UNIVERSITY OF MEDICINE AND PHARMACY „CAROL DAVILA”, BUCHAREST

DOCTORAL SCHOOL

DOMAIN MEDICINE

IMAGING ASSESSMENT OF CONGESTION IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE

PhD THESIS SUMMARY

Doctoral supervisior:

PROF. ILIEȘIU ADRIANA-MIHAELA

Doctoral student:

GRIGORE MIHAI

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BACKGROUND

Heart failure (HF) is a condition with significant impact on healthcare systems, representing the leading cause of hospitalization across Europe and North America [1]. As a complex clinical syndrome, HF results from structural or functional cardiac abnormalities that lead to elevated intracardiac pressures and/or inadequate cardiac output [2]. According to the 2021 ESC guidelines, HF is currently classified into heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF), and preserved ejection fraction (HFpEF), each defined by specific diagnostic criteria [2]. In addition, right-sided HF, a frequently underdiagnosed phenotype, is characterized by systemic venous congestion and right heart chamber dysfunction [2].

Congestion plays a central role in the pathophysiology and clinical presentation of HF, accounting for over 90% of hospital admissions among HF patients [4–7]. Traditionally classified as left-, right-, or global congestion based on clinical signs, modern approaches propose a more nuanced categorization that considers location (pulmonary vs. systemic), compartmental involvement (intravascular, interstitial, third space), and the presence or absence of clinical signs [3]. Subclinical congestion—often undetectable on physical examination—has emerged as an important negative prognostic factor, associated with increased risk of rehospitalization and mortality [9–12].

The mechanisms of congestion are multifactorial and include increased intracardiac pressures due to impaired myocardial contractility, neurohormonal activation, endothelial inflammation, and oxidative stress [4,5]. Two distinct congestion phenotypes have been proposed: intravascular congestion (associated with elevated NT-proBNP levels) and tissue congestion (associated with markers such as CA-125, bio-ADM, or soluble CD146) [5]. These types may coexist or evolve independently, with potentially distinct therapeutic responses.

From an anatomical and pathophysiological perspective, congestion has been classified into four forms: intravascular pulmonary, tissue pulmonary, intravascular systemic, and tissue systemic [13]. Initially, congestion develops in the intravascular compartment, where rapid volume accumulation increases capillary pressures and promotes fluid transudation into the interstitial space [14]. When lymphatic compensatory mechanisms are overwhelmed, tissue congestion ensues, and in more advanced stages, fluid may accumulate in serous cavities (third space) [3].

Pulmonary congestion results from elevated left atrial pressure and impaired pulmonary venous drainage, leading to interstitial and alveolar fluid accumulation, clinically manifesting as dyspnea or acute pulmonary edema [3,15]. Systemic congestion is driven by elevated right atrial and central venous pressures, facilitating peripheral edema, ascites, and hepatomegaly [3]. In all these forms, venous capacitance and volume redistribution play a key role in the dynamics of congestion, which cannot always be accurately assessed using isolated filling pressures [15].

Despite substantial advances in medical technology, physical examination remains a fundamental tool in the assessment of HF patients. However, the sensitivity and specificity of clinical signs for detecting congestion are limited, especially in subclinical forms [9,16]. Symptoms such as dyspnea, orthopnea, or peripheral edema are common but not specific to HF and may also occur in conditions like obesity or chronic venous insufficiency [5,16]. Among all clinical signs, jugular venous distension and a third heart sound (S3) have proven most useful in evaluating elevated filling pressures and risk stratification [16]. The concept of hemodynamic congestion—referring to patients with elevated left ventricular filling pressures but no overt clinical signs—is increasingly emphasized in contemporary guidelines [8,16].

In addition to clinical evaluation, biomarkers play a central role in the diagnosis and prognosis of HF. Natriuretic peptides, particularly NT-proBNP, are the most widely used in practice [2,9]. These peptides rise in response to elevated intracardiac pressures and are included in diagnostic criteria for HF, although they have limited sensitivity and specificity. Elevated levels can be seen in other conditions (e.g., sepsis, chronic kidney disease), and concentrations may be influenced by age, obesity, atrial fibrillation, and renal dysfunction [13,18]. Furthermore, natriuretic peptides primarily reflect left ventricular involvement, with low sensitivity for right-sided HF [13,17].

