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Peer Reviewer of *World Journal of Critical Care Medicine*, Deng-Gao Peng, MD, Associate Chief Physician, Associate Professor, Department of Emergency Medicine, The Third People's Hospital of Shenzhen, Shenzhen 518112, Guangdong Province, China. 1370211295@qq.com

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Point-of-care ultrasound in diagnosis and management of congestive nephropathy

Michael Turk, Thomas Robertson, Abhilash Koratala

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Michael Turk, Thomas Robertson, Department of Medicine, Allegheny Health Network, Pittsburgh, PA 15222, United States

Abhilash Koratala, Division of Nephrology, Medical College of Wisconsin, Milwaukee, WI 53226, United States

Corresponding author: Abhilash Koratala, MD, Associate Professor, Division of Nephrology, Medical College of Wisconsin, 8701 W Watertown Plank Rd, Milwaukee, WI 53226, United States. akoratala@mcw.edu

Abstract

Congestive nephropathy is kidney dysfunction caused by the impact of elevated venous pressures on renal hemodynamics. As a part of cardiorenal syndrome, the diagnosis is usually made based on history and physical examination, with findings such as jugular venous distension, a third heart sound, and vital signs as supporting findings. More recently, however, these once though objective measures have come under scrutiny for their accuracy. At the same time, bedside ultrasound has increased in popularity and is routinely being used by clinicians to take some of the guess work out of making the diagnosis of volume overload and venous congestion. In this mini-review, we will discuss some of the traditional methods used to measure venous congestion, describe the role of point-of-care ultrasound and how it can ameliorate a clinician's evaluation, and offer a description of venous excess ultrasound score, a relatively novel scoring technique used to objectively quantify congestion. While there is a paucity of published large scale clinical trials evaluating the potential benefit of ultrasonography in venous congestion compared to gold standard invasive measurements, more study is underway to solidify the role of this objective measure in daily clinical practice.

Key Words: Ultrasound; Point-of-care ultrasonography; Doppler; Venous excess ultrasound score; Congestion; Hemodynamics; Heart failure; Nephrology

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Core Tip: Congestive nephropathy denotes kidney dysfunction in fluid overload states as a result of venous congestion. Conventional methods to assess congestion at the bedside lack sensitivity and diagnostic accuracy. Point-of-care ultrasound is emerging as an enhancement to physical examination for objective assessment of congestion and guide therapy. Future research should focus on its impact on practical outcomes such as freedom from congestive symptoms, quality of life, and recurrent hospitalizations.

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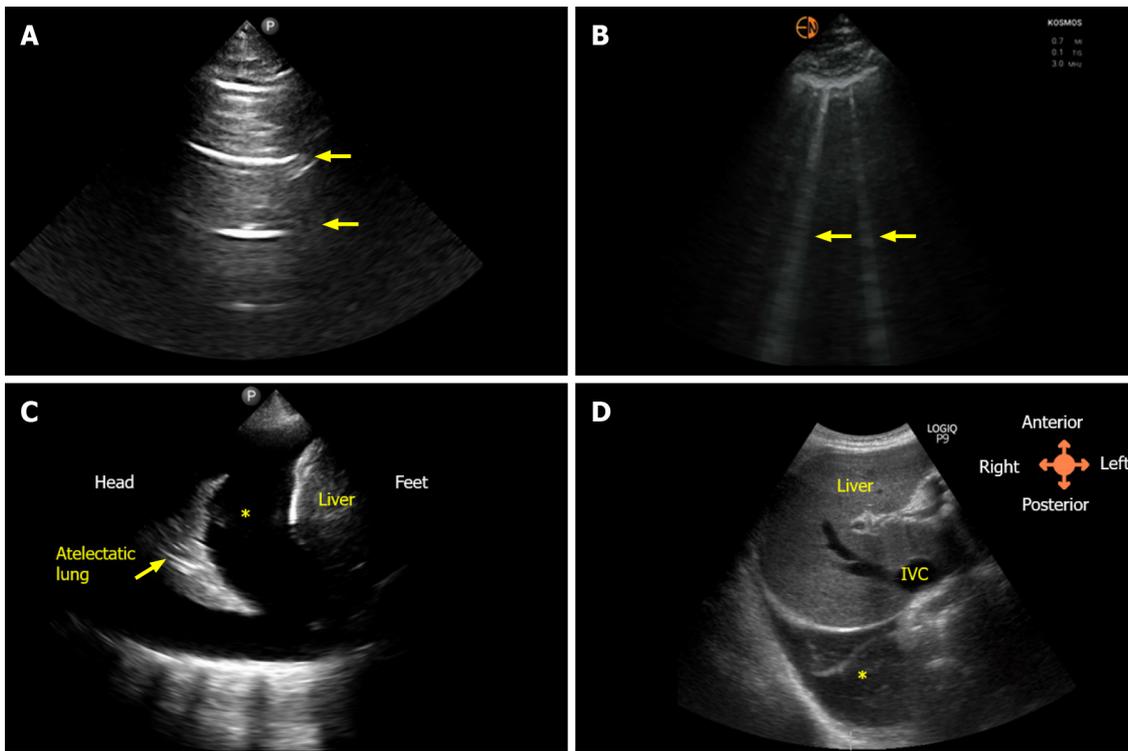
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INTRODUCTION

