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Abstract:

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Point of care Ultrasound in Cirrhosis-associated Acute Kidney Injury: beyond Inferior Vena Cava

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Acute kidney injury (AKI) in patients with cirrhosis poses a diagnostic challenge owing to a multitude of etiologic possibilities with overlapping presentations. The shortcomings of conventional physical examination are well-recognized, especially in clinical scenarios associated with derangements in fluid status. Even laboratory data are insufficient to discern certain etiologies. For example, low urine sodium can be observed in volume depletion, congestive nephropathy, iodinated contrast exposure, intra-abdominal hypertension (IAH), and hepatorenal syndrome (HRS) as well as some cases of tubular injury. While careful history taking helps to some extent, physicians often rely on their clinical judgement to guide management in these cases, which is influenced by experience, pattern recognition skills and internal biases. Further, current blanket recommendation of plasma volume expansion with albumin infusion (1 g/kg body weight per day) in patients with cirrhosis presenting with AKI adds to the problem, potentially leading to iatrogenic fluid overload. In a randomized controlled trial including patients with decompensated cirrhosis, repeated daily infusion of intravenous albumin with a targeted serum level did not improve kidney function compared to standard care; however, it did increase the incidence of pulmonary edema/fluid overload [1]. As such, there is an obvious need to augment our bedside clinical assessment using novel diagnostic tools, preferably non-invasive ones. Over the past several years, point of care ultrasonography (POCUS) has evolved as a valuable adjunct to physical examination though it remains largely underutilized in nephrology. We have previously discussed the general principles of POCUS, scope of practice and training program development [2, 3], and therefore will not delve into details here. In the context of AKI in cirrhosis, Velez, et al. have demonstrated that inferior vena cava (IVC) ultrasound helps to better characterize the fluid status and potentially prevents misclassification as HRS [4]. Because of the perceived ease of image acquisition, there is a growing interest among nephrologists to learn IVC ultrasound. However, it is important to understand that isolated use of IVC is laden with pitfalls. In our experience-based opinion, multi-organ POCUS is the key to proper assessment of hemodynamics at the bedside and herein, we will explain the rationale.

Estimation of right atrial pressure (RAP) based on the size and collapsibility of IVC in spontaneously breathing patients is a standard practice in echocardiography. Nevertheless, the
correlation between IVC parameters and cardiac catheterization-derived RAP is only modest and is not applicable in mechanically ventilated patients [5]. Moreover, as the collapsibility of IVC depends on the strength of breath, relying on an absolute percentage is error-prone especially in frail patients or those who cannot follow instructions (e.g., patients with hepatic encephalopathy). In cases where the cirrhotic liver is hyperechoic, it can be technically challenging to visualize the vessel and knowledge of alternate sonographic windows/imaging planes is necessary. It is not uncommon for POCUS users to mistake adjacent aorta for IVC in such scenarios, which may result in incorrect clinical decision-making. In some cases, cirrhosis-related local factors such as caudate lobe hypertrophy may alter the diameter of IVC independent of fluid status [6, 7]. Additionally, it is well-known that raised intra-abdominal pressure can result in collapsed IVC despite intravascular volume excess [8]. Demonstration of large amount of ascites or distended bowel on POCUS should alert the physician to consider IAH in the differential diagnosis. Focal narrowing of the upper intrahepatic IVC had been suggested to indicate IAH [9] but we found that to be an unreliable finding in our practice. In settings where intra-abdominal pressure measurement is not readily available, we suggest using internal jugular vein (IJV) ultrasound to assess RAP. The vein can be easily located using POCUS and measuring the height of the collapse point provides an estimate of RAP (analogous to the highest point of venous pulsation when assessing jugular venous pressure by inspection). In patients who can follow instructions, change in the IJV cross-sectional area with valsalva maneuver predicts RAP (the vessel is more distensible when the RAP is low) [10]. Interestingly, a study in patients undergoing laparoscopic surgery demonstrated that IVC collapsibility correlated well with that of IJV in the pre-operative phase \( (r^2 = 0.86, p < 0.01) \) but lost correlation once the abdomen was insufflated to 15 mmHg \( (r^2 = 0.26, p = 0.42) \). The mean IVC diameter was reduced by 5 mm during the insufflation phase [11]. On a note of caution, IJV POCUS is subject to errors due to inappropriate head elevation angle, inadvertent application of excess transducer pressure, limited access to the neck because of the presence of dialysis catheters, tracheostomy collars or braces.

