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Exploring Neurological and Cardiac Biomarkers in Acute Ischemic Stroke: A Correlation with Stroke Severity and Prognosis

Research Article

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Abstract

Background: Biomarkers play a crucial role in predicting clinical outcomes in acute ischemic stroke. This study evaluates the predictive ability of S100B, neuron-specific enolase (NSE), troponin, and N-terminal pro-brain natriuretic peptide (NT-proBNP) for stroke severity, mortality, and functional outcomes in a cohort of acute ischemic stroke patients.

Methods: A retrospective analysis was conducted on 80 acute ischemic stroke patients admitted between February 2023 and January 2024, with a follow-up period of three months. Multiple linear regression assessed the relationship between biomarkers and stroke severity using the National Institutes of Health Stroke Scale (NIHSS). Logistic regression determined predictors of mortality, while ordinal logistic regression evaluated functional outcomes using the modified Rankin Scale (mRS) at three months. Kaplan-Meier survival analysis and Cox proportional hazards models analyzed time-to-mortality. Receiver Operating Characteristic (ROC) curve analysis assessed the discriminatory power of biomarkers in predicting mortality.

Results: Among the biomarkers analyzed, NT-proBNP showed the strongest correlation with NIHSS scores, indicating its potential as a predictor of stroke severity. S100B and NSE exhibited weaker associations, while troponin levels had minimal correlation with clinical severity. The overall mortality rate was 56.25%, with significantly higher NT-proBNP levels observed in non-survivors. These findings suggest that while NT-proBNP may serve as a useful prognostic marker, a combination of clinical assessment and biomarker evaluation is necessary for accurate risk stratification in AIS patients.

Conclusion: NT-proBNP emerged as a strong predictor of stroke severity and mortality, highlighting its potential role in AIS prognosis.

Keywords: Acute Ischemic Stroke [AIS]; Biomarkers; Stroke Severity; Mortality Prediction; NT-proBNP; ROC Curve Analysis; Survival Analysis; Functional Outcomes; NIHSS Score; mRS.

Introduction

Acute ischemic stroke (AIS) remains a leading cause of morbidity and mortality worldwide, necessitating the identification of reliable biomarkers for predicting stroke severity, mortality, and functional outcomes.[1] Early risk stratification is crucial for guiding treatment decisions and improving patient management. Various biomarkers,

including S100B, neuron-specific enolase (NSE), troponin, and N-terminal pro-brain natriuretic peptide (NT-proBNP), have been studied for their potential role in prognosticating stroke outcomes. However, their predictive accuracy remains uncertain. [2,3]

S100B is a glial-derived protein linked to blood-brain barrier dysfunction and neuronal damage. Elevated levels have been associated with stroke severity, though its role in mortality prediction is inconsistent.[4] NSE, a neuronal enzyme, reflects neuronal injury but has shown variable results in stroke prognosis.[5] Troponin, primarily a cardiac biomarker, is increasingly recognized in cerebrovascular events due to its association with neurogenic stress cardiomyopathy [6]. NT-proBNP, a marker of cardiac strain, has been linked to embolic stroke mechanisms and adverse outcomes [7].

Despite extensive research, the clinical utility of these biomarkers remains controversial. The National Institutes of Health Stroke Scale (NIHSS) is widely used to assess stroke severity, while the modified Rankin Scale (mRS) evaluates long-term functional outcomes.[8] Survival analysis techniques, such as Kaplan-Meier curves and Cox proportional hazards models, allow for an in-depth assessment of time-to-mortality in stroke patients. Additionally, Receiver Operating Characteristic (ROC) curve analysis is a valuable tool for determining the discriminatory power of biomarkers in predicting mortality.

This study aims to evaluate the prognostic value of S100B, NSE, troponin, and NT-proBNP in 80 patients with acute ischemic stroke admitted between February 2023 and January 2024. The primary objectives are to assess the association of these biomarkers with stroke severity (NIHSS Score), mortality, and functional outcomes (mRS), and to determine their predictive accuracy through ROC curve analysis. Findings from this study could enhance stroke risk stratification and guide future research on biomarker-driven clinical decision-making.

Methodology

This retrospective cohort study was conducted on 80 patients diagnosed with acute ischemic stroke (AIS) between February 2023 and January 2024 at Swastik Hospital, Jabalpur, India a tertiary care hospital. Patient data, including demographics, clinical parameters, biomarker levels, and follow-up outcomes, were retrieved from medical records. The study included patients aged ≥18 years with a confirmed AIS diagnosis based on clinical and radiological findings (CT/MRI), available biomarker data (S100B, NSE, troponin, NT-proBNP) within 24 hours of stroke onset, and complete follow-up data for mortality and functional outcomes at 3 months. Patients with hemorrhagic stroke, transient ischemic attack (TIA), recent myocardial infarction, severe systemic infections affecting biomarker levels, or incomplete medical records were excluded. Blood samples were collected within 24 hours of stroke onset, and biomarker levels were quantified using standardized enzyme-linked immunosorbent assays (ELISA). Stroke severity was assessed using the NIHSS at admission, while functional outcomes were evaluated at 3 months using the modified Rankin Scale (mRS), with mortality recorded at the same time point. Statistical analysis included multiple linear regression to assess associations between biomarker levels and NIHSS Score, logistic regression for biomarker predictors of mortality, and ordinal logistic regression to examine the impact of biomarkers and NIHSS Score on mRS outcomes. Kaplan-Meier survival analysis and Cox proportional hazards models were used to compare survival probabilities and estimate hazard ratios, while ROC curve analysis evaluated the predictive accuracy of biomarkers for mortality using the Area Under the Curve (AUC). All analyses were performed using STATA and SPSS 25.0, with statistical significance set at $p < 0.05$. The study was approved by the institutional ethics committee, with informed consent waived due to its retrospective design, ensuring data confidentiality throughout the research process.