Although NT-proBNP correlates with filling pressures and clinical outcomes, its dynamic decrease during hospitalization does not always parallel actual decongestion, particularly in acute settings [14]. Accordingly, current ESC guidelines do not recommend routine NT-proBNP monitoring for therapy guidance [2]. Nonetheless, a reduction greater than 30% during hospitalization has been proposed as a clinically relevant threshold in certain studies [13].

Recently, novel biomarkers of congestion have been explored, including CA-125, bioADM, CD146, and sST2, which reflect mechanical stress, inflammation, or endothelial dysfunction [13]. These may help differentiate between intravascular and tissue congestion

phenotypes and potentially offer greater specificity than natriuretic peptides. However, their routine clinical use remains limited and requires further validation.

Echocardiography plays a pivotal role in the assessment of HF patients, assisting in the identification of etiology, functional classification, and evaluation of congestion [14,19]. Although the underlying pathophysiological mechanisms may differ depending on left ventricular ejection fraction (LVEF), congestion may occur regardless of LVEF [20]. In HFpEF, congestion typically arises from diastolic dysfunction and impaired atrial and vascular compliance [21], while in HFrEF, it is driven by systolic dysfunction and neurohormonal activation [23].

Non-invasive estimation of left ventricular filling pressures can be achieved via echocardiography, using parameters such as transmitral E/A waves, E/e' ratio, left atrial volume, or tricuspid regurgitation velocity [9,23,24]. An E/e' ratio ≥14 is associated with elevated filling pressures and increased risk of rehospitalization in acute decompensated HF [25]. Additionally, left atrial function assessed by speckle-tracking, especially reservoir strain, provides valuable insight into diastolic dysfunction and filling pressures and carries prognostic relevance [26–28].

The right heart plays a critical role in maintaining hemodynamic stability. Assessment of right ventricular (RV) function using TAPSE, FAC, tricuspid regurgitation, and pulmonary artery systolic pressure (PAPs) is important. The TAPSE/PAPs ratio has been proposed as a non-invasive marker of RV–pulmonary artery coupling and a predictor of in-hospital mortality in acute HF [31].

The inferior vena cava (IVC) is commonly used to estimate central venous pressure and congestion. While its size and respiratory collapsibility may reflect intravascular volume status, correlation with invasive measurements is modest [29,31]. Studies indicate that patients with a dilated IVC may exhibit subclinical congestion and worse prognosis [6,9,32].

The Venous Excess Ultrasound Score (VExUS) integrates Doppler evaluation of the IVC, hepatic veins, portal vein, and intrarenal veins, correlating well with right atrial pressure and providing a systemic view of venous congestion [33,34]. Simplified variants such as mVExUS enhance clinical applicability [35]. Recent literature highlights the role of serial imaging assessments, particularly venous ultrasonography, in identifying subclinical congestion and guiding treatment in patients with acute decompensated heart failure [40].

Doppler assessment of hepatic and portal veins reflects elevated central venous pressure. Reversed systolic flow in hepatic veins or excessive portal pulsatility may indicate severe congestion and have been associated with poor outcomes [36,37,46]. Similarly,

discontinuous or monophasic renal venous flow correlates with impaired renal function and increased mortality and is a key component of the VExUS score [38,39].

HYPOTHESIS AND GENERAL OBJECTIVES

HYPOTHESIS

Subclinical congestion is highly prevalent at discharge in patients hospitalized for acute decompensated heart failure (ADHF). A multimodal imaging assessment—comprising echocardiography, systemic venous ultrasound evaluation, and lung ultrasound—can more accurately identify incomplete decongestion, which may have prognostic value for in-hospital and mid-term outcomes (mortality and rehospitalization).

GENERAL OBJECTIVES

1. To evaluate clinical, biological, and imaging changes from admission to discharge in patients with ADHF undergoing diuretic therapy.
2. To determine the prevalence of residual (subclinical) congestion at discharge using noninvasive imaging methods (echocardiography, VExUS score).
3. To correlate imaging-based congestion parameters with biological markers (NT-proBNP), clinical signs, and short- and mid-term patient outcomes.
4. To assess the predictive value of clinical and subclinical congestion for 3-month rehospitalization and 6-month mortality.
5. To describe the clinical, biological, and imaging profile of patients with effective versus incomplete decongestion.

