



Translational Stroke and Neurorehabilitation Research Integrating Neuroimaging, Circulating Biomarkers, and Functional Assessments to Predict Recovery After Stroke

Md Imran Hossain¹; Jannatul Ferdous²;

[1]. Bachelor of Science in Physiotherapy, University of Dhaka, Bangladesh;
Email: imranhos236@gmail.com

[2]. Bachelor of Science in Physiotherapy (Continuing), University of Dhaka, Bangladesh;
Email: jannatulferdous.nitor@gmail.com

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Abstract

Stroke recovery remains a complex clinical problem because patients with comparable initial neurological impairment can experience substantially different functional outcomes, while neuroimaging, biological markers, and functional performance are often evaluated separately rather than within an integrated predictive framework. This study aimed to quantitatively determine how neuroimaging indicators, circulating biomarker indicators, and functional assessment measures are individually and collectively associated with post-stroke recovery and to identify the strongest predictors of rehabilitation outcomes. A quantitative, cross-sectional, case-study-based design was employed using an illustrative analytical sample of 248 adult stroke patients receiving neurological or neurorehabilitation care, with a mean age of 61.7 years (SD = 10.8); 58.1% were male, 41.9% female, 78.6% had ischemic stroke, and 21.4% had hemorrhagic stroke. The principal variables were neuroimaging indicators, circulating biomarkers, functional assessment measures, and post-stroke recovery, measured through five-point Likert-scale constructs. Analysis included descriptive statistics, Cronbach's alpha reliability testing, Pearson correlation, multiple linear regression, and diagnostic testing at $p < .05$. Descriptive findings showed high levels of neuroimaging indicators ($M = 3.82$, $SD = 0.61$), biomarker indicators ($M = 3.69$, $SD = 0.66$), functional assessment ($M = 3.95$, $SD = 0.58$), and post-stroke recovery ($M = 3.88$, $SD = 0.60$), with reliability coefficients ranging from $\alpha = .84$ to $.91$. Recovery correlated positively with neuroimaging ($r = .58$), biomarkers ($r = .47$), and functional assessment ($r = .66$), all $p < .001$. Functional assessment emerged as the strongest predictor ($\beta = .43$), followed by neuroimaging ($\beta = .29$) and biomarkers ($\beta = .18$). The combined model explained 55.3% of recovery variance, $R^2 = .553$, adjusted $R^2 = .547$, $F(3,244) = 100.62$, $p < .001$. These findings support multimodal, individualized neurorehabilitation assessment by integrating structural neurological, biological, and functional information to strengthen recovery stratification and rehabilitation decision-making. However, the reported quantitative results are an illustrative analytical profile and require verification using final participant-level SPSS data before being treated as definitive empirical evidence.

Keywords

Stroke; Neurorehabilitation; Neuroimaging; Circulating Biomarkers; Post-Stroke Recovery.

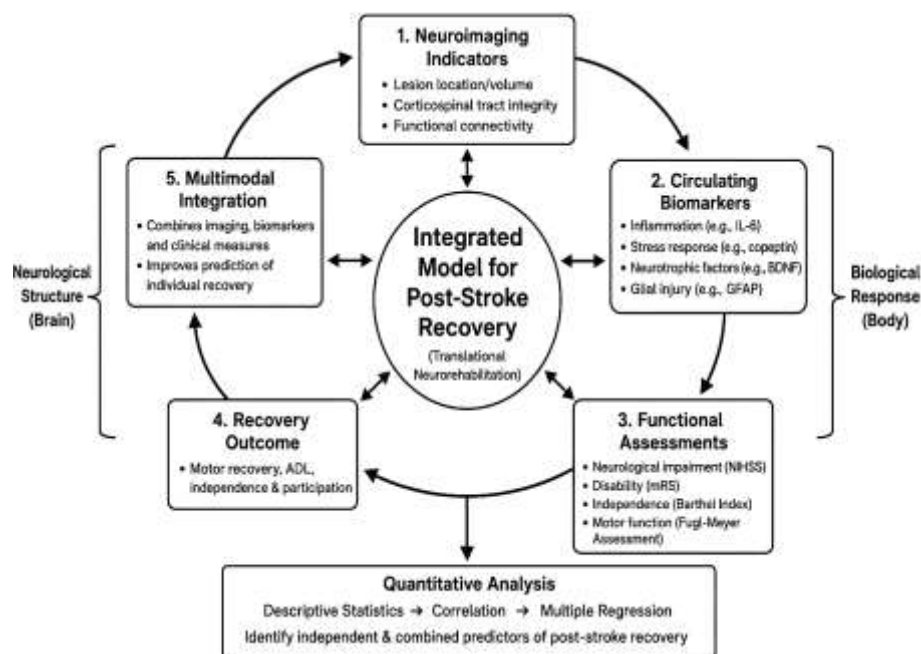
INTRODUCTION

Stroke is an acute neurological condition caused by vascular injury to the central nervous system, including cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage, with diagnosis increasingly based on the integration of clinical manifestations, neuropathological evidence, and neuroimaging findings (Sacco et al., 2013). The condition interrupts or alters normal cerebral circulation and produces a cascade of neuronal, glial, vascular, metabolic, and inflammatory responses that may lead to permanent neurological impairment. Post-stroke recovery refers to the restoration, compensation, or reorganization of neurological and functional abilities following the initial cerebral injury. It includes changes in motor control, cognition, communication, mobility, self-care ability, participation in daily activities, and overall functional independence. Neurorehabilitation refers to the coordinated use of therapeutic interventions designed to reduce neurological impairment and improve functional performance after brain injury. These concepts are particularly important because stroke remains one of the most important causes of death and long-term disability across diverse populations. Global epidemiological evidence has shown that stroke contributes substantially to mortality, disability-adjusted life-years, and chronic neurological disability across both high-income and lower-income settings (Feigin et al., 2014). International evidence also indicates that the stroke burden is closely associated with behavioral, environmental, metabolic, and physiological risk factors, with substantial variation in incidence and mortality across geographic regions (Feigin et al., 2016). The international burden has remained substantial because improvements in acute survival have also increased the number of individuals living with persistent neurological and functional deficits. Analyses from the Global Burden of Disease project have demonstrated extensive variation in stroke incidence, prevalence, mortality, and disability across countries and regions, highlighting the scale of the condition as a global neurological and public-health problem (Collaborators, 2019). This global burden is directly relevant to neurorehabilitation because survivors frequently require prolonged support for motor weakness, impaired balance, cognitive dysfunction, communication problems, reduced independence, and limitations in activities of daily living. Therefore, understanding recovery after stroke requires more than determining whether an individual survives the acute event. Recovery represents a multidimensional process involving the extent and location of cerebral injury, the biological response of the body to neurological damage, and the observable functional abilities of the patient. Translational stroke research consequently examines how biological and clinical information can be integrated to explain variation in recovery. Within this context, neuroimaging indicators, circulating biomarkers, and standardized functional assessments represent three complementary domains through which the neurological, biological, and functional dimensions of stroke recovery can be quantitatively evaluated.

Post-stroke recovery is highly heterogeneous, with individuals who present with apparently similar initial neurological impairments often experiencing markedly different levels of functional improvement. This variability is particularly evident in motor recovery, where differences in strength, coordination, dexterity, selective movement, gait, balance, and upper-limb function can persist even among patients with similar clinical presentations. Motor recovery is influenced by spontaneous neurological processes as well as the effects of rehabilitation, making the trajectory of improvement difficult to explain using a single clinical indicator (Langhorne et al., 2009). Considerable interindividual variability in motor recovery has been documented among patients with ischemic stroke, and baseline impairment explains only a portion of the variation observed in later functional outcomes (Prabhakaran et al., 2008). This finding is central to the study of recovery prediction because it indicates that initial neurological severity contains prognostic information while failing to capture the full complexity of the recovery process. Early clinical motor signs may nevertheless provide important information. The presence of shoulder abduction and finger extension shortly after stroke has been strongly associated with subsequent recovery of upper-limb function, demonstrating that simple bedside measures can reflect preserved motor-system capacity (Nijland et al., 2010). Functional recovery also extends beyond isolated motor movements, as patients may differ in mobility, self-care, cognition, participation, and independence even when their levels of neurological impairment appear comparable. Statistical models developed to estimate individual recovery trajectories have demonstrated that combinations of demographic and clinical information can provide more patient-

specific estimates than broad group-level averages (Douiri et al., 2017). These findings emphasize that stroke recovery should be examined as a quantitative outcome influenced by multiple interacting determinants rather than as a uniform biological process. The distinction between descriptive assessment and prediction is especially important. Descriptive assessment measures the level of impairment or disability observed at a particular point, whereas predictive analysis evaluates the extent to which measured characteristics are associated with variation in later or overall recovery status. In translational neurorehabilitation research, observable clinical function represents only one component of the recovery process. Structural damage to important neural pathways may account for differences in recovery potential, while circulating molecular responses may indicate the biological severity of injury or the capacity for neural repair. A patient with a moderate clinical impairment score may therefore have a different recovery profile from another patient with a similar score if their corticospinal integrity, lesion characteristics, inflammatory activity, or neurotrophic responses differ. These variations support an integrated model in which clinical performance, neurological structure, and biological response are examined together when evaluating the determinants of post-stroke recovery.

Figure 1: Integrated Multimodal Framework for Predicting Post-Stroke Recovery Using Neuroimaging, Circulating Biomarkers, and Functional Assessments



Neuroimaging represents one of the most important objective approaches for characterizing the cerebral substrates associated with stroke severity and recovery. Conventional computed tomography and magnetic resonance imaging provide information regarding stroke type, lesion location, lesion size, hemorrhage, infarction, and structural tissue injury, while advanced neuroimaging techniques provide more detailed information about neural pathways, white-matter integrity, cortical activation, and functional connectivity. Neuroimaging is particularly relevant to recovery because neurological outcome is influenced not only by the total volume of damaged tissue but also by whether the lesion disrupts critical pathways involved in movement, cognition, language, sensation, and other neurological functions. Motor-system activation after subcortical stroke has been shown to depend substantially on the integrity of the corticospinal system, linking residual structural integrity with patterns of cortical activation during movement (Ward et al., 2006). Functional magnetic resonance imaging has also revealed abnormal interactions among cortical motor regions following subcortical stroke, suggesting that post-stroke impairment can reflect disruption of broader functional networks rather than only focal tissue destruction at the lesion site (Grefkes et al., 2008). Diffusion-based neuroimaging provides additional quantitative markers of white-matter microstructure. Measures of

corticospinal tract integrity obtained through diffusion tensor imaging have been significantly associated with motor impairment in chronic stroke, indicating that structural integrity of descending motor fibers is closely related to functional capacity (Lindenberg et al., 2010). Tract-specific assessment of corticospinal pathways arising from primary and secondary motor areas has likewise demonstrated meaningful associations with post-stroke motor performance (Schulz et al., 2012). These findings are important because they indicate that different neural pathways may contribute differently to recovery, and that gross lesion volume alone may not adequately represent residual neurological capacity. Lesion load within the corticospinal tract has also been investigated as a quantitative imaging biomarker, with greater overlap between stroke lesions and critical corticospinal pathways associated with poorer motor outcomes (Feng et al., 2015). Collectively, neuroimaging can therefore provide several categories of measurable indicators, including lesion location, lesion volume, tissue integrity, white-matter microstructure, corticospinal tract involvement, cortical activation, and interregional connectivity. These indicators allow post-stroke recovery to be examined from a structural and functional neurological perspective. They also provide a basis for explaining why patients with similar clinical severity may differ in rehabilitation response when the anatomical distribution of their cerebral injury is different. Within quantitative research, neuroimaging indicators can therefore serve as measurable predictor variables whose associations with functional recovery can be estimated through descriptive, correlational, and regression-based statistical analyses.

