Article

Usefulness of Serial Multiorgan Point-of-Care Ultrasound in Acute Heart Failure: Results from a Prospective Observational Cohort

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Abstract: *Background and Objectives*: Acute Heart Failure (AHF) is a common disease and a cause of high morbidity and mortality, constituting a major health problem. The main purpose of this study was to determine the impact of multiorgan ultrasound in identifying the pulmonary hypertension (PH) in patients admitted due to AHF, predict the evolution of the disease during hospitalization and identify areas of improvement in the care of patients with AHF. *Materials and Methods*: Patients were evaluated with a standard exam of lung ultrasound, echocardiography, inferior vena cava (IVC) and femoral, renal, hepatic, portal venous Doppler flow patterns at admission and on the day of discharge. *Results*: Thirty patients were enrolled during November 2021. The mean age was seventy-nine years (Standard Deviation – SD 13,4). Seven patients (23.3%) had a renal function worsening. Regarding ultrasound findings, venous excess ultrasonography score (VExUS) score was calculated at admission and at discharge, surprisingly remaining unchanged or even worsened in most of them (21 patients, 70.0%). The area under the curve for the Lung Score was 83.9% ($p = 0.008$), obtaining a cutoff value of 10 that showed a sensitivity of 82.6% and a specificity of 71.4% in the identification of intermediate and high PH. It was possible to monitor significant changes between both exams on the lung score ($p < 0.001$), hepatic vein Doppler ($p < 0.001$), portal vein Doppler ($p = 0.030$), intra-renal vein Doppler ($p = 0.025$) and VExUS score ($p = 0.023$), remaining similar the femoral vein Doppler ($p = 0.177$) and IVC ($p = 0.132$). *Conclusions*: Our study results suggest that performing serial multiorgan Point-of-Care ultrasound can help us to better identify high and intermediate probability of PH patients with AHF. Currently proposed multi-organ, venous Doppler scanning protocols, such as the VExUS score, should be further studied in different populations before expanding its use in AHF patients.

Keywords: acute heart failure (AHF); venous congestion; Point-of-Care Ultrasound (POCUS); VExUS (venous excess ultrasonography score)

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1. Introduction

Acute heart failure (AHF) is a clinical syndrome whose diagnosis is based on the probability of symptoms and signs coupled with ultrasound and the determination of biochemical markers (1). AHF is very frequently linked to high resource utilization, emergency services visits, hospital admissions, and despite this, it presents a non-negligible complication rate, hovering according to the series of almost 15% mortality and a 32% of hospital readmissions (2) . Moreover, patients with AHF with pulmonary hypertension (PH) tend to have a worse prognosis (3). PH may have important consequences such as liver stasis (4), enteropathy (5), encephalopathy (6) and kidney failure (7,8).

Point-of-Care ultrasound (POCUS), performed at the bedside of the patient, allows to determine the probability of PH (9,10), based on the combination of different echocardiographic parameters; not easy to obtain in real practice and in exacerbated patients (11,12). Therefore, we are in the need of simpler ultrasound parameters that bring us closer to determine the probability of PH and its systemic consequences (13). Furthermore, PH can cause a decrease in NT-proBNP levels, a pillar biochemical marker of AHF, challenging the diagnosis.

Traditionally, we have relied on measuring the inferior vena cava (IVC) as a marker of central venous pressure (CVP). However, CVP does not accurately reflect the patient's venous preload or congestion. In PH, certain valvular heart diseases, advanced chronic obstructive pulmonary disease (COPD) associated with PH or even in young and athletic patients, it is possible to find a dilated IVC without systemic congestion (14).

Currently, there is an increasing use of ultrasound parameters in the systemic congestion based on the vein Doppler assessment, such as the hepatic and portal veins assessment (15–19), described more than 20 years ago, or more recent one, such as the intrarenal vein Doppler (20). Recently, it has been demonstrated to be useful when integrated into a multiorgan POCUS protocol, such as the venous excess ultrasonography score (VExUS) in cardiac surgical patients (13,21). To our best knowledge, the formulation of such an approach is in need in hospitalized AHF patients.