It is well known that unresolved congestion is associated with adverse outcomes in patients with heart failure, increasing the risk of re-hospitalization and death[1,2]. In 2017 alone, heart failure admissions occurred at a rate of approximately 5 per 1000 United States adults with about a quarter of those patients experiencing readmissions, which highlights the magnitude of this problem[3]. The deleterious effects of fluid overload are now being recognized outside of heart failure, with multiple studies showing a positive fluid balance being associated with increased mortality[4,5]. Though seemingly straightforward, evaluation and management of congestion require a thorough understanding of the pathophysiology and hemodynamic principles. Multiple bedside diagnostic methods and tools exist for clinicians to assess congestion including signs and symptoms, physical examination, laboratory data, and radiography, but these all have limitations. On the other hand, timely diagnosis is vital as faster rates of decongestion are associated with a reduced risk of mortality and hospitalization[6]. In addition, end-organ effects of fluid overload are being increasingly recognized, which brings us to the topic of congestive nephropathy. Congestive nephropathy is defined as renal dysfunction that occurs due to venous congestion leading to impaired organ perfusion[7]. While this term was recently coined[8], several studies have previously shown that elevated central venous pressure (CVP) is associated with worsening renal function despite preserved cardiac index[9]. This does have pathophysiologic basis as the renal perfusion pressure is the difference between mean arterial pressure and CVP; if the CVP is elevated, the perfusion pressure drops, impairing renal blood flow. In addition, activation of the renin-angiotensin-aldosterone system and consequent sodium and water retention, interstitial edema, endothelial dysfunction, and increased intra-abdominal pressure all contribute to increased pressure within the encapsulated kidney (*renal tamponade*), ultimately leading to organ dysfunction. Further, renal dysfunction can exacerbate the existing fluid overload, resulting in a vicious cycle. In this article, we will provide a kidney-centric overview of the bedside tools available to assess congestion, focusing on advances in point-of-care ultrasonography (POCUS).

CONVENTIONAL METHODS TO ASSESS CONGESTION

The bedside assessment of a patient's intravascular volume is challenging. Traditionally, this assessment involves taking a thorough history and performing cardiopulmonary physical examination. A patient's given history can often be misleading or not reflective of their hemodynamic physiology. Physical examination, including assessment of jugular venous pressure, lower extremity edema, presence of an 'S3', and auscultation of the lungs for evidence of pulmonary edema, has traditionally been a common way for clinicians to assess intravascular volume status at the bedside. This is wrought with subjectivity and inaccuracies, and has almost no correlation with right heart catheterization, which is the invasive gold-standard assessment[10,11]. Similarly, chest X-ray remains a common modality to diagnose pulmonary congestion resulting from heart failure or other etiologies, despite having considerable diagnostic limitations including high false negative rate[12]. The degree of venous congestion beyond that of the jugular vein, specifically the alteration of blood flow in the hepatic, portal, and renal veins leading to congestive organ injury, cannot be assessed by physical examination or an X-ray. All these traditional approaches have significant limitations and cannot reliably detect hemodynamic congestion. Diagnosis of congestive nephropathy is challenging as no gold standard exists. Traditionally, the diagnosis of congestive nephropathy has been based on clinician gestalt after a trial-and-error period without any objective way to evaluate renal hemodynamics. POCUS using vascular Doppler analysis is emerging as a promising modality to assess for venous congestion along the continuum from the heart to the kidneys.



