Review Article

Contribution of Lung Ultrasound and VExUS in the Diagnosis and Monitoring of Patients with Heart Failure

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Abstract

Despite advancements in the treatment of heart failure (HF), accurately assessing and monitoring fluid status and congestion remains a challenge. Traditional methods, including clinical evaluation, biomarker analysis, and imaging techniques, exhibit limitations in their capacity for real-time evaluation and monitoring of venous and pulmonary congestion. Lung ultrasound (LUS) detects B-lines and provides a rapid, sensitive assessment of pulmonary congestion, crucial for both acute and chronic HF management. Venous Excess Ultrasound Score (VExUS) provides a comprehensive assessment of systemic venous congestion by evaluating venous flows in hepatic, portal, and renal veins, alongside the inferior vena cava measurement. This review explores the integration of LUS and VExUS as innovative non-invasive, bedside technologies poised to enhance diagnostic accuracy, predict outcomes, and guide therapeutic decisions, potentially improving patient care.

Keywords

Heart Failure; Pulmonary Edema; Ultrasonography.

Central Illustration: Contribution of Lung Ultrasound and VExUS in the Diagnosis and Monitoring of Patients with Heart Failure

VExUS application

• Diagnosis in CRS
• Guiding therapy in CRS
• Prognosis in HF

LUS application

• Diagnosis of lung edema
• Guiding therapy in HF
• Prognosis in HF

Hepatic flow - grade 1
Hepatic flow - grade 3
Portal flow - grade 1
Portal flow - grade 3
LUS - A pattern
LUS - B pattern

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with clinical examination, promises to significantly transform and personalize treatment strategies in both acute and chronic HF scenarios.

Introduction

Heart failure (HF) continues to pose a substantial challenge in cardiology, marked by its widespread prevalence, significant morbidity, and considerable burden on healthcare systems worldwide.\(^1\) Despite advancements in cardiac care, diagnosis and monitoring of patients with HF, as well as accurate assessment of congestion, continue to present considerable obstacles. While traditional methodologies such as physical exams, X-rays, and biomarkers provide effective means of assessment, they exhibit inherent limitations, particularly in real-time assessment and monitoring of fluid status.

The onset of congestion is a strong predictor of poor patient outcomes in HF.\(^2\) However, its identification and assessment can be complex. Clinical symptoms and signs of congestion, such as orthopnea, jugular venous distension, peripheral edema, and the presence of third heart sound are essential for recognizing decompensated HF. Yet, they are capable of detecting only moderate to high levels of congestion, presenting low sensitivity and poor predictive value when used in isolation.\(^3\) While the combination of signs and symptoms in clinical scores has improved diagnostic accuracy, these scores have primarily been employed as prognostic tools, rather than assisting in the acute management of decompensated HF at the bedside.\(^4\)

The integration of signs and symptoms with biomarkers, such as brain natriuretic peptide (BNP), and imaging tests is recommended to enhance differentiation among potential differential diagnoses.\(^5\) However, traditional chest X-rays exhibit reasonable specificity but limited sensitivity in assessing congestion.\(^6\) Furthermore, despite the diagnostic and prognostic value of BNP, the GUIDE-IT multicenter randomized clinical trial revealed that using BNP levels to guide therapy for decompensated HF was not proven effective.\(^7\)

In certain challenging clinical scenarios, pulmonary artery catheterization (PAC) is used to assess both right and left ventricular filling pressures and hemodynamic congestion. The ESCAPE trial evaluated the impact of using PAC to achieve decongestion in patients hospitalized with severe, symptomatic, and recurrent HF. Patients were randomized to receive therapy guided by both clinical assessment and PAC or by clinical assessment alone. In both groups, the instituted therapeutic interventions led to a significant reduction in symptoms, jugular venous pressure, and the presence of edema. However, there was no difference in the primary endpoint of days alive out-of-hospital during the first 6 months (133 days vs. 135 days; HR=1.00; 95% CI 0.82-1.21; p=0.99), and in-hospital adverse events were more common among patients in the PAC group (21.9% vs. 11.5%; p=0.04).\(^8\)

In this complex clinical landscape, the demand for accurate, non-invasive, and real-time diagnostic and monitoring tools is paramount. Lung Ultrasound (LUS)\(^9\) and Venous Excess Ultrasound Score (VExUS)\(^10\) have emerged as promising technologies in this regard. LUS offers a non-invasive, bedside approach for detecting pulmonary congestion, a common and significant complication in HF. VExUS assesses venous congestion and provides crucial insights into patients’ hemodynamic status, an aspect often overlooked by conventional diagnostic methods.