2. Materials and Methods

This was a prospective study performed in an academic hospital, conducted in accordance with the Declaration of Helsinki, and approved by the Research Ethics Committee of our University Hospital. We obtained informed consent from each patient.

2.1. Patient Selection

We included patients admitted to an internal medicine ward due to the main diagnosis of AHF. These patients had to exhibit signs attributable to congestion (any of the following: peripheral edema, ascites, jugular engorgement, crackles on pulmonary auscultation, signs of pulmonary congestion on chest X-ray), dyspnea and a NT-proBNP levels> 1000 pg / ml at admission.

We excluded patients <18 years, with hemodynamic instability (vital compromise) or those who declined to participate. A sample of 30 consecutive patients who met these inclusion criteria were enrolled and prospectively studied.

2.2. Initial patient assessment

Demographic data (age, sex, weight), medical history (comorbidities, medications), risk factors for AHF (ie, cardiopulmonary diseases), physical exam (weight, negative balance performed), heart rate (HR), sinus rhythm / atrial fibrillation , laboratory tests (creatinine, urea, hemoglobin, white blood cells, platelets, NT-proBNP at admission and before discharge), chest X-ray were registered.

2.3. Ultrasound data collection

Patients underwent a multiorgan ultrasound study in the first 24 hours of admission and the same day of discharge.

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We collected the different ultrasound parameters that could be associated to volume overload, the diameters of the IVC, the number of lung B-lines (Lung Score), echocardiographic findings (left ventricular diastolic diameter, left ventricular systolic diameter, interventricular septum and posterior wall thickness in diastole and systole, left ventricular ejection fraction, left and right atrial area, transmitral filling pattern, basal diameter of the right ventricle in apical plane, TAPSE, tricuspid regurgitation velocity, pulmonary artery diameter, right ventricle outflow acceleration time, pulmonary regurgitation velocity , presence of moderate or severe valvular heart disease), intra-renal Doppler ultrasound (polyphasic, biphasic, monophasic), portal vein Doppler ultrasound (pulsatility index <30%, 30-49%,> 50%), hepatic vein Doppler ultrasound (venous flow pattern type S> D, S <D, S wave inversion), femoral vein Doppler ultrasound (pulsatility index <30%, 30-49%,> 50%).

The exam was performed by an ultrasound fellowship-trained internal medicine physician, who had a long-standing experience in cardiac, vascular and lung US (more than 5 years). A Mindray M7 diagnostic ultrasound system with Phased Array, Curvilinear and linear transducer (Mindray España, Madrid, Spain) and a Kosmos ultrasound handheld device (EchoNous, WA, USA) were used in the study.

The sonographer was blinded to the patient's past medical history, vital signs, symptoms, laboratory measurements, and therapy.

2.4. Outcome measures and definitions

Our study aims to determine the impact on accuracy of currently proposed multiorgan, venous Doppler scanning protocols, such as the VExUS score (13), in determining the probability of PH and the presence of developing renal failure during the hospitalization.

We defined worsening renal failure as a 25% increase in baseline serum creatine or an increase of 0.3 mg / dL during hospitalization.

The EVEREST grading score (22), as a clinical course marker of congestion during hospitalization, was calculated for each patient, at admission and at discharge.

Our hypothesis is that multiorgan ultrasound would help us to better identify high and intermediate probability of PH patients with AHF. Likewise, we intended to make a prediction of the evolution of the disease during hospitalization and identify areas of improvement in the care of patients with AHF.

2.5. Statistical analysis

Baseline characteristics are presented as mean and standard deviation (SD) for continuous variables and count and proportions for categorical variables.

Comparisons of means were made using T-Student test and Chi-square test or Fisher's exact two-tailed test was used for categorical variables when it was appropriate. A sample of 30 patients was obtained as previously recommended in reliability studies (23).

We assumed an α-value of 0.05 for two-sided hypothesis testing. Analyzes were conducted with the statistical IBM SPSS software v25.0 (SPSS Inc., Chicago, IL, USA).

3. Results

During November 2021, a total of 39 patients were screened and fulfilled the inclusion criteria (summarized in figure 1 and table 1), 1 patient declined to participate and 8 were excluded after inclusion: 3 patients died, 1 had a cardiac valve replacement, 1 could not finish the exam, and 3 had other diagnosis than AHF (1 had diffuse lung interstitial disease and 2 had pneumonia, without echocardiographic signs of AHF). 30 patients were included into the final analysis.