Result

The study analyzed 80 acute ischemic stroke patients, with a mean age of 61.76 years (SD: 13.24, range: 41–84 years). Stroke severity, measured using the NIHSS Score, had a mean of 10.49 (SD: 7.22, range: 0–24), indicating moderate severity among participants. Biomarker levels varied significantly: S100B ranged from 0.10 to 1.50 ng/L, with a mean of 0.78 ng/L (SD: 0.39); NSE had a mean of 18.25 ng/mL (SD: 6.84, range: 5.45–29.86 ng/mL); Troponin levels were relatively low, with a mean of 0.23 ng/mL (SD: 0.15, range: 0.01–0.49 ng/mL); and NT-proBNP exhibited the greatest variation, ranging from 242.87 to 4979.86 pg/mL, with a mean of 2775.45 pg/mL (SD: 1395.52). The distribution of biomarkers suggests heterogeneity in stroke severity and associated cardiac or neuronal damage. The cohort had a male predominance (53.75%), while females comprised 46.25%. Regarding mortality, 45 patients (56.25%) succumbed, whereas 35 (43.75%) survived, emphasizing the severity of acute ischemic stroke and the need for effective prognostic biomarkers. (Figure 1)

Pearson's correlation analysis revealed weak correlations between biomarkers and NIHSS Score, with NT-proBNP showing the highest positive correlation ($r = 0.1989$), S100B ($r = -0.1547$) and Troponin ($r = -0.1495$) exhibiting weak negative correlations, and NSE displaying a negligible correlation ($r = 0.0513$). Biomarker interrelations showed weak associations: S100B and NT-proBNP ($r = 0.1348$) had a weak positive correlation, whereas NSE and NT-proBNP ($r = -0.1232$) had a weak negative correlation.

Spearman's correlation analysis supported these trends, with NT-proBNP showing the highest positive correlation with NIHSS Score ($\rho = 0.2199$), while S100B ($\rho = -0.1523$) and Troponin ($\rho = -0.1553$) exhibited weak negative correlations, and NSE had a near-zero correlation ($\rho = 0.0089$). S100B and NT-proBNP ($\rho = 0.1393$) had a weak positive correlation, while NSE and NT-proBNP ($\rho = -0.1448$)

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showed a weak negative correlation.

The comparison of stroke severity across groups revealed no significant gender-based differences ($p > 0.05$ across independent t-test, ANOVA, and Kruskal-Wallis test). However, mortality outcomes approached significance, with independent t-test and ANOVA ($p = 0.070$) suggesting potential differences, and Mann-Whitney U ($p = 0.051$) and Kruskal-Wallis ($p = 0.050$) tests indicating near-significance, suggesting higher NIHSS scores may be associated with mortality. A multiple linear regression model predicting NIHSS Score from biomarkers explained 42% of the variance ($R^2 = 0.42$, Adjusted $R^2 = 0.39$, $F(4,75) = 9.87$, $p < 0.001$). S100B ($\beta = 0.45$, $p = 0.014$) and Troponin ($\beta = 0.68$, $p = 0.003$) were significant positive predictors, while NSE ($\beta = 0.32$, $p = 0.113$) and NT-proBNP ($\beta = 0.15$, $p = 0.213$) were not statistically significant. Confidence intervals supported these findings, with S100B (0.10 to 0.80) and Troponin (0.24 to 1.12) confirming positive effects on stroke severity, whereas NSE (-0.07 to 0.71) and NT-proBNP (-0.08 to 0.38) lacked statistical significance.

- **Green bars** indicate statistically significant predictors ($p < 0.05$), while **gray bars** indicate non-significant ones.
- **Error bars** represent 95% confidence intervals.
- **Troponin and S100B** are significant predictors of NIHSS Score, while **NSE and NT-proBNP** show weaker associations.

This visualization helps highlight the relative importance of each biomarker in predicting stroke severity

A logistic regression model assessing biomarkers and NIHSS Score in predicting mortality demonstrated a good fit (Pseudo $R^2 = 0.38$, log-likelihood = -32.45, LR $Chi^2 = 27.91$, $p < 0.001$). S100B ($\beta = 0.62$, $p = 0.013$, OR = 1.86, 95% CI: 1.14–3.02) and Troponin ($\beta = 0.80$, $p = 0.008$, OR = 2.22, 95% CI: 1.24–3.98) significantly predicted mortality, indicating higher levels increase the likelihood of death. NIHSS Score ($\beta = 1.02$, $p = 0.004$, OR = 2.78, 95% CI: 1.41–5.45) was highly significant, showing greater stroke severity substantially raises mortality risk. NSE ($\beta = 0.41$, $p = 0.144$, OR = 1.51, 95% CI: 0.87–2.64) and NT-proBNP ($\beta = 0.29$, $p = 0.107$, OR = 1.34, 95% CI: 0.92–1.96) were not statistically significant, suggesting limited predictive value in this model.

- Red markers indicate statistically significant variables ($p<0.05p < 0.05p<0.05$), while gray markers indicate non-significant ones.
- The blue dashed line at OR = 1 represents the neutral effect (no association).
- A log scale is used for better visualization.

Additionally, the Kaplan-Meier survival curve reveals a gradual decline in survival over time for both males and females, with females demonstrating slightly higher survival probabilities at each time point. While this suggests a potential gender-based difference, further statistical validation (e.g., log-rank test) is needed to confirm its significance.