The incorporation of these modalities into routine HF management has the potential to significantly enhance the current approach by offering more precise diagnoses, improving monitoring of disease progression, and potentially reducing hospital readmissions. This review aims to explore the roles of LUS and VExUS in the contemporary management of HF, highlighting their impact on improving patient outcomes and alleviating healthcare burdens (Central Illustration).

LUS in HF

LUS has revolutionized the management of HF, providing sophisticated diagnostic, monitoring, and prognostic capabilities.\(^11\) As an echographic technique, LUS is instrumental in detecting B-lines, which are sonographic reverberation artifacts indicative of interstitial pulmonary edema, thus playing a crucial role in assessing pulmonary congestion. The acquisition of LUS images involves placing a transducer perpendicular to the chest wall in intercostal spaces to avoid rib shadowing, ensuring optimal visualization of the pleural line and lung parenchyma beneath. Depth settings are adjusted to adequately display the pleura and the underlying lung tissue. B-lines typically extend from the pleural line to the bottom of the screen, obliterating A-lines and moving with the patient’s breath.\(^12\)

Various protocols exist for conducting LUS, each differing in the number of lung fields examined.\(^13\) However, the eight-zone LUS protocol is most commonly utilized in clinical practice, particularly following its endorsement in the latest consensus by the European Association of Cardiovascular Imaging (EACVI).\(^14\) This protocol involves scanning bilateral anterior and lateral chest areas, dividing each hemithorax into four zones. The detection of three or more B-lines in two or more zones is indicative of pulmonary congestion. A higher number of B-lines correlates with elevated pulmonary capillary wedge pressure, as validated by invasive hemodynamic measurements,\(^15\) providing a non-invasive yet reliable method to assess the severity of ventricular filling pressure.

Acute HF

Diagnosis in Emergency Department

In the context of acute HF, LUS has become an indispensable diagnostic tool within emergency settings, providing rapid, non-invasive assessment with enhanced sensitivity over traditional imaging methods. LUS significantly outperforms auscultation in diagnosing pulmonary congestion in critically ill patients.\(^16\) Furthermore, in patients with acute decompensated HF, a LUS-integrated approach was more accurate than the use of chest x-ray and NT-proBNP,\(^17\) leading to a 33.5% reduction in time to disposition decision and a 33.7% decrease in length of hospital stay, as shown in Table 1.\(^18\)
Guiding treatment

The dynamic nature of LUS, capable of monitoring real-time changes in pulmonary congestion, is significantly beneficial for monitoring the effectiveness of decongestive therapy and titrating it accordingly. Notably, a decrease in B-lines is a direct indicator of a positive response to diuretic therapy and fluid management, highlighting LUS’ potential role in managing acute HF. For example, the combination of focused echocardiographic evaluation of cardiac filling pressures and inferior vena cava (IVC) index with LUS through CaTUS protocol resulted in significantly greater decongestion when compared with standard care, as defined by a reduction in symptoms, cardiac filling pressures, natriuretic peptides, cumulative fluid loss, and resolution of pulmonary congestion on LUS (p < 0.05 for all). Also, CaTUS-guided therapy led to shorter mean length of hospitalization (3.74±2.02 days vs. 6.85±4.22 days; p=0.002) and better survival regarding the combined endpoint of all-cause mortality and readmission due to acute HF at 6 months, primarily driven by a reduction in rehospitalizations.

Prognosis

LUS adeptly quantifies residual pulmonary congestion at discharge, addressing a critical gap often overlooked by physical examination alone. In a single-center cohort study, residual pulmonary congestion, as assessed by LUS at discharge, emerged as an independent predictor of both mortality (HR=11.3; 95% CI 2.4–53.2; p=0.002) and hospitalization for worsening HF (HR=8.1; 95% CI 2.1–32.1; p=0.003) within 90 days, using a simplified 4-zone LUS method (positive if the sum of B-lines across 4 zones was ≥7 B-lines). Residual congestion is also linked to more adverse outcomes over 6 months, as defined by a composite endpoint of HF readmission or all-cause death (HR=2.01; 95% CI: 1.11–3.64; p=0.021), assessed by a B-line count ≥30 obtained with the 28 scanning regions method. Similar results were observed utilizing the eight-zone method, with the best cut-off being ≥1 zone with ≥3 B-lines on each hemithorax. Interestingly, levels of NT-proBNP, a conventional biomarker in HF, did not substantially predict these long-term outcomes.