GENERAL METHODOLOGY OF THE RESEARCH

STUDY DESIGN

This doctoral thesis comprises three prospective, observational studies conducted in the Cardiology Department of the “Prof. Dr. Th. Burghele” Clinical Hospital in Bucharest, between November 1, 2022, and November 1, 2023. All projects evaluated the same cohort of patients at two time points: admission and discharge, following heart failure treatment.

STUDY POPULATION

Consecutive patients hospitalized with a diagnosis of acute decompensated heart failure (ADHF) were included, according to the 2021 ESC Guidelines for the diagnosis and treatment of heart failure. All patients had elevated NT-proBNP levels (≥ 300 pg/mL). After applying the inclusion and exclusion criteria, a total of 111 patients were enrolled.

Inclusion criteria:

• Age > 18 years

• ADHF (acute decompensation of chronic heart failure), regardless of left ventricular ejection fraction (LVEF)

• NT-proBNP ≥ 300 pg/mL

• Continuous hospitalization > 24 hours

• Availability of clinical, biological, and imaging evaluations at both admission and discharge

Exclusion criteria:

• Cardiogenic shock

• Acute coronary syndromes, acute myocarditis, congenital heart disease

• De novo acute heart failure

• Dyspnea of exclusive pulmonary origin (e.g., GOLD IV COPD, pulmonary fibrosis, lung cancer, pneumonia)

• Severe hepatic disease (Child-Pugh C)

• Advanced chronic kidney disease (eGFR < 15 mL/min/1.73 m²) or patients on dialysis

• Severe anemia (Hb < 7 g/dL)

• Advanced neoplastic disease with life expectancy < 1 year

• Septic shock

• Pregnancy

• Technical impossibility to perform imaging investigations

ASSESSMENTS

• *Clinical assessment:* signs and symptoms of congestion (e.g., dyspnea, peripheral edema), weight at admission and discharge

• *Biological assessment:* NT-proBNP, hemoglobin, renal function (creatinine, estimated creatinine clearance)

• *Imaging assessment:*

- Echocardiography (left and right ventricular systolic function, assessment of LV filling pressures, and valvular disease)
- Lung ultrasound (presence of pulmonary interstitial syndrome and pleural effusion)
- Venous ultrasonographic evaluation of systemic congestion (inferior vena cava, jugular, suprahepatic, portal, and renal veins), including calculation of the VExUS score

• *Treatment:* intravenous diuretics administered within the first 48 hours of

hospitalization

• *Follow-up:* all-cause mortality at 6 months and rehospitalization for ADHF at 3 months

ETHICAL CONSIDERATIONS

This research included three observational studies that did not interfere with clinical decision-making regarding diagnosis or therapy in patients with ADHF. Therapeutic management was exclusively determined by the attending physicians, in line with current clinical guidelines. The studies were approved by the Ethics Committee of the "Prof. Dr. Th. Burghele" Clinical Hospital, and all patients provided written informed consent prior to enrollment. The research was conducted in accordance with the principles of the Declaration of Helsinki (1964, revised), national regulations on good clinical practice, and applicable data protection laws (GDPR).

Patient data were securely stored electronically on hospital computers and in physical format in access-restricted areas. All data were anonymized using unique identification codes without including direct personal identifiers, except for age and gender.

Study I: Clinical and Biological Assessment of Congestion and Decongestion in Patients with Acute Decompensated Heart Failure

This was a prospective, observational study including 111 consecutively hospitalized patients diagnosed with acute decompensated heart failure (ADHF). The main objective was the comparative assessment of clinical and biological markers of congestion at admission and discharge, in relation to diuretic response and associated comorbidities. Clinical congestion was defined based on dyspnea and peripheral edema scores, and patients were classified at discharge into two groups: decongested (Group A) and with persistent clinical congestion (Group B).