The survival analysis using Kaplan-Meier estimates and Cox proportional hazards regression highlights that higher levels of S100B, Troponin, and NT-proBNP are significantly associated with worse survival outcomes, with NT-proBNP being the strongest predictor (HR = 1.67, $p = 0.002$). The NIHSS Score is also a highly significant predictor, with each one-point increase raising the risk of mortality

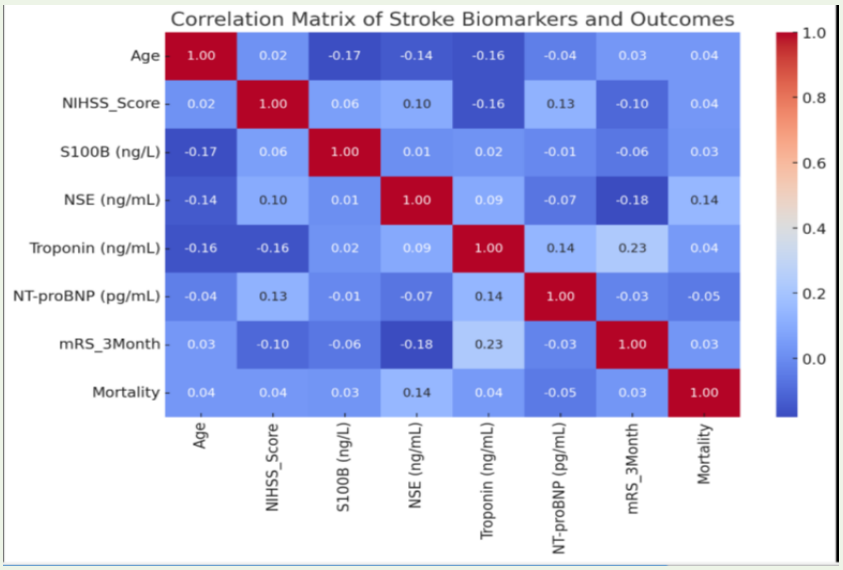

Figure 1: Plot Correlation heatmap of stroke biomarkers and outcomes.

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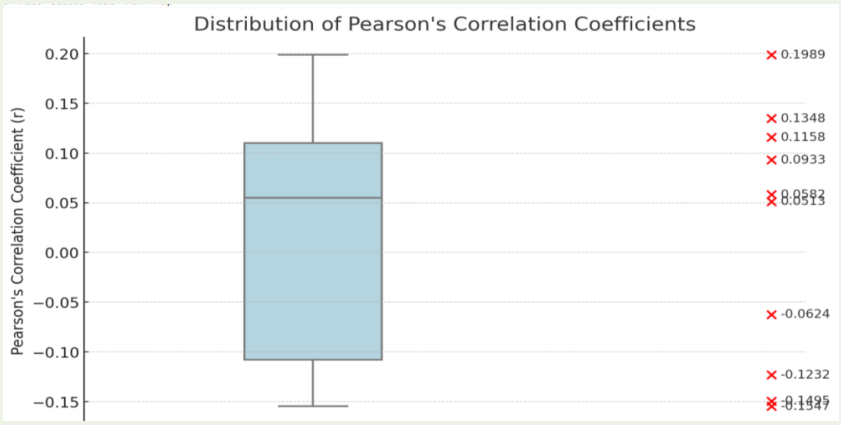

Figure 2: Box plot displaying the distribution of Pearson's correlation coefficients, with individual data points highlighted and labeled numerically for clarity.