While the IVC and/or IJV ultrasound helps to estimate RAP, the downstream effects of elevated RAP on organs such as congestive nephropathy can be gauged by Doppler ultrasound of the
abdominal veins typically hepatic, portal, and renal parenchymal veins. This technique, also known as venous excess ultrasound or VExUS can be used to monitor the efficacy of decongestive therapy in patients with fluid overload thanks to the dynamic nature of these Doppler waveforms [12]. However, in cirrhosis, hepatic and portal venous waveforms maybe unreliable due to local factors. As such, we use renal parenchymal vein Doppler and an extra-abdominal vessel such as femoral vein or superior vena cava (accessed via suprasternal, supraclavicular or parasternal windows) where feasible [13, 14] to assess the flow patterns. Femoral vein Doppler is technically easier, and a pulsatile waveform demonstrates good correlation with elevated RAP; however, the sensitivity is relatively low [specificity 94% and sensitivity 46% in one study [15]]. Moreover, it is less reliable in cases of severe IAH compromising the venous return from the lower limbs. In addition to IVC and VExUS, assessment of the right ventricular function, relative cardiac chamber size, and tricuspid regurgitation allow better elucidation of the right-sided hemodynamics and monitor response to therapy.

Left heart dysfunction and pulmonary congestion can potentially go unnoticed resulting in inappropriate management or care delays if solely relying on right-sided parameters. Lung ultrasound is an easy-to-learn skill that allows rapid detection of extravascular lung water often before the onset of symptoms. Its diagnostic superiority compared to chest auscultation is well-documented, particularly in patients with heart failure and end-stage kidney disease [16]. In the liver intensive care units, lung POCUS is often used to adjust ventilator settings, determine readiness for extubation, guide ultrafiltration as well as screen for procedural complications such as pneumothorax after central venous catheter placement [17]. In addition, ability to assess left ventricular (LV) filling pressures using Doppler ultrasonography provides valuable insights into fluid tolerance. This would also help when there is a question about cardiogenic (due to elevated LV filling pressures) versus non-cardiogenic pulmonary edema. In a recent study, 62% of patients diagnosed with HRS by clinical criteria were found to have elevated cardiac filling pressures determined by right heart catheterization. Interestingly, when switched from volume loading to diuretic therapy, these patients showed significant reductions in serum creatinine values suggesting superimposed or misclassified (as HRS) cardiorenal
pathophysiology [18]. Furthermore, estimation of stroke volume using Doppler ultrasonography aids in distinguishing between hypovolemic and high cardiac output states as both are associated with small, collapsible IVC and a hyperdynamic LV on greyscale ultrasound. This allows early initiation of vasopressors and prevents empiric volume expansion if the cardiac output is already high due to cirrhosis-associated splanchnic vasodilation [19]. Being a clinician-performed study, POCUS facilitates individualized patient management by enabling serial, goal-directed assessment of hemodynamics.

As in any AKI, hydronephrosis and bladder outlet obstruction can be quickly ruled out at the bedside using POCUS without having to wait for consultative imaging. Concurrent assessment of intra-renal arterial resistive index (RI) may provide useful information in a carefully selected subset of patients despite being a non-specific measure. For example, RI has shown to be elevated in patients with IAH and HRS compared to those with volume depletion [20]. **Figure 1** provides a visual summary of POCUS applications used in the evaluation and management of cirrhotic patients with AKI.

Some may perceive multi-organ ultrasound to be overwhelming and time-consuming. However, with proper training and thorough understanding of image acquisition principles, bedside hemodynamic assessment should take no more than 15-20 minutes in our experience. This time can be simultaneously used to elicit history or for patient education. Moreover, not every patient requires a comprehensive evaluation using all the Doppler techniques mentioned above. **Figure 2** is a representation of our thought process when approaching hemodynamic AKI in cirrhosis using POCUS as a diagnostic aid. While POCUS is within the scope of appropriately trained physicians [2, 3] performing it with inadequate knowledge and skills can lead to patient harm. Establishing image archiving and a robust quality assessment system at the institutional level is vital for the success of any POCUS program. POCUS should never be considered a substitute for meticulous history-taking, urine microscopy or consultative imaging. Future studies in patients with cirrhosis and AKI should consider exploring the impact of POCUS-guided therapy on safety endpoints such as fluid overload.
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Author Contributions:
Abhilash Koratala: Conceptualization; Data curation; Formal analysis; Methodology; Writing - original draft. Nathaniel Reisinger: Conceptualization; Data curation; Methodology; Supervision; Writing - review and editing.