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Figure 1 Lung ultrasound images. A: Normal lung showing horizontal artifacts, *i.e.*, A-lines (arrows); B: Vertical artifacts (arrows) known as B-lines indicating interlobular septal thickening, typically seen in congestion; C: Pleural effusion (asterisk) as seen on lateral scan; D: Right pleural effusion (asterisk) as seen from subxiphoid scanning window. IVC: Inferior vena cava.

POINT-OF-CARE ULTRASOUND

POCUS is a limited ultrasound examination performed at the bedside and interpreted by the treating physician. It is used to answer focused clinical questions, and is integrated with the patient's history, physical examination, and other available data to narrow the differential diagnosis and inform management. POCUS is becoming more accessible to clinicians owing to the recent advances in ultrasound technology and availability of the low-cost, highly portable equipment. Compared to conventional examination, POCUS offers substantially higher diagnostic accuracy[13]. In the context of heart failure and congestion, POCUS not only aids in the diagnosis, but also guides decongestive therapy with potential implications for patient outcomes. In this section, we will outline the various components of sonographic evaluation of a patient with suspected fluid overload/venous congestion.

Lung ultrasound

Lung ultrasound (LUS) has shown superiority over chest X-ray for nearly all clinical indications[14] and can detect extravascular edema prior to the onset of clinical symptoms. From diagnosing pneumonia[15] to identifying pulmonary edema[16], LUS has proven to be more accurate, and in some settings, more accessible. In a meta-analysis of six studies and more than 1800 patients, LUS had better sensitivity (88% *vs* 73%) when compared to chest X-ray for the diagnosis of cardiogenic pulmonary edema[17]. LUS findings are shown to have prognostic significance in various clinical scenarios including heart failure and end-stage renal disease[18,19]. With respect to guiding therapy, in the recent LUST trial[20], LUS-guided ultrafiltration strategy was associated with a reduction in the recurrence of decompensated heart failure and other cardiovascular events in hemodialysis patients. Similarly, in heart failure patients, LUS-guided management has shown to reduce acute decompensation events and urgent care visits[21, 22]. LUS is an important diagnostic, prognostic, and management tool in the assessment of clinical or subclinical fluid overload. While it does not directly diagnose congestive nephropathy, it influences the treatment by establishing fluid tolerance *vs* intolerance. For example, in a patient with acute kidney injury, presence of extravascular lung water on LUS would sway away the clinician from administering empiric intravenous fluids, thus avoiding iatrogenic fluid overload. Figure 1 illustrates normal and abnormal LUS findings seen in fluid overload.

