venous flow **(A)** has changed to pulsatile flow **(B)**.

In the hepatic vein, as right atrial pressure (RAP) increases, systolic anterograde flow (S wave) starts to become smaller than the diastolic anterograde flow (D wave). With severe fluid congestion and further rise in RAP, the S wave develops reversal of flow (Figure 2). In the portal vein, normal continuous monophasic flow pattern starts to become progressively pulsatile with 30-49% pulsatility in mild and ≥50% pulsatility in severe congestion (Figure 3). In the interlobar renal veins, the continuous flow pattern changes to an interrupted flow pattern (Figure 4) and later to isolated diastolic flow pattern. The sequential changes in the flow pattern with increasing congestion is summarized in Figure 5. Final VExUS grade using the combination of these flow patterns is given in Table 1.

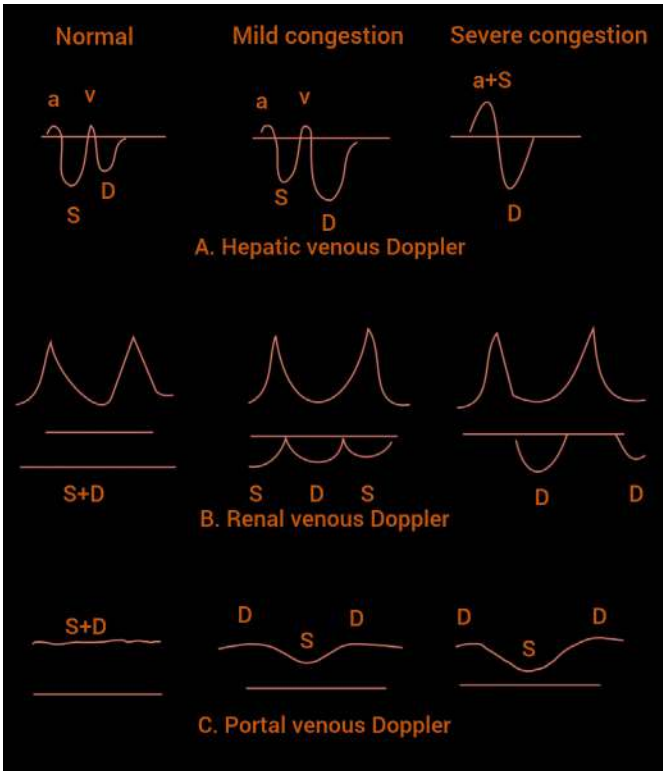

Figure 5. Schematic diagram showing changes in the venous flow patterns with increasing congestion. **(A)** In the hepatic veins, from the normal relation of S>D, mild congestion will decrease the size of S waves as compared to D waves. Severe congestion causes the reversal of S wave (Video supplement 1). **(B)** In the renal veins, the normal continuous venous flow in the renal veins gradually becomes pulsatile in mild congestion. With severe congestion, the systolic flow is lost and only diastolic wave remains. **(C)** The continuous flow of portal vein normally has a pulsatility index [(maximum velocity- minimum velocity)/maximum velocity] of <30%. In mild congestion, the pulsatility index increases to 30-49% while severe congestion increases it to ≥50%. (Video supplement 2)

Table 1. VExUS Grading

VExUS Grade	Findings
Grade 0	IVC <2 cm
Grade 1	IVC ≥2cm with normal/mild abnormalities
Grade 2	IVC ≥2cm with severe abnormality in at least one of the veins
Grade 3	IVC ≥2cm with severe abnormalities in multiple veins

Image acquisition

The assessment technique involves using a curvilinear or a phased array probe. A single probe positioned in the subcostal area can be used to acquire all the required images. Firstly, IVC diameter is measured. Then pulsed wave Doppler is used to obtain he venous flow waveforms of the hepatic vein, portal vein and interlobar renal vein. The degree of congestion is rated in each vein to quantify a final VExUS grade[17,18]. Alternatively, images can also be obtained from the mid-axillary position as shown in Figure 1. Table 2 summarizes the technique of attaining images.

