Original Article

Correlation Between Venous Excess Ultrasound and N-Terminal Pro-B-Type Natriuretic Peptide Levels in Patients With Acute Decompensated Heart Failure

Marcella Pereira Flores,[1,2] Alexandre Costa Souza,[1,2] Marcus Vinicius Silva Freire de Carvalho,[1,2] Rodrigo Morel Vieira de Melo,[1,2] Lívia Rodrigues Sampaio Cavalcante,[1,2] Natália Duarte Barroso,[1,2] Yuri Xavier de Carvalho,[1,2] Raisa Mainarte Franco Barros,[1,2] Clara Talita Silva Lobo,[1,2] Adriano Chaves de Almeida Filho[1,2]

Hospital São Rafael,[1] Salvador, BA – Brazil

Instituto D'Or de Pesquisa e Ensino,[2] Rio de Janeiro, RJ – Brazil

Abstract

Background: **The Venous Excess Ultrasound (VExUS) score has been proposed as an ultrasonographic method for assessing systemic venous congestion in patients with acute decompensated heart failure (ADHF). However, the relationship between VExUS and the biomarker N-terminal pro-B-type natriuretic peptide (NT-proBNP) remains unclear in literature.**

Objectives: **To evaluate the correlation between the VExUS score and serum NT-proBNP levels in patients with ADHF.**

Methods: **This retrospective observational study included 117 patients hospitalized with ADHF. Systemic venous congestion was assessed using the VExUS score, and serum NT-proBNP levels were obtained from laboratory records. Comparisons between groups were performed using the Kruskal-Wallis test, followed by Dunn's test for multiple comparisons. The strength of association between variables was analyzed using Spearman's correlation coefficient.**

Results: **NT-proBNP levels increased progressively with increasing VExUS severity, with median values of 2,890 pg/mL (VExUS 0), 4,700 pg/mL (VExUS 1), 5,430 pg/mL (VExUS 2), and 13,200 pg/mL (VExUS 3). Statistical analysis demonstrated a significant difference between groups (Kruskal-Wallis: $\chi^2 = 39.18$; $p < 0.0001$). Dunn's test indicated that patients with VExUS 3 had significantly higher NT-proBNP levels compared with the other groups ($p < 0.01$). A moderate positive correlation was observed between the variables (Spearman's coefficient $\rho = 0.567$; $p < 0.0001$).**

Conclusion: **The results indicate that the VExUS score is associated with NT-proBNP levels and may be integrated into clinical reasoning when assessing venous congestion in patients with ADHF.**

Keywords: **Heart Failure; Ultrasonics; Inpatients.**

Introduction

Heart failure (HF) is a highly prevalent condition worldwide, affecting more than 64 million people and associated with significant impact on morbidity, mortality, and healthcare costs.[1] Over the past decades, a continuous increase has been observed in both the incidence and the clinical complexity of HF, accompanied by a higher number of hospitalizations and worse outcomes across different populations.[2] Recurrent hospitalizations after episodes of decompensation are common, occurring in approximately half of patients during early follow-up, which increases the demand for specialized care.[3]

Early recognition of signs of hypervolemia is essential in the management of acute decompensated HF (ADHF), particularly in emergency departments and specialized cardiology care units. Accurate identification of congestion allows timely therapeutic interventions, reduces the risk of hemodynamic deterioration, and is associated with better clinical outcomes. In the hospital setting, systematic assessment of volume status is crucial to guide decisions related to the use of diuretics, adjustment of perfusion-guided therapies, and the need for advanced support, contributing to greater safety and effectiveness of treatment.[4,5]

Among the complementary tests used in the evaluation of ADHF, the N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) plays a relevant role in the characterization of congestion and prognostic stratification. Elevated levels of this biomarker are associated with greater clinical severity, increased risk of adverse events, and higher probability of rehospitalization, which reinforces its usefulness in monitoring patients during hospitalization and at the time of discharge.[6]