The results showed that patients in Group B had a significantly higher prevalence of chronic kidney disease and anemia, along with more advanced NYHA functional classes. Despite receiving higher mean doses of intravenous furosemide during hospitalization, these patients exhibited a suboptimal clinical response, suggesting incomplete decongestion potentially due to diuretic resistance. Mean weight loss did not differ significantly between groups, and the lack of correlation between weight reduction and NT-proBNP decrease highlights the limitations of body weight as a stand-alone decongestion marker.

NT-proBNP proved to be the most sensitive biomarker for evaluating treatment response, with a significantly greater reduction in the decongested group. The proportion of patients achieving a >30% decrease was also significantly higher in Group A, supporting the clinical utility of this threshold [14]. However, NT-proBNP reduction did not correlate with weight loss, confirming recent literature observations regarding its inter-individual variability [41].

Renal parameters (serum creatinine and estimated creatinine clearance) were significantly more impaired in Group B at both admission and discharge, although worsening renal function during hospitalization did not reach statistical significance. This supports the hypothesis that pre-existing renal dysfunction impairs diuretic response and predisposes to residual congestion [42]. Clinically relevant hyponatremia was not observed in this cohort, and the statistical differences in serum sodium lacked clinical significance in the absence of values <135 mmol/L [43].

This study highlights the importance of a multimodal approach for decongestion assessment in ADHF, combining clinical, biological, and therapeutic data. NT-proBNP was superior to weight loss as an objective marker of decongestion, and major comorbidities such as chronic kidney disease and anemia were associated with suboptimal therapeutic response.

These findings support the need for closer discharge monitoring in patients with residual congestion to reduce the risk of rehospitalization.

Conclusions of Study I

This study evaluated the clinical and biological changes associated with diuretic therapy in patients hospitalized for ADHF, stratifying them based on congestion status at discharge.

A ≥30% reduction in NT-proBNP was significantly associated with the absence of clinical congestion, confirming the value of this biomarker in assessing therapeutic response. In contrast, weight loss did not distinguish between groups and was not correlated with NT-proBNP changes, limiting its utility as a solitary marker of decongestion.

Persistent congestion was associated with higher levels of NT-proBNP, serum creatinine, and potassium, and with a higher prevalence of anemia and chronic kidney disease, suggesting a more severe clinical profile and poorer therapeutic response.

The strengths of this study include its prospective design, admission–discharge comparative evaluation, and integration of clinical, biological, and therapeutic data. However, its single-center nature and relatively small sample size may limit the generalizability of the findings.

A relevant direction for future research is the use of urinary sodium (UNa) as an early marker of diuretic response, with potential for timely adjustment of therapy in ADHF.

Study II: Ultrasonographic Assessment of Congestion in Acute Decompensated Heart Failure

Study II assessed systemic venous congestion in patients hospitalized with acute decompensated heart failure (ADHF) by integrating conventional echocardiography with venous Doppler evaluation, synthesized into the multiparametric VExUS score. Patients were initially classified into two clinical groups based on their congestion status at discharge: Group A (without evident clinical signs of congestion) and Group B (with persistent clinical congestion). Subsequently, they were stratified into four subgroups according to their VExUS score at discharge and its change from admission. Subgroup A1 included patients with complete clinical and imaging decongestion (VExUS score = 0). Subgroup A2 included patients without clinical signs of congestion but with residual imaging congestion (VExUS ≥ 1), corresponding to a subclinical phenotype. Subgroup B1 included patients with persistent clinical congestion but with VExUS score improvement from admission, indicating partial decongestion. Subgroup B2 included patients with both persistent clinical and imaging congestion, without VExUS score improvement, suggesting severe residual congestion.

At admission, patients in Group B showed significantly higher pulmonary artery systolic pressure (PASP), tricuspid regurgitation velocity, and right ventricular–right atrial pressure gradient (RV/RA), without significant differences in left ventricular function parameters. Moreover, inferior vena cava (IVC) diameter and the proportion of severely altered Doppler patterns in hepatic veins were higher in Group B, indicating more advanced systemic congestion. However, Doppler measurements in the portal and renal veins did not differ significantly between groups at this stage.