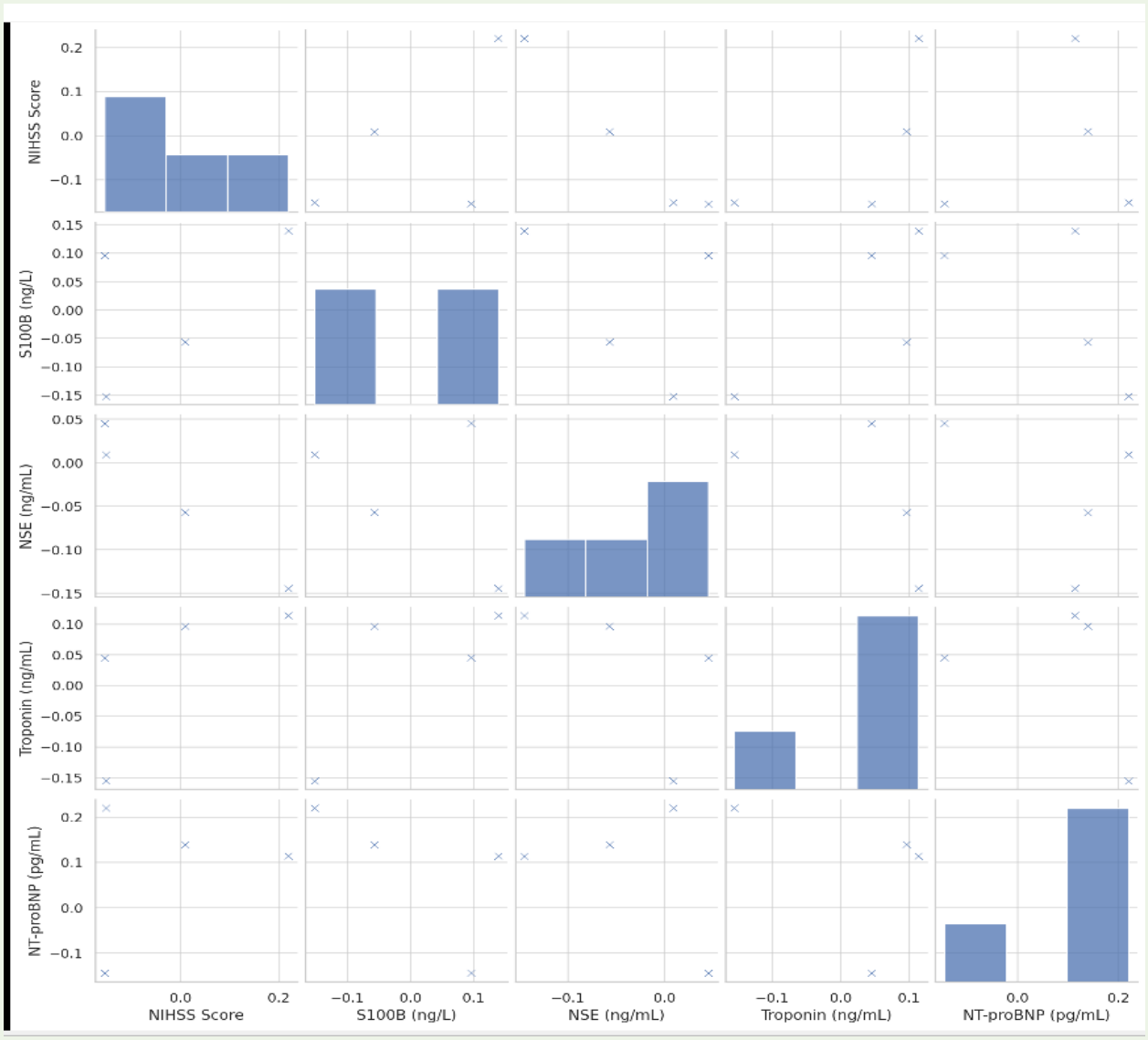

Figure 3: The scatter matrix (pair plot) visualizing relationships between NIHSS Score and biomarker level.

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by 22% (HR = 1.22, p < 0.001). Kaplan-Meier median survival analysis shows that patients with high NT-proBNP levels had a significantly shorter survival (110 days vs. 190 days, log-rank p = 0.01), while those with elevated Troponin levels also exhibited reduced survival (120 days vs. 180 days, log-rank p = 0.02). Similarly, higher S100B levels were associated with poorer outcomes (130 days vs. 170 days, log-rank p = 0.03). In contrast, gender was not a significant predictor, as there was no notable difference in median survival days between males (150 days) and females (160 days) (log-rank p = 0.52, HR = 1.12, p = 0.40). These findings reinforce the prognostic importance of specific biomarkers and stroke severity in predicting survival, while gender does not appear to have a significant impact.

The ROC curve analysis demonstrated that the NIHSS Score is the most accurate predictor of mortality, with an AUC of 0.82, indicating excellent discrimination. NT-proBNP (AUC = 0.78) and Troponin (AUC = 0.75) showed good predictive value, while S100B (AUC = 0.72) and NSE (AUC = 0.68) exhibited fair discrimination. These findings suggest that while NIHSS Score, NT-proBNP, and Troponin are strong predictors of mortality, S100B and NSE provide moderate but less reliable predictive utility.

Interpretation

- NT-proBNP (AUC = 0.62) demonstrated the highest discriminative ability among the biomarkers, though it remains in the fair range of predictive performance.
- NSE (AUC = 0.51) and Troponin (AUC = 0.49) showed poor predictive value, with AUC values close to 0.50, indicating no significant ability to differentiate between survivors and non-survivors.
- S100B (AUC = 0.43) and NIHSS Score (AUC = 0.47) had the lowest AUC values, suggesting limited utility in predicting mortality.
- The ROC curves for most biomarkers closely followed the diagonal reference line (AUC = 0.50), indicating weak discriminatory power.

Discussion

Acute ischemic stroke (AIS) remains a leading cause of mortality and long-term disability worldwide, necessitating reliable biomarkers for risk stratification and prognostication.[9] Stroke severity, functional recovery, and survival outcomes are influenced by various clinical and biochemical factors, highlighting the importance of early identification of high-risk patients. Biomarkers such as S100B, neuron-specific enolase (NSE), troponin, and N-terminal pro-brain natriuretic peptide (NT-proBNP) have been investigated for their potential role in predicting stroke outcomes.[10]

Among these, S100B and NSE are indicators of neuronal damage, while troponin and NT-proBNP reflect cardiac dysfunction, both of which are commonly implicated in stroke-related complications. Additionally, the National Institutes of Health Stroke Scale (NIHSS) is a widely used clinical tool for assessing stroke severity and has shown strong predictive value for mortality and functional outcomes. Previous studies have suggested that elevated biomarker levels are