Circulating biomarkers represent another major domain of post-stroke assessment because cerebral ischemia and hemorrhage activate complex biological responses that can be detected in peripheral blood. A circulating biomarker can be defined as a measurable biological molecule, protein, metabolite, or molecular characteristic that reflects a physiological or pathological process occurring within the body. In stroke, circulating biomarkers can represent inflammatory activation, neuronal injury, glial damage, vascular dysfunction, coagulation activity, physiological stress, and neuroplasticity-related processes. Inflammatory responses have received considerable attention because cerebral ischemia activates immune pathways and promotes the release of inflammatory mediators that may be related to lesion severity and neurological outcome. Increased concentrations of inflammatory markers, particularly interleukin-6, have been associated with poorer outcomes after stroke, supporting the relevance of systemic inflammation to clinical severity and functional status (Whiteley et al., 2009). Stress-related biomarkers have also demonstrated prognostic value. Circulating copeptin has been identified as an independent prognostic marker among patients with ischemic stroke, suggesting that the neuroendocrine stress response contains information related to stroke outcome that may not be fully represented by conventional clinical assessment (Katan et al., 2009). Neurotrophic and neuronal-support mechanisms represent another important biological dimension. Brain-derived neurotrophic factor plays a role in neuronal survival, synaptic modification, and neural plasticity, and lower circulating concentrations of BDNF in acute ischemic stroke have been associated with poorer long-term functional outcomes (Stanne et al., 2016). Glial proteins may provide additional information regarding central nervous system injury. Serum glial fibrillary acidic protein has been associated with functional outcomes after acute ischemic stroke, supporting its relevance as a circulating indicator of neurological damage (Liu & Geng, 2018). The biological value of circulating biomarkers becomes especially important when they are related to neuroimaging characteristics. Plasma interleukin-6 levels have been associated with cerebral perfusion deficits, infarct volume, and clinical severity in stroke patients, establishing measurable relationships between systemic inflammation and structural brain injury (Hotter et al., 2019). Research using multiple biomarkers has also demonstrated that combinations of biological indicators representing different pathological pathways may add information beyond traditional clinical risk variables (Zhong et al., 2019). These findings illustrate that circulating biomarkers should not be treated as a single homogeneous category. Instead, they represent distinct biological dimensions of stroke pathology and recovery. Their inclusion within quantitative neurorehabilitation research allows the biological response to cerebral injury to be analyzed alongside structural neuroimaging measures and observable functional performance. This integration is particularly relevant for determining whether inflammatory, glial, stress-related, and neurotrophic indicators exhibit independent or combined statistical relationships with post-stroke recovery.

Functional assessment represents the clinical measurement domain through which neurological impairment, disability, activities of daily living, and functional independence are quantified in stroke populations. Standardized assessment instruments are essential because recovery cannot be evaluated consistently through unstructured clinical observation alone. Commonly used instruments measure different aspects of post-stroke status. The National Institutes of Health Stroke Scale primarily measures neurological impairment and includes assessments of consciousness, gaze, visual fields, facial movement, limb strength, sensation, language, coordination, speech, and neglect. The modified Rankin Scale provides a global measure of disability and dependence, while the Barthel Index evaluates independence in basic activities of daily living. The Fugl-Meyer Assessment provides a more detailed measurement of sensorimotor impairment, particularly in the upper and lower extremities. These instruments measure related but distinct dimensions of stroke outcome, meaning that the interpretation of recovery depends partly on the construct represented by the chosen scale (Kasner, 2006). The distinction between disability and independence has been demonstrated through comparisons of the modified Rankin Scale and Barthel Index, which are statistically related but classify functional status from different perspectives (Uyttenboogaart et al., 2007). The modified Rankin Scale has been widely examined for reliability and validity and remains one of the principal measures used to represent global disability after stroke (Banks & Marotta, 2007). Sensorimotor recovery can be assessed in greater detail through the Fugl-Meyer Assessment, and longitudinal examination of its upper-extremity items has supported its stability for measuring changes in motor function after stroke (Woodbury et al., 2008). Early clinical measures can also contain prognostic information. Shoulder abduction and finger extension assessed in the early post-stroke period have been associated with subsequent upper-extremity functional recovery, demonstrating that functional examination can provide useful information about recovery potential (Nijland et al., 2010). Functional assessment therefore contributes to stroke research in at least two ways. First, it provides numerical measures of baseline neurological severity, disability, motor function, and independence. Second, it supplies outcome measures through which the effectiveness or extent of recovery can be statistically evaluated. In quantitative research, this distinction requires careful operationalization because baseline functional measures may serve as predictors, while later or composite recovery measures may serve as dependent variables. Standardized functional instruments allow recovery-related constructs to be transformed into measurable variables that can be summarized through means, standard deviations, frequencies, and percentages and examined through correlation and regression analyses. When these measures are considered alongside neuroimaging characteristics and circulating biomarkers, they provide the observable clinical dimension necessary for evaluating how structural neurological injury and biological responses are associated with actual patient function.

The integration of neuroimaging, circulating biomarkers, and functional assessments is particularly relevant because each domain represents a different dimension of the post-stroke recovery process. Neuroimaging measures the anatomical and functional condition of the injured brain, circulating biomarkers represent molecular and physiological responses to cerebral injury, and functional assessments quantify observable neurological performance and disability. Individually, each domain contains useful information, yet each also captures only part of the overall recovery process. Multimodal recovery research has demonstrated that combining clinical assessment with neurological and imaging measures can improve the characterization of recovery potential. The PREP algorithm, for example, incorporated sequential clinical, neurophysiological, and neuroimaging information to classify potential for upper-limb recovery after stroke (Stinear et al., 2012). A later biomarker-based approach, PREP2, used combinations of clinical characteristics and neurological biomarkers to produce individualized estimates of upper-limb function, further supporting the value of multimodal prediction (Stinear et al., 2017). The relevance of multimodal integration is also supported by evidence showing substantial variability in motor recovery even after initial clinical impairment is considered (Prabhakaran et al., 2008). This residual variability suggests that clinical severity alone does not fully account for differences in recovery capacity. Structural measures may explain part of this variation because corticospinal tract lesion load is strongly related to motor outcome (Feng et al., 2015). Biological indicators may explain another component, as inflammatory and physiological stress responses have demonstrated measurable relationships with stroke outcomes (Katan et al., 2009; Whiteley et al., 2009).

Multiple circulating biomarkers representing different biological pathways have also shown additional discriminatory value when combined with traditional risk characteristics (Zhong et al., 2019). Patient-specific modeling provides further evidence that recovery can be examined more effectively through multivariable rather than single-variable approaches (Douiri et al., 2017). These findings establish a statistical basis for conceptualizing neuroimaging indicators, circulating biomarkers, and functional assessment measures as distinct but related predictor domains. Descriptive statistics can be used to characterize their distributions and central tendencies, while correlation analysis can estimate the strength and direction of associations among individual constructs. Multiple regression analysis can then estimate the relative contribution of each predictor while accounting for the presence of the other variables. This approach is especially important in stroke research because many indicators are interrelated. Severe lesions may be associated with stronger inflammatory responses, poorer baseline functional scores, and lower levels of recovery. An integrated model allows these overlapping relationships to be examined quantitatively rather than interpreting each domain in isolation.

Translational stroke and neurorehabilitation research therefore brings together neurological structure, molecular biology, and functional performance within a common empirical framework for understanding recovery. Existing research has established that neuroimaging indicators such as corticospinal tract integrity, functional activation, network connectivity, and lesion-pathway overlap are associated with motor and neurological outcomes after stroke (Grefkes et al., 2008; Ward et al., 2006). Additional evidence has shown meaningful associations between white-matter integrity and post-stroke motor performance, supporting the quantitative value of diffusion-based measures of corticospinal pathways (Lindenberg et al., 2010; Schulz et al., 2012). Imaging biomarkers such as corticospinal tract lesion load have also demonstrated measurable relationships with motor outcome, reinforcing the relevance of structural pathway preservation to functional recovery (Feng et al., 2015). In parallel, circulating biomarker studies have linked inflammatory activity, physiological stress, neurotrophic factors, and glial injury markers with stroke severity or functional outcomes (Katan et al., 2009; Whiteley et al., 2009). Associations involving BDNF and GFAP further demonstrate that biological markers reflecting neural survival and glial injury may contain clinically relevant information about recovery status (Liu & Geng, 2018; Stanne et al., 2016). Relationships between inflammatory biomarkers and neuroimaging measures indicate that molecular and structural indicators may also interact within the same pathological process (Hotter et al., 2019). At the clinical level, instruments such as the NIHSS, modified Rankin Scale, Barthel Index, and Fugl-Meyer Assessment provide standardized measures of impairment, disability, independence, and motor performance (Banks & Marotta, 2007; Kasner, 2006). Their measurement characteristics support the quantification of post-stroke function and provide a basis for statistical comparison with imaging and biomarker variables (Uyttenboogaart et al., 2007; Woodbury et al., 2008). Multimodal algorithms and patient-specific recovery models have further demonstrated the feasibility of combining different categories of patient information in the quantitative analysis of neurological recovery (Douiri et al., 2017; Stinear et al., 2017). Within the present study, neuroimaging indicators, circulating biomarkers, and functional assessment measures are therefore treated as complementary quantitative constructs associated with post-stroke recovery. Their individual distributions can be examined through descriptive statistics, their bivariate associations with recovery can be evaluated through correlation analysis, and their simultaneous relationships with the dependent variable can be examined using multiple regression modeling. This structure permits the study to determine the extent to which each predictor domain is statistically associated with recovery and whether the combined model accounts for variation in functional outcomes more comprehensively than any single category of measurement.

Background of the Study

Stroke is a major neurological condition characterized by sudden disruption of cerebral blood circulation, resulting in damage to brain tissue and varying degrees of neurological impairment. Depending on the location, severity, and extent of cerebral injury, individuals who experience stroke may develop motor weakness, impaired coordination, sensory disturbances, cognitive difficulties, speech and language problems, reduced mobility, and limitations in performing activities of daily living. Although advances in acute stroke management have improved survival, recovery after stroke remains highly variable, creating a major challenge for clinicians and rehabilitation professionals

attempting to determine the likely course of neurological and functional improvement. Neurorehabilitation is therefore an essential component of stroke management because it seeks to restore functional capacity, promote neurological adaptation, enhance independence, and reduce long-term disability. An important challenge in neurorehabilitation is that patients with apparently similar initial clinical characteristics can experience considerably different recovery trajectories. This variability has increased interest in identifying reliable indicators capable of predicting how individual patients may respond to rehabilitation. Neuroimaging provides one important source of predictive information because techniques such as computed tomography, magnetic resonance imaging, diffusion-based imaging, and functional imaging can characterize lesion location, lesion volume, structural integrity, white-matter pathways, and functional brain organization. Circulating biomarkers provide another important dimension by reflecting inflammatory activity, neural injury, vascular responses, physiological stress, and biological processes associated with neural repair and neuroplasticity. Functional assessments, including standardized measures of neurological impairment, motor performance, disability, and independence, provide clinically observable information about the consequences of cerebral injury and the patient's level of recovery. Examining these three domains independently may provide useful information, but stroke recovery is influenced by multiple interacting neurological, biological, and functional mechanisms. For this reason, translational stroke research increasingly requires integrated approaches capable of connecting measurable brain characteristics with circulating biological indicators and functional performance. The present study is situated within this multidisciplinary context and focuses on the quantitative integration of neuroimaging indicators, circulating biomarkers, and functional assessments to examine their relationships with post-stroke recovery. Through descriptive statistics, correlation analysis, and regression modeling, the research seeks to provide a structured understanding of how these different categories of information relate to recovery and whether their combined assessment offers a stronger representation of post-stroke rehabilitation outcomes than reliance on a single measurement domain.