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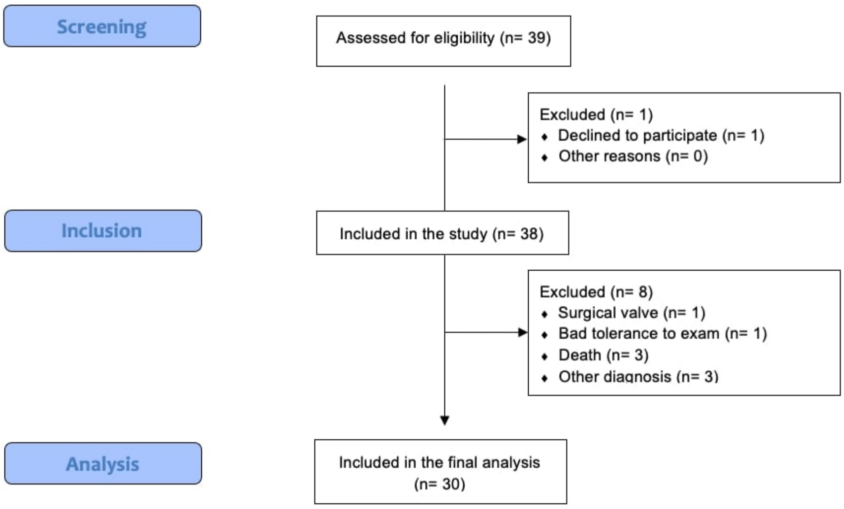

Figure 1. STROBE flow diagram.

The mean age was 79 years (SD 13,4) and 50% were female. 19 patients (63.3%) had an underlying cardiovascular illness. The mean creatinine level was 1.13 mg / dL (SD 0.5, Normal Value-NV: <0.90) and NT-proBNP was 10846.7 pg / L (SD 11693, NV: <400) at admission. The mean creatinine level was 1.44 mg / dL (SD 0.8) and NT-proBNP was 6987.3 pg / L (SD 8999.1) at discharge. 7 patients (23.3%) had a renal function worsening. Regarding the multiorgan ultrasound exam performed (figure 2), all patients had at least two exams performed, at admission and at discharge (see Table 1). It was possible to monitor significant changes between both exams on the lung score (p <0.001), hepatic vein Doppler profile (p <0.001), portal vein Doppler (p = 0.030), intra-renal vein Doppler (p = 0.025) and VExUS score (p = 0.023), remaining similar to the femoral vein Doppler (p = 0.177) and IVC (p = 0.132).

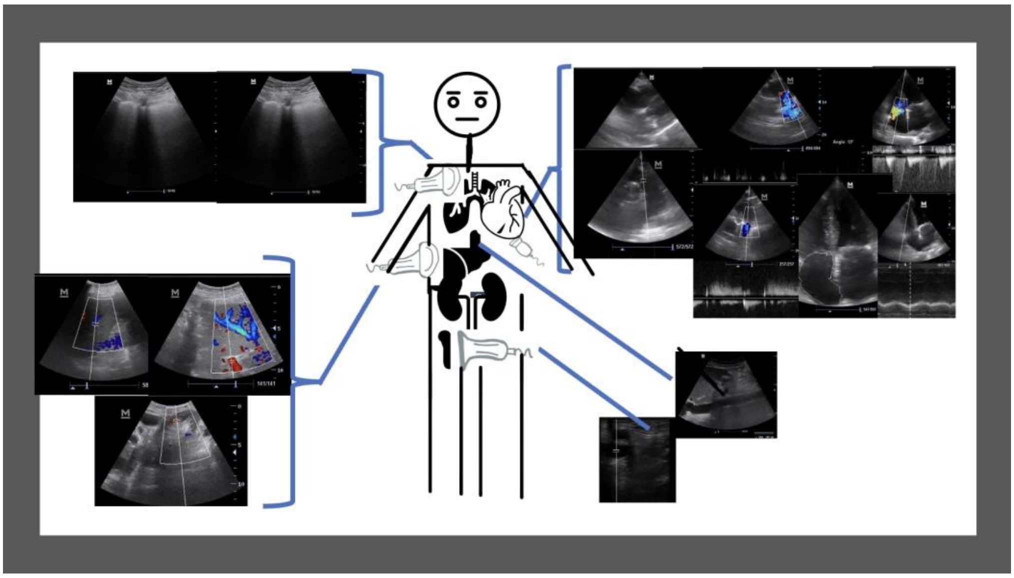

Figure 2. Representation of the ultrasound exam performed in all patients (N=30).