Thereafter, employing LUS before discharge in acute HF patients can effectively detect persistent pulmonary congestion, assisting in the identification of those with an elevated risk of HF-related readmission or mortality. This underscores the importance of optimizing decongestion, as highlighted in the 2021 European Society of Cardiology (ESC) Guidelines for the management of HF.

Chronic HF

Decompensation in HF typically manifests with minimal clinical symptoms for the majority of patients, often becoming noticeable only in advanced stages when urgent intervention is required due to congestion. Consequently, the incorporation of LUS into routine clinical assessments of outpatients could provide a means for early detection of subclinical congestion. In chronic HF management of ambulatory patients, LUS-guided diuretic strategies have demonstrated substantial benefits, in particular to titrate diuretic therapy and reduce HF-related adverse outcomes.

The LUS-HF trial highlighted that personalized LUS-directed management of pulmonary congestion in the post-discharge follow-up of patients recently hospitalized for HF reduced the number of urgent visits for worsening HF (21% vs. 5%; p=0.008) and improved functional capacity in 6-min walking test compared with baseline (37 m (IQR: 5–70 m) vs. 60 m (IQR: 29–125 m); p=0.023), during a 6-month follow-up period. Following this, the CLUSTER-HF trial demonstrated that treatment guided by LUS performed in every patient visit resulted in a noteworthy 45% risk reduction in the primary endpoint, a composite of urgent HF visits, rehospitalization for worsening HF and death from any cause at 6 months, mainly driven by a reduction in urgent HF visits (HR=0.28; 95% CI 0.13–0.62; p=0.001). Furthermore, in a randomized multicenter unblinded study, individuals with chronic HF undergoing optimized medical therapy and randomized to LUS-guided management experienced a notable decrease of 56% in acute HF-related hospitalizations at 90 days (RR=0.44; 95% CI 0.23–0.84; p=0.01). Additionally, there was a concurrent reduction in NT-proBNP levels (p=0.01) and an improvement in overall quality of life (p=0.02).

### Table 1 – LUS application in HF

<table>
<thead>
<tr>
<th>Category</th>
<th>Application</th>
<th>Description</th>
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</tr>
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<tbody>
<tr>
<td>Acute HF</td>
<td>Diagnosis in emergency department</td>
<td>Rapid, non-invasive assessment with enhanced sensitivity over traditional methods. Outperforms auscultation and is more accurate than chest x-ray and NT-proBNP.</td>
<td>Reduces time to disposition decision and hospital stay length.</td>
</tr>
<tr>
<td>Guiding treatment</td>
<td>Monitors real-time changes in pulmonary congestion, guiding decongestive therapy. Decrease in B-lines indicates positive response to treatment.</td>
<td>Leads to larger decongestion, shorter hospitalization, and reduced HF rehospitalization.</td>
<td></td>
</tr>
<tr>
<td>Prognosis</td>
<td>Quantifies residual pulmonary congestion at discharge.</td>
<td>Assists in identifying high-risk patients for readmission or mortality, underscoring the importance of optimizing decongestion.</td>
<td></td>
</tr>
<tr>
<td>Chronic HF</td>
<td>Guiding treatment</td>
<td>Early detection of subclinical congestion in outpatients.</td>
<td>Reduces urgent visits for worsening HF, improves physical capacity and quality of life.</td>
</tr>
</tbody>
</table>

HF: heart failure.
In conclusion, LUS has emerged as a non-invasive, clinically efficacious, and simple modality, pivotal in the management of pulmonary congestion across the HF spectrum. Its diagnostic accuracy, real-time therapeutic feedback, and prognostic value in both acute and chronic HF settings underscore its essential role in contemporary HF management protocols.

**VExUS in HF**

**Diagnosis**

Accurate assessment of central venous pressure (CVP) is essential for optimizing volume management in patients with HF. In this context, measurement of the IVC is the most commonly utilized non-invasive method. CVP can be estimated by evaluating IVC diameter and its inspiratory variability, which has been shown to predict elevations in right atrial pressure (RAP) with greater frequency and accuracy than physical examination of the jugular venous pulse. The size and inspiratory variability of the IVC, despite being part of the initial assessment of systemic congestion, should not be used in isolation, as its correlation with RAP measured from right heart catheterization is only moderate. Furthermore, there are several limitations in its analysis, such as mechanical ventilation, pulmonary hypertension, variable breathing patterns during spontaneous ventilation, and lung hyperinflation with auto-PEEP in patients with obstructive lung disease.

Venous congestion leads not only to dilation of the IVC but also to pressure transmission to peripheral organs, altering the pattern of venous blood flow predictably. In this regard, VExUS has emerged as a significant advancement in the assessment of systemic venous congestion. By evaluating venous flows in hepatic, portal, and renal veins, along with IVC measurement, VExUS provides a comprehensive overview of venous status. Initially developed in the post-cardiac surgery setting, where it demonstrated high accuracy in identifying patients at risk for developing cardiorenal syndrome (CRS), VExUS has proven its value across other clinical scenarios.

The assessment of the VExUS score begins with the identification of IVC, in the subcostal window, in a supine position. IVC diameter should be measured one to two centimeters from the right atrium. If dilated, (≥ 2 cm), further evaluation should be conducted by the analysis of hepatic, portal, and intra-renal vein flow using Pulse-wave Doppler, as illustrated in Table 2. For flow assessment, a phased array transducer can be used through the subcostal window, or a convex transducer along the anterior axillary line. A non-dilated IVC (<2 cm) indicates no significant venous congestion (VExUS 0). Mild congestion (VExUS 1) is defined by the presence of an IVC ≥ 2 cm with either a combination of normal patterns (systolic [S] wave higher than the diastolic [D] wave at hepatic vein Doppler, non-pulsatile portal vein Doppler with maximum and minimum velocity variability of <30%, continuous pattern at intra-renal vein Doppler) or mild findings (S < D wave at hepatic vein Doppler, pulsatility index between 30-50% at portal vein Doppler, pulsatile flow at intra-renal vein Doppler with distinct S and D components). Moderate congestion (VExUS 2) is considered when an IVC ≥ 2 cm presents with at least one severely abnormal pattern (S wave reversed at hepatic vein Doppler, pulsatility index ≥ 50% at portal vein Doppler, monophasic flow with a D-only pattern at intra-renal vein Doppler). Severe congestion (VExUS 3) is indicated by a dilated IVC with two or more severely abnormal patterns, as shown in Table 3.

When compared with invasive hemodynamic measurements by right heart catheterization, a high classification in the VExUS score was associated with an increase in RAP (p<0.001, R²=0.68), presenting better performance than IVC in predicting values ≥ 12 mmHg (AUC=0.99; 95% CI 0.96-1.0 vs. AUC=0.79; 95% CI 0.65-0.92).

**Guiding therapy**

VExUS plays a potential role in guiding therapy, particularly in the context of CRS. The technique’s ability to dynamically track venous congestion could aid clinicians in adjusting diuretic therapy, aiming for an improvement in VExUS grade, which is associated with better outcomes in CRS, as illustrated in Table 4.

In a prospective cohort study of CRS patients including decompensated HF (57% of study subjects), resolution of acute kidney injury showed a significant correlation with improvement in VExUS score (p=0.003) and there was a significant association between changes in VExUS grade and fluid balance (p=0.006). Additionally, this study was the first to validate the use of the VExUS protocol without the need for renal flow, simplifying image acquisition and enhancing the clinical applicability of the method.

VExUS is especially relevant in cases of renal function deterioration, where there’s uncertainty about reducing diuretic therapy. Higher VExUS scores would suggest that renal impairment is linked to systemic venous congestion, supporting the continuation of diuretic treatment.

The sole clinical trial assessing the impact of VExUS-guided decongestion therapy on kidney function recovery and decongestion metrics in patients with CRS type 1 (worsening kidney function due to acute HF) revealed that, compared to standard evaluation, VExUS-guided decongestion did not significantly enhance kidney function recovery (26% vs. 24%; p=0.09). However, VExUS demonstrated a more than twofold increase in the likelihood of achieving decongestion (OR=2.6; 95% CI 1.9-3.0; p=0.01) and reaching a >30% reduction in BNP levels (OR=2.4; 95% CI 1.3-4.1; p=0.01). Additionally, the time required to achieve decongestion was shorter in the VExUS group by 2 days [5 days (IQR: 3-8 days) vs. 7 days (IQR: 4-11 days); p=0.004]. Notably, patients randomized to VExUS exhibited a greater rise in serum creatinine compared to the control group (p=0.005), suggesting that VExUS enables more precise identification of congestion, leading to more aggressive treatment.

This paradoxical increase in serum creatinine during decongestion in acute decompensated HF has been associated with improved cardiorenal survival, raising the possibility that the greater increases in serum creatinine in VExUS-guided decongestion were indicative of more effective treatment.

This potential relationship between VExUS findings and renal outcomes underscores the importance of VExUS in...
managing fluid overload, ensuring patients receive optimal care tailored to their specific venous congestion status.

**Prognosis**

Prior research has elucidated the significance of systemic congestion in predicting outcomes accurately. In a population of patients hospitalized with acute HF, abnormal portal vein pulsatility at discharge was significantly associated with mortality (HR=1.03; 95% CI 1.01-1.04; p<0.001) and a high renal venous stasis index (cardiac cycle time-venous flow time/cardiac cycle time) have demonstrated worse prognosis in terms of cardiac death or worsening HF (HR=1.91; 95% CI 1.05–3.48;
Among VExUS score prognostic value. Each Doppler venous waveforms. renal disease may also have the potential to affect intra-renal the main renal vein instead of the interlobar vein. Parenchymal acquisition, often resulting in suboptimal recordings. Erroneous presents the highest technical challenge due to its difficulty in with a low body mass index, without raised RAP. portal vein flow can also occur in young, healthy individuals indicate congestion in cirrhotic patients. Interestingly, pulsatile be present in parenchymal liver disease and might not truly tricuspid regurgitation. as atrial fibrillation, right ventricular systolic excursion, and interpretation can be influenced by factors beyond RAP, such as inflammation, previous HF or chronic kidney mechanisms such as inflammation, previous HF or chronic kidney disease, suggesting other underlying mechanisms such as inflammation, previous HF or chronic kidney disease could contribute to lung congestion.43 For accurate interpretation of VExUS, electrocardiogram tracing is essential to correctly identify venous waves. Each VExUS component also has its limitations. Hepatic vein Doppler interpretation can be influenced by factors beyond RAP, such as atrial fibrillation, right ventricular systolic excursion, and tricuspid regurgitation. Diminished portal vein pulsatility can be present in parenchymal liver disease and might not truly indicate congestion in cirrhotic patients. Interestingly, pulsatile portal vein flow can also occur in young, healthy individuals with a low body mass index, without raised RAP. Among the three components of VExUS, intra-renal vein Doppler presents the highest technical challenge due to its difficulty in acquisition, often resulting in suboptimal recordings. Erroneous interpretation often arises when sampling a larger vessel like the main renal vein instead of the interlobar vein. Parenchymal renal disease may also have the potential to affect intra-renal Doppler venous waveforms.44,45 Considering these limitations, it is crucial to avoid interpreting any of these exams in isolation. Assessing the images within the relevant clinical context and advocating for multiorgan evaluation can mitigate the risk of misinterpretation.

Future directions
As Point-of-Care Ultrasonography (PoCUS) becomes increasingly common in modern medical practice, its importance in assessing the volume status of HF patients is expected to grow significantly. However, a gap remains in PoCUS training, which is an unmet need in the healthcare field. Consequently, the development and implementation of comprehensive training programs, along with supervision and quality assurance mechanisms, should be prioritized by healthcare organizations. Enhancing training and minimizing inter-rater variability are essential steps toward ensuring more accurate and reliable evaluations. Such improvements can help prevent misdiagnoses and provide valuable guidance in therapy management, thereby improving patient care in HF management.

The employment of LUS and venous Doppler has the potential to significantly improve the clinical detection and quantification of congestion. Despite this advantage, robust evidence is currently insufficient to demonstrate that interventions aimed specifically at ameliorating these parameters lead to enhanced hard outcomes in patients with HF, both in emergency departments and critical care environments. This gap underscores the need for further research to validate the impact of targeted treatment strategies on improving patient outcomes in these acute care settings. Also, additional investigation is required to assess whether the adoption of an integrative approach, rather than individual sonographic parameters, would have a beneficial impact on outcomes.

Conclusions
Congestion represents a significant clinical challenge among patients with decompensated HF, often resulting in frequent hospitalizations and poorer clinical outcomes. Timely and accurate identification of congestion is paramount for appropriate management and mitigating adverse consequences. In this context, LUS and VExUS play a crucial role as indispensable and effective tools, providing objective insights into pulmonary and systemic congestion that surpass traditional methods. When combined, these modalities aid clinicians in differential diagnosis, therapeutic strategies, and prognosis assessment for individuals with decompensated HF, thereby enhancing the overall quality of care.

Author Contributions
Conception and design of the research, Writing of the manuscript and Critical revision of the manuscript for content: Telo GH, Saadi MP, Silvano GP, Silveira AD, Biolo A.

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References


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