Mailing Address: Marcella Pereira Flores •
Hospital São Rafael. Avenida São Rafael, 2152. Postal code: 41253-190. São Marcos, Salvador, BA – Brazil
E-mail: marcellapflavigne@gmail.com
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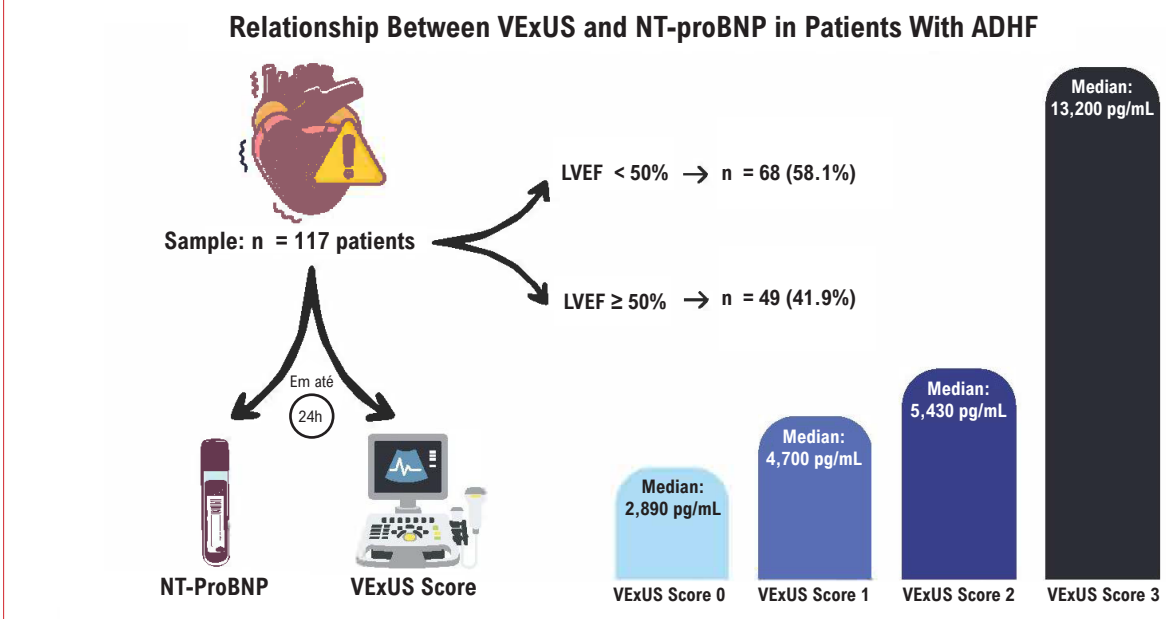
Central Illustration: Correlation Between Venous Excess Ultrasound and N-Terminal Pro-B-Type Natriuretic Peptide Levels in Patients With Acute Decompensated Heart Failure



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Correlation Between Venous Excess Ultrasound and N-Terminal Pro-B-Type Natriuretic Peptide Levels in Patients With Acute Decompensated Heart Failure. ADHF: acutely decompensated heart failure; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-B-type natriuretic peptide; VExUS: Venous Excess Ultrasound.

Point-of-care ultrasound (POCUS) has emerged as a complementary tool in the assessment of congestion in patients with ADHF, as it allows direct analysis of venous structures and provides additional information to clinical examination and laboratory markers. The Venous Excess Ultrasound (VExUS) score was proposed as a structured method to quantify systemic venous congestion, integrating findings from the inferior vena cava and patterns of hepatic, portal, and renal venous flow.[7] Recent studies have demonstrated that VExUS may assist in identifying residual congestion and contribute to therapeutic decision-making during hospitalization.[8] In addition, POCUS shows satisfactory interobserver agreement in the evaluation of venous parameters, which reinforces its usefulness in emergency departments and cardiology units.[8]

Despite advances in the use of POCUS and the growing application of the VExUS score in the assessment of systemic venous congestion, the relationship between this method and laboratory markers widely used in clinical practice, such as NT-proBNP, remains poorly explored. Understanding this potential association may contribute to improving the characterization of volume status in patients with ADHF. Therefore, the present study aimed to evaluate the correlation between the VExUS score and serum NT-proBNP levels in patients hospitalized with ADHF.

Methods

Study design and population

This was a cross-sectional observational study conducted with patients admitted with ADHF. The sample included 117 hospitalized patients, all evaluated for systemic venous congestion using the VExUS score and undergoing serum measurement of the NT-proBNP biomarker.

Ultrasound assessment and laboratory sampling were performed within the first 24 hours after admission to the emergency department of a tertiary referral hospital in the city of Salvador, state of Bahia, between November 2023 and December 2024.