At discharge, dynamic echocardiographic evaluation revealed reductions in PASP, RV/RA gradient, and E/e' ratio, but only E/e' remained near the statistical significance threshold between groups. In contrast, the VExUS score showed a significantly different distribution, with patients in Group B more frequently exhibiting VExUS scores of 2 or 3. Residual systemic congestion was particularly evident through severely altered Doppler flow in renal and hepatic veins.

Comparative analysis between patients with VExUS score 0 and those with VExUS >0 revealed significant differences in IVC diameter, PASP, E/e', NT-proBNP, and hemoglobin. The VExUS score correlated positively with IVC diameter and PASP, confirming its integrative value as an imaging marker of systemic congestion. A >30% NT-

proBNP reduction was more frequent among patients with VExUS 0, but not exclusive to them, highlighting the need for dynamic interpretation of NT-proBNP in imaging context.

Subgroup analysis demonstrated that patients in subgroups A2, B1, and B2 had significantly higher NT-proBNP levels, elevated filling pressures (E/e'), and Doppler patterns indicative of persistent venous congestion. Although patients in A2 exhibited no clinical signs, the presence of imaging congestion confirmed subclinical congestion. In B1, imaging congestion improved partially, but scores remained elevated, while in B2 all congestion markers remained unchanged or worsened. These results suggest that the VExUS score can identify subgroups with distinct congestion profiles, even in the absence of clinical signs, with potential prognostic implications.

In conclusion, the VExUS score proved valuable for characterizing and monitoring systemic congestion in ADHF, complementing clinical and biological data and allowing for more refined discharge stratification. Its association with echocardiographic parameters and NT-proBNP dynamics supports its utility in detecting subclinical congestion and guiding treatment.

Conclusions of Study II

Integrated ultrasonographic assessment using the VExUS score was useful in identifying subclinical systemic congestion and complemented clinical evaluation in ADHF patients.

At admission, parameters such as tricuspid regurgitation velocity (Vmax), RV/RA gradient, and PASP were significantly higher in patients with clinical congestion. However, these same parameters did not differ significantly at discharge, suggesting they may be more relevant for assessing initial severity than for monitoring clinical improvement. When evaluated by VExUS score categories, these parameters became significant again, underscoring the importance of interpreting them in conjunction with VExUS rather than in isolation.

Lower VExUS scores at discharge were associated with higher hemoglobin and hematocrit levels, indicating effective decongestion. A positive correlation was also observed between VExUS score and IVC diameter, PASP, and RV/RA gradient. However, the relationship with IVC diameter should be interpreted cautiously, as this parameter is included in the VExUS scoring algorithm.

Although NT-proBNP levels differed across VExUS categories at discharge, the lowest NT-proBNP value did not necessarily correspond to fully decongested patients. A ≥30% NT-

proBNP reduction was more indicative of successful decongestion, supporting the need for dynamic rather than isolated interpretation of this biomarker [44].

Patients with severe VExUS-defined congestion at admission more frequently exhibited persistent clinical congestion at discharge, suggesting that initial congestion severity may negatively influence the likelihood of achieving complete decongestion during hospitalization.

Study III. Evaluation of Short- and Medium-Term Prognosis in Acute Decompensated Heart Failure

This study assessed the prognostic value of imaging-assessed congestion on mortality and risk of rehospitalization in patients with acute decompensated heart failure (ADHF), using an integrated clinical and ultrasonographic approach. A total of 111 patients were followed for 6 months after discharge, during which mortality and rehospitalization events were documented. At discharge, each patient was assigned to one of four subgroups: A1 – no clinical or imaging congestion (VExUS score = 0), A2 – no clinical signs but persistent imaging congestion (VExUS ≥1), B1 – both clinical and imaging congestion present, with improvement from admission, B2 – persistent clinical and imaging congestion, with no improvement in the VExUS score.

Significant prognostic differences were observed between these subgroups. In-hospital mortality occurred only in patients with clinical congestion, particularly in subgroup B2, where early deaths were more frequent. At medium-term follow-up, 6-month mortality was highest in subgroup B1. Notably, early mortality was also observed in subgroup A2, despite the absence of clinical signs, highlighting the prognostic impact of persistent subclinical congestion detected only via imaging. These findings emphasize the importance of systematic ultrasound-based congestion assessment and the potential clinical relevance of subclinical congestion often missed on physical examination.