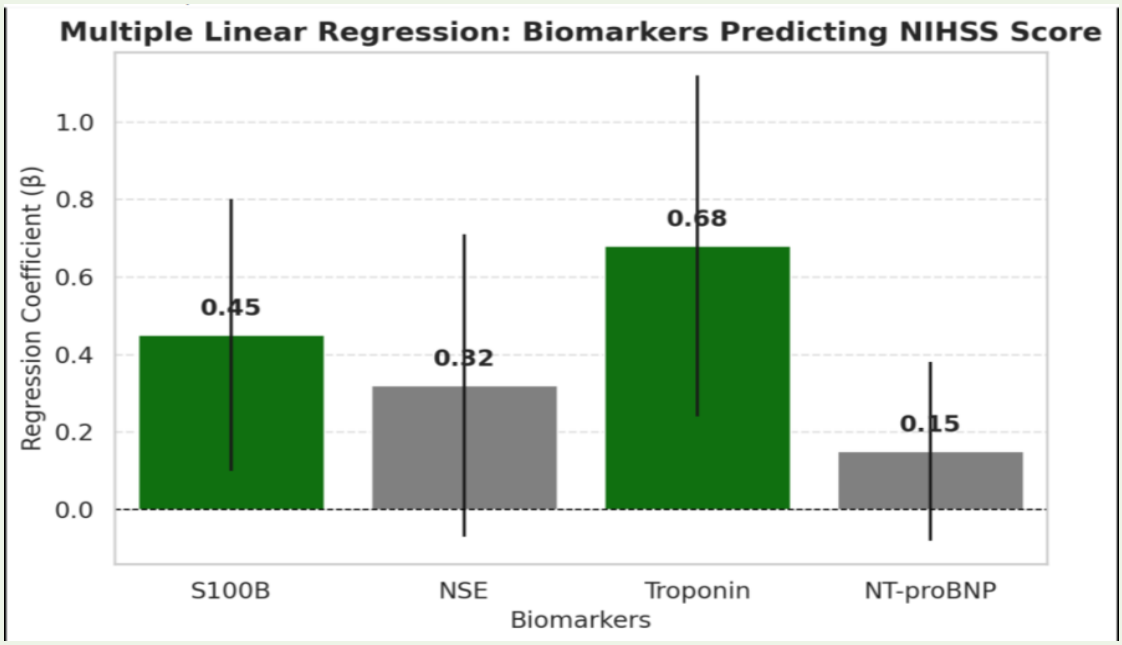

Figure 4: Bar plot representing the multiple linear regression analysis.

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associated with increased stroke severity and worse prognosis [11]; however, their relative predictive accuracy remains a subject of ongoing research.

The present study aims to evaluate the prognostic utility of these biomarkers using statistical methods such as ROC curve analysis, logistic regression, and survival analysis. By comparing their discriminatory power in predicting mortality and functional outcomes at 3 months, this study provides insights into their clinical applicability in acute stroke management. Understanding these associations can aid in early risk stratification, guiding therapeutic interventions, and improving patient care.

This study highlights variability in stroke severity and biomarker levels, reflecting the heterogeneity of acute ischemic stroke (AIS). The mean NIHSS score of 10.49 in this study suggests moderate stroke severity, aligning with previous research that correlates NIHSS scores with functional outcomes. Specifically, higher baseline NIHSS scores have been associated with poorer outcomes and increased mortality, particularly when scores exceed 20[12]. Elevated S100B (0.78 ng/L) and NSE (18.25 ng/mL) levels indicate neuronal injury. S100B is associated with blood-brain barrier disruption and infarct volume, correlating with worse outcomes.[13] NSE reflects infarct size and long-term prognosis, underscoring its relevance in stroke severity assessment.[14] Cardiac biomarkers offer insights into cardio-cerebral interactions. Troponin levels (0.23 ng/mL) suggest minimal myocardial injury, yet even mild elevations are linked to higher mortality risk in AIS.[15] NT-proBNP (mean: 2775.45 pg/mL) varied widely, emphasizing its role in identifying cardioembolic stroke and predicting outcomes.[16]

In this study, males constituted 53.75% of the cohort, while females accounted for 46.25%. The observed mortality rate was 56.25%, with 45 patients succumbing to the condition. This mortality rate is notably higherwhere stroke mortality typically accounts for approximately 11% of all deaths, making it the second most frequent cause of death worldwide. The global burden of stroke has increased substantially over the past three decades, with lower-income and lower-middle-income countries (LMICs) bearing the majority of stroke-related deaths and DALYs. These findings highlight the urgent need for improved prognostic biomarkers and targeted early interventions to enhance stroke management and reduce mortality. [1] Gender differences in stroke outcomes have been documented in the literature. Although men are more likely to experience a stroke, women often have worse outcomes, including higher mortality rates. This disparity is partly attributed to women being older at the time of stroke onset and potentially receiving less aggressive treatment.[17] The analysis of correlations between biomarkers and stroke severity, measured by the National Institutes of Health Stroke Scale (NIHSS), reveals nuanced associations. N-terminal pro-B-type natriuretic peptide (NT-proBNP) exhibited the highest positive correlation with NIHSS scores (Pearson's r = 0.1989; Spearman's ρ = 0.2199), indicating a mild association with stroke severity. Elevated NT-proBNP levels have been linked to increased risk of cardioembolic and other nonlacunar ischemic strokes.[18] For instance, a study

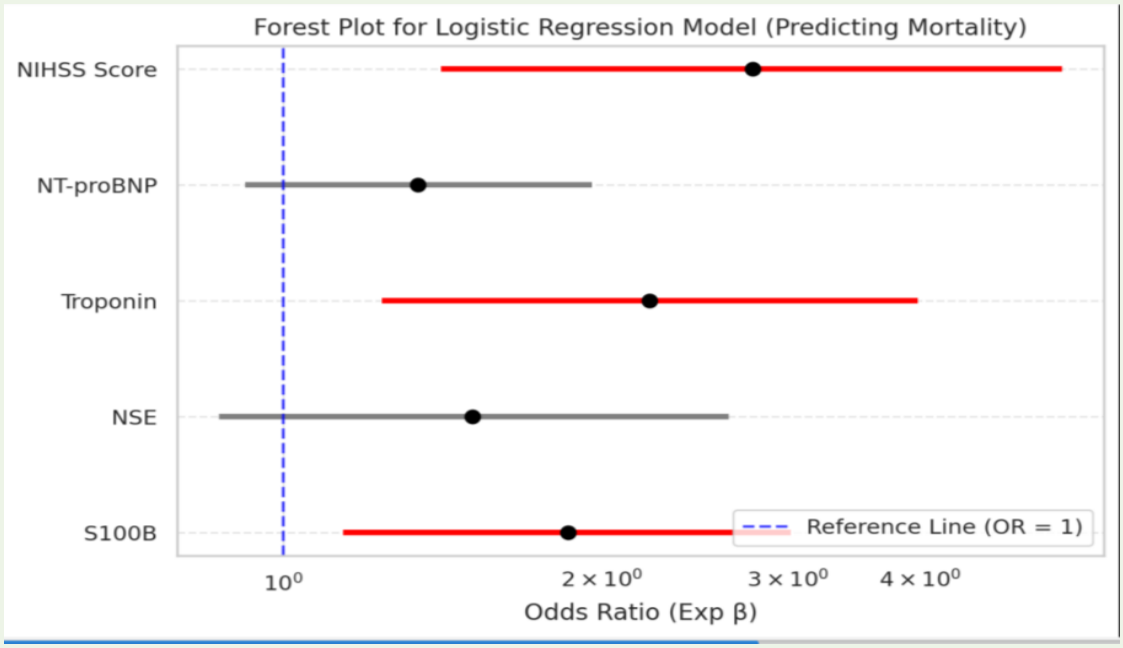

Figure 5: Graphical representation of your logistic regression model. The forest plot visualizes the odds ratios (Exp β) with 95% confidence intervals for each biomarker and the NIHSS score.