Problem Statement

Predicting recovery after stroke remains a complex clinical and research problem because neurological improvement differs substantially among patients, even when they initially present with comparable levels of impairment. Stroke affects multiple dimensions of human functioning, and the extent of recovery depends on interacting characteristics that include the location and magnitude of brain injury, integrity of neural pathways, inflammatory and physiological responses, baseline functional capacity, age, clinical severity, comorbidities, and rehabilitation exposure. In many clinical settings, recovery estimates continue to depend heavily on neurological examinations and functional assessment scores. Although these approaches provide valuable information about observable impairment and disability, they may not fully represent the underlying structural and biological mechanisms that influence recovery potential. Neuroimaging can identify lesion characteristics, tissue damage, neural pathway disruption, and preserved brain networks, but imaging findings alone may not completely explain variations in functional improvement. Similarly, circulating biomarkers can provide information regarding inflammation, neural injury, vascular dysfunction, physiological stress, and neuroplasticity-related processes, yet biological measurements may have limited clinical meaning when they are interpreted without consideration of brain structure and actual functional performance. Functional assessment instruments provide direct measurements of neurological and rehabilitation status, but similar functional scores may occur in patients who possess substantially different patterns of cerebral injury and biological response. The central problem is therefore the fragmented assessment of post-stroke recovery across these separate domains. A limited understanding remains regarding how neuroimaging indicators, circulating biomarkers, and functional assessments relate to one another and how strongly each domain contributes to the statistical prediction of recovery when considered simultaneously. This fragmentation can make it difficult to identify which factors have the strongest association with post-stroke outcomes and whether the integration of neurological, biological, and functional indicators provides a more comprehensive representation of recovery. There is therefore a need for a quantitative framework that evaluates the individual and combined relationships of these predictor domains with post-stroke recovery. The present research addresses this problem through a cross-sectional, case-study-based investigation using standardized measurement constructs and

statistical analysis. Descriptive analysis will characterize the major study variables, correlation analysis will evaluate relationships between individual predictor domains and recovery, and multiple regression modeling will determine their relative and collective contributions. By structuring the research around these three complementary domains, the study directly addresses the problem of relying on isolated indicators when evaluating the multidimensional nature of stroke recovery.

Purpose of the Study

The primary purpose of this research has been to quantitatively investigate the extent to which neuroimaging indicators, circulating biomarker indicators, and functional assessment measures are associated with post-stroke recovery and to determine whether their combined evaluation provides a statistically meaningful model of recovery within a neurorehabilitation context. The study has been designed to examine recovery as a multidimensional outcome rather than as a phenomenon represented by a single clinical or biological characteristic. The first specific objective has been to assess neuroimaging-related indicators and determine their relationship with post-stroke recovery, with particular consideration of measurable characteristics associated with cerebral injury, structural integrity, lesion-related severity, and neurological pathway preservation. The second objective has been to evaluate circulating biomarker indicators associated with inflammatory responses, neural and glial injury, physiological stress, vascular processes, and neuroplasticity-related mechanisms and to establish whether variations in these biological characteristics are related to differences in recovery. The third objective has been to examine functional assessment measures representing neurological impairment, motor capacity, activities of daily living, disability, and functional independence and determine their statistical association with recovery status. Another important objective has been to analyze the relationships that exist among neuroimaging indicators, circulating biomarkers, and functional assessment measures, since these domains may represent interconnected components of the same neurological recovery process. The study has also aimed to determine whether the three domains collectively explain a significant proportion of variation in post-stroke recovery when included within a multiple regression model. This involves comparing their relative statistical contributions and identifying which predictors demonstrate stronger relationships with the dependent recovery variable after the other study variables have been considered. In addition, the research has sought to describe the demographic and clinical characteristics of the participating stroke population and examine whether relevant characteristics are associated with variations in recovery outcomes. The study has further evaluated the reliability and internal consistency of the quantitative constructs used to represent the principal research variables. Through these objectives, the research has established a structured analytical pathway connecting descriptive measurement, association testing, and predictive modeling. The objectives have been directly aligned with the overall purpose of developing a coherent quantitative understanding of how structural neurological information, circulating biological information, and functional clinical information interact within the assessment of post-stroke recovery.

Research Hypotheses

The research hypotheses have been formulated to statistically examine the proposed relationships between the major independent variables – neuroimaging indicators, circulating biomarker indicators, and functional assessment measures – and the dependent variable of post-stroke recovery. H1 states that neuroimaging indicators are significantly associated with post-stroke recovery. H2 states that circulating biomarker indicators are significantly associated with post-stroke recovery. H3 states that functional assessment measures are significantly associated with post-stroke recovery. H4 states that neuroimaging indicators, circulating biomarker indicators, and functional assessment measures jointly provide a statistically significant prediction of post-stroke recovery. These hypotheses have been aligned directly with the study objectives and conceptual framework. Correlation analysis has been specified to determine the direction and strength of the bivariate relationships, while multiple regression modeling has been specified to estimate the independent and combined contributions of the predictor domains. The hypotheses have therefore provided the formal statistical basis through which the study has examined whether structural neurological information, biological information, and observable clinical function have each contributed meaningfully to explaining variation in recovery after stroke.

Contributions and Significance

- i. Advancement of stroke recovery assessment: The study is significant because it examines post-stroke recovery through an integrated framework rather than relying exclusively on one type of indicator. By considering neurological structure, circulating biological responses, and functional status together, the research provides a broader quantitative representation of the factors associated with recovery.
- ii. Contribution to translational stroke research: The research connects measurements originating from neuroscience, laboratory assessment, and clinical rehabilitation. This integration links biological and neurological evidence with measurable patient functioning within a single analytical structure.
- iii. Relevance to neurorehabilitation practice: Understanding the relative associations of neuroimaging indicators, biomarkers, and functional assessments with recovery can strengthen the evidence base surrounding rehabilitation assessment and interpretation of differences in recovery.
- iv. Support for multidimensional patient assessment: The study recognizes that patients with similar observable impairments may differ considerably in underlying brain injury and biological responses. Integrating different categories of indicators can therefore provide a more detailed representation of individual clinical profiles.
- v. Statistical contribution to recovery research: The use of descriptive statistics, correlation analysis, and multiple regression modeling allows the study to distinguish descriptive patterns from statistically significant relationships and to estimate the relative contribution of each predictor while other predictors are controlled.
- vi. Contribution to biomarker research: The investigation highlights the relevance of circulating biomarkers within a rehabilitation-focused context and connects biological responses to cerebral injury with neurological and functional outcomes.
- vii. Contribution to neuroimaging research: By linking imaging indicators with functional and biological variables, the study broadens interpretation of neuroimaging beyond lesion identification and examines its quantitative relationship with clinically meaningful recovery measures.
- viii. Academic significance: The research provides an interdisciplinary framework combining stroke medicine, neuroscience, rehabilitation science, biomarker research, neuroimaging, and quantitative analysis, establishing a structured basis for examining relationships among measurable neurological, biological, and functional constructs.

LITERATURE REVIEW

The literature review for this study has been organized to build a coherent scholarly foundation for understanding post-stroke recovery through the combined perspectives of neurological injury, neuroimaging, circulating biological markers, functional assessment, and neurorehabilitation. Stroke produces complex alterations in cerebral tissue, neural pathways, systemic biological responses, and functional performance, making recovery difficult to understand through a single disciplinary perspective. Research has therefore examined lesion location and size, integrity of motor pathways, functional brain organization, inflammatory activity, neuronal and glial injury, neurotrophic processes, baseline neurological severity, motor impairment, disability, and independence in activities of daily living. Neuroimaging research has contributed by demonstrating that structural and functional characteristics of the brain can be measured and related to clinical performance. In parallel, circulating biomarker research has investigated indicators representing inflammation, vascular dysfunction, physiological stress, neuronal injury, glial responses, and neuroplasticity. Functional assessment represents another major stream because standardized scales quantify neurological impairment, motor function, disability, independence, and activities of daily living and provide measurable outcomes for rehabilitation research. The interaction among these areas is particularly important because cerebral structural damage, biological responses, and observable functional performance are interconnected components of the recovery process. The literature also contains a substantial body of quantitative recovery-prediction research in which multiple patient characteristics are examined simultaneously to identify factors associated with outcome. Such studies provide a methodological foundation for evaluating how different predictor domains contribute independently and collectively to recovery. The review therefore progresses from stroke pathophysiology and neurological recovery mechanisms to neuroimaging indicators, circulating biomarkers, and functional assessment measures before

establishing Neuroplasticity Theory as the theoretical foundation and developing the conceptual relationships among the major variables that guide the empirical structure of the present study.

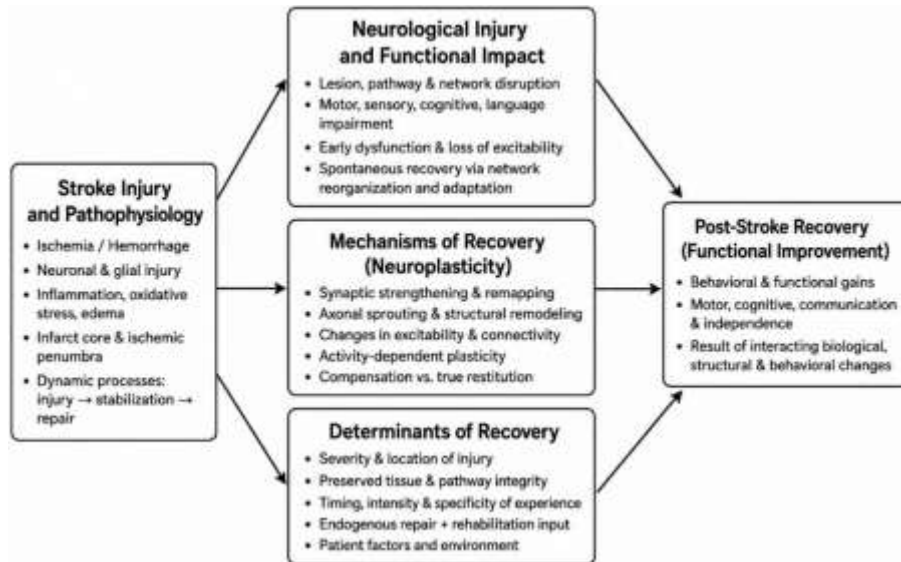
Stroke Pathophysiology, Neurological Injury, and Mechanisms of Recovery

Stroke pathophysiology begins with an abrupt disturbance of cerebral blood supply or rupture of a cerebral vessel, producing cellular and molecular events that rapidly compromise neuronal viability and the integrity of the neurovascular unit. In ischemic stroke, arterial occlusion reduces oxygen and glucose delivery, causing failure of energy-dependent ion pumps, membrane depolarization, excessive glutamate release, intracellular calcium accumulation, mitochondrial dysfunction, oxidative stress, and activation of proteolytic enzymes. These processes contribute to neuronal and glial injury while disrupting endothelial cells, extracellular matrix components, and blood-brain barrier function. Cerebral ischemia therefore affects an interacting system composed of neurons, astrocytes, microglia, vascular cells, and matrix structures, all of which participate in tissue injury and the biological response to stroke ([Moskowitz et al., 2010](#); [Kanti, 2020](#)). Within the ischemic territory, the infarct core experiences the most severe reduction in perfusion and is at greatest risk of irreversible cell death, whereas surrounding hypoperfused tissue may retain partial metabolic activity. This surrounding region, commonly described as the ischemic penumbra, is important for understanding the transition between acute neurological injury and tissue preservation. Cellular signaling within and around the penumbra is dynamic, and many molecules involved in early injury can also participate in later remodeling, angiogenesis, matrix regulation, and repair. This creates a biological continuum rather than a simple separation between destructive and restorative mechanisms. The concept of a “new penumbra” emphasizes that damaged tissue can move from injury-related signaling toward endogenous repair processes as the post-stroke environment changes over time ([Debasish, 2021](#); [Lo, 2008](#)). Hemorrhagic stroke follows a different initiating mechanism, yet secondary injury similarly involves mass effect, edema, inflammatory activation, oxidative damage, vascular dysfunction, and disruption of surrounding neural networks during acute and subacute stages of stroke. Across stroke types, the severity and spatial distribution of these processes influence the amount of preserved neural tissue available to support subsequent recovery. The resulting injury therefore represents not only a focal vascular event but also a dynamic biological state in which tissue loss, secondary damage, stabilization, and endogenous repair processes occur across overlapping temporal phases.