Patients without complete records of the ultrasound examination required for VExUS score determination, without available NT-proBNP measurement within the established period, or with a diagnosis of advanced liver disease were excluded because of the potential interference with the venous parameters analyzed. After applying these criteria, the final sample consisted of 117 patients.

Clinical assessment and definition of variables

Clinical data were obtained through review of medical records, including age, sex, left ventricular ejection fraction

(LVEF), and hemodynamic profile at admission according to the Stevenson classification. Other clinical and laboratory variables were used to characterize the sample.

The main exposure variable was the VExUS score, considered in four categories (0, 1, 2, and 3), corresponding to the grading of systemic venous congestion. The main outcome variable was the serum NT-proBNP level (pg/mL), analyzed as a continuous variable.

Ultrasound assessment and Venous Excess Ultrasound score

Systemic venous congestion was assessed by POCUS using a Vivid™ iq Ultrasound System (GE HealthCare, USA). Different transducers were used according to the evaluation window: a sector transducer for cardiac windows and a convex transducer for evaluation of the abdominal and retroperitoneal venous system.

Examinations were performed with the patient in the supine position, with the head of the bed elevated to approximately 30°. During acquisition of venous flow signals, brief periods of apnea were attempted whenever clinically feasible to reduce respiratory artifacts and improve the definition of Doppler waveforms, particularly in smaller vessels such as the renal interlobar veins.

During evaluation of hepatic venous flow, simultaneous electrocardiographic recording was used, allowing more precise identification of the S (systolic) and D (diastolic) waves and ensuring greater uniformity in the interpretation of flow patterns.

The ultrasound windows analyzed included the inferior vena cava, hepatic venous flow, portal flow, and renal venous flow, according to the VExUS score protocol. The diameter of the inferior vena cava and the venous flow patterns in the three abdominal territories were recorded and classified according to the criteria established for the VExUS system. Based on these findings, patients were classified into VExUS scores 0, 1, 2, or 3, representing increasing degrees of systemic venous congestion.

Measurement of N-terminal pro-B-type natriuretic peptide

Serum NT-proBNP levels were obtained from laboratory tests performed during hospitalization for ADHF, according to the institutional routine of the service. Measurements were performed using standardized immunometric methods in the local laboratory.

Values were expressed in pg/mL and used in the statistical analyses without additional transformation in the original protocol.

Statistical analysis

Initially, patients were stratified into four groups according to the VExUS score (0, 1, 2, and 3). Comparison of NT-proBNP levels between groups was performed using the Kruskal-Wallis test, followed by Dunn's test for multiple pairwise comparisons.

The strength of association between the VExUS score and NT-proBNP levels was evaluated using Spearman's correlation coefficient (ρ), considering the ordinal nature of VExUS and the expected asymmetric distribution of NT-proBNP values.

To model the relationship between the VExUS score and NT-proBNP, a Gamma regression model with a logarithmic link function was used, with NT-proBNP as the dependent variable and the VExUS score as the explanatory variable. Model fit was evaluated using McFadden's pseudo R^2.

Continuous variables were assessed for distribution using the Shapiro-Wilk test. Given the asymmetry observed in most variables, results were presented as median and interquartile range. Categorical variables were expressed as absolute frequencies and proportions.

The significance level adopted was 5% ($p < 0.05$). All analyses were performed using R software, version 4.4.3.

Results

Sample characteristics

In the present study, 117 patients hospitalized with ADHF were evaluated. The median age was 79 years. Of the total, 53 patients were female (45.3%) and 64 were male (54.7%).

Regarding left ventricular function, 68 patients had LVEF $< 50\%$, whereas 49 had LVEF $\geq 50\%$. Concerning the hemodynamic profile at admission, profile B (warm and wet) was observed in 110 patients (94.0%), while profile C (cold and wet) was identified in seven patients (6.0%).

All patients included in the study had a complete ultrasound assessment required for VExUS score classification and serum NT-proBNP measurement performed within the first 24 hours after hospital admission.

Distribution of the Venous Excess Ultrasound score

Patients were stratified into four groups according to the VExUS score: VExUS 0 ($n = 21$), VExUS 1 ($n = 35$), VExUS 2 ($n = 31$), and VExUS 3 ($n = 30$). This distribution allowed comparison of serum NT-proBNP levels across different degrees of systemic venous congestion assessed by the score.

N-terminal pro-B-type natriuretic peptide levels according to the Venous Excess Ultrasound score

A progressive increase in the median NT-proBNP levels was observed as the VExUS score increased. The medians were 2,890 pg/mL in the VExUS 0 group, 4,700 pg/mL in the VExUS 1 group, 5,430 pg/mL in the VExUS 2 group, and 13,200 pg/mL in the VExUS 3 group.

Statistical analysis using the Kruskal-Wallis test demonstrated a significant difference between groups ($\chi^2 = 39.18$; $p < 0.0001$). In the multiple comparisons performed with Dunn's test, statistically significant differences were observed in comparisons involving the VExUS 3 group ($p < 0.01$).

Correlation between the Venous Excess Ultrasound score and the N-terminal pro-B-type natriuretic peptide

Correlation analysis between the VExUS score and serum NT-proBNP levels demonstrated a moderate positive correlation, with a Spearman coefficient of 0.567 ($p < 0.0001$).

In the Gamma regression model with a logarithmic link function, the VExUS score showed a β coefficient of 0.584 ($p < 0.0001$). The McFadden pseudo R^2 obtained was 0.024.

Discussion

Using POCUS in the assessment of systemic venous congestion has expanded in the context of cardiovascular diseases, particularly in ADHF. The analysis of hepatic, portal, and renal venous flow patterns, integrated with measurements of the inferior vena cava, has been recognized as an approach that complements clinical examination and provides a more comprehensive assessment of the patient's hemodynamic status.[9] The VExUS score emerged as a structured method to synthesize ultrasound findings related to venous overload, with increasing application in different clinical settings.[10] Recent reviews indicate that this tool provides a standardized and reproducible evaluation of systemic venous congestion, contributing to the understanding of the hemodynamic impact of increased venous pressures in different clinical conditions.[7,11,12]

NT-proBNP values showed progressively higher distribution across the categories of the VExUS score, as illustrated in the boxplot (Figure 1). A gradual increase in medians was observed between groups, accompanied by a greater interquartile range at higher score levels. In the VExUS 3 group, greater variability was observed, with the presence of values higher than those seen in the other categories. This graphical pattern demonstrates an upward trend in the distribution of the biomarker as the degree of systemic venous congestion estimated by VExUS increases, complementing the results obtained in the statistical analyses (Central Illustration).

Graphical analysis also demonstrated an ascending distribution of NT-proBNP values across the categories of the VExUS score. Figure 2 presents the scatter plot with the line fitted by Spearman correlation, showing a positive linear trend consistent with the observed coefficient ($\rho = 0.567$). Figure 3 illustrates the curve estimated by the Gamma regression model with a logarithmic link function, in which a progressive increase in predicted NT-proBNP values is observed across the different levels of the VExUS score.

Using Gamma regression with a logarithmic link function allowed appropriate modeling of the asymmetric distribution of NT-proBNP, characterized by wide dispersion and the presence of extreme values at higher levels of congestion. This model captured the exponential relationship between increasing VExUS score and rising biomarker levels, demonstrating a progressive intensification of NT-proBNP values as systemic venous congestion worsens. This approach complements the Spearman analysis by showing that the observed correlation, of moderate magnitude, accompanies the gradual increase in NT-proBNP levels as the VExUS score increases.[10,13,14]

This pattern suggests that the VExUS score, by quantifying the hemodynamic impact of increased venous pressures, objectively reflects the severity of volume decompensation, which is physiologically translated into the release of NT-proBNP.[15,16]

Consistent with the prognostic value of isolated congestion markers, the VExUS 3 score has been associated in other cohorts with more unfavorable clinical outcomes, including higher risk of worsening renal function, reduced natriuretic response, and resistance to diuretic therapy, in addition to worse overall prognosis. The ability of VExUS to dynamically monitor systemic venous congestion makes it potentially useful for guiding diuretic therapy, particularly in cases of cardiorenal syndrome, in which higher scores may support continuation of the diuretic strategy.[17-19]

NT-proBNP predominantly reflects myocardial stress and increased cardiac filling pressures, whereas the VExUS score expresses the hemodynamic consequences of systemic venous congestion by integrating ultrasound signs related to elevated venous pressure and the risk of organ dysfunction. Thus, both methods assess distinct and complementary pathophysiological dimensions of congestion in heart failure and may contribute to a more comprehensive and individualized clinical approach.[20-22]

Limitations of the study

This study has some limitations. It is a cross-sectional observational study conducted at a single center, with a final sample of 117 patients. The cross-sectional design limits the ability to infer causal relationships or to evaluate dynamic changes in venous congestion and NT-proBNP levels during hospitalization.

Although a strategy was adopted to reduce temporal bias, with both VExUS score assessment and NT-proBNP measurement performed within the first 24 hours after hospital admission, this time window, although short, represents a potential limitation considering the dynamic nature of ADHF and the therapeutic interventions initiated during this period.

The application of the VExUS score also has limitations inherent to its components and the clinical context in which it is used. Interpretation of hepatic vein Doppler may be influenced by the presence of significant tricuspid regurgitation and atrial fibrillation, conditions that may alter the venous flow pattern independently of the degree of congestion. Similarly, pulsatility of portal flow may be observed in young and healthy individuals, whereas its reduction may occur in parenchymal liver diseases. For this reason, patients with relevant structural liver disease were excluded from the analysis. Although integration of different venous territories in the VExUS score reduces dependence on a single parameter, these limitations should be considered when interpreting the findings.[10,22,23]

Future studies, preferably with a longitudinal design, will be necessary to evaluate the dynamic evolution of the

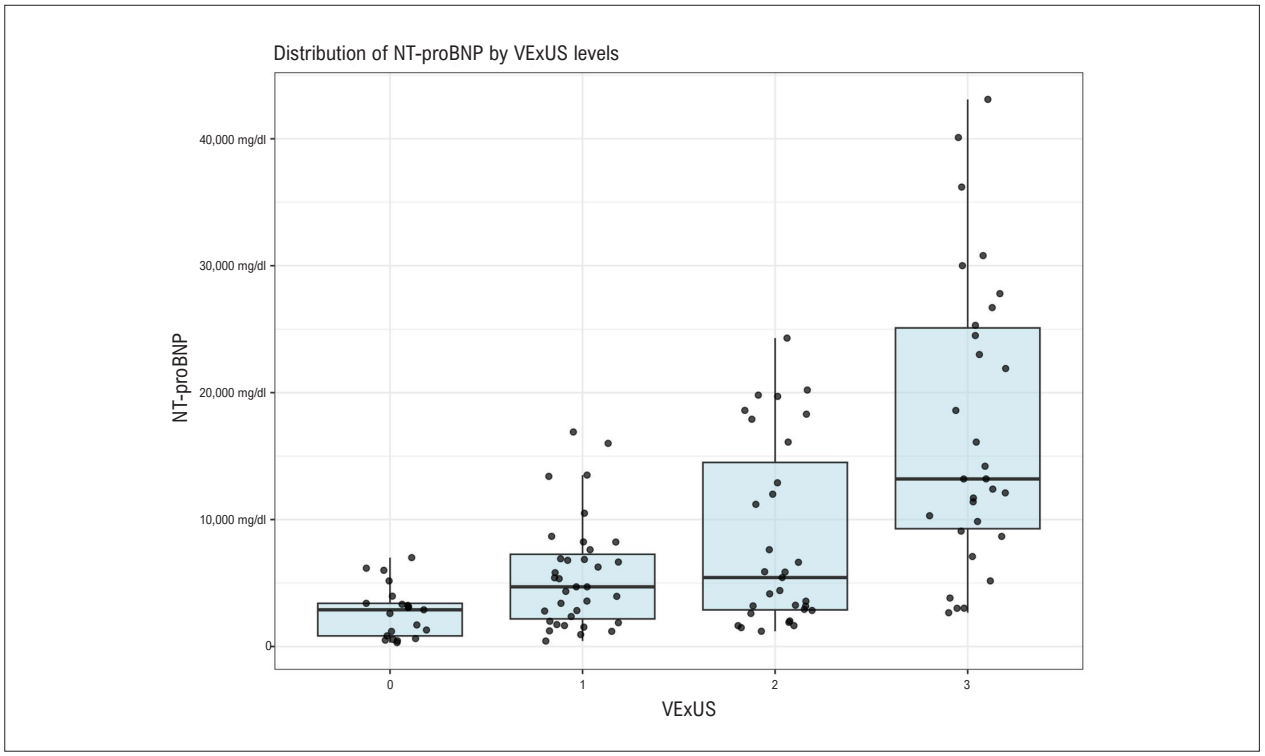

Figure 1 – *Distribution of NT-proBNP levels according to VExUS score categories. NT-proBNP: N-terminal pro-B-type natriuretic peptide; VExUS: Venous Excess Ultrasound.*

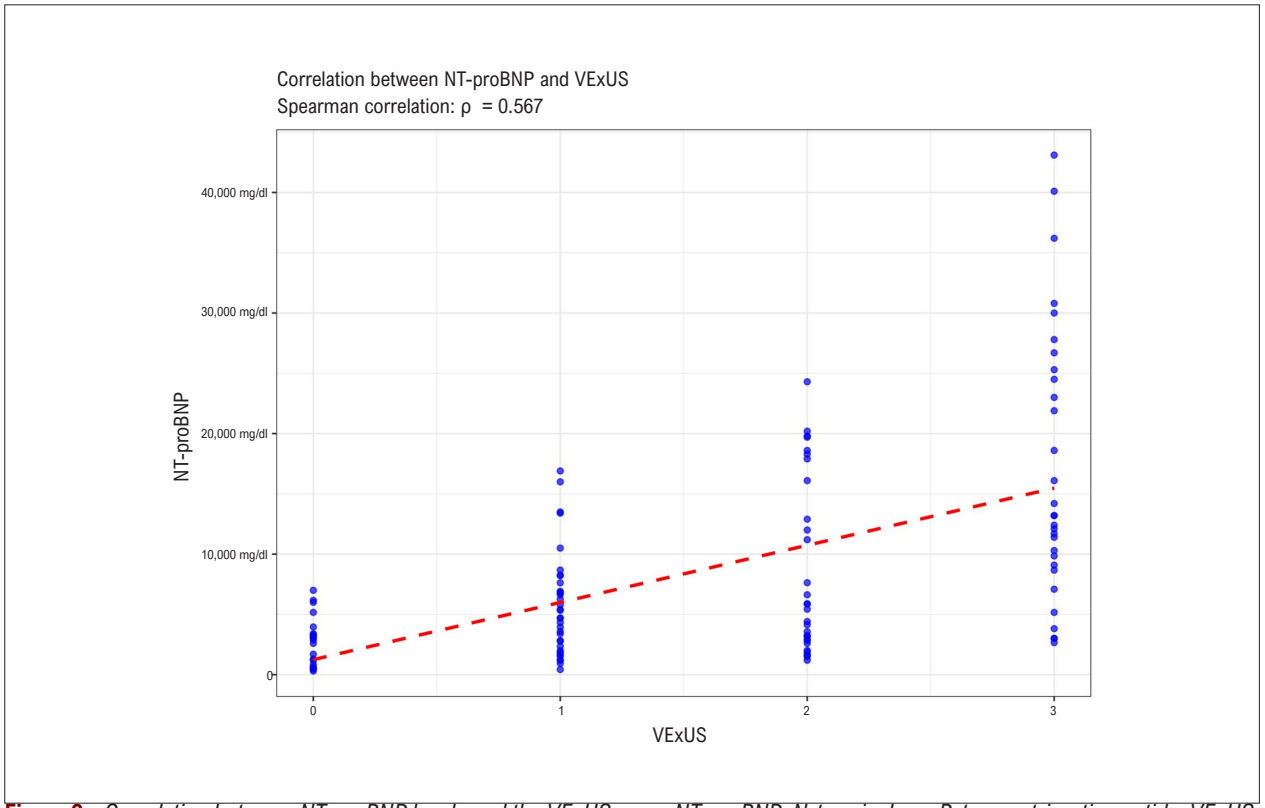

Figure 2 – *Correlation between NT-proBNP levels and the VExUS score NT-proBNP: N-terminal pro-B-type natriuretic peptide; VExUS: Venous Excess Ultrasound.*

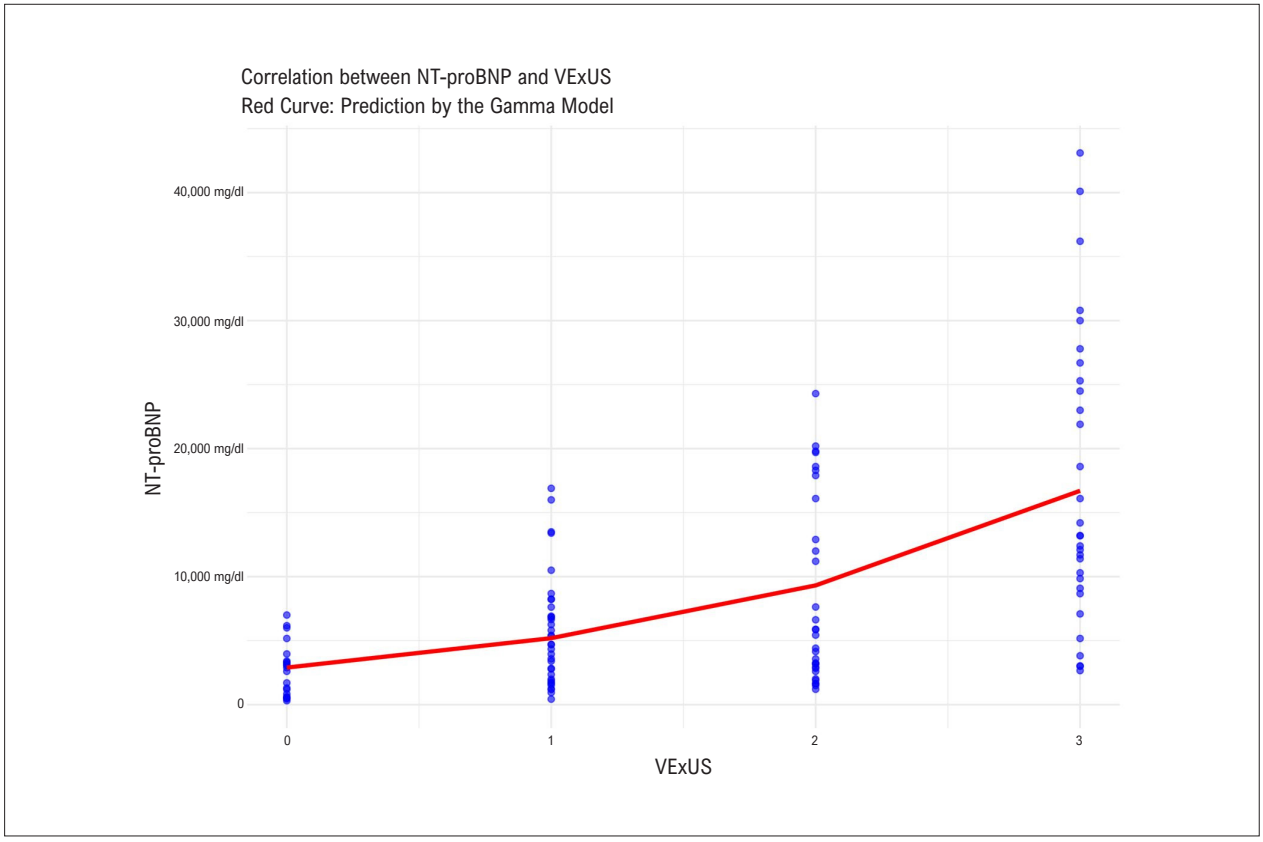

Figure 3 – *Relationship between NT-proBNP and the VExUS score estimated by a Gamma regression model. NT-proBNP: N-terminal pro-B-type natriuretic peptide; VExUS: Venous Excess Ultrasound.*

VExUS score during hospitalization and its relationship with the therapeutic strategies used. This type of approach may provide a more precise understanding of the role of systemic venous congestion assessed by VExUS in the clinical management of patients with ADHF.

Conclusion

The results of this study indicate that the VExUS score is associated with NT-proBNP levels, reinforcing its potential as a complementary tool in the evaluation of systemic venous congestion in patients with ADHF.

The integration of VExUS into clinical reasoning and biomarker interpretation may provide a more comprehensive perspective on volume status, contributing to a more individualized diagnostic and therapeutic approach.

Author Contributions

Conception and design of the research: Almeida Filho AC, Morel RV; acquisition of data: Cavalcante LRS, Carvalho YX, Barros RMF, Lobo CTS; analysis and interpretation of the data and statistical analysis: Souza AC; writing of the manuscript: Flores MP; critical revision of the manuscript for intellectual content: Carvalho MVSF, Barroso ND.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of CONEP under the protocol number 84674724.7.0000.0048.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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