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# PREDICTIVE VALUE AND ANALYSIS OF PATHOPHYSIOLOGICAL INTERRELATIONSHIPS BETWEEN MARKERS OF CARDIAC INJURY AND PARAMETERS OF COMPLEX METABOLIC DYSFUNCTION

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**Abstract.** Heart diseases are among the conditions with high incidence, morbidity, and mortality rates. Research and studies focus both on understanding the pathophysiological mechanisms underlying these conditions and on their interrelationships with associated secondary conditions, such as metabolic disorders. The analysis of biological markers is important for predictability, diagnosis, or staging. Furthermore, numerous studies are focused on potential future therapies based on this research. The aim of present study was an observational, retrospective design and was conducted on a cohort of patients with heart failure. Status was analyzed based on the absence or presence of metabolic comorbidities (diabetes mellitus, dyslipidemia, renal disease). For the correlation analysis, values of cardiovascular, inflammation, and fibrosis biomarkers were used, along with established metabolic markers for renal, hepatic, and glycemic impairment. Distribution of biomarker values was evaluated using descriptive analysis and coefficients for parametric data and non-Gaussian distributions, normality tests, or tests for comparing biological variables in patients with heart failure, systemic cardiovascular disease, and metabolic impairment in cases with associated metabolic dysfunction. The approach to these evaluations must be a multimarker that correlates pathophysiological processes. Assessment of the interdependence of the studied routine analytes has immediate practical value, and the results can be immediately applicable, being easily manageable and financially viable. The need for a multimarker approach also includes new, emerging biomarkers that bring added value and speed to clinical and laboratory evaluation.

**Kewords:** Cardiovascular Markers, Metabolic Disorders, Inflammation, Renal Markers, Liver Markers, Blood Glucose Levels.

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## INTRODUCTION

Cardiovascular diseases are still considered a major global health problem, with significant morbidity and mortality. The impact of these diseases is major on health systems around the world (Lupu, A.,et.al., 2021) A challenge for health systems is the prevalence of these diseases for elderly populations in low and middle-income countries, where the increase is significant. Global deaths due to cardiovascular diseases according to the World Health Organization include 32% of all deaths, with risk factors specific to these countries also intervening: level of organization and functioning of public health systems, access to these services (Netala, V. R.et.al., 2024).

Worldwide, prevention and monitoring programs have further improved mortality rates. For evaluation and monitoring, new biomarkers are constantly being studied in addition to the already established ones (Lupu, A.,et.al., 2023) such as – brain natriuretic peptide (BNP), N-terminal prohormone of BNP (NT-proBNP), troponins, cardiac enzymes creatine kinase (CK) and creatine kinase (CK) enzyme (MB), reactive protein (CK) enzyme-myodynamic (CRP). (Blanda, V., et.al., 2020).

New emerging biomarkers are being evaluated and researched to improve laboratory and clinical evaluation for patients with cardiovascular diseases (Lupu, A., et.al., 2026). In the case of heart failure, numerous biomarkers have been studied (Lupu, S. A.,et.al., 2025), promising candidates for diagnostic, prognostic or staging value.

The present study evaluates established analytes in the evaluation of cardiovascular and metabolic dysfunctions and adds analytical considerations and performance regarding interrelationships in laboratory analyses. The design is a retrospective cross-sectional study for established markers. For multimarker evaluation, there are significant studies and research for the introduction of new biomarkers.

The tests for NT-proBNP and BNP have specificity for differential diagnosis in heart failure and can be considered clinically comparable tests. Diagnostic correlation and concordance are relatively low, especially in patients with chronic kidney disease (Farnsworth, C.W., et., al., 2018). It is important to note that patients can be stratified by age, according to the ranges of values according to it. In patients with heart failure, chronic kidney disease can vary the values of natriuretic peptides, NT-proBNP more than in the case of BNP (Farnsworth, C.W., et., al., 2018). There are studies that have demonstrated the usefulness of BNP and NT-proBNP determinations in diagnosis and monitoring. Elevated BNP and NT-proBNP values correlate with the severity of heart failure, assessed according to the functional classification of the New York Heart Association (NYHA), and are also associated with an unfavorable prognosis. It can be influenced in the case of other metabolic diseases. BNP values correlate poorly with the glomerular filtration factor in renal function. (McCullough, P.A., et al., 2003).