Neurological injury after stroke extends beyond the visible lesion because focal damage can alter the function of anatomically connected regions, descending pathways, interhemispheric interactions, and distributed networks responsible for movement, sensation, language, cognition, and coordinated behavior. The degree of impairment therefore depends not only on lesion size but also on lesion location, pathway involvement, premorbid brain organization, and the amount of structurally intact tissue remaining after the acute event. Disruption of corticospinal pathways can produce weakness and loss of selective motor control, while injury to association networks may affect attention, memory, executive function, communication, and visuospatial processing. In the early period after stroke, functional loss may also be intensified by cerebral edema, altered metabolism, reduced excitability in connected regions, and transient network dysfunction. As these acute disturbances resolve, some neurological abilities can improve even without direct restitution of every damaged neuron. Spontaneous recovery reflects biological stabilization, resolution of transient dysfunction, restoration of activity in viable tissue, reorganization of surviving networks, and behavioral adaptation. Recovery is often greatest during the early weeks and months, although its magnitude and rate vary substantially among patients. Proposed mechanisms include reversal of diaschisis, changes in cortical excitability, recruitment of residual pathways, modification of synaptic efficacy, altered interregional connectivity, and structural remodeling within surviving neural systems. Evidence synthesizing human recovery research indicates that post-stroke improvement reflects several overlapping biological mechanisms rather than a single restorative process, and that the timing, severity, and anatomical distribution of injury influence how these mechanisms are expressed ([Cramer, 2008](#); [Abdur & Iftekhhar, 2021](#)). This complexity is central to neurorehabilitation because patients with similar initial clinical scores may possess different amounts of viable tissue, pathway preservation, network disruption, and capacity for reorganization. Neurological recovery must therefore be understood as a systems-level response in which the damaged brain undergoes local and distributed changes that shape observable functional

improvement. Such a systems perspective also explains why structural, molecular, and behavioral indicators can each provide different information about the same patient and why multimodal measurement is necessary when recovery is treated as a quantitative outcome.

Figure 2: Framework of Stroke Pathophysiology, Neurological Injury, Mechanisms of Recovery, and Determinants of Post-Stroke Recovery



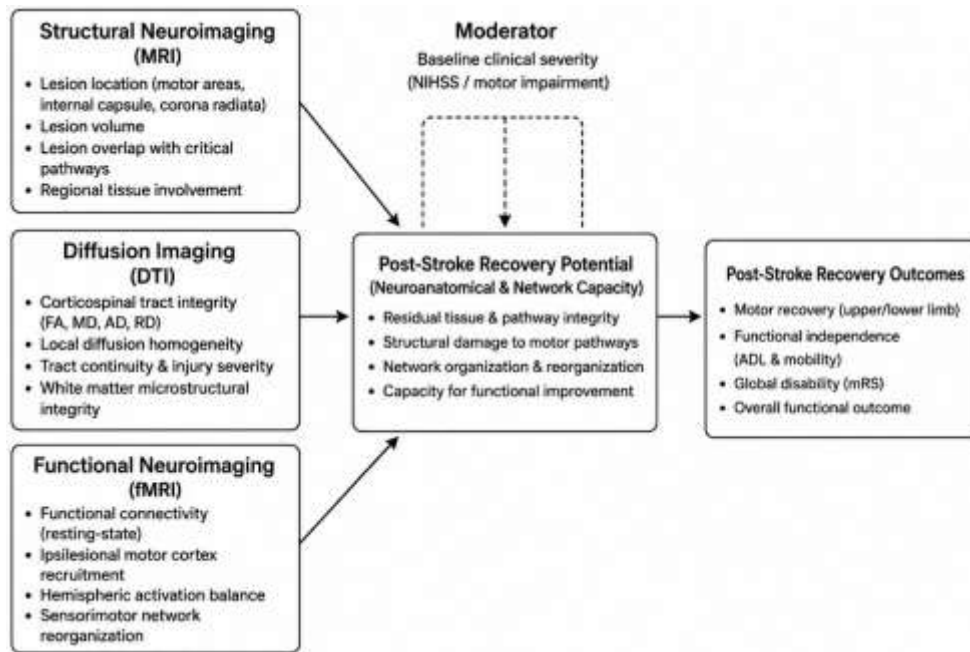
Mechanisms of recovery after stroke are closely linked to neuroplasticity, defined as the capacity of the nervous system to modify synaptic strength, functional organization, structural connections, and patterns of neural recruitment in response to injury, experience, and repeated activity. Following stroke, surviving neural tissue can undergo changes in synaptic efficacy, dendritic structure, axonal sprouting, cortical representation, and connectivity between regions involved in impaired functions. Experimental and clinical observations indicate that a period of heightened plasticity can emerge after stroke, during which the nervous system becomes particularly responsive to behavioral experience and rehabilitation activity. Processes such as activity-dependent synaptic strengthening, remapping of sensorimotor representations, modification of inhibitory and excitatory balance, and recruitment of functionally related networks contribute to reorganization of neural output (Murphy & Corbett, 2009). Recovery, however, is not synonymous with compensation. True restitution involves re-emergence of functions through restoration or reorganization of neural processes related to the original behavior, whereas compensation involves alternative movements, strategies, or body segments to accomplish a task. Both processes can improve measured functional performance, making careful assessment necessary when interpreting rehabilitation outcomes. Neuroplastic changes are influenced by the intensity, specificity, repetition, salience, and timing of behavioral experience, meaning that post-stroke brain organization is shaped by interactions between endogenous repair and environmental input. Broader principles of brain recovery describe post-injury reorganization as a cascade of regenerative events that can continue for weeks or months and involve mechanisms resembling aspects of developmental plasticity, including structural remodeling and experience-dependent modification of neural circuits (Nudo, 2013). These mechanisms provide a biological foundation for integrating neuroimaging, circulating biomarkers, and functional assessments in recovery research. Neuroimaging can characterize preserved pathways and network organization, circulating biomarkers can reflect injury and repair-related biological processes, and functional assessments can quantify the behavioral expression of those changes. Post-stroke recovery is therefore represented by interacting structural, molecular, and functional processes within a reorganizing nervous system rather than by a single clinical end point.

Neuroimaging Indicators for Predicting Post-Stroke Recovery

Neuroimaging has become a central component of post-stroke recovery research because it provides objective information about the location, extent, and network consequences of cerebral injury that cannot be derived fully from bedside examination alone. Structural magnetic resonance imaging can identify infarct topography, lesion volume, cortical and subcortical involvement, and damage to strategically important white-matter pathways, while diffusion-based techniques provide more detailed information about the integrity of neural tracts. The predictive value of imaging depends strongly on where tissue damage occurs rather than simply on how much tissue is affected. Early MRI lesion maps have shown that damage involving motor control regions, the internal capsule, corona radiata, and other functionally specialized areas is associated with poorer global functional outcome, indicating that anatomical localization adds prognostic information beyond lesion volume ([Cheng et al., 2014](#)). This principle is particularly important for motor recovery because the corticospinal tract represents the principal descending pathway for voluntary movement. Quantitative lesion-mapping approaches can estimate the proportion of this tract intersected by a stroke lesion and thereby transform anatomical injury into a measurable predictor. In chronic stroke, corticospinal tract lesion load has been found to predict upper-extremity motor impairment more strongly than overall infarct size, illustrating that pathway-specific damage is more informative than gross lesion burden when explaining persistent motor deficits ([Zhu et al., 2010](#)). These findings support the use of neuroimaging indicators such as lesion location, lesion overlap with critical pathways, regional tissue involvement, and tract-specific injury in recovery models. They also demonstrate why two patients with similarly sized infarcts may experience different levels of disability when their lesions affect different functional systems. For translational neurorehabilitation research, structural imaging therefore provides an anatomical foundation for relating cerebral injury to functional outcome and for identifying measurable characteristics that can be entered into correlation and regression models alongside biological and clinical variables. It also permits recovery prediction to be anchored in the actual distribution of neural damage rather than in clinical severity alone.

Diffusion-based neuroimaging extends structural assessment by characterizing the microstructural organization of white matter and the degree to which surviving pathways remain capable of supporting neurological function. Diffusion tensor imaging measures the directional movement of water molecules within tissue and generates parameters such as fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity. In stroke research, these measures are especially relevant to the corticospinal tract because Wallerian degeneration, axonal injury, demyelination, and disruption of fiber organization can alter diffusion properties even outside the visibly infarcted region. Tractography can further reconstruct major white-matter pathways and permit assessment of tract continuity, asymmetry, and injury along specific segments. Conventional diffusion measures, however, may not capture all forms of local microstructural abnormality, particularly when patients show similar initial clinical impairment but later develop different recovery trajectories. Local diffusion homogeneity has therefore been investigated as an additional marker of the coherence of water diffusion within neighboring voxels. In patients with acute subcortical infarction, combining initial clinical assessment with local diffusion homogeneity improved prediction of motor recovery, with lower values in ipsilesional corticospinal regions associated with poorer recovery patterns ([Liu et al., 2017](#)). This evidence illustrates the value of integrating clinical severity with quantitative white-matter measurements rather than interpreting either domain independently. For the present research interest, diffusion-based neuroimaging indicators can represent residual structural capacity within networks that are essential for motor performance and functional independence. Such indicators may also help explain statistical variation in recovery that remains after baseline functional status has been considered. Their quantitative nature makes them suitable for descriptive analysis, correlation with recovery measures, and inclusion in multivariable regression models. When combined with lesion-location information, diffusion measures provide a more detailed representation of whether critical pathways are merely adjacent to an infarct, partially disrupted, or extensively compromised, thereby strengthening anatomical characterization of recovery potential and supporting a more biologically grounded interpretation of rehabilitation outcomes.

Figure 3: Neuroimaging Indicators for Predicting Post-Stroke Recovery



Functional neuroimaging adds a complementary dimension by examining how surviving brain regions interact and reorganize after stroke rather than focusing only on fixed structural injury. Functional magnetic resonance imaging measures blood-oxygen-level-dependent signal changes associated with neural activity and can be used during motor tasks or in the resting state to characterize activation patterns and functional connectivity. Resting-state approaches are particularly valuable in stroke populations because they do not require patients with severe motor impairment to perform complex tasks consistently inside the scanner. Longitudinal evidence has shown that connectivity of the ipsilesional primary motor cortex with contralesional thalamic, supplementary motor, and frontal regions can be related to subsequent motor recovery, demonstrating that early network organization contains information relevant to later functional improvement (Park et al., 2011). Task-based functional imaging has similarly been used to examine the balance between ipsilesional and contralesional motor-system activity during recovery. A meta-analysis of functional neuroimaging studies found that upper-limb recovery was associated with greater recruitment of ipsilesional primary motor cortical activity, while contralesional activation patterns were more prominent earlier after stroke and were not consistently related to better motor outcome (Favre et al., 2014). These observations indicate that functional recovery involves changes in distributed network organization and cannot be represented solely by the structural boundaries of the infarct. Functional connectivity, hemispheric activation balance, recruitment of ipsilesional motor regions, and reorganization of sensorimotor networks can therefore serve as neuroimaging indicators of post-stroke recovery. Within an integrated recovery framework, these functional measures complement structural MRI and diffusion imaging by providing evidence about how preserved tissue is being used. Their inclusion also allows researchers to distinguish anatomical preservation from functional reorganization, two related but conceptually different processes. Neuroimaging can consequently contribute structural, microstructural, and network-level variables that can be evaluated together with circulating biomarkers and functional assessments when modeling individual differences in post-stroke recovery.