Focused cardiac ultrasound

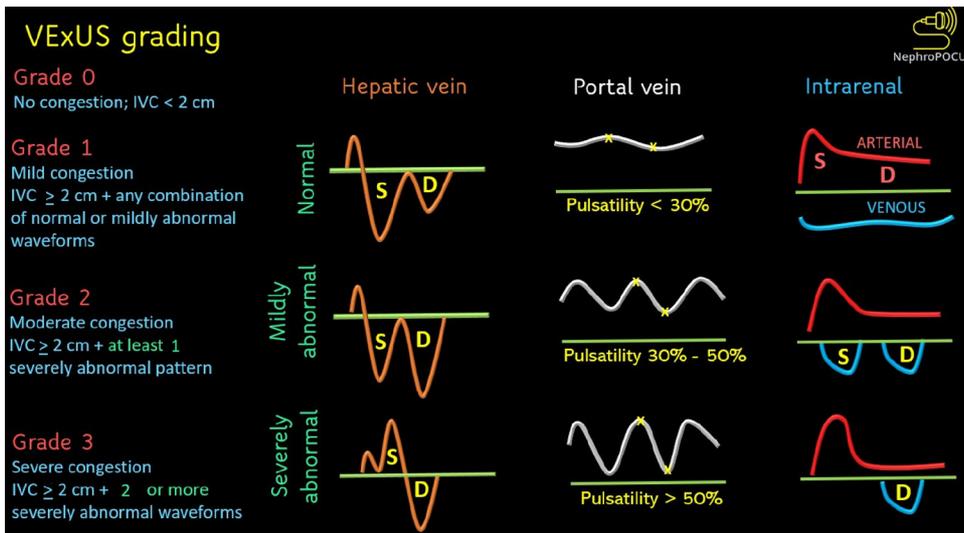
Focused cardiac ultrasound (FoCUS) is a POCUS examination of the heart and inferior vena cava (IVC). Essentially, it is a limited and problem-focused evaluation performed by any clinician trained in POCUS

analogous to auscultation and not restricted to cardiologists. On the contrary, consultative echocardiography involves a comprehensive evaluation documenting a predefined set of parameters and measurements. FoCUS has a much higher diagnostic accuracy than conventional physical examination [23] and quickly provides vital information related to cardiac structure and function. Pathologies requiring immediate attention such as pericardial effusion, impaired contractility, gross chamber enlargement, and valvular anomalies can be diagnosed at the bedside and promptly addressed. In addition, IVC ultrasound allows non-invasive estimation of the CVP/right atrial pressure (RAP). As mentioned, elevated CVP is the starting point of venous congestion and is associated with impaired renal function as well as mortality[24]. In spontaneously breathing patients, current guidelines recommend stratifying RAP as follows. RAP is estimated to be 3 mmHg (0-5 mmHg) if the maximal anteroposterior diameter of the IVC is < 2.1 cm with > 50% collapse during a sniff. If the IVC is > 2.1 cm and collapses < 50%, RAP is documented as 15 mmHg (10-20 mmHg). An intermediate value of 8 mmHg (5-10 mmHg) is assigned where IVC parameters do not fit this paradigm. Elevated RAP estimated by IVC ultrasound is associated with hospital readmissions and mortality[25,26]. Despite its simplicity and apparent clinical utility, isolated IVC ultrasound has several pitfalls. First, estimation of RAP by IVC ultrasound is not accurate in mechanically ventilated patients. Even in those who are spontaneously breathing, strength of 'sniff' considerably varies among patients, leading to false impressions. Moreover, trained athletes and active young adults can have a chronically dilated IVC without elevated RAP whereas patients with elevated intra-abdominal pressure may have a collapsed IVC despite high RAP. In addition, IVC POCUS in long axis is subject to cylinder effect, which means when the ultrasound beam bisects the three-dimensional vessel (presumably a cylinder) in the periphery rather than the center, a falsely low diameter will be recorded. This leads to incorrect interpretation during follow-up studies, particularly when different operators are performing the study. Therefore, the IVC must be examined in both long and short axis views, where feasible[27,28]. Also, in conditions such as cirrhosis, IVC size/shape may be altered by the local structural changes, making it unreliable to predict RAP. Furthermore, it must be noted that isolated IVC POCUS does not provide real-time information on end-organ congestion, which in turn depends on both RAP and venous compliance. In other words, a plethoric IVC increases the probability of congestive organ injury but cannot objectively demonstrate it.