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**Figure legend:**

**Figure 1:** Summary of common point of care ultrasound parameters we use in the assessment of hemodynamics in patients with cirrhosis and acute kidney injury.

IJ, internal jugular; RAP, right atrial pressure; TR, tricuspid regurgitation; IVC, inferior vena cava; US, ultrasound; VExUS, Venous excess ultrasound; LV, left ventricular; LVOT, left ventricular outflow tract

*Normal sonographic images shown for illustration purposes.*

**Figure 2:** Proposed diagnostic algorithm in a case of cirrhosis and suspected hemodynamic acute kidney injury.

Color coding: blue boxes indicate right heart and red boxes left heart-related sonographic parameters. Green outlines indicate volume tolerance phenotype, and the orange outlines signify volume intolerance.

POCUS, point of care ultrasonography; IVC, inferior vena cava; IJ, internal jugular; LVOT, left ventricular outflow tract; VTI, velocity time integral; RAP, right atrial pressure; E/e’, ratio of the early diastolic waves of the mitral inflow Doppler and mitral annular tissue Doppler; LA, left atrium, TR, tricuspid regurgitation; RV, right ventricle; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion, S’, tricuspid annular systolic velocity; SVC, superior vena cava, ARDS, acute respiratory distress syndrome; HV, hepatic vein, PV, portal vein

*Incorrect angle of insonation is a frequent source of error when assessing LVOT VTI (surrogate for stroke volume) and other Doppler measurements listed.*
Figure 1

- IJ VEIN: Estimate RAP
- TR JET DOPPLER: Right ventricular systolic pressure
- IVC & ABDOMEN: Estimate RAP via IVC US, Ascites, bowel distension
- VExUS: Venous congestion, Resistive index
- LVOT DOPPLER: Estimate stroke volume & Cardiac output
- MITRAL VALVE DOPPLER: LV Diastolic function
- GREYSCALE CARDIAC: LV systolic function, Chamber enlargement, Pericardial effusion
- Venous congestion, Portal vein, Hepatic vein, Intra-renal vein & artery, Femoral vein
Figure 2

SUSPECTED HEMODYNAMIC ACUTE KIDNEY INJURY IN CIRRHOSIS

Distributive pathophysiology
- Initiate vasopressor therapy
- High + Preserved/hyperdynamic LV squeeze

Stroke volume (LVOT VTI)
- Low (often increased variability) + Preserved/hyperdynamic LV squeeze
- True volume depletion
  - Volume expansion, stop diuretics

Lungs
- A-lines
  - Small with respiratory variation
  - Volume tolerant phenotype
  - VOLUME TOLERANT PHENOTYPE
  - VOLUME INTOLERANCE
  - B-lines
  - and/or Plethoric IVC

IVC
- Low/normal RAP based on blood column height or variation of size with valsalva or respiration
- IVC indeterminate
- Consider paracentesis
- IJ vein
- Suggestive of high RAP
  - IVC indeterminate
  - Elevated RAP
    - Volume removal (or appropriate management per cause [?pressure overload])

Elevated
- Cardiogenic
  - Pulmonary edema
  - Volume removal

Assess LV filling pressures
- (E/e’ ratio, LA size, TR jet velocity)

Normal
- (often irregular pleural line, spared areas in the lung)
- Consider ARDS/infection/aspiration
  - Cause-directed therapy

Consider cirrhotic cardiomyopathy
- Inotropes if indicated

Stroke volume
- Low + decreased LV squeeze
- Consider right heart
  - (RV size, TR, RVSP, TAPSE/S’)

Assess Venous congestion by Doppler
- (Hepatic, portal and renal parenchymal veins)

Monitor for improvement with treatment (assess adequacy of decongestion)
- SVC and/or femoral vein Doppler

Abnormal
- HV/PV indeterminate