Table 1. Demographics and clinical characteristics of patients included (N = 30).

Demographics	N (%)
Gender (female) - N (%)	15 (50.0)
Age (years) mean (SD)	79 (13.4)

Previolus diseases	**N (%)**
Hypertension - N (%)	25 (83.3)
Dyslipidemia - N (%)	12 (40.0)
Diabetes Mellitus - N (%)	8 (26.7)
Chronic Kidney Disease (stage 3 or more) - N (%)	8 (26.7)
Previous recent hospitalization - N (%)	5 (6.7)
Cardiovascular disease - N (%)	19 (63.3)
Atrial Fibrillation - N (%)	8 (26.7)
Reduced Ejection Fraction - N (%)	3 (10.0)
Pulmonary disease - N (%)	9 (30.0)
Phyisical exam	**N (%)**
Weight (kg) at admission mean (SD)	81.1 (16.7)
Weight (kg) at discharge (SD)	65,6 (19.2)
Laboratory results - Mean (SD)	
NT-proBNP at admission pg/L (SD)	10846,7 (11693,8)
Urea at admission mg/dL (SD)	58,3 (29,2)
Sodium at admission mg/dL (SD)	137,5 (6,5)
Creatinine at admission - mg/dL (SD)	1,13 (0,5)
Hemoglobin at admission - g/dL (SD)	12,9 (2,4)
NT-proBNP at discharge pg/L (SD)	6987,3 (8999,1)
Urea at discharge mg/dL (SD)	88,7 (41,1)
Sodium at discharge mg/dL (SD)	141,1 (3,9)
Creatinine at discharge - mg/dL (SD)	1,44 (0,8)
Hemoglobin at discharge - g/dL (SD)	12,9 (2,2)
Ultrasound exam – at admission	**N (%)**
Heart rhythm during ultrasound exam	
Sinusal rhythm	10 (33.3)
Atrial fibrillation	18 (60)
Atrial flutter	2 (6.7)
Inferior Vena Cava of > 2,1 cm and <50% of collapsability	12 (40,0)
Inferior Vena Cava of < 2,1 cm and >50% of collapsability	9 (30,0)
Lung score at admission - mean (SD)	16,5 (9,2)
Tricuspid regurgitation	
Moderate tricuspid regurgitation - N (%)	6 (20.0)
Severe tricuspid regurgitation - N (%)	9 (30.0)
Pericardial effusion – N (%)	4 (13,3)
Low TAPSE – N (%)	11 (36,7)
Mildly reduced Ejection Fraction - N (%)	5 (16,7)

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Reduced Ejection Fraction - N (%)	5 (16,7)
Probability of pulmonary hypertension	
Low	7 (23,3)
Intermediate	12 (40,0)
High	11 (36,7)
Hepatic Vein at admission	
S > D	1 (3,3)
S < D	17 (56,7)
S Reversal	11 (36,7)
Not measurable	1 (3,3)
Portal Vein at admission	
Pulsatility < 30%	15 (23,3)
Pulsatility 30-50%	9 (40,0)
Pulsatility >50%	6 (36,7)
Intra-Renal Vein at admission	
Continuous Monophasic	13 (33,3)
Biphasic flow	13 (43,3)
Discontinuous Monophasic	4 (13,3)
Femoral Vein at admission	
Pulsatility < 30%	8 (26,7)
Pulsatility 30-50%	3 (10,0)
Pulsatility >50%	19 (63,3)
Ultrasound exam – at discharge	**N (%)**
Inferior Vena Cava of > 2,1 cm and <50% of collapsability	12 (40,0)
Inferior Vena Cava of < 2,1 cm and >50% of collapsability	9 (30,0)
Lung score at discharge - mean (SD)	9,3 (8,1)
Change in Lung score - mean (SD)	6,7 (10.4)
Inferior Vena Cava of > 2,1 cm and <50% of collapsability	8 (26,7)
Inferior Vena Cava of < 2,1 cm and >50% of collapsability	10 (33,3)
Improve in Inferior Vena Cava - N (%)	14 (46.7)
Hepatic Vein at discharge	
S > D	9 (30,0)
S < D	11 (36,7)
S Reversal	9 (30,0)
Not measurable	1 (3,3)
Improve in Hepatic Vein profile - N (%)	22 (73.3)
Portal Vein at admission	
Pulsatility < 30%	23 (76,3)