Venous excess ultrasound score: Venous excess ultrasound score (VExUS) stands for venous excess Doppler ultrasound. It involves Doppler evaluation of the abdominal veins (hepatic, portal, and intrarenal) to assess the flow pattern and thereby detect venous congestion that effects organ perfusion. While the Doppler patterns in these individual veins have been studied long before[29-32], the concept of VExUS is fairly new and first documented by Beaubien-Souligny *et al*[33] in 2020. In their study including 145 cardiac surgery patients, the investigators found that severe flow abnormalities in at least two of the three above-mentioned veins together with a dilated IVC (≥ 2 cm) predicts the risk of acute kidney injury (*i.e.*, congestive nephropathy) with a hazard ratio of 3.69, outperforming isolated CVP measurement. Therefore, adding VExUS to IVC ultrasound improves the risk prediction of organ dysfunction. Based on the degree of flow alteration in individual veins, a scoring system was proposed to quantify systemic venous congestion, which is illustrated in Figure 2. In addition to diagnosing congestion, VExUS allows objective monitoring of congestion while the patient is receiving decongestive therapy as these waveforms are dynamic[34]. For example, Argaiz *et al*[35] have demonstrated that improvement in portal vein pulsatility coincides with improvement in renal function in patients with heart failure receiving diuretic therapy. In addition, several case reports exist demonstrating this phenomenon in multiple veins[36-41]. While there have not been published randomized clinical trials to date, outcome data for VExUS is emerging in the literature. For example, a high VExUS score, indicating severe hemodynamic congestion, has been shown to be associated with development of acute kidney injury in various clinical settings[34,42]. Specifically in heart failure patients, altered renal vein flow has been shown to confer worse outcomes[32,43,44]. In isolation, all these waveforms have limitations, which we have discussed in detail previously and is beyond the scope of this manuscript[45,46]. Of particular note, VExUS cannot distinguish between volume and pressure overload. For instance, a patient with precapillary pulmonary hypertension can have the same Doppler stigmata of congestion as a patient with iatrogenic fluid overload. It is up to the clinician to interpret the findings in the appropriate clinical context and in conjunction with other sonographic parameters (*e.g.*, Doppler echocardiography). Having said that, congestion from any cause (pressure or volume) still leads to congestive nephropathy. In a large cohort of patients with pulmonary hypertension, Husain-Syed *et al* [47] showed that intrarenal venous congestion correlates with renal dysfunction as well as mortality/morbidity end point, which exemplifies this concept.

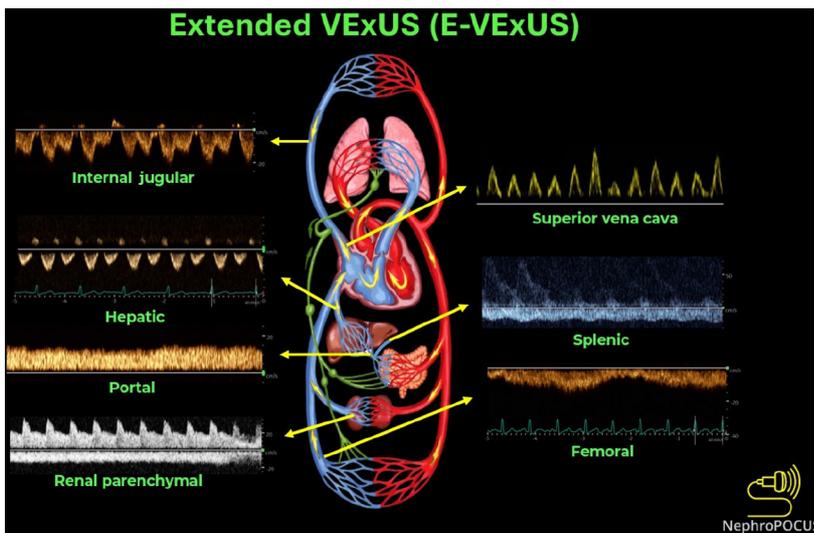
Extended VExUS

The term extended venous excess ultrasound score (E-VExUS) or extended VExUS has been proposed to include Doppler interrogation of additional veins such as the internal jugular, superior vena cava, splenic, and femoral veins in situations where the primary veins (*e.g.*, hepatic, portal in cirrhosis, and intrarenal in advanced kidney disease) suffer from limitations[28,48]. This also includes estimation of RAP by greyscale POCUS of the internal jugular vein where IVC is not accessible or unreliable. Doppler