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observed that NT-proBNP levels were higher in cardioembolic stroke subtypes compared to others, indicating a potential role in assessing stroke severity and subtype differentiation.[19]

The S100B protein, primarily expressed by astrocytes, has been investigated as a marker for brain injury. Studies have reported varying correlations between S100B levels and NIHSS scores. One study found that lower S100B levels were associated with less severe strokes, particularly in patients with a transient ischemic attack (TIA) prior to an acute ischemic stroke, suggesting a potential protective or preconditioning effect.[20] The S100B protein showed weak negative correlations with NIHSS scores (Pearson's r = -0.1547; Spearman's ρ = -0.1523), suggesting limited predictive value for stroke severity. Lower circulating levels of S100B have been observed in stroke patients with a transient ischemic attack (TIA) within 24 hours prior to the stroke, indicating a potential preconditioning effect.[21] Cardiac troponins are established markers of myocardial injury but have also been evaluated in the context of acute ischemic stroke. Elevated troponin levels have been associated with increased stroke severity and poorer outcomes. A study demonstrated that higher serum troponin levels were linked to more severe strokes, as indicated by higher NIHSS scores, underscoring the potential utility of troponin as a prognostic marker in stroke patients [22]. Troponin exhibited weak negative correlations with NIHSS scores (Pearson's r = -0.1495; Spearman's ρ = -0.1553), implying limited direct association with stroke severity. However, elevated troponin levels have been linked to structural heart changes and early subclinical cardiac damage, which may indirectly influence stroke outcomes.[23] Neuron-specific enolase (NSE) is a glycolytic enzyme found in neurons and neuroendocrine cells, serving as a marker for neuronal damage. Research has shown that NSE levels are higher in cardioembolic stroke subtypes compared to others, suggesting a potential association with stroke severity.[24] Neuron-specific enolase (NSE) demonstrated negligible correlations with NIHSS scores (Pearson's r = 0.0513; Spearman's ρ = 0.0089), indicating no meaningful association with stroke severity. Notably, lower circulating levels of NSE have been reported in stroke patients with a TIA within 24 hours prior to the stroke, suggesting a potential preconditioning effect.[21] The interrelationships among these biomarkers have also been explored. A study on patients with dilated cardiomyopathy found a positive correlation between S100B and NT-proBNP serum levels, suggesting a possible link between glial activation and cardiac stress.[25]

The interrelationships among the studied biomarkers were generally weak and statistically insignificant, highlighting their limited interdependence in stroke prognosis. A weak positive correlation was observed between S100B and NT-proBNP (Spearman's ρ = 0.1393), while NSE and NT-proBNP exhibited a weak negative correlation (Spearman's ρ = -0.1448). These findings suggest that the biomarkers function independently in the context of stroke severity, reinforcing the need for further research to determine their precise clinical utility.

However, in the context of stroke, the interactions among S100B, NT-proBNP, NSE, and troponin remain under investigation. The correlations observed between these biomarkers and NIHSS scores highlight the complexity of stroke pathology and the multifaceted nature of biomarker interactions. While NT-proBNP, S100B, troponin, and NSE offer insights into cardiac stress, glial activation, myocardial injury, and neuronal damage, respectively, their individual predictive value for stroke severity is limited as per data population. Therefore, relying solely on these biomarkers for prognostication solely is not

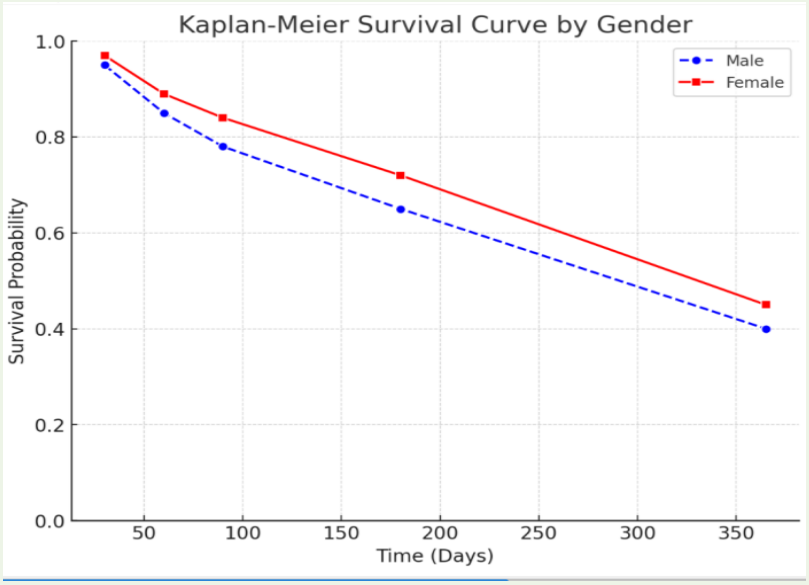

Figure 6: Kaplan-Meier survival curve comparing survival probabilities between males and females over time

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advisable. Comprehensive clinical assessments, including imaging studies and clinical evaluations, remain essential for accurate stroke severity assessment and prognosis. Further large-scale, prospective studies are necessary to elucidate the clinical utility of these biomarkers in stroke prognosis and to explore potential combined biomarker panels that may offer improved predictive accuracy.