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Pulsatility 30-50%	3 (10,0)
Pulsatility >50%	4 (13,3)
Improve in Portal Vein profile - N (%)	9 (30.0)
Worsening in Portal Vein profile - N (%)	2 (6,7)
Intra-Renal Vein at admission	
Continuous Monophasic	17 (56,7)
Biphasic flow	9 (30,0)
Discontinuous Monophasic	4 (13,3)
Improve in Intra-Renal Vein profile - N (%)	6 (20.0)
Worsening in Intra-Renal Vein profile - N (%)	4 (13,3)
Femoral Vein at admission	
Pulsatility < 30%	13 (43,3)
Pulsatility 30-50%	1 (3,3)
Pulsatility >50%	16 (53,3)
Improve in VExUS score - N (%)	9 (30.0)
Worsening in VExUS score - N (%)	7 (23.3)
VExUS score unchanged - N (%)	14 (46.7)
Improve in Femoral Vein profile - N (%)	9 (30.0)
Worsening in Femoral Vein profile - N (%)	3 (10,0)
Follow-up	
EVEREST score at admission	10,1 (3,1)
EVEREST score at discharge	0,7 (0,8)
NYHA at admission	
NYHA I	1 (3.3)
NYHA II	9 (30.0)
NYHA III	18 (60.0)
NYHA IV	2 (6.7)
NYHA at discharge	
NYHA I	21 (70,0)
NYHA II	8 (26,7)
NYHA III	1 (3,3)
NYHA IV	0 (0,0)

NT-proBNP: NT-proB-type Natriuretic Peptide; NYHA: New York Heart Association; SD: standard deviation; VExUS: venous excess ultrasonography score.

Probability of PH was calculated (9,10), resulting in a low probability in 7 patients (23.3%), intermediate in 12 (40%) and high in 11 (36.7%). VExUS score was also calculated at admission and at discharge (table 2), with an improvement in the score in only 9 patients (30%) and unchanged or worsening in most of them (21 patients, 70.0%). We calculated the EVEREST score at admission (10.1, SD 3.1) and discharge (0.74, SD 0.8). This score had a low to moderate correlation with VEXUS at admission (0.532; p = 0.004), similar to hepatic vein (0.470; p = 0.011), portal vein (0.478; p = 0.012), intra-renal vein (0.429;

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p = 0.12) Doppler at admission. Regarding the EVEREST score at discharge, it was possible to correlate it to the VEXUS score at discharge (0.461; p = 0.015), Portal vein (0.675; p <0.001), intra-renal vein (0.549; p = 0.003) and femoral vein Doppler (0.510; p = 0.007).

Table 2. Changes between ultrasound parameters at admission and discharge of patients included (N = 30).