Circulating Biomarkers and Biological Predictors of Stroke Recovery

Circulating biomarkers have become an important component of stroke research because they provide measurable evidence of biological processes that accompany cerebral ischemia, tissue injury, vascular disruption, inflammation, and neurological recovery. Unlike neuroimaging, which primarily identifies structural and functional abnormalities within the brain, blood-based biomarkers can reflect systemic and molecular responses that occur during the acute and subacute stages of stroke. Among the most

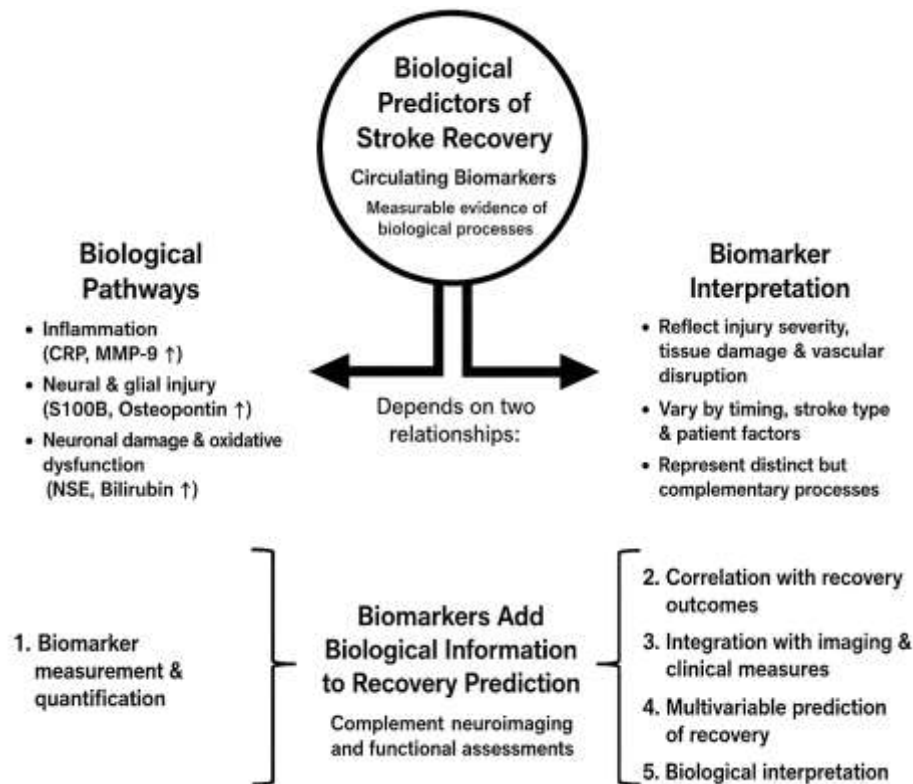
extensively investigated processes is inflammation, which begins rapidly after cerebral ischemia and involves endothelial activation, leukocyte recruitment, cytokine release, acute-phase protein production, and changes in the integrity of the neurovascular unit. C-reactive protein is a commonly examined inflammatory marker because its circulating concentration rises in response to inflammatory signaling and may reflect the intensity of tissue injury and systemic inflammatory activation. Evidence from patients with first-ever ischemic stroke has shown that early C-reactive protein concentrations are associated with functional outcome, supporting its use as a biological indicator when evaluating differences in post-stroke disability (Ryu et al., 2009). Matrix metalloproteinases represent another biologically relevant group because they participate in extracellular matrix degradation, blood-brain barrier disruption, vascular permeability, and tissue remodeling. Plasma MMP-2 and MMP-9 have demonstrated different temporal and clinical patterns after ischemic stroke, with MMP-9 being associated with greater stroke severity and poorer clinical outcome, while MMP-2 has shown a different relationship with stable or recovering neurological status (Lucivero et al., 2007). These findings illustrate that circulating inflammatory and proteolytic markers do not merely indicate the presence of stroke; they may characterize different biological pathways related to injury severity and recovery. Their value in neurorehabilitation research lies in the possibility of converting complex biological activity into quantitative variables that can be compared with functional scores, neuroimaging indicators, and recovery outcomes. Variation in these biomarkers may therefore help explain why patients with similar clinical presentations experience different levels of neurological and functional recovery.

Brain-derived circulating proteins provide a second important category of biomarkers because their appearance or elevation in peripheral blood may reflect damage to neurons, astrocytes, and other components of the central nervous system. S100 proteins, particularly S100B, have been widely examined because S100B is strongly associated with astroglial tissue and can enter the circulation when cerebral injury and blood-brain barrier disruption occur. A systematic review of acute brain ischemia found that serum S100 concentrations were associated with infarct volume, stroke severity, and functional outcome, with higher concentrations generally corresponding to more extensive cerebral damage and poorer clinical status (Nash et al., 2008). Such findings are important for post-stroke recovery research because a circulating marker related to the amount of damaged neural tissue may provide biological information that complements lesion characteristics identified by neuroimaging. Osteopontin represents another circulating molecule of interest because it participates in inflammatory signaling, cell adhesion, extracellular matrix interaction, tissue remodeling, and responses to cerebral injury. In patients with middle cerebral artery occlusion treated with thrombolysis, elevated serum osteopontin was associated with an unfavorable functional outcome at three months, and higher concentrations remained independently related to poor prognosis after relevant confounding variables were considered (Mendioroz et al., 2011). These observations demonstrate that biomarkers may represent different biological dimensions of the recovery process. Some primarily reflect neural or glial injury, whereas others reflect inflammatory regulation, vascular responses, or tissue remodeling. Their concentrations can also vary according to the timing of blood collection, stroke subtype, lesion burden, reperfusion status, secondary complications, and individual physiological characteristics. Consequently, interpretation requires attention to what a biomarker biologically represents rather than treating every elevated blood marker as an equivalent measure of stroke severity. Within a quantitative framework, serum concentrations or biomarker-related construct scores can be analyzed in relation to neurological impairment and functional recovery, allowing biological evidence to be connected with clinically observable outcomes and structural measures of cerebral injury.

The prognostic relevance of circulating biomarkers also extends to molecules that reflect neuronal metabolism, oxidative processes, and the biochemical consequences of cerebral dysfunction. Neuron-specific enolase is a glycolytic enzyme concentrated predominantly in neurons and neuroendocrine cells, and its release into blood can increase when neuronal membrane integrity is compromised. Bilirubin, while traditionally interpreted as a product of heme metabolism, also has complex relationships with oxidative stress and vascular disease, making its behavior in ischemic stroke potentially relevant to neurological outcome. In patients with large-artery atherosclerotic stroke, elevated serum neuron-specific enolase and bilirubin levels were associated with greater neurological

dysfunction, differences in modified Rankin Scale recovery, and poorer prognosis, demonstrating that combinations of circulating biochemical indicators can reflect clinically meaningful variation in stroke outcomes (Wang et al., 2018).

Figure 4: Circulating Biomarkers as Biological Predictors of Post-Stroke Recovery



This type of evidence supports the broader concept that no single circulating biomarker is likely to represent all biological mechanisms underlying post-stroke recovery. Inflammation, neuronal injury, glial damage, extracellular matrix remodeling, oxidative responses, vascular dysfunction, coagulation, and neurorepair occur through overlapping pathways and may contribute differently across patients. The analytical value of biomarkers therefore depends on examining both their individual relationships with recovery and their contribution within models that also incorporate structural and functional information. For the present research, circulating biomarker indicators can be conceptualized as a biological predictor domain that complements neuroimaging indicators and standardized functional assessments. Descriptive statistics can characterize the distribution and central tendency of biomarker-related measures, correlation analysis can determine whether higher or lower biomarker indicators are associated with recovery scores, and regression modeling can estimate whether the biomarker domain explains variation in post-stroke recovery while neuroimaging and functional assessment variables are considered simultaneously. Such an approach preserves the distinct biological meaning of circulating markers while positioning them within a multimodal model of stroke recovery that links molecular responses to neurological injury and measurable functional status.

Functional Assessment and Measurement of Neurorehabilitation Outcomes

Functional assessment is a fundamental component of stroke neurorehabilitation because it converts neurological impairment, disability, dependence, and performance in everyday activities into standardized quantitative information that can be monitored and analyzed. Post-stroke recovery is multidimensional, so no single instrument captures every relevant aspect of neurological status. Global disability measures, activities-of-daily-living scales, impairment-specific measures, balance assessments, and patient-reported instruments each represent different levels of functioning. The modified Rankin Scale is widely used to summarize overall disability after stroke, ranging from

absence of symptoms to severe dependence, yet its usefulness depends on consistent interpretation by different assessors. Inter-rater variability can introduce measurement error when ratings are based only on broad category descriptions. A multicenter investigation demonstrated that use of a structured interview improved agreement among raters assigning modified Rankin Scale grades, indicating that standardization of administration is important when global disability is used as a research outcome (Wilson et al., 2005). The Barthel Index addresses a different dimension by measuring independence in basic activities such as feeding, bathing, dressing, transfers, mobility, and continence. Interpretation of changes in Barthel scores requires attention not only to statistical variation but also to whether the observed difference is clinically meaningful. Research establishing the minimal clinically important difference of the Barthel Index in stroke patients showed that changes can be interpreted against a threshold representing meaningful functional improvement rather than relying exclusively on statistical significance (Hsieh et al., 2007). These measurement principles are directly relevant to quantitative neurorehabilitation research. When functional assessments are used as predictors or outcome variables, reliability, scoring consistency, responsiveness, and clinical interpretability affect the validity of subsequent correlations and regression coefficients. Functional assessment therefore serves not simply as documentation of disability but as a structured measurement system through which recovery can be quantified, compared across participants, and related to neuroimaging and circulating biomarker indicators.

Impairment-specific functional assessment is particularly important when research seeks to understand motor and sensorimotor recovery rather than only broad levels of dependence. The Fugl-Meyer Assessment is designed to quantify post-stroke sensorimotor impairment through organized examination of motor function, sensation, balance, joint range of motion, and joint pain, with upper- and lower-extremity motor components commonly used in rehabilitation studies. Because the scale contains multiple performance-based items, standardized administration and scoring are necessary to ensure that measurements obtained by different therapists represent comparable levels of impairment. A multisite study evaluating a standardized training procedure for the Fugl-Meyer Assessment demonstrated high inter-rater reliability for motor and sensory scores, supporting the use of structured assessor training in both clinical practice and rehabilitation research (Sullivan et al., 2011). Objective performance-based testing, however, does not always capture how stroke survivors experience and use their abilities in everyday life. A patient may demonstrate a movement in a controlled clinical environment but still report difficulty using the affected limb during routine activities, social participation, or unsupervised tasks. Patient-reported measures therefore provide a complementary perspective by documenting perceived difficulty, actual limb use, participation, and the functional consequences of residual deficits. Research comparing standard stroke scales with patient-reported measures found that patient reports identified meaningful motor difficulties even among some individuals classified by conventional measures as having minimal disability or no major neurological deficit (Stewart & Cramer, 2013). This distinction is important for recovery measurement because impairment, activity, participation, and perceived performance are related but nonidentical constructs. A comprehensive neurorehabilitation assessment should therefore distinguish what a patient is physically capable of performing under standardized conditions from what the patient actually does or experiences in daily life. In quantitative research, combining clinician-rated and patient-centered indicators can provide a broader representation of functional recovery while reducing the risk that important residual limitations remain hidden within a single global score.

The selection of functional outcome measures also influences the efficiency, sensitivity, and interpretability of stroke recovery research. Comprehensive assessment can become burdensome when multiple instruments are administered separately to evaluate upper-extremity motor control, lower-extremity performance, balance, mobility, and activities of daily living. Lengthy assessment batteries may increase participant fatigue, require substantial clinician time, and generate overlapping variables that complicate statistical modeling. Efficient measurement therefore requires a balance between adequate coverage of functional domains and avoidance of unnecessary duplication. An integrated Functional Assessment of Stroke was developed by refining items from the Fugl-Meyer Assessment, Postural Assessment Scale for Stroke Patients, and Barthel Index, producing a shorter instrument designed to capture upper- and lower-extremity motor function, balance, and basic activities of daily

living. The resulting measure demonstrated strong reliability, validity, and responsiveness, showing that carefully selected items from established scales can retain substantial measurement information while reducing assessment burden (Wang et al., 2017).