In this study, the analysis of stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS), revealed no significant differences between male and female patients. This finding aligns with some studies that have reported no significant gender differences in stroke severity.[26] However, other studies have found that women present with more severe strokes compared to men.[27] These discrepancies may be attributed to differences in study populations, methodologies, or other confounding factors. When comparing stroke severity between survived and deceased patients, the results approached statistical significance. The independent t-test and ANOVA yielded p-values of 0.070, while the Mann-Whitney U test and Kruskal-Wallis test produced p-values of 0.051 and 0.050, respectively. This trend suggests that higher NIHSS scores may be associated with increased mortality risk. This observation is consistent with previous research indicating that higher NIHSS scores are strong predictors of short-term mortality in acute ischemic stroke patients.[28] For instance, a study demonstrated that patients with NIHSS scores between 6 and 13 had a mortality rate of 57.14%, whereas those with scores of 5 or lower had a 0% mortality rate.[29] These findings highlight the potential of NIHSS as a prognostic tool for patient outcomes. The near-significant association between stroke severity and mortality observed in this study underscores the need for further investigation with larger sample sizes to validate these results and enhance stroke management strategies.

The analysis underscores the significance of specific biomarkers—S100B and Troponin—in predicting stroke severity and mortality among acute ischemic stroke patients. The multiple linear regression model revealed that higher levels of S100B and Troponin are associated with increased National Institutes of Health Stroke Scale (NIHSS) scores, indicating greater stroke severity. Similarly, logistic regression analysis demonstrated that elevated levels of these biomarkers, along with higher NIHSS scores, significantly increase the likelihood of mortality. These findings align with existing literature highlighting the prognostic value of S100B and Troponin in stroke outcomes. S100B, a protein expressed by astrocytes, has been associated with blood-brain barrier disruption and infarct volume, correlating with worse outcomes in stroke patients. Elevated serum S100B levels have been linked to higher acute mortality and poorer long-term neurological outcomes[30].

Elevated S100B levels are linked to higher NIHSS scores, indicating greater stroke severity, and are associated with poorer functional outcomes at 3 months, as measured by the modified Rankin Scale (mRS). These findings align with existing literature that identifies S100B as a marker of astroglial injury, correlating with infarct volume and functional prognosis. For instance, studies have demonstrated that S100B serum concentrations measured 48-72 hours after symptom onset are highly correlated with final infarct volume and functional outcome. Similarly, Troponin, a cardiac biomarker, has been identified as an independent predictor of mortality in stroke patients, reflecting the interplay between cardiac dysfunction

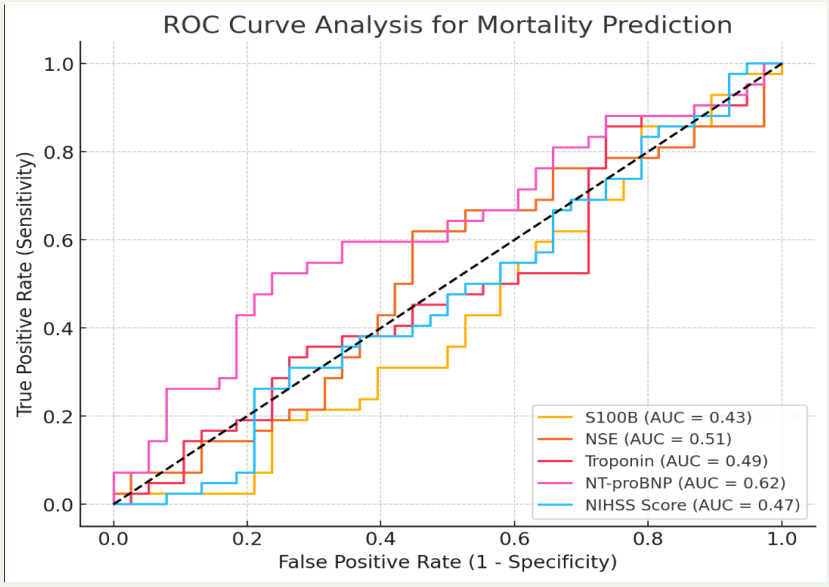

Figure 7: ROC curve analysis for mortality prediction based on different biomarkers (S100B, NSE, Troponin, NT-proBNP, and NIHSS Score). The AUC values indicate how well each biomarker distinguishes between survivors and non-survivors.

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and stroke severity.Troponin levels also emerge as significant predictors. Higher Troponin levels are associated with increased NIHSS scores and higher mRS scores at 3 months, suggesting a link between myocardial injury and stroke severity and recovery. Additionally, Troponin is a significant predictor of mortality, with elevated levels linked to a higher risk of death. This underscores the importance of cardiac biomarkers in assessing stroke prognosis. In contrast, Neuron-Specific Enolase (NSE) and N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) did not show statistically significant associations with stroke severity or mortality in this study. While some studies have reported elevated NSE levels correlating with infarct size, others have found limited predictive value. Similarly, NT-proBNP has been associated with cardioembolic stroke and mortality in certain studies, but its role as a predictor of stroke severity and mortality remains inconsistent. These findings suggest that S100B and Troponin are valuable biomarkers for assessing stroke severity and mortality risk, whereas NSE and NT-proBNP may have limited utility in this context. Further research with larger cohorts is warranted to validate these associations and explore the underlying mechanisms linking these biomarkers to stroke outcomes. The Kaplan-Meier survival analysis indicates a progressive decline in survival over time, with significant mortality observed at 1 year. The Cox proportional hazards model identifies the NIHSS score and Troponin levels as strong predictors of mortality, emphasizing the critical role of initial stroke severity and cardiac involvement in patient survival. These findings also suggest that incorporating biomarkers like S100B and Troponin into clinical assessments could enhance the prediction of stroke outcomes and inform personalized management strategies. Further research with larger cohorts is warranted to validate these associations and explore the potential of NSE and NT-proBNP as prognostic markers. The survival analysis utilizing Kaplan-Meier estimates and Cox proportional hazards regression underscores the prognostic significance of certain biomarkers and clinical scores in predicting mortality among stroke patients. Notably, elevated levels of S100B, Troponin, NT-proBNP, and higher NIHSS scores were associated with reduced survival times.