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Figure 2 Venous excess ultrasound grading. When the diameter of the inferior vena cava is > 2 cm, three grades of congestion are defined based on the severity of abnormalities on hepatic, portal, and renal parenchymal venous Doppler. Hepatic vein Doppler is considered mildly abnormal when the systolic (S) wave is smaller than the diastolic (D) wave, but still below the baseline; it is considered severely abnormal when the S-wave is reversed. Portal vein Doppler is considered mildly abnormal when the pulsatility is 30% to 50%, and severely abnormal when it is ≥ 50%. Asterisks represent points of pulsatility measurement. Renal parenchymal vein Doppler is mildly abnormal when it is pulsatile with distinct S and D components, and severely abnormal when it is monophasic with D-only pattern. Figure adapted from NephroPOCUS.com with permission.



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Figure 3 Doppler components of extended venous excess ultrasound score examination. Figure adapted from NephroPOCUS.com with permission.

components of E-VExUS are illustrated in **Figure 3**. Similar to the components of original VExUS, these veins have also been studied individually and shown to be useful to gauge the effects of elevated RAP [49-53]. Of late, femoral vein Doppler is gaining attention due to relative ease of image acquisition. In a recent study including 57 patients undergoing right heart catheterization, femoral vein flow alteration graded by stasis index showed excellent diagnostic performance to detect elevated RAP (specificity: 92.3% [80.0-99.3]; diagnostic accuracy: 90.4 [77.4-97.3]; positive likelihood ratio: 12.5 [3.01-51.97])[54]. However, caution must be exercised in 'excluding' elevated RAP/venous congestion based on the femoral vein alone as earlier studies showed a relatively low sensitivity[55]. This VExUS expansion is still in its early stages of adoption, so there is need for more data to establish its clinical utility in routine practice. **Figure 4** is the sonographic representation of chain of venous congestion from the right heart to femoral vein. **Table 1** summarizes the key sonographic findings and limitations of each application in the context of congestive nephropathy.

Table 1 Key sonographic findings and limitations of each application in the evaluation of congestive nephropathy

Sonographic application	Possible findings in the context of congestive nephropathy	Limitations
Lung ultrasound	Elevated extravascular lung water (B-lines) and pleural effusion	B-lines are non-specific and can be seen in non-cardiogenic pulmonary edema, lung fibrosis, contusion, and alveolar hemorrhage
Focused cardiac ultrasound (basic)	LV systolic dysfunction (qualitative and M-mode); RV systolic dysfunction (qualitative and M-mode); Pericardial effusion; Gross chamber enlargement (<i>e.g.</i> , RV dilation leading to interventricular septal flattening); Gross valvular dysfunction (<i>e.g.</i> , tricuspid regurgitation on color Doppler); Elevated right atrial pressure (plethoric IVC)	Lack of spectral Doppler provides limited information. Qualitative assessment relies on operator experience. IVC cannot reliably estimate RAP in mechanically ventilated patients. IVC can be small in intra-abdominal hypertension despite elevated RAP. IVC can be dilated without elevated RAP in trained athletes
Focused cardiac ultrasound (advanced)	Reduced stroke volume assessed by LV outflow tract velocity time integral. Elevated LV filling pressures assessed by mitral inflow Doppler and mitral annular tissue Doppler. Elevated pulmonary artery pressures/right ventricular systolic pressure assessed by continuous wave Doppler through the RV outflow tract and tricuspid valve. Elevated right atrial pressure assessed by tricuspid inflow and tissue Doppler	Requires higher operator skill level and training than basic cardiac ultrasound. Suboptimal views/Doppler angle limit the accuracy of measurements obtained. Some of the parameters lack validation in critical illness
Hepatic vein Doppler	Reduced amplitude or reversal of the systolic wave (Normally, systolic wave is larger than the diastolic wave)	Prone to erroneous interpretation without EKG. Cannot differentiate pressure and volume overload (applies to all components of VExUS and E-VExUS). Influenced by factors other than RAP (<i>e.g.</i> , atrial fibrillation, RV systolic excursion). Diminished pulsatility in cirrhosis; may not accurately reflect the degree of congestion
Portal vein Doppler	Increased pulsatility (normal waveform is near-continuous)	Pulsatile portal vein can be seen in cirrhosis and healthy, young individuals without an elevated RAP. Can appear falsely normal despite elevated RAP in patients with portal hypertension
Intra-renal venous Doppler	Increased pulsatility, systolic wave reversal (normal waveform is near-continuous)	Most technically challenging of the three components of VExUS. Sampling a larger vessel such as the main renal vein instead of interlobar vein leads to mistaken interpretation
E-VExUS	IJ vein: Reduced amplitude or reversal of the systolic wave (normally, systolic wave is larger than the diastolic wave); Splenic vein: Increased pulsatility (normal waveform is near-continuous); SVC: Reduced amplitude or reversal of the systolic wave (normally, systolic wave is larger than the diastolic wave); Femoral: Increased pulsatility and elevated velocity of the retrograde component (normal waveform is near-continuous)	Not validated as a combination score though individual components are studied. EKG is required when there is no simultaneous arterial trace to delineate cardiac cycles. IJ vein: Susceptible to probe pressure due to its relatively superficial location. Splenic vein: Similar limitations as portal vein. SVC: Technically challenging to access <i>via</i> transthoracic windows. Femoral: Relatively less sensitive to detect elevated RAP. Severe intra-abdominal hypertension may influence the waveform