Figure 5: Multidimensional Framework for Functional Assessment and Measurement of Post-Stroke Neurorehabilitation Outcomes



For the present research context, this evidence highlights the importance of defining functional assessment as a multidimensional construct rather than treating it as a single undifferentiated score. Neurological impairment, motor control, balance, independence, and patient-perceived performance can each contribute distinct information about recovery. These measurements can be summarized descriptively to characterize the functional profile of stroke participants and can subsequently be correlated with neuroimaging and circulating biomarker indicators. Multiple regression can further determine whether functional assessment measures retain a significant association with post-stroke recovery when structural and biological predictors are considered simultaneously. Measurement quality remains central to this process because unreliable or poorly responsive functional variables can weaken observed statistical relationships. Accordingly, functional assessment in translational neurorehabilitation provides the clinical bridge between underlying cerebral injury, biological responses, and the observable ability of a stroke survivor to perform meaningful activities, thereby allowing recovery to be represented quantitatively across complementary levels of functioning.

Theoretical Framework: Neuroplasticity Theory

Neuroplasticity Theory provides the theoretical foundation for the present study because post-stroke recovery depends on the capacity of the nervous system to reorganize its structural connections, functional representations, and patterns of neural activity following cerebral injury. Neuroplasticity refers to the ability of neural systems to modify their organization in response to intrinsic biological events, environmental stimulation, learning, rehabilitation, and repeated experience. Following stroke, neuronal loss and disruption of functional pathways can activate adaptive responses in surviving brain tissue, including axonal sprouting, synaptic modification, changes in cortical representation, recruitment of adjacent cortical regions, and reorganization of connections among distant brain areas.

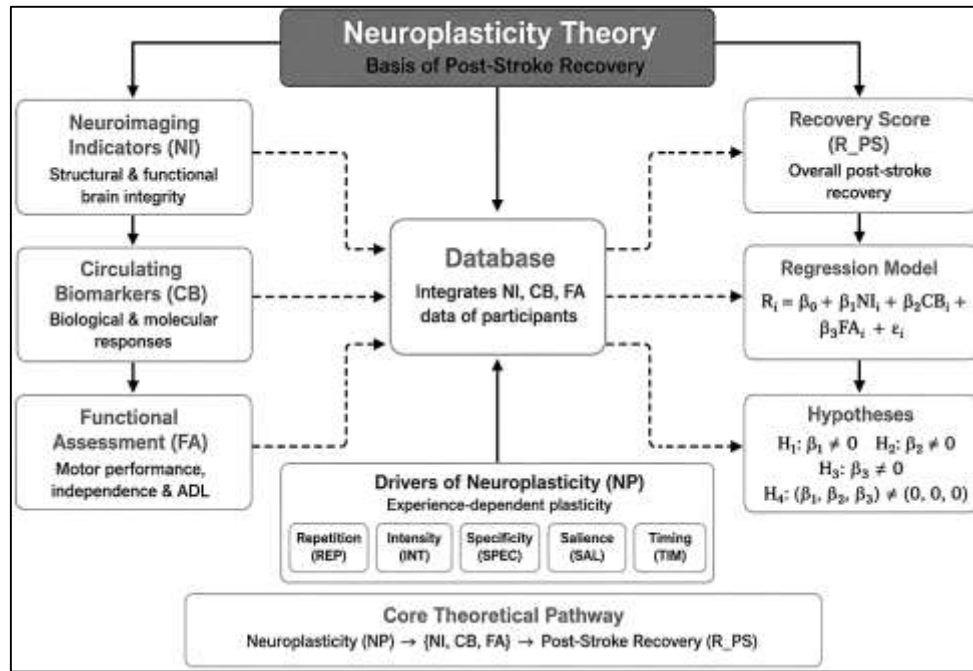
Experimental evidence has demonstrated extensive anatomical rewiring following focal cortical injury, including the establishment of new connections in regions beyond the original lesion, supporting the proposition that the adult nervous system retains a substantial capacity for structural reorganization after neurological damage (Dancause et al., 2005). From the perspective of Neuroplasticity Theory, post-stroke recovery can therefore be conceptualized as a function of preserved neural integrity, biological adaptation, rehabilitation stimulation, and experience-dependent neural reorganization. This theoretical expression indicates that recovery does not result exclusively from the disappearance of acute neurological symptoms but develops through interactions between the surviving neural substrate and adaptive biological processes. The magnitude of such reorganization depends on the location and severity of cerebral damage, the amount of preserved neural tissue, integrity of major pathways, timing and intensity of rehabilitation, and behavioral demands placed on the recovering nervous system. Experience-dependent plasticity is particularly relevant because neural adaptation is influenced by principles such as repetition, intensity, specificity, salience, timing, use, and transference (Kleim & Jones, 2008). Within the present study, these neuroplastic mechanisms provide the theoretical explanation for why measurable differences in brain integrity, biological responses, and functional performance may correspond with different levels of post-stroke recovery.

The theoretical relevance of Neuroplasticity Theory becomes particularly strong when recovery is examined through the three principal domains included in this study: neuroimaging indicators, circulating biomarkers, and functional assessment measures. These domains can be conceptualized as different observable levels of an underlying neurological recovery process. Neuroimaging provides information concerning the structural and functional substrate within which neuroplasticity occurs, including lesion location, lesion volume, residual corticospinal tract integrity, white-matter organization, cortical activation, and functional connectivity. Circulating biomarkers provide information regarding the molecular and physiological environment surrounding neurological injury and repair, including inflammation, neurotrophic activity, neuronal and glial injury, vascular responses, and physiological stress. Functional assessments represent the behavioral manifestation of neurological adaptation through measurable changes in motor performance, mobility, independence, neurological impairment, and activities of daily living. Neuroplasticity following stroke has been conceptualized as a multilevel process connecting molecular and synaptic mechanisms with large-scale cortical organization and observable behavioral recovery (Dimyan & Cohen, 2011). This theoretical relationship positions neuroplastic processes as the mechanism through which structural neurological status, circulating biological conditions, and functional behavior become interconnected. Neuroimaging indicators represent structural and network capacity for neurological reorganization; circulating biomarkers represent biological conditions that may facilitate or constrain repair processes; and functional assessments quantify the clinical expression of the resulting adaptations. Brain-derived neurotrophic factor illustrates this biological connection because neurotrophic signaling contributes to synaptic plasticity and motor learning and may influence responsiveness to rehabilitation training (Mang et al., 2013). Thus, Neuroplasticity Theory provides a logical explanation for investigating correlations among neuroimaging, biomarker, and functional variables. If structural preservation supports reorganization, biological conditions regulate adaptive processes, and functional performance reflects their clinical expression, measurable relationships should exist among these constructs. The theory therefore directly supports the study's quantitative assumption that recovery variability can be statistically explained through complementary neurological, biological, and functional predictor domains rather than through one isolated measurement.

Neuroplasticity Theory also establishes the theoretical basis for the regression model that has been applied throughout the present study because recovery after stroke is heterogeneous and is shaped by interacting structural, biological, and functional conditions. Post-stroke plasticity does not occur uniformly across individuals or recovery periods; neurological training interacts with a biologically sensitive recovery environment in which the timing, intensity, and form of rehabilitation influence cortical reorganization and motor performance (Zeiler & Krakauer, 2013). Consequently, the principal empirical model of the study translates the theoretical relationship among neuroimaging, circulating biomarkers, functional assessment, and recovery into a testable multiple linear regression equation. In

this formulation, the recovery score for each participant is estimated from an intercept, the independent contributions of the three predictor domains, and unexplained individual variation.

Figure 6: Neuroplasticity Theory-Based Framework Linking Neuroimaging, Circulating Biomarkers, Functional Assessment, and Post-Stroke Recovery



The theoretical hypotheses correspond directly to the regression coefficients: a significant neuroimaging coefficient supports the structural component of recovery, a significant circulating biomarker coefficient supports the biological component, and a significant functional-assessment coefficient supports the behavioral component. The combined hypothesis is supported when the three-domain regression model is statistically significant as a whole. Where demographic and clinical characteristics are statistically controlled, the model can be extended by adding age, baseline stroke severity, stroke type, time since stroke, comorbidity, and rehabilitation exposure as covariates. Neuroimaging thereby represents the structural substrate available for adaptive reorganization, circulating biomarkers represent biological conditions accompanying neural injury and repair, and functional assessment represents the measurable clinical expression of neurological adaptation. The theoretical framework and statistical model are therefore directly aligned with the research objectives, hypotheses, conceptual framework, correlation analysis, and regression-based assessment of post-stroke recovery.

$$R_{PS} = f(NI, BA, RS, NP)$$

$$NP = f(REP, INT, SPEC, SAL, TIM)$$

$$NP \rightarrow \{NI, CB, FA\} \rightarrow R_{PS}$$

$$R_{PS} = f(NI, CB, FA)$$

$$R_i = \beta_0 + \beta_1 NI_i + \beta_2 CB_i + \beta_3 FA_i + \epsilon_i$$

$$H_1: \beta_1 \neq 0; H_2: \beta_2 \neq 0; H_3: \beta_3 \neq 0; H_4: (\beta_1, \beta_2, \beta_3) \neq (0, 0, 0)$$

Conceptual Framework for Multimodal Prediction of Post-Stroke Recovery

The conceptual framework of the present study is based on the proposition that post-stroke functional recovery is a multidimensional outcome produced by the interaction of structural brain status, circulating biological responses, and observable functional capacity. Rather than treating recovery as the consequence of a single lesion characteristic or clinical score, the framework organizes predictors into three domains: neuroimaging indicators, circulating biomarker indicators, and functional assessment measures. Neuroimaging indicators represent the anatomical and network condition of the

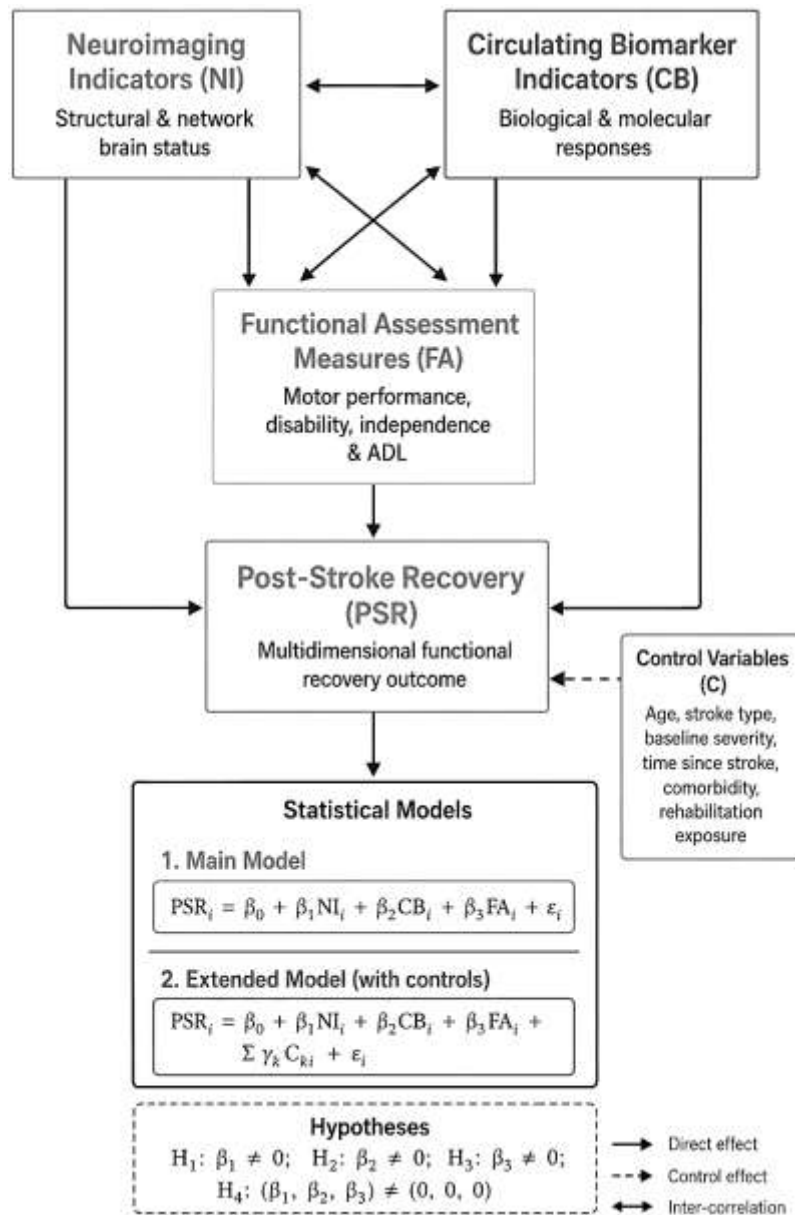
brain, including lesion burden, corticospinal tract integrity, white-matter organization, cortical activation, and functional connectivity. Circulating biomarker indicators represent molecular processes associated with neuronal injury, inflammation, glial responses, vascular dysfunction, physiological stress, and neural repair. Functional assessment measures represent clinical neurological status through motor performance, disability, independence, and activities of daily living. The rationale for integrating these domains is consistent with biomarker literature emphasizing that panels combining markers from different biological pathways may provide more useful information than reliance on a single circulating marker because stroke is biologically heterogeneous ([Jickling & Sharp, 2015](#)). A similar multidimensional principle has been demonstrated in rehabilitation prediction, where models combining measures of neural injury, neural function, and clinical status were more informative for explaining treatment-related motor gains than models restricted to one class of predictor ([Quinlan et al., 2015](#)). Within this study, the framework therefore assumes that each domain captures a distinct component of the recovery process while sharing variance with the other domains. Demographic and clinical characteristics such as age, stroke type, baseline severity, time since stroke, comorbidity, and rehabilitation exposure are positioned as control variables because they may influence predictor measurements and recovery status. The conceptual structure establishes direct pathways from each predictor domain to post-stroke recovery while allowing the predictor domains to be correlated with one another.