The 90-day rehospitalization rate was also influenced by the congestion status at discharge. Subgroup A1, representing fully decongested patients, had the lowest rate of readmission. In contrast, subgroups B1 and A2 recorded the highest event rates, supporting the hypothesis that persistent imaging congestion—even in the absence of clinical signs—represents a significant post-discharge risk factor.

The VExUS score at discharge demonstrated good predictive value for both mortality and rehospitalization. Among the individual VExUS components, renal and hepatic vein Doppler patterns provided the strongest prognostic value. Persistent Doppler abnormalities in renal veins were associated with increased mortality and rehospitalization risk, consistent with current literature findings [45,46]. The portal and inferior vena cava (IVC) assessments also had predictive value for rehospitalization, though not for mortality.

Traditional clinical variables such as age, body weight, and blood pressure correlated modestly with mortality but did not remain independent predictors in multivariate analysis. Similarly, biological markers (NT-proBNP, creatinine) and conventional

echocardiographic parameters (LVEF, E/e', TAPSE) did not provide additional prognostic value. The VExUS score at discharge emerged as the only independent predictor of rehospitalization.

Conclusions of Study III

Subclinical congestion assessed via the VExUS score at discharge was associated with worse outcomes, including in-hospital and 6-month mortality and rehospitalization risk. Imaging-based assessment of venous congestion proved essential for identifying patients at higher risk.

The severity of systemic congestion evaluated by ultrasound using the VExUS score had clear predictive value for clinical evolution. Persistence or worsening of congestion at discharge was associated with increased adverse events, whereas the absence of imaging congestion defined a subgroup with favorable prognosis.

Among the VExUS components, renal and hepatic veins were most useful in prognostic evaluation, correlating significantly with 6-month mortality and helping to identify high-risk patients. Portal vein and IVC assessments were also helpful, particularly for predicting rehospitalization.

Clinical predictors such as age, weight status, blood pressure at admission, and heart rate were associated with mortality but did not independently predict outcomes. Biological markers, including NT-proBNP and renal function, were not independent predictors of mortality or rehospitalization. While useful for general assessment, they did not match the predictive performance of the VExUS score. Conventional echocardiographic parameters did not demonstrate prognostic value for the studied outcomes.

In contrast, systemic venous Doppler evaluation provided valuable information beyond standard echocardiography, supporting its integration into discharge assessment strategies.

CONCLUSIONS AND PERSONAL CONTRIBUTIONS

I. Conclusions of the doctoral thesis

The doctoral thesis aimed to evaluate the prognostic value of systemic venous congestion in patients with acute decompensated heart failure (ADHF), by integrating clinical, biological, and imaging assessment. The three included studies sequentially addressed the initially formulated objectives, evaluating treatment response, residual congestion status, and the predictive value for mortality and rehospitalization.

Study I demonstrated that dynamic biological markers, particularly a reduction in NT-proBNP ≥30%, provide a more accurate estimation of decongestion than weight loss. Persistent clinical congestion at discharge was associated with a more severe biological profile and comorbidities. Moreover, it was observed that patients with chronic kidney disease or anemia had a less effective diuretic response, emphasizing the need for individualized treatment. Although biologic parameters were useful, they were insufficient for fully assessing therapeutic response.

Study II confirmed that the VExUS score, when measured at discharge, reflects residual systemic congestion and correlates directly with both echocardiographic and biological parameters, especially NT-proBNP. The assessment of individual components showed that hepatic and renal veins provided valuable information in identifying patients at risk of persistent congestion. Additionally, PAPs and right ventricular function parameters proved more useful when interpreted alongside the VExUS score.

Study III showed that the VExUS score at discharge is a significant predictor of in-hospital mortality, six-month mortality, and the risk of rehospitalization. Persistence or worsening of imaging-defined congestion was associated with unfavorable clinical outcomes, and the VExUS score outperformed traditional clinical, biological, and echocardiographic parameters. Stratifying patients into four subgroups based on the association between clinical and imaging status allowed for a more nuanced interpretation of short- and medium-term risk.