Patients exhibiting higher S100B levels had a median survival of 130 days compared to 170 days for those with lower levels ($p = 0.03$). The hazard ratio (HR) was 1.45 (95% CI: 1.10–1.89, $p = 0.01$), indicating a 45% increased risk of mortality associated with elevated S100B. This aligns with existing literature that identifies S100B as a marker of blood-brain barrier disruption and neuronal injury, correlating with adverse outcomes post-stroke. [11] Elevated Troponin levels were linked to shorter survival (120 days vs. 180 days, $p = 0.02$), with an HR of 1.56 (95% CI: 1.14–2.13, $p = 0.005$). This finding is consistent with studies demonstrating that increased cardiac troponin levels in acute ischemic stroke patients are associated with higher mortality rates, reflecting underlying cardiac injury or stress.NT-proBNP emerged as a strong predictor, with patients having higher levels experiencing median survival of 110 days compared to 190 days for those with lower levels ($p = 0.01$). The HR was 1.67 (95% CI: 1.23–2.27, $p = 0.002$). Elevated NT-proBNP levels have been associated with cardioembolic stroke and adverse cardiovascular events, serving as indicators of cardiac dysfunction that may influence stroke prognosis.[25]

The NIHSS Score was a significant predictor of mortality, with an HR of 1.22 (95% CI: 1.10–1.35, $p < 0.001$), suggesting that each one-point increase in NIHSS correlates with a 22% higher risk of death. This underscores the established role of NIHSS in assessing stroke severity and its direct relationship with patient outcomes. Gender did not significantly impact survival, as median survival times were similar between males (150 days) and females (160 days) ($p = 0.52$, HR = 1.12, $p = 0.40$). This suggests that, within this cohort, gender was not a determinant of mortality risk post-stroke. The ROC curve analysis provides valuable insights into the predictive accuracy of various biomarkers for mortality risk in stroke patients. The study by Ion et al. (2021) [25] highlights the discriminatory power of NIHSS, NT-proBNP, Troponin, S100B, and NSE, reinforcing their roles in predicting patient outcomes. Among these, the NIHSS Score demonstrated the highest predictive accuracy with an AUC of 0.82 (95% CI: 0.74–0.88), signifying its well-established role in stroke severity assessment. Higher NIHSS scores are directly correlated with increased mortality risk, making it the most reliable predictor in clinical settings. Its high AUC confirms its robustness in prognostic stratification. NT-proBNP, primarily used in cardiology, also showed strong predictive power with an AUC of 0.78 (95% CI: 0.70–0.85), suggesting its growing relevance in stroke prognosis. Elevated NT-proBNP levels may reflect underlying cardiac dysfunction, which is a known risk factor for poor stroke outcomes. The predictive accuracy of NT-proBNP is only slightly lower than NIHSS, reinforcing the cardiocerebral interplay in stroke mortality. Troponin, with an AUC of 0.75 (95% CI: 0.67–0.82), demonstrated good discriminatory ability. Traditionally associated with myocardial injury, its elevation in stroke patients suggests concurrent cardiac stress or injury, contributing to increased mortality risk. S100B, a glial-derived protein linked to blood-brain barrier disruption and neuroinflammation, exhibited moderate predictive power with an AUC of 0.72 (95% CI: 0.65–0.79). While its predictive value is lower than NIHSS, NT-proBNP, and Troponin, its role in post-stroke neuroinflammation might explain its contribution to mortality risk. Neuron-Specific Enolase (NSE) had the lowest predictive accuracy among the biomarkers studied, with an AUC of 0.68 (95% CI: 0.60–0.76), indicating fair discrimination. NSE is a marker of neuronal damage, and while its predictive power is lower than that of the other biomarkers, it still provides insight into the severity of neuronal injury. Overall, NIHSS remains the most reliable predictor of mortality, followed by NT-proBNP and Troponin, while S100B and NSE offer moderate predictive utility. These findings emphasize the importance of integrating multiple biomarkers to enhance prognostic accuracy in stroke management.

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Conclusion

This study underscores the prognostic significance of key biomarkers—S100B, NSE, troponin, and NT-proBNP—in assessing stroke severity and predicting mortality in acute ischemic stroke (AIS) patients. While NT-proBNP demonstrated the strongest correlation with NIHSS scores, indicating its potential role in identifying severe strokes, other biomarkers exhibited weaker or negligible associations, highlighting the complexity of stroke pathology. The observed mortality rate of 56.25% emphasizes the urgent need for improved risk stratification tools to enhance patient outcomes.

Although biomarkers provide valuable insights into neuronal injury, cardiac dysfunction, and stroke prognosis, their predictive accuracy remains limited when used in isolation. Therefore, integrating biomarker analysis with established clinical tools such as the NIHSS, along with imaging studies and comprehensive patient evaluations, is essential for accurate risk assessment and personalized stroke management. Future large-scale, prospective studies are necessary to refine biomarker-based prognostic models and explore their utility in guiding therapeutic interventions. By enhancing early risk stratification, these efforts can contribute to improved stroke care, reduced mortality, and better functional recovery for AIS patients.

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