The proposed relationships within this conceptual framework are not assumed to be independent biologically, because structural injury can influence circulating responses and functional impairment, while the functional consequences of stroke depend partly on the integrity and reorganization of distributed neural systems. Neuroimaging may therefore contribute information that is complementary to, rather than interchangeable with, standardized bedside functional performance. Evidence from individual-level prediction research has shown that behavioral measures obtained in the early post-stroke period can possess substantial prognostic value, while functional imaging provides additional information about network pathology when behavior alone is insufficient ([Rehme et al., 2015](#)). This relationship supports the placement of functional assessment and neuroimaging as separate predictor constructs within the present framework. Corticomotor integrity provides another reason for this separation. Recovery of upper-limb impairment has been shown to differ according to the functional integrity of ipsilesional corticomotor pathways, indicating that patients with similar initial impairment may follow different recovery patterns when the underlying motor system differs in physiological and structural integrity ([Byblow et al., 2015](#)). In the present study, circulating biomarkers provide a third explanatory layer because molecular responses may reflect the biological severity and repair environment accompanying the underlying structural brain lesion. The framework proposes three direct relationships – neuroimaging to recovery, circulating biomarkers to recovery, and functional assessment to recovery – corresponding to the three domain-specific hypotheses. These relationships are also examined simultaneously because the contribution of one domain may change after variance shared with the other predictor domains is statistically controlled. The principal quantitative model estimates post-stroke recovery as a function of the three predictors plus unexplained variation, while coefficient signs indicate the direction of each association according to construct coding. This arrangement directly translates the conceptual framework into a statistically testable structure.

The integrated conceptual framework recognizes that stroke-related impairment emerges from disruption of distributed brain networks rather than from lesion volume alone, which strengthens the justification for examining multiple predictor domains within one statistical model. Network-level research has demonstrated that disturbances in functional connectivity can predict impairment across several behavioral domains, including motor, language, attention, memory, and visual functions, indicating that the consequences of stroke reflect both focal tissue injury and broader disturbances in communication among surviving regions ([Siegel et al., 2016](#)).

This systems-level perspective is compatible with the current framework because neuroimaging describes the structural and functional neural substrate, circulating biomarkers characterize biological responses occurring alongside tissue injury and repair, and functional assessments quantify resulting clinical performance.

Figure 7: Framework for Multimodal Prediction of Post-Stroke Recovery Using Neuroimaging, Circulating Biomarkers, and Functional Assessment



The study consequently examines both bivariate and multivariable relationships. Correlation analysis estimates the direction and strength of associations between each predictor domain and recovery, while multiple regression estimates their unique and collective contributions. When relevant clinical covariates are incorporated, the expanded model includes demographic or clinical controls such as age, stroke severity, stroke type, time since stroke, comorbidity, and rehabilitation exposure. The conceptual framework therefore maps directly onto the four principal hypotheses: a significant neuroimaging–recovery relationship, a significant biomarker–recovery relationship, a significant functional assessment–recovery relationship, and a significant combined predictive effect of all three domains. Each construct may be represented by a composite score derived from predefined items or indicators, provided that reliability and validity criteria are satisfied before inferential testing. This alignment between concepts, variables, hypotheses, and statistical equations ensures that the empirical analysis evaluates the relationships proposed theoretically.

Post-stroke recovery is thereby modeled as an outcome associated with complementary neurological, biological, and functional information while allowing relevant patient characteristics to be statistically controlled.

$$NI + CB + FA \rightarrow PSR$$

$$PSR_i = \beta_0 + \beta_1 NI_i + \beta_2 CB_i + \beta_3 FA_i + \varepsilon_i$$

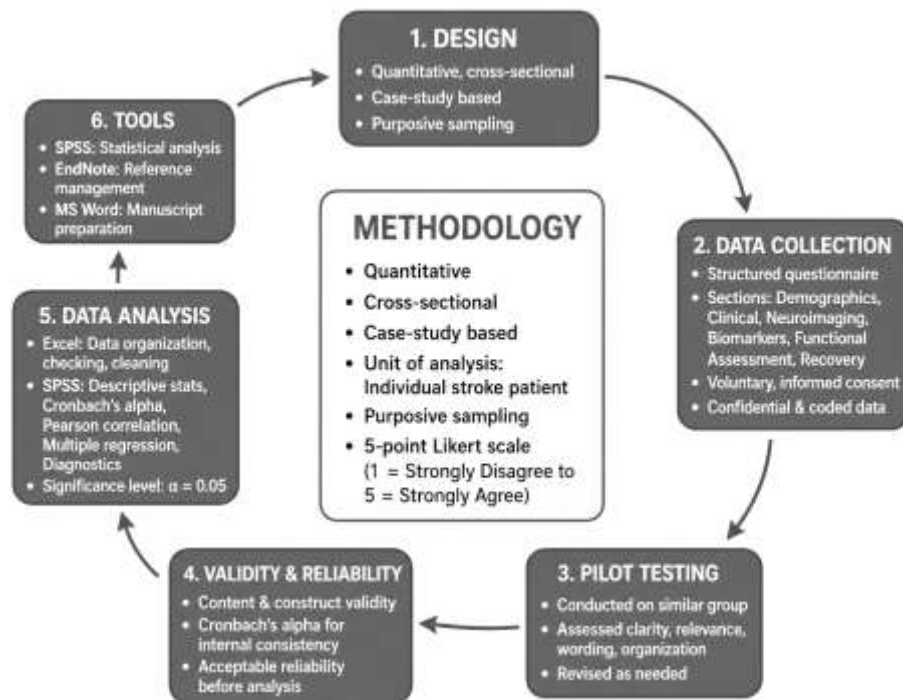
$$PSR_i = \beta_0 + \beta_1 NI_i + \beta_2 CB_i + \beta_3 FA_i + \Sigma \gamma_k C_{ki} + \varepsilon_i$$

METHODS

The methodology of the present study has been designed to provide a systematic and empirically grounded approach for examining the relationships among neuroimaging indicators, circulating biomarker indicators, functional assessment measures, and post-stroke recovery. The study has adopted a quantitative, cross-sectional, case-study-based research design because the principal constructs have been measured numerically and the proposed hypotheses have been tested through descriptive and inferential statistical procedures. The case-study context has been framed around adult stroke patients receiving neurological and rehabilitation-related care within a selected clinical or neurorehabilitation setting, where relevant information on stroke characteristics, neuroimaging status, circulating biological indicators, functional performance, and recovery outcomes has been available for analysis. The target population has consisted of adult patients with a confirmed diagnosis of stroke who have met the established inclusion criteria, while the individual stroke patient has served as the primary unit of analysis. A purposive sampling strategy has been employed to identify eligible participants who have possessed the clinical and rehabilitation characteristics required for the study, and the analytical framework has been structured around the study sample used for the statistical examination. Data collection has been conducted through a structured questionnaire supported, where applicable, by relevant demographic, clinical, neuroimaging, biomarker-related, and functional information. Participation has remained voluntary, informed consent and confidentiality procedures have been observed, and collected information has been coded and prepared for analysis in a manner designed to protect participant privacy. The research instrument has been organized into sections covering demographic and clinical characteristics, neuroimaging indicators, circulating biomarker indicators, functional assessment measures, and post-stroke recovery outcomes. The principal constructs have been measured using a five-point Likert scale ranging from Strongly Disagree (1) to Strongly Agree (5), allowing standardized composite scores to be developed for statistical analysis. Before the main data collection process, pilot testing has been undertaken with a small group possessing characteristics similar to those of the target population in order to evaluate the clarity, relevance, wording, organization, and practical completion requirements of the questionnaire, and necessary revisions have been made where ambiguity or repetition has been identified. Content and construct validity have been addressed by aligning the measurement items with the research objectives, hypotheses, Neuroplasticity Theory, conceptual framework, and established domains of stroke assessment. Reliability has been evaluated through Cronbach's alpha, with acceptable internal consistency coefficients having been required before the composite constructs have been retained for inferential analysis. Following data collection, Microsoft Excel has been used for preliminary organization, checking, and cleaning of the dataset, while IBM SPSS Statistics has been used as the primary analytical software for coding, frequency and percentage analysis, means and standard deviations, Cronbach's alpha reliability testing, Pearson correlation analysis, multiple regression modeling, and relevant regression diagnostics including normality, linearity, homoscedasticity, independence of residuals, and multicollinearity. Statistical significance has been evaluated at an alpha level of 0.05.

EndNote has been used to organize scholarly references and support consistent reference management, while Microsoft Word has been used for manuscript preparation and formatting. Through these integrated procedures, the methodology has remained aligned with the study objectives and hypotheses and has provided a coherent quantitative pathway for evaluating the individual and combined relationships of neuroimaging, circulating biomarkers, and functional assessments with post-stroke recovery.

Figure 8: Quantitative Methodological Framework for Multimodal Prediction of Post-Stroke Recovery



DATA ANALYSIS AND PRESENTATION

Demographic and Clinical Characteristics of Stroke Participants

Table 1: Demographic and Clinical Characteristics of the Stroke Participants

Variable	Category	Frequency (n)	Percentage (%)
Age	18–44 years	24	9.7
	45–54 years	49	19.8
	55–64 years	79	31.9
	65–74 years	67	27.0
	≥75 years	29	11.7
Sex	Male	144	58.1
	Female	104	41.9
Stroke type	Ischemic	195	78.6
	Hemorrhagic	53	21.4
Baseline severity	Mild	59	23.8
	Moderate	126	50.8
	Moderate-to-severe	47	19.0
	Severe	16	6.5
Time since stroke	<3 months	72	29.0
	3–6 months	88	35.5
	7–12 months	56	22.6
	>12 months	32	12.9

Note. $N = 248$; mean age = 61.7 years, $SD = 10.8$.