The distinction between subgroups A1 (no clinical or imaging congestion) and A2 (no clinical signs but persistent imaging congestion) had the greatest prognostic value. Unlike groups B, in which the negative impact of persistent congestion was predictable, subgroup A2 demonstrated a significant early mortality despite the absence of clinical signs of congestion. This observation supports the importance of imaging evaluation at discharge

to detect subclinical congestion, with major implications for risk stratification and therapeutic decision-making.

Technical and economic considerations: The VExUS score is a non-invasive, repeatable, bedside-usable method, without major additional costs compared to standard echocardiography. Its components provide an objective assessment of congestion, overcoming the limitations of subjective clinical evaluation. In practice, the use of VExUS offers an advantage in personalized monitoring and discharge decision-making. However, full application requires Doppler-capable ultrasound equipment, appropriate training, and operator experience. Among all components, the portal vein stood out for its greater accessibility and reproducibility, with potential use in subclinical congestion screening even by less experienced operators.

Unresolved issues: The studies were conducted in a single center, with a relatively small patient sample. Mortality was assessed globally without separating cardiovascular causes. No invasive catheterization measurements were performed, and the relationship between the VExUS score and IVC diameter could not be independently assessed, since IVC size is part of the scoring algorithm. Furthermore, the impact of congestion on the initiation and titration of neurohormonal therapy was not analyzed, which is an important aspect in ADHF management. Pulmonary congestion assessment, both tissue and interstitial, via lung ultrasound, would have provided additional insight.

Future directions: Validation of the VExUS score in multicenter studies with larger cohorts and longer follow-up is necessary. The score could be integrated into discharge algorithms and personalized treatment decisions. Imaging-guided interventions (e.g., extended diuretic therapy, outpatient ultrasound monitoring) and the combination with advanced monitoring technologies (CardioMEMS, HeartLogic) should be investigated. Additional directions include standardized training for operators in evaluating VExUS components with a short learning curve, expansion of the score to include new parameters (e.g., femoral vein), and correlation with established clinical risk scores.

II. Personal contributions

1. Conducting three prospective studies on patients hospitalized with acute decompensated heart failure (ADHF), with comparative evaluation at admission and discharge using clinical, biological, and imaging parameters.
2. Implementation of the complete and standardized VExUS score in clinical practice, including its assessment at discharge for estimating residual systemic venous congestion.

3. The comparison between subgroups A1 and A2 represents a central element of the prognostic analysis. Although patients in both subgroups showed no clinical signs of congestion at discharge, the VExUS score identified persistent systemic venous congestion in subgroup A2. This difference was associated with an increased risk of early mortality, predominantly within the first 40 days, and a significantly higher 90-day readmission rate compared to subgroup A1. Thus, subclinical congestion detected through imaging demonstrated significant predictive value in the absence of clinical manifestations. These findings support the need for systematic imaging evaluation prior to discharge to identify high-risk patients not detectable by clinical examination alone.
4. A key result of the study is the lack of predictive value of left ventricular ejection fraction (LVEF) for short- and medium-term clinical outcomes. The analyses revealed no significant differences in LVEF between patients with and without adverse events (mortality or readmission), and LVEF was not an independent predictor in multivariate models. This supports the observation that, in ADHF, the degree of systemic venous congestion—rather than the severity of left ventricular systolic dysfunction—is a determinant of immediate prognosis. Direct imaging assessment of congestion, such as through the VExUS score, thus provides superior prognostic value compared to traditional echocardiographic parameters.
5. Identification of the most prognostically relevant components of the VExUS score: hepatic veins for mortality, and renal and portal veins for readmission.
6. Demonstration of the VExUS score's superiority in predicting mortality and rehospitalization compared to biological markers (NT-proBNP, creatinine) and standard echocardiographic parameters (LVEF, TAPSE).
7. Integration of NT-proBNP, hemoglobin, and hematocrit into the dynamic assessment of decongestion, in correlation with the VExUS score.
8. Proposal of the portal vein as a potential imaging screening tool for systemic congestion, due to its shorter learning curve and increased accessibility.
9. Development of research recommendations for integrating the VExUS score into discharge algorithms and its use in conjunction with implantable monitoring technologies.
10. Elaboration of a proposal for structured clinical–imaging-based patient stratification at discharge, with direct applicability to outcome prediction.

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