Ultrasound exam	At admission	At discharge	*p* -Value
Inferior Vena Cava of > 2,1 cm and <50% of collapsibility – N (%)	12 (40.0)	12 (40.0)	0.132
Inferior Vena Cava of < 2,1 cm and >50% of collapsibility – N (%)	9 (30.0)	9 (30.0)	0.132
Lung score - mean (SD)	16.5 (9.2)	9.3 (8.1)	<0.001
Hepatic Vein			
S > D – N (%)	1 (3.3)	9 (30.0)	< 0.001
S < D – N (%)	17 (56.7)	11 (36.7)	
S Reversal – N (%)	11 (36.7)	9 (30.0)	
Not measurable – N (%)	1 (3.3)	1 (3.3)	
Portal Vein			
Pulsatility < 30% – N (%)	15 (23.3)	23 (76.3)	0.030
Pulsatility 30-50% – N (%)	9 (40.0)	3 (10.0)	
Pulsatility >50% – N (%)	6 (36.7)	4 (13.3)	
Intra-Renal Vein			
Continuous Monophasic – N (%)	13 (33.3)	17 (56.7)	0.025
Biphasic flow – N (%)	13 (43.3)	9 (30.0)	
Discontinuous Monophasic – N (%)	4 (13.3)	4 (13.3)	
VExUS score			
0 – N (%)	8 (26.7)	10 (33.3)	0.023
1 – N (%)	11 (36.7)	9 (30.0)	
2 – N (%)	6 (20.0)	7 (23.3)	
3 – N (%)	5 (16.7)	4 (13.3)	
Femoral Vein			
Pulsatility < 30% – N (%)	8 (26.7)	13 (43.3)	0.177
Pulsatility 30-50% – N (%)	3 (10.0)	1 (3.3)	
Pulsatility >50% – N (%)	19 (63.3)	16 (53.3)	

NT-proBNP: NT-proB-type Natriuretic Peptide; SD: standard deviation; VExUS: venous excess ultrasonography score.

Regarding NYHA status, most of the patients were in a functional status of NYHA III (18 patients, 60%) at admission and NYHA I (21 patients, 70%) at discharge.

Receiver operating characteristic (ROC) curve was calculated for predicting intermediate and high probability of PH according to VExUS score, vein Doppler ultrasound (hepatic, portal, intra-renal and femoral), lung score (figure 3a). The area under the curve (AUC) for the Lung Score was 83.9% (p = 0.008), obtaining a cutoff value of 10 that showed a sensitivity of 82.6% and a specificity of 71.4%. Followed by VExUS score (AUC 80.1%; p = 0.017) and Hepatic vein Doppler (AUC 79.5%; p = 0.020).

The ROC curve was calculated for predicting the probability of renal failure during hospitalization without any significant results (figure 3b).

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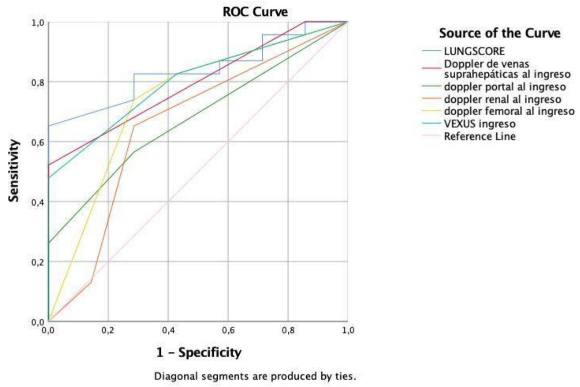
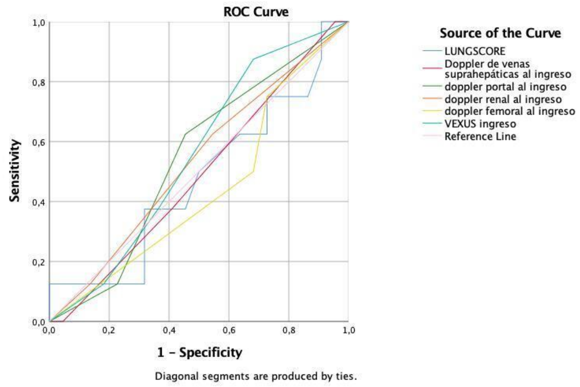


(**a**)



(**b**)

Figure 3. Receiver operating characteristic (ROC) curve for predicting intermediate and high probability of Pulmonary Hypertension (PH) according to Lung Score (area under the curve - AUC - 83.9%; p = 0.008), VExUS score (AUC 80.1%; p = 0.017) and Hepatic vein Doppler (AUC 79.5%; p = 0.020); (**b**) receiver operating characteristic (ROC) curve for predicting the probability of creatinine worsening during hospitalization, without any significant results (AUC between 47.4% to 55.4%).

4. Discussion

The importance of venous congestion lies in its correlation with adverse events (10). Traditionally measured with the IVC, its use is endorsed by the European heart failure guidelines (1), however of restricted use due to its numerous limitations (14). Easy to access and reliable diagnostic methods of venous congestion which can accurately guide management in AHF are vital.

Beaubien-Souligny proposes a venous congestion quantification system called the VExUS protocol through hepatic, portal and intra-renal venous Doppler assessment, which seems to be useful in the postoperative cardiac surgery patient to predict renal failure (13,21). However, in acute heart failure, there is an underestimation of creatinine at the beginning of the disease due to hemodilution, so it is not a parameter we must base therapeutic changes (1). As seen in our cohort, there was a worsening in the creatinine levels at discharge, because of hemoconcentration due to the therapy, as well as weight loss and improve in the NYHA status.

In our study, we showed that several ultrasound parameters might be useful for monitoring the intrahospital course of the disease, such as the Lung score, VExUS score and hepatic, portal, intra-renal vein Doppler flow. However, unexpectedly, the dynamics of the VExUS score on admission and discharge remained the same or even disimproved. This raises the question whether the VExUS might be a good parameter, time consuming and cost-effective, to guide the adjustment of the therapy in AHF patients.

In previous studies, left heart failure is more efficiently diagnosed with the Lung score than chest X-ray and NT-proBNP (2); comparable to our findings, Lung score and VExUS score correlated very good with an intermediate and high probability of PH, pointing out that could be a first-line diagnostic tool alternative to advanced echocardiographic studies. Therefore, this group believes, that one of the potential roles of the VExUS protocol is aiding in the diagnosis of PH in AHF, since its diagnosis is complicated and many times we are unable to acquire all the parameters to calculate its probability (3).

Moreover, some exams included in the VExUS protocol, showed in isolation a good correlation with the probability of PH, such as the hepatic vein or in the monitoring of the evolution, such as the portal vein, suggesting being reasonable to adopt different flexible approaches. Additionally, the hepatic veins in patients with rhythm disorders or with intracardiac devices might be difficult to interpret (24). Therefore selecting patients with a portal determination could be sufficient, as supported by other studies (16–19). Regarding, intra-renal Doppler, some observational studies pointed out that severe congestion (monophasic pattern) was associated with an adverse prognosis in AHF (25,26). However, obtaining adequate images can be challenging, especially in the tachypneic patient and has not been studied in patients with structural abnormalities or chronic kidney disease (27).

The femoral vein is an attractive and rapid method for the detection of PH and right ventricular failure as proposed by Denault (32) through the assessment of the pulsatility, retrograde flow and the absence of respiratory fasicity (14,32); but in our study it seems an insufficient method to be used in isolation. This could be in part owing that our patients could not be positioned in supine ulna (orthopnea), as described in previous studies (14,32). As in our study, we found that the femoral vein could have a similar role as the IVC.

To our best of our knowledge, our study is the first to assess the evolution of the different multi-organ venous Doppler flows in patients with AHF.

We acknowledge some study limitations. First, a small sample of AHF patients, the expert sonographer performed all ultrasound scans on patients consecutively admitted to our department, which limits the generalizability of our results, and ought to be validated in future studies. Second, our study did not analyze the dynamic changes according to the therapy received in different stages, and the patient outcomes, which would have a higher clinical impact. Therefore, for this purpose, we suggest the study can be considered hypothesis generating.

Another limitation is the poor performance of VExUS (and any other ultrasound parameters) in predicting the renal function deterioration, therefore the results from this study provides insights on the need to search other meaningful outcomes, and an opportunity to further investigate the role of ultrasound in this prevalent disease.

5. Conclusions

In conclusion, our study suggests that performing serial multiorgan Point-of-Care ultrasound can help us to better identify high and intermediate probability of Pulmonary Hypertension patients with Acute Heart Failure. Currently proposed multi-organ, venous Doppler scanning protocols, such as the VExUS score, should be further studied in different populations before expanding its use.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Hospital Universitario Puerta de Hierro (protocol code MIR/HPDH_2021_02 and date of approval July 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The authors confirm that the data supporting the findings of this study are available from the corresponding author, upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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