LV: Left ventricle; RV: Right ventricle; M-mode: Motion mode; IVC: Inferior vena cava; EKG: Electrocardiogram; VExUS: Venous excess ultrasound; RAP: Right atrial pressure; RV: Right ventricle; E-VExUS: Extended venous excess ultrasound; IJ: Internal jugular; SVC: Superior vena cava.

KNOWLEDGE GAPS AND FUTURE DIRECTIONS

While POCUS has gained a lot of traction over the last several years, it is sometimes met with a degree of skepticism. Detractors are quick to point out that a significant mortality benefit with use of POCUS has not been shown. For example, the SHoC-ED trial randomized almost 300 patients with undifferentiated shock into a POCUS plus standard of care *vs* standard of care without ultrasonography to help diagnose the etiology of shock and help manage the condition. This showed no mortality benefit, no decrease in length of stay, decrease in intravenous fluid use, or decrease in rates of computed tomography scanning[55]. Conversely, the supporters of POCUS are quick to point out that achieving a mortality benefit in an intervention that is not therapeutic is a mountain that may prove too high to climb; in essence, unfair to expect of a diagnostic modality. In most cases, POCUS and VExUS scoring help quantify congestion in an objective manner and allow clinicians to rely much less on other unreliably recorded measures such as daily weights and intake-output documentation. Several randomized controlled trials incorporating VExUS are currently underway to determine its efficacy not only in the diagnosis but also in guiding the management such as for dosing diuretics. The use of elements of the extended VExUS examination needs to be further validated in population wide studies before becoming mainstays of the evaluation. Due to the medical community's long-standing affinity for objective scoring systems, VExUS will without a doubt become more commonplace. However, there will continue to be significant demand from clinicians for a show of mortality reduction before the practice becomes widely adopted. In the meantime, it is important to give weight to other outcomes such as time to diagnosis, readmission rates, recovery of renal function, symptom burden from heart failure and congestion, and quality of life in the judgment of this emerging technique. On the other hand, we do acknowledge that POCUS training remains an unmet need currently. Applications such as Doppler echocardiography, VExUS, and E-VExUS require solid technical skills that can only be garnered by longitudinal training. Especially in nephrology, there are a very few fellowship programs that offer