At the plasma level, lipoprotein spheres are found that contain cholesterol, phospholipids, and proteins in their internal structure, along with triglycerides in addition to cholesterol. The role of these lipoprotein particles is to transport triglycerides and cholesterol. Classification according to their structure and size:

-Very low-density lipoproteins – chylomicrons – VLDL
-Low-density lipoproteins – LDL
-High-density lipoproteins – HDL

These lipoproteins are known to have various effects related to the risk of coronary disease (Gotto A.M., 1988).

The role of HDL is significant in lipid metabolism, acting as a cardioprotective mechanism (NIH Publication). It consists of transporting cholesterol from peripheral tissues to the liver. Due to this cardioprotective role, low plasma HDL values are considered an indicator of increased cardiovascular risk (Williams P. et al., 1979; Cleeman J.I. et al., 2001).

C-reactive protein (CRP) is synthesized in the liver. It is a highly sensitive acute-phase reactant that increases following tissue injury or inflammation. Elevated values occur after myocardial infarction, inflammation, stress, infections, and even in cancer (Grange J. et al., 1997).

## MATERIALS AND METHODS

The study was conducted on a group of patients in whom clinical and biological parameters with cardiovascular, inflammatory, metabolic, renal, and hepatic relevance were analyzed. The data were statistically processed using IBM SPSS Statistics 25 software, focusing both on the descriptive characteristics of the variables and on the relationships between the main biomarkers analyzed.

To evaluate the relationships between quantitative variables, the **Spearman correlation** coefficient was used, considering the biological nature of the data and the possibility of non-normal distributions. The interpretation of correlations took into account the direction and strength of the Spearman rho coefficient, the p-value, and the number of valid cases included in each analysis. A positive coefficient value indicated a direct relationship, while a negative value indicated an inverse relationship. The threshold for statistical significance was set at **p < 0.05, w**hile **p-values < 0.01** were considered highly statistically significant.

Additionally, the AST/ALT ratio was calculated by dividing the AST value by the ALT value for cases in which both parameters were available. For this derived variable, the mean, median, standard deviation, minimum and maximum values, range, skewness, and kurtosis were analyzed. The distribution of the AST/ALT ratio was also evaluated using a Stem-and-Leaf plot in order to identify extreme values.

The statistical study included analyses performed on patients with heart failure, focusing on the correlations between these parameters and their pathophysiological interdependencies, including their predictive value.

**1. The Myocardial Stress – Inflammation – Remodeling Axis.**

**Correlations**

| | | | BNP | NT-proBNP | PCR |
|---|---|---|---|---|---|
| Spearman's rho | BNP | Correlation Coefficient | 1,000 | . | ,350 |
| | | Sig. (2-tailed) | . | . | ,111 |
| | | N | 26 | 1 | 22 |
| | NT-proBNP | Correlation Coefficient | . | 1,000 | ,086 |
| | | Sig. (2-tailed) | . | . | ,872 |
| | | N | 1 | 7 | 6 |
| | PCR | Correlation Coefficient | ,350 | ,086 | 1,000 |
| | | Sig. (2-tailed) | ,111 | ,872 | . |
| | | N | 22 | 6 | 40 |

**Spearman correlation analysis** did not reveal statistically significant associations between natriuretic markers and CRP. BNP showed a weak to moderate positive correlation with CRP, without reaching the threshold for statistical significance (rho = 0.350; p = 0.111; N = 22), suggesting only a possible trend toward an association between cardiac stress and inflammatory status. NT-proBNP was not significantly correlated with CRP (rho = 0.086; p = 0.872; N = 6), the coefficient indicating a very weak positive association. The correlation between BNP and NT-proBNP could not be validly assessed because only one case had simultaneously available values for both markers.

**2. The Cardio-Renal Axis.**

**Correlations**

| Spearman's rho | | Creatinina | Ureea |
|---|---|---|---|
| Creatinina | Correlation Coefficient | 1,000 | ,702** |
| | Sig. (2-tailed) | . | ,000 |
| | N | 49 | 49 |
| Uree | Correlation Coefficient | ,702** | 1,000 |
| | Sig. (2-tailed) | ,000 | . |
| | N | 49 | 49 |

**. Correlation is significant at the 0.01 level (2-tailed).

Creatinine showed a strong positive correlation with urea (rho = 0.702; p < 0.001; N = 49), confirming the biological relationship between these two markers of renal function.

**3. The Complex Metabolic and Atherosclerotic Axis.**

**Correlations**

| | | | Glicemie | BNP | NT-proBNP |
|---|---|---|---|---|---|
| Spearman's rho | Glicemie | Correlation Coefficient | 1,000 | ,048 | ,250 |
| | | Sig. (2-tailed) | . | ,815 | ,589 |
| | | N | 49 | 26 | 7 |
| | BNP | Correlation Coefficient | ,048 | 1,000 | . |
| | | Sig. (2-tailed) | ,815 | . | . |
| | | N | 26 | 26 | 1 |
| | NT-proBNP | Correlation Coefficient | ,250 | . | 1,000 |
| | | Sig. (2-tailed) | ,589 | . | . |
| | | N | 7 | 1 | 7 |

Spearman correlation analysis did not reveal statistically significant associations between blood glucose levels and natriuretic markers. Blood glucose did not correlate significantly with BNP (rho = 0.048; p = 0.815; N = 26), the coefficient indicating a very weak positive association. Likewise, blood glucose showed a weak positive correlation with NT-proBNP, but without statistical significance (rho = 0.250; p = 0.589; N = 7). The correlation between BNP and

NT-proBNP could not be validly assessed due to the existence of only one common case with available values for both parameters.

**Correlations**

| | | | HDL | BNP | NT-proBNP |
|---|---|---|---|---|---|
| Spearman's rho | HDL | Correlation Coefficient | 1,000 | -,245 | -,600 |
| | | Sig. (2-tailed) | . | ,379 | ,400 |
| | | N | 31 | 15 | 4 |
| | BNP | Correlation Coefficient | -,245 | 1,000 | . |
| | | Sig. (2-tailed) | ,379 | . | . |
| | | N | 15 | 26 | 1 |
| | NT-proBNP | Correlation Coefficient | -,600 | . | 1,000 |
| | | Sig. (2-tailed) | ,400 | . | . |
| | | N | 4 | 1 | 7 |

Spearman correlation analysis did not reveal statistically significant associations between blood glucose levels and natriuretic markers. Blood glucose did not correlate significantly with BNP (rho = 0.048; p = 0.815; N = 26), the coefficient indicating a very weak positive association. Likewise, blood glucose showed a weak positive correlation with NT-proBNP, but without statistical significance (rho = 0.250; p = 0.589; N = 7). The correlation between BNP and NT-proBNP could not be validly assessed due to the existence of only one common case with available values for both parameters.

## CONCLUSIONS

Metabolic dysfunction has a negative impact on the cardiovascular system. These conditions are interconnected, and the analyzed biomarkers may have potential utility in diagnostic strategies, as well as in assessing disease progression and evolution. The studied biomarkers are relevant for the clinical evaluation of patients with heart failure and metabolic disorders, and are also important in associated conditions such as diabetes mellitus and renal disease. Further studies and research into new analytes, with the aim of developing a multimarker approach, may be of significant value.

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