Original article

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Venous excess ultrasound score in patients with sepsis and cardiorenal syndrome

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Abstract

***Background*: Fluid overload and venous congestion are deleterious in critically ill patients with cardiorenal syndrome. There is scarce literature on venous excess ultrasound score (VExUS) assessment characteristics in cardiorenal syndromes with hypoxia and sepsis.**

***Methods*: This study was an observational, prospective, single-center study that included patients with sepsis and heart failure who were transferred to the cardiac care unit (CCU). An intensivist in critical care ultrasound performed a serial ultrasound examination until acute kidney injury (AKI) was resolved or the patient was initiated on dialysis. VExUS, comprising the inferior vena cava, hepatic vein waveform, and portal vein pulsatility, was assessed. Patients with grade 0 and I were allowed to receive boluses of IV fluid on admission, according to the decision of the treating intensivist. Patients with grades II and III were observed only with fluid restriction and diuresis until renal replacement therapy if needed.**

***Results*: Of the 109 patients with suspected sepsis, 33 (30%) with renal and cardiac failure were selected. The median patient age was 73 (57-85) years, and 15 (45.5%) patients were men.**

The mean left ventricular ejection fraction was 46%, the tissue Doppler right ventricle S' was 8.8 cm, the right ventricular diameter was 3.9 cm, the mean pulmonary hypertension was 51 mmHg, and the mean creatinine was 377 µmol/l. There were 17 (51.5%) patients with acute kidney injury. Seventeen patients (51.5%) had VExUS grade III. The resolution of AKI was significantly correlated with improvement in VExUS grade (p-value 0.005). Renal replacement therapy was needed acutely for seven (24%) VExUS grade III patients. There was a significant association between changes in VExUS grade and fluid balance (p-value 0.006).

***Conclusion*: In populations with sepsis and cardiorenal disease, the combined grading of IVC, hepatic vein, and portal vein (VExUS) can aid in managing fluid and predict the need for renal replacement therapy.**

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Introduction

Treating patients with hypotension due to sepsis in critically ill conditions focuses on intravenous fluid resuscitation and vasopressors to maintain cardiac output with early administration of antibiotics. (1) Administering intravenous fluid boluses to patients with distributive shock is a common practice and a treatment strategy in the Sepsis Campaign 1-hour bundle. (2) Although volume responsiveness is a recommended step for the administration of fluid, there is a concern and growing evidence that fluid administration needs to be supported by strong evidence. (3)

Fluid administration leads to a further increase in pressures in both the right and left atrium in patients with cardiorenal syndrome from physiological aspects. The left atrial pressures are commonly assessed by imaging pulmonary edema clinically and radiologically and evaluating oxygen saturations and indicators, such as partial pressure of oxygen/fraction of inspired oxygen.
Identifying an increase in right atrial pressure and right ventricular function in the setting of sepsis is challenging. (4) Central venous monitors and pulmonary artery catheters can assess the right side of the heart. However, these methods are still invasive, with false results with positive pressure ventilation, and have not affected the outcomes. (5,6) Point-of-care ultrasonography (POCUS) is helpful in assessing the right atrial pressures and venous congestion because the venous excess or congestion leads to distinct patterns in Doppler venous return flow from the liver and kidneys. Doppler flow patterns of the inferior vena cava (IVC), left hepatic veins (HVs), portal veins (PVs), and intrarenal vessels (IRVs) are noninvasive and can identify early right-sided venous congestion. (7) Abnormal waveforms are associated with acute kidney injury after cardiac surgery. (8) In septic cardiorenal patients with hypotension, abnormal waveforms might help determine whether to avoid fluid administration and start vasopressors as initial management. In this prospective observational study, we present POCUS techniques to assess congestion and venous excess systems and describe their clinical implications and outcomes in the sepsis population with cardiorenal syndrome.

Materials and methods

This was a single-center observational prospective study. The study was conducted at the Critical Care Unit (CCU) at Ahmadi Hospital in Kuwait. Patients were recruited from January 2022 to July 2022. The Ahmadi Hospital Ethics Committee approved the study.
The inclusion criteria were patients older than 18 with suspicion of cardiorenal syndrome who needed a CCU with a provisional diagnosis of sepsis and were eligible for the study.
The exclusion criteria were patients with liver cirrhosis, portal hypertension, and IVC thrombus.
Patients enrolled in the study underwent echocardiography and ultrasound of the IVC, PV, and renal vessels with serial evaluation until sepsis resolved.
The primary objective was to assess the correlation between the serial VExUS and acute kidney injury (AKI) in patients with cardiorenal syndrome and sepsis. The secondary objective was to assess the correlation between the VExUS and fluid balance, right heart function, and clinical signs of fluid overload.

Data collection

Data, including demographic details, admission diagnosis, and kidney disease staging, were documented. Creatinine and blood urea nitrogen (BUN) measurements with urine output, daily fluid balance and sequential organ failure assessment (SOFA) score, mean arterial blood pressure, vasopressors, and inotropes use were recorded. Moreover, if needed, mechanical/noninvasive mechanical ventilation was provided. Echocardiographic recordings on admission were documented daily, including left ventricle ejection fraction, mean pulmonary artery pressure, and tricuspid annular plane systolic excursion (TAPSE). The daily VExUS was recorded. Kidney function was documented, and Acute Kidney Injury Network (AKIN) criteria staging was used and defined as an increase in serum creatinine of more than 0.3 mg/dl or a decrease in urine output within 48 hours. (9)

Ultrasound and Doppler assessment

For ultrasound examination, we used the SonoSite Edge II Ultrasound System. A 3-5 MHz curvilinear probe was used for the assessment of the hepatic vessel and renal vessel. The examiner was certified in point-of-care ultrasound.
The IVC was interrogated in long and short axes along the intrahepatic segment, and a visual average was used (**Figure 1**). (10) Respiratory variation was defined as a 20% or more change in surface area on the short axis.

- Grade 0: <5 mm with respiratory variation
- Grade I: 5-9 mm with respiratory variation
- Grade II: 10-20 mm with respiratory variation
- Grade III: >20 mm with respiratory variation
- Grade IV: >20 mm with minimal or no respiratory variation

The portal vein Doppler protocol has previously been described (11,12) and is presented in **Figure 1**. The peak (VMax) and nadir velocities (VMin) during the cardiac cycle were recorded. The pulsatility index (PI) was calculated ([PVmax - PVmin]/PVmax × 100%).
A Doppler study was performed on the left hepatic vein 2 cm from the origin of the inferior vena cava in the epigastric region. (9,10) The pattern of hepatic vein flow was recorded according to the classification.
The hepatic vein (HV) was interrogated by pulsed wave Doppler, and the identification and analysis of A, S, and D waves were as follows:

- Grade 0: normal S>D
- Grade I: S<D with antegrade S
- Grade II: S flat or inverted or biphasic trace

We have chosen the approach of the S wave.

Renal vessel Doppler assessment was performed with pulsed wave Doppler at the corticomedullary junction. The wave was obtained in all three segments during a respiratory pause after the end of expiration to obtain 2 to 3 consecutive cardiac cycles (**Figure 2**). The VMax and the VMin were recorded during the cardiac cycle. The pattern of intrarenal venous flow was recorded according to a classification described by Iida et al. (13)

Portal vein Doppler (PD)

Portal vein (PV) interrogation

- Grade 0: <0.3 pulsatility index
- Grade I: 0.3-0.49 pulsatility index
- Grade II: 0.5-1.0 pulsatility index

The pulsatility index was calculated as (Vmax - Vmin)/Vmax. The normal and abnormal waves of Doppler forms are shown in **Figure 3**. VExUS is graded according to: (10)

- Grade 0: IVC grade <III, HV grade 0, PV grade 0
- Grade I: IVC grade IV, but normal HV/PV pattern
- Grade II: IVC grade IV with mild flow pattern abnormalities in HV/PV
- Grade III: IVC grade IV with severe flow pattern abnormalities in HV/PV

Results

Of the 109 patients with suspected sepsis, 33 (30%) with renal and cardiac failure were selected. The median patient age was 73 (57-85) years, and 15 (45.5%) patients were men. The clinical characteristics of the patients with confirmed coronavirus disease 2019 (COVID-19) pneumonia are shown in **Table 1**.

The mean left ventricular ejection fraction was 46%, the tissue Doppler right ventricle S' was 8.8 cm, the right ventricular diameter was 3.9 cm, the mean pulmonary hypertension was 51 mmHg, and the mean creatinine was 377 µmol/l. There were 17 (51.5%) patients with AKI. Seventeen patients (51.5%) had VExUS grade III. The resolution of AKI was significantly correlated with improvement in VExUS grade (p-value 0.005). Renal replacement therapy was needed acutely for VExUS grade III in seven patients (24%) (**Table 2**). Fluid resuscitation followed by renal replacement therapy was required for one patient with grade I and three patients with grade 2 (**Tables 2 and 3**), and no renal replacement therapy was conducted in patients with grade 0. Patients with grade 0 and I received fluid for the resolution of AKI. There was a significant association between changes in VExUS grade and fluid balance (p-value 0.006).

Discussion

AKI refers to a rapid deterioration in kidney function resulting from increased urea and other nitrogenous compounds and the disturbance of the extracellular volume, metabolic status, and electrolyte regulation. AKI in the intensive care unit (ICU) increases morbidity and mortality by 40-65%. (14)

Sepsis, heart and circulatory failure, and nephrotoxic drugs are the main causes of AKI. To pursue normal volemic status and mean arterial pressure in sepsis, aggressive fluid therapy and vasopressors are part of sepsis management that can lead to venous congestion and might decrease organ perfusion. (14)

Solid evidence supports the major role of renal venous congestion as a primary driver of cardiorenal syndrome. Patients presenting with acute heart failure were analyzed through invasive hemodynamics, glomerular filtration rate, and renal blood flow with other invasive hemodynamics. In patients with acute heart failure, the lower ranges of renal blood flow (<400 ml/min/1.73 m^2) were the most determinant factor of kidney function. (15) However, although renal blood flow is the major factor affecting the glomerular filtration rate in patients with heart failure, backward failure and venous congestion are also related to the glomerular filtration rate. (15) Treatment to preserve the glomerular filtration rate should not only focus on the improvement of renal perfusion but also on decreasing venous congestion. (15)

The proposed pathophysiology behind worsening renal function is increased pressure in venous vessels followed by increased interstitial pressure and possible tubular obstruction. (16) This then increases renin-angiotensin system activation in sodium avidity. (16) The renal capsule plays a role in creating a tamponade effect and impairing renal perfusion pressure. (17)

Volume status assessment is challenging for patients with acute heart failure and sepsis because physical assessment findings correlate poorly with invasive venous congestion measures. (18) POCUS has been increasingly adapted in intensive care and emergency settings for evaluating volume status through Doppler venous blood flow evaluation. The Doppler venous flow evaluation that identifies venous congestion includes the inferior vena cava, hepatic and portal veins, and intrarenal veins. (14) The unique population of septic patients with cardiorenal syndrome is a challenge for physicians, as they need to determine whether to start intravenous fluid or vasopressors. According to our results, the population with grade 0 and grade I received fluid without worsening renal function, but only one in grade I needed renal replacement therapy. Renal replacement was required in 6% of patients with grade II and 18% of patients with grade III.

The limitation of the study was the small population size. In addition, the management needed to be protocolized and left to the treating physician and our local protocol on how to proceed with the initial management of patients with sepsis and cardiorenal syndrome.

Conclusion

In populations with sepsis and cardiorenal disease, the combined grading of IVC, hepatic vein, and portal vein (VExUS) might aid fluid management and predict the need for renal replacement therapy.

Table 1. Baseline characteristics of the study subjects

Variables	Description
Age (years)	73 (57-85)
Sex (male), n (%)	15 (45.5)
Diabetes mellitus, n (%)	30 (90)
Hypertension, n (%)	20 (66)
Acute kidney injury, n (%)	17 (51.5)
Renal replacement therapy, n (%)	8 (24)
VExUS, n (%)	
- 0	2 (6.1)
- 1.00	7 (21.2)
- 2.00	7 (21.2)
- 3.00	17 (51.5)
Respiratory status, n (%)	
- Pulmonary edema with ultrasound chest B lines	21 (64)
- Pleural effusion	26 (78)
- Artificial ventilation	22 (66)
Cardiac function (mean)	
- Left ventricle ejection fraction (%)	46.4±14.6
- PASP (mmHg)	52±11.2
- Tissue Doppler right ventricle S' (mm)	8±2.1
- TAPSE (mm)	14±3.2
- Right ventricle diameter (cm)	3.9±0.7

Legend: VExUS=venous excess ultrasound score; PASP=pulmonary artery systolic pressure; TAPSE=tricuspid annular plane systolic excursion.
Continuous variables are expressed as the mean and standard deviation. Categorical variables are expressed as frequencies and percentages.

Table 2. VExUS and intervention crosstabulation

	Intervention (number of patients)					Total
	Fluid	Fluid followed by dialysis	Furosemide	Furosemide followed by dialysis	Dialysis	
Score						
- 0	2	0	0	0	0	2
- 1	6	1	0	0	0	7
- 2	2	0	2	2	1	7
- 3	1	1	9	5	1	17
Total	11	2	11	7	2	33

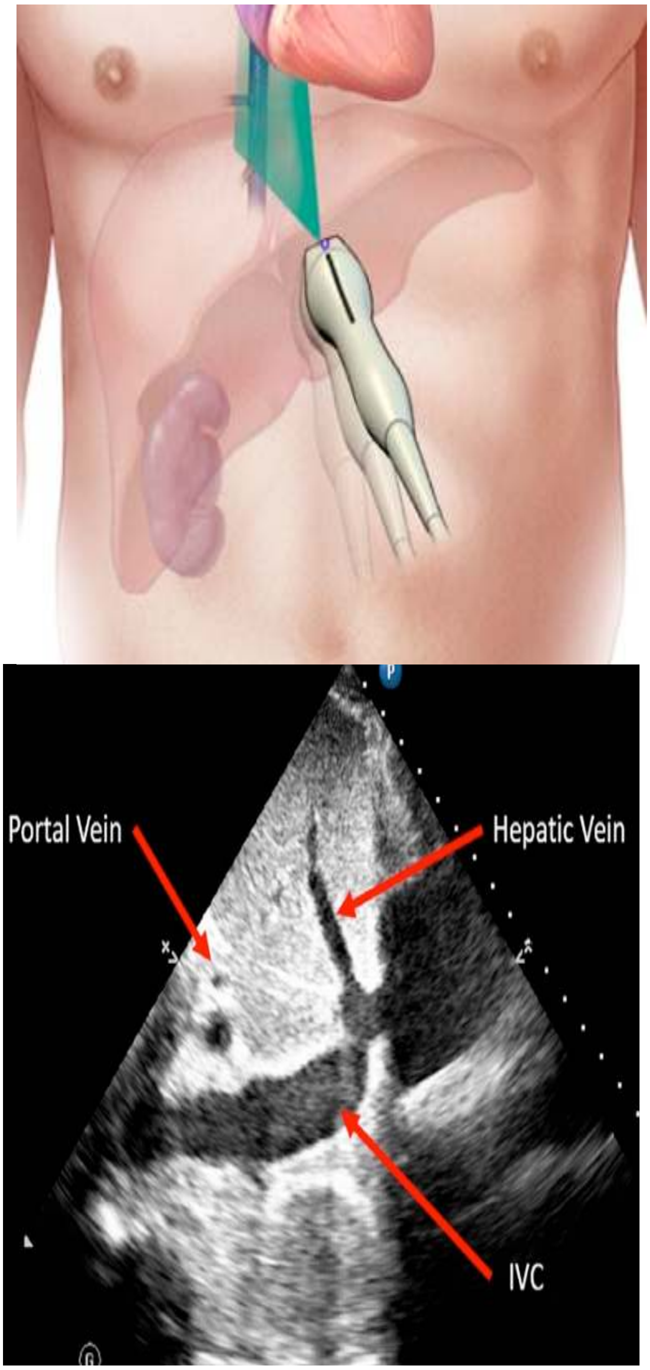
Legend: VExUS=venous excess ultrasound score.

Table 3. Association of VExUS with treatment

Treatment	VExUS			p-value
	Improving	No change	Worsening	
IV fluid, n (%)				0.55
- Yes	13 (39)	0	2 (6)	
- No	20 (60)	4 (12)	2 (6)	
Dialysis, n (%)				0.1
- Yes	11 (33)	0	0	
- No	22 (66)	0	4 (12)	
Diuretics, n (%)				0.8
- Yes	18 (55)	4 (12)	3 (9)	
- No	15 (45)	2 (6)	2 (6)	

Legend: VExUS=venous excess ultrasound score; IV=intra venous.
The statistical test used was the Fischer exact test. All patients received inotropes.

Figure 1. Acquiring hepatic and portal vein images by placing an ultrasound probe at the epigastrium



Legend: IVC=inferior vena cava.

Figure 2. Obtaining kidney Doppler waveforms with ultrasound probe placement

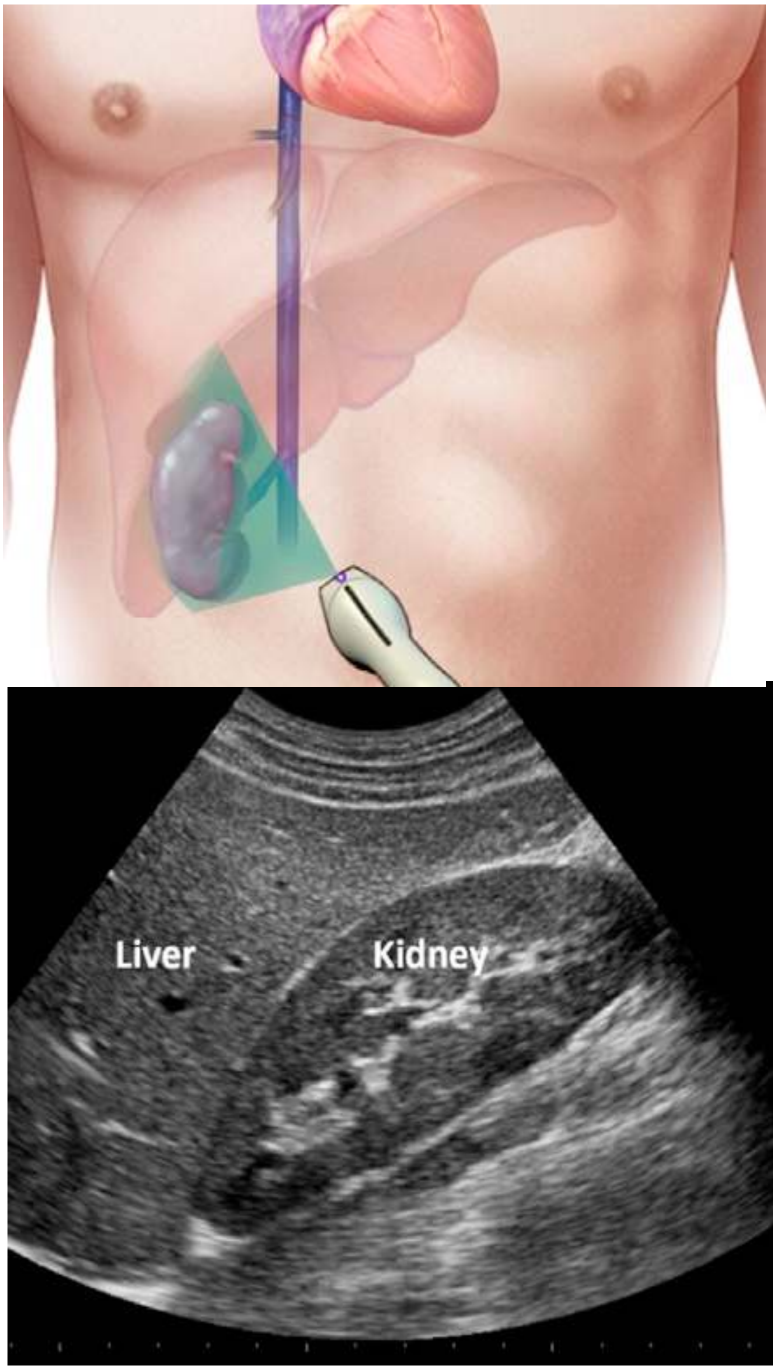
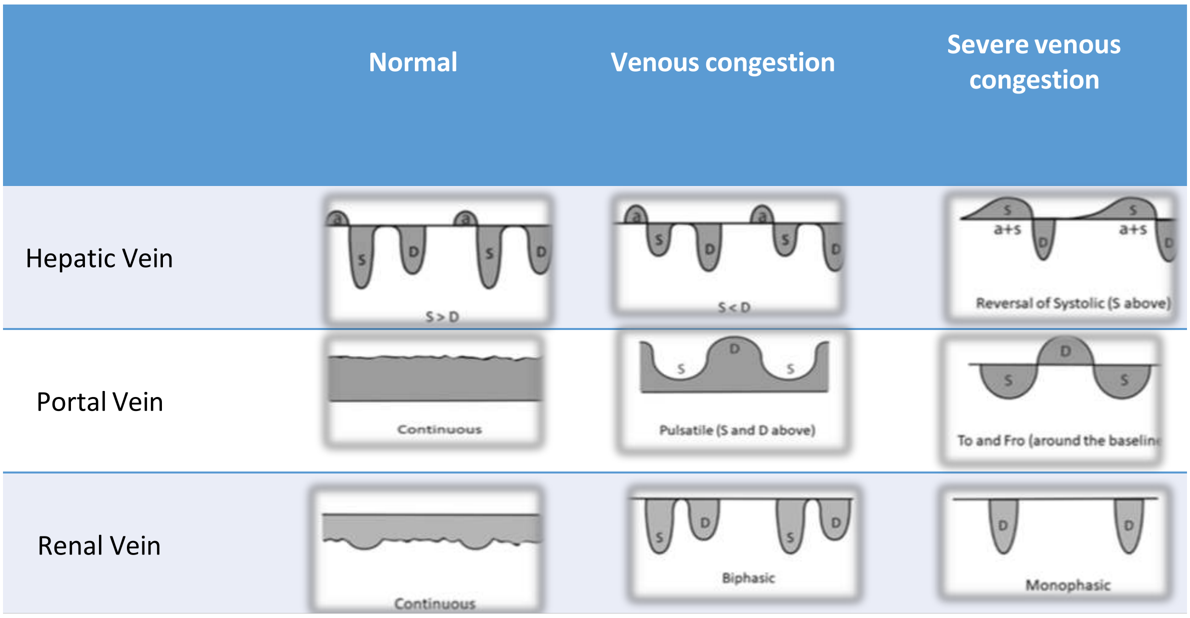


Figure 3. Changes in venous Doppler waveforms



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