Table 2. Summary of imaging technique of different veins[15,18,19]

Vein	Identification and image acquisition	Common errors	Remarks
IVC	• An anechoic structure entering the right atrium • Hepatic vein draining into it as it traverses the liver • Measured within 2cm caudal to the drainage into the right atrium.	• Cylinder tangent effect: measurement of anywhere other than the largest diameter of the cylinder (troubleshooting: measurement in both long and short axis) • Measurement of the intrathoracic part • Confusion with aorta or duodenum.	• Size may be affected by increased right atrial pressures as in pulmonary artery hypertension and tricuspid regurgitation. • Size may vary with body habitus
Hepatic	• Anechoic 3 structures (right, middle and left hepatic veins) converging into the IVC • Anechoic walls as compared to portal vein • Appear blue on Color Doppler • Doppler wave form is similar to a CVP wave form with S, V, D and A waves	• S and D waves may be wrongly interpreted. • Troubleshooting: simultaneous ECG for identification	• Is not reliable in pathological conditions involving the veins (eg. cirrhosis, Budd-Chiari malformation) and arrhythmias
Portal	• Hypoechoic structure with echogenic walls crossing over the IVC (vs. hepatic vein which drains into the IVC) • Main portal vein is red in Color Doppler but branches may be blue	• Angle of insonation to be kept as close to 0 degree as possible by angle correction (holds true for all Doppler studies) • Since VExUS is more qualitative than quantitative form of Doppler imaging, there is somewhat independence from the angle of insonation.	• May be unreliable in patients with portal hypertension • Doppler scale of 40cm/s for portal and hepatic veins assessment while 20cm/s for renal vein assessment is recommended
Renal	• Interlobar veins to be identified • Appears blue but mostly have accompanying red arterial flow	• Not reliable in chronic kidney disease.	• Technically the most difficult to obtain • Added difficulty with respiratory movements

Evidences in favor of VExUS

Preliminary works had already been done in the past which included isolated assessment of IVC, portal vein and the renal vein independently to determine venous congestion.[20–23] This was the first time that venous congestion could be systematically graded. This congestion was found to have clinical implications in that acute kidney injury (AKI) could be predicted with VExUS. They had reported good predictive values of VExUS for AKI in their validation cohort. They had found a specificity of 96%.[16] Since then, the medical community has been enthusiastic about it and no doubt it gained so much popularity in a short time given the myriad of possibilities associated with it in clinical practice. Early case reports and case series of successful management of patients with heart failure with aggressive fluid removal using this protocol were published.[24,25]

Bhardwaj et al published an original research to find the association between AKI and VExUS grades. In his prospective study of patients with cardiorenal syndrome, they found that improvement in AKI was significantly associated with improvement with the VExUS scores at day 2. In addition, improving VExUS scores were associated with decreasing fluid balance. The authors also had proposed a systematic approach to the evaluation and management of AKI based on VExUS scan. In this study, a modification was made in their scanning protocol such that they had omitted renal venous Doppler evaluation. Thus fluid overload that was detected could have thus been representative of systemic congestion. It only makes sense that the organ at question, kidneys with AKI for this specific objective, should not have been skipped.[26]

Another pilot study done among patients undergoing maintenance hemodialysis for chronic kidney disease also had to skip renal venous ultrasound since they couldn't record any flow in the intra-renal veins. This could be because of the altered, mostly decreased blood flow in the kidneys in end stage renal diseases. Furthermore, they had included lung and cardiac ultrasound to assess the effects of congestion on lung and cardiac function. The sample size was only 33, but their results add insight to the utility of VExUS. They found that VExUS scores improved after dialysis and so did lung ultrasound scores. But the cardiac functions did not improve in terms of left ventricular outflow tract- velocity time integral (LVOT-VTI) or tricuspid annular plane systolic excursion (TAPSE).[27]

We believe the work of Spiegel et al which was published in Critical Care in 2020 needs a special mention here. They had studied 114 patients using Doppler ultrasonography to predict major adverse kidney events (MAKE-30). They found that S/D reversal in hepatic Doppler was associated with an odds ratio of >4 for developing MAKE-30. Similarly, portal vein pulsatility index of >30% had an odds ratio of 2.28. The patient population in this study was from a general ICU and the findings suggest that congestion could have a significant contribution in development of AKI in critically ill patients based on the increased odds ratios. But the results are very difficult to interpret without further information on the sample regarding the cumulative fluid balance and markers of fluid congestion.[28]

In a recent study by Anastasiou et al published in JASE, the prevalence and clinical utility of VExUS score was explored in 358 hospitalized patients with acute heart failure and they found that VExUS score 3 was independently associated with markers of adverse RV remodeling and had incremental prognostic value[29,30]

Another recent prospective study from two centers in Spain was published in 2023. This study was done in 74 patients admitted with the diagnosis of acute heart failure with an admitting NT-proBNP level of above 500 pg/mL. This study aimed to look at clinical outcomes of death and readmissions in patients with acute heart failure and if VExUS could predict them. Results showed that VExUS grade of 3 was found to predict mortality with a sensitivity of 92% and specificity of 79%. The correlation of VExUS grade 3 with heart failure related mortality was found to be strong (r=0.55).[31]

Limitations of VExUS

Andrei et al in their prospective multicentric study in general ICUs tried to demonstrate the association of venous congestion by VExUS grading and AKI or 28-day mortality. Of note, although this cohort had an AKI prevalence of 47% at inclusion, of which only 6 patients (that is 4%) had evidence of severe grades of venous congestion. This study did not find any association of AKI or 28 day mortality with VExUS.[32] The results of these studies could mean that although VExUS may help in guiding fluid status in volume overload conditions, improvements in cardiac function or the renal functions may not be associated with it.

The findings from Islas-Rodriguez et al also corroborated these and add some points for debate against the clinical utility of VExUS. This study was done in patients with cardiorenal syndrome. The 70 patients of cardiorenal syndrome who were managed with diuretics based on VExUS compared with a control group of 70 patients, attained a decrease in NT-proBNP levels by >30% (defined as decongestion) twice as faster. These early decongested patients had initial increase in their creatinine levels compared with the control group. The authors attributed this to rapid decongestion with aggressive use of diuresis. However no difference in outcomes were noted which included recovery of renal function or 90 days mortality.[33]

Even the 2023 Spanish study by Torres-Arrese, which was done among heart failure patients had shown a predictive capacity for death only for VExUS of grade 3. No other grades predicted clinically significant outcomes.[31]

Verdict

From the above pertinent literature presented, a few inferences can be drawn. First, congestion or fluid overload is detected by VExUS. This is supported by the observational study from Longino et al. They found a strong correlation of 0.68 between right atrial pressure and VExUS in addition to an accuracy of 99% for detection of RAP of >12mm Hg.[34] However, the congestion may not be clinically relevant. Its effects are pronounced and clinically appreciable only in patients who are prone to develop significant adverse effects due to low reserve to tolerate volume overload like those with cardiac failure or CKD. Second, AKI in a general critical care patient is often caused by multiple factors. In these patients, venous congestion may have a significantly less contribution to the development of AKI as compared to those with decompensated heart failure.[35–37] Third, since fluid congestion is predicted by VExUS, it could theoretically be used to guide management for decongestion. Albeit, the patient selection for its optimal use is important. Only severe congestion seems to be reliably predicted hence it cannot be generalized for all patients for fluid de-resuscitation. If used in an appropriately selected cohort, VExUS could improve fluid management and possibly improve clinical outcomes including AKI and mortality.

At the time of writing of this review, 11 studies on VExUS were found to be registered in clinical trials registry. Results from these and many other studies may help to establish the definitive role of VExUS in clinical usage in near future.

CONCLUSION

VExUS has emerged as a promising bedside tool to detect venous congestion in critically ill patients. Embracing the inherent limitations, at present, we await the evidences to emerge in the future, that will guide us as how we can best utilize this technique to guide fluid management and to improve patient outcome.

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