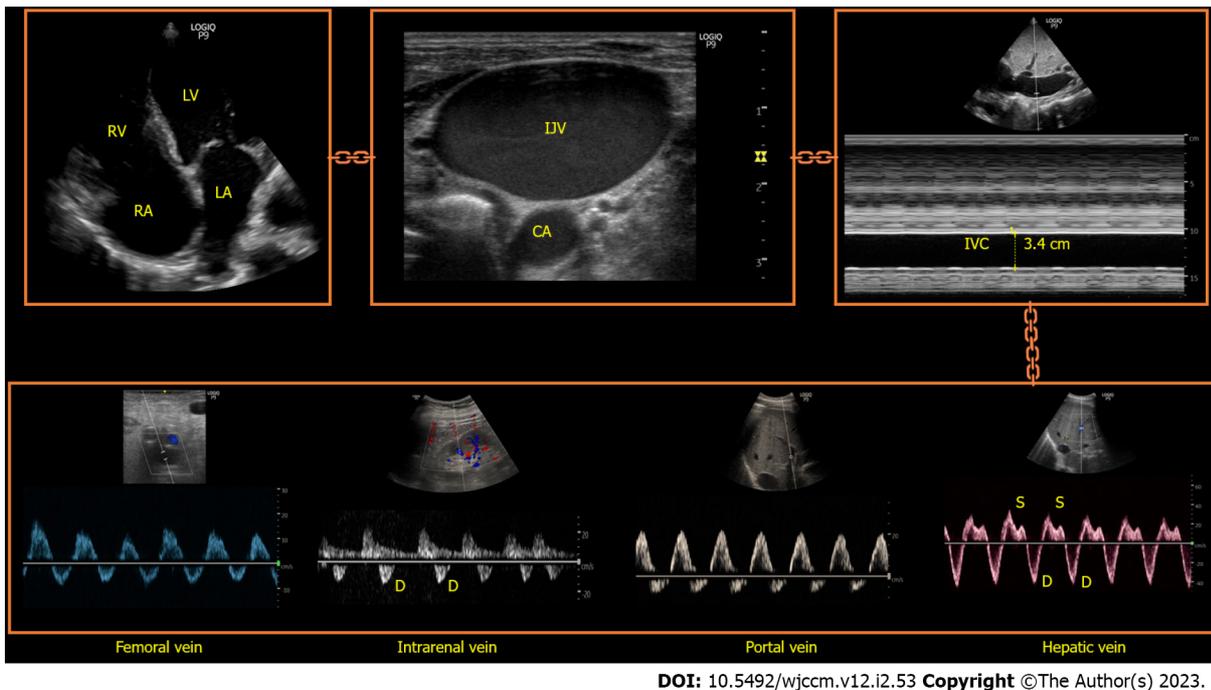


Figure 4 The chain of venous congestion: Apical view of the heart is shown in the upper left corner where bulging of the interatrial septum into the left atrium can be noted suggestive of high right atrial pressure. Next image shows significantly dilated internal jugular vein followed by a plethoric inferior vena cava. Lower panel represents the commonly assessed Doppler parameters to assess systemic venous congestion, all of which are severely abnormal. Please see Figure 3 for the normal appearance of these waveforms and Figure 2 for venous excess ultrasound score grading. RA: Right atrium; RV: Right ventricle; LA: Left atrium; LV: Left ventricle; CA: Carotid artery; S: Systolic wave; D: Diastolic wave.

training in comprehensive hemodynamic assessment at this time[56,57]. This is ironic given that most of the consults in a typical nephrology practice revolve around managing fluid disorders. While the situation is slightly better in critical care medicine, guideline-mandated training requirements remain vague. As such, professional organizations must step up and establish robust POCUS certification and competency assessment standards. Otherwise, performance of advanced sonographic applications by inadequately trained physicians may potentially result in patient harm.

CONCLUSION

It is well known that hemodynamic congestion has adverse effects on multi-organ function and is associated with adverse clinical outcomes. Ultrasonographic techniques have long been used to quantify venous congestion and have been validated extensively in the medical literature. The combination of Doppler findings from several organ systems into an objective evaluation is a process that has been undergoing significant study in recent years. While VExUS has its limitations, it has promise as a dependable tool in the management of congestive nephropathy and is superior to any other bedside noninvasive assessment. As with other diagnostic tools, it is critical that clinicians analyze their findings as just one part of the larger clinical puzzle in conjunction with other objective data points. In the correct clinical context, using VExUS findings to apply individualized changes to care plans may ultimately help deliver more accurate care to patients with suspected congestive nephropathy.

FOOTNOTES

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Country/Territory of origin: United States

ORCID number: Abhilash Koratala 0000-0001-5801-3574.

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