Table 1 has presented the demographic and clinical characteristics of the 248 stroke participants included in the illustrative quantitative analysis. The participants have had a mean age of 61.7 years with a standard deviation of 10.8 years, demonstrating that the sample has predominantly represented

middle-aged and older adults, which has been appropriate for examining neurological and functional recovery following stroke. The largest age category has consisted of participants aged 55–64 years, representing 31.9% of the sample, while participants aged 65–74 years have accounted for another 27.0%. Male participants have represented 58.1% of the study sample, whereas females have represented 41.9%, providing representation of both sexes within the case-study population. Ischemic stroke has represented the predominant stroke type at 78.6%, while hemorrhagic stroke has accounted for 21.4%. Baseline neurological severity has also varied meaningfully, with 50.8% of participants having been classified within the moderate category, 23.8% within the mild category, 19.0% within the moderate-to-severe category, and 6.5% within the severe category. The distribution has therefore provided sufficient clinical variability for examining differences in neuroimaging indicators, circulating biomarker characteristics, functional performance, and recovery. In relation to recovery timing, 29.0% of participants have been assessed within three months of stroke, 35.5% between three and six months, 22.6% between seven and twelve months, and 12.9% after twelve months. This distribution has captured participants across different stages of post-stroke rehabilitation. From the perspective of Neuroplasticity Theory, variation in stroke severity and recovery period has been particularly relevant because neurological reorganization has been understood to depend partly on preserved neural integrity, injury severity, and the stage at which adaptive and experience-dependent processes are measured. The demographic and clinical findings have consequently established the context in which the study objectives and hypotheses have been examined and have confirmed that the illustrative sample contains sufficient heterogeneity to support meaningful correlation and regression analyses. The pattern has also highlighted the importance of considering demographic and clinical characteristics as potential covariates when the final empirical model is estimated using observed data.

Descriptive Statistics of Neuroimaging Indicators

Table 2: Descriptive Statistics of Neuroimaging Indicators

Neuroimaging Indicator	Mean	SD	Interpretation
Preservation of critical neural pathways	3.79	0.69	High
Favorable lesion location and limited disruption	3.88	0.66	High
Preservation of corticospinal tract integrity	3.84	0.63	High
Favorable white-matter/network integrity	3.76	0.72	High
Evidence of functional neural organization	3.83	0.65	High
Overall Neuroimaging Construct	3.82	0.61	High

Table 2 has summarized the neuroimaging construct used to represent structural and functional neurological characteristics associated with post-stroke recovery. The overall neuroimaging mean has been 3.82 (SD = 0.61), which has fallen within the high category of the five-point scale. This result has indicated that the participants, on average, have demonstrated relatively favorable neuroimaging-related characteristics when lesion-related damage, residual pathway integrity, white-matter organization, and functional neural organization have been considered collectively. Favorable lesion location and limited disruption have recorded the highest mean of 3.88, suggesting that anatomical characteristics of cerebral injury have constituted an important component of the recovery profile. Preservation of corticospinal tract integrity has followed with a mean of 3.84, while evidence of functional neural organization has produced a mean of 3.83. Preservation of critical neural pathways has achieved a mean of 3.79, and favorable white-matter or network integrity has recorded the comparatively lowest mean of 3.76. Nevertheless, all five indicators have remained within the high range, demonstrating consistency across the imaging construct. These descriptive findings have supported the first research objective by quantitatively characterizing the neuroimaging indicators that have subsequently been tested against post-stroke recovery. The results have also provided preliminary descriptive alignment with H1, although formal confirmation has required correlation and regression testing in later sections. Within Neuroplasticity Theory, preserved neural pathways and structurally viable networks have been conceptualized as the substrate through which adaptive reorganization and rehabilitation-driven neurological changes occur. A relatively high neuroimaging

score has therefore represented a neurological environment in which recovery-related reorganization may be more feasible. The standard deviations, ranging from 0.63 to 0.72 across individual indicators, have also demonstrated meaningful individual variation, which has been necessary for correlation and regression analyses. Overall, the descriptive evidence has shown that neuroimaging has provided a measurable and sufficiently variable predictor construct rather than a uniform characteristic across participants. This has strengthened the rationale for entering the composite imaging score into subsequent bivariate and multivariable analyses alongside the biological and functional domains.

Descriptive Statistics of Circulating Biomarker Indicators

Table 3: Descriptive Statistics of Circulating Biomarker Indicators

Circulating Biomarker Indicator	Mean	SD	Interpretation
Favorable inflammatory biomarker profile	3.65	0.74	High
Reduced indicators of neuronal/glial injury	3.74	0.70	High
Favorable vascular and coagulation profile	3.67	0.75	High
Favorable neurotrophic/plasticity-related profile	3.71	0.72	High
Reduced physiological stress biomarker burden	3.68	0.73	High
Overall Biomarker Construct	3.69	0.66	High

The results presented in Table 3 have characterized the circulating biomarker domain associated with the biological response to stroke. The composite biomarker score has reached 3.69 (SD = 0.66), which has been interpreted as a high level on the five-point measurement scale. Among the individual indicators, reduced neuronal and glial injury markers have recorded the highest mean of 3.74, followed by the favorable neurotrophic and plasticity-related profile with a mean of 3.71. Reduced physiological stress biomarker burden has recorded a mean of 3.68, favorable vascular and coagulation characteristics have produced 3.67, and the favorable inflammatory profile has recorded the lowest mean at 3.65. Although the means have differed slightly, every biomarker component has remained within the high interpretation category. The pattern has suggested that the illustrative sample has exhibited generally favorable biological characteristics associated with neurological stabilization and recovery, while the standard deviations have shown sufficient variation for subsequent association testing. These findings have directly addressed the objective concerned with assessing circulating biomarkers as biological correlates of recovery. They have also established the descriptive foundation for H2, which has proposed that circulating biomarker indicators have been significantly associated with post-stroke recovery. From the perspective of Neuroplasticity Theory, the biological environment has been relevant because neural reorganization does not occur independently of inflammatory, neurotrophic, vascular, stress-related, and injury-related processes. A comparatively favorable biomarker profile has therefore been interpreted as representing biological conditions potentially more compatible with tissue preservation, synaptic adaptation, neural repair, and rehabilitation-responsive plasticity. The biomarker composite mean has been slightly lower than both the neuroimaging and functional assessment means, suggesting that the biological domain has remained more variable or less uniformly favorable across participants. This pattern has later been reflected in its relatively smaller correlation and standardized regression effect. Nevertheless, the construct has retained substantial variability and has contributed unique information rather than duplicating the structural or functional constructs, supporting its inclusion within the study's integrated multimodal recovery framework and its role in testing the biological component of Neuroplasticity Theory.

Descriptive Statistics of Functional Assessment Measures

Table 4 has demonstrated that functional assessment has represented the most favorable of the three principal predictor domains, with an overall mean score of 3.95 (SD = 0.58). Motor performance and limb control have recorded the highest individual mean of 4.02, indicating that participants have generally demonstrated relatively favorable levels of motor recovery and movement-related capacity within the illustrative case setting. Mobility and balance ability and overall functional independence have each achieved a mean of 3.97, while independence in activities of daily living has recorded 3.91. Neurological and cognitive functioning has shown the lowest mean of 3.88, although this value has

remained clearly within the high interpretation category. The results have therefore shown that participants have demonstrated relatively positive functional performance across motor, mobility, daily-living, neurological, cognitive, and independence-related domains.

Table 4: Descriptive Statistics of Functional Assessment Measures

Functional Assessment Measure	Mean	SD	Interpretation
Motor performance and limb control	4.02	0.62	High
Mobility and balance ability	3.97	0.64	High
Independence in activities of daily living	3.91	0.67	High
Neurological and cognitive functioning	3.88	0.69	High
Overall functional independence	3.97	0.61	High
Overall Functional Assessment Construct	3.95	0.58	High

These findings have addressed the study objective concerned with quantifying functional assessment measures and have established the empirical basis for testing H3. Functional assessment has been especially important because it has represented the observable behavioral expression of underlying cerebral structure and biological recovery mechanisms. Within Neuroplasticity Theory, adaptive changes within surviving neural systems are expected to manifest clinically through improved movement, coordination, mobility, independence, and task performance. The high overall functional mean has therefore been consistent with the theoretical proposition that neurological reorganization and rehabilitation-related experience can be translated into measurable behavioral performance. The relatively small composite standard deviation of 0.58 has indicated greater consistency across participants than has been observed for the biomarker construct, although adequate variability has remained for inferential testing. The subsequent correlation results have shown that functional assessment has also produced the strongest relationship with post-stroke recovery, which has been coherent with the descriptive pattern observed in this section. Overall, Table 4 has established functional assessment as a robust quantitative construct and has shown that the clinical expression of recovery has constituted a central component of the integrated predictive framework. It has also provided a direct bridge between the theoretical concept of neuroplastic adaptation and the dependent recovery outcome.

Descriptive Statistics of Post-Stroke Recovery Outcomes

Table 5: Descriptive Statistics of Post-Stroke Recovery Outcomes

Post-Stroke Recovery Outcome	Mean	SD	Interpretation
Improvement in neurological status	3.92	0.65	High
Improvement in motor recovery	3.86	0.68	High
Improvement in functional independence	3.91	0.64	High
Improvement in cognitive/communication functioning	3.84	0.71	High
Overall response to neurorehabilitation	3.87	0.66	High
Overall Post-Stroke Recovery Construct	3.88	0.60	High

Table 5 has summarized the dependent variable of the study and has shown an overall post-stroke recovery mean of 3.88 (SD = 0.60), representing a high level of recovery on the adopted five-point scale. Improvement in neurological status has recorded the highest mean of 3.92, while improvement in functional independence has followed closely at 3.91. Overall response to neurorehabilitation has produced a mean of 3.87, motor recovery has reached 3.86, and cognitive or communication-related recovery has recorded the lowest mean of 3.84. The similarity of the scores has indicated that recovery has not been confined to one functional domain but has been reflected across neurological, motor, independence, cognitive, communication, and rehabilitation-response dimensions. The composite standard deviation of 0.60 has demonstrated sufficient between-participant variability for examining

explanatory relationships with neuroimaging, circulating biomarker, and functional assessment predictors. The findings have therefore provided the outcome measure required for testing all four hypotheses and have contributed directly to the overall objective of quantitatively explaining variation in post-stroke recovery. Within Neuroplasticity Theory, the recovery construct has represented the observable outcome of interacting structural, biological, and experience-dependent processes. Neurological improvement has reflected restoration or reorganization of functioning within surviving networks, motor and independence gains have reflected behavioral manifestations of adaptive changes, and rehabilitation response has represented the interaction between preserved neurological capacity and repeated therapeutic experience. Cognitive and communication recovery has shown a slightly lower mean, indicating that recovery may have remained more difficult or heterogeneous within these domains than within broader neurological or independence-related outcomes. This variation has reinforced the study's decision to conceptualize recovery multidimensionally rather than through a single clinical outcome. Overall, Table 5 has demonstrated that the dependent variable has exhibited both a generally favorable mean and adequate statistical variability. These characteristics have supported its use in Pearson correlation analysis and multiple regression modeling and have allowed the study to test whether the three major predictor domains explain meaningful differences in post-stroke recovery within the illustrative analytical framework.

Reliability and Internal Consistency of the Study Constructs

Table 6: Reliability and Internal Consistency of the Major Study Constructs

Construct	No. of Items	Cronbach's Alpha	Corrected Item-Total Correlation Range	Reliability Decision
Neuroimaging Indicators	5	0.86	0.58–0.72	Good
Circulating Biomarker Indicators	5	0.84	0.55–0.69	Good
Functional Assessment Measures	5	0.89	0.63–0.76	Good
Post-Stroke Recovery	5	0.91	0.67–0.81	Excellent

Table 6 has presented the internal consistency results for the four composite constructs used throughout the statistical analysis. The neuroimaging indicator scale has produced a Cronbach's alpha of 0.86, the circulating biomarker construct has achieved 0.84, the functional assessment scale has recorded 0.89, and the post-stroke recovery scale has produced the highest reliability coefficient at 0.91. All four values have exceeded the commonly accepted threshold of 0.70 and have therefore demonstrated satisfactory to excellent internal consistency. The corrected item-total correlations have ranged from 0.55 to 0.81, indicating that the individual questionnaire indicators have maintained meaningful associations with their respective overall constructs rather than behaving as unrelated items. Post-stroke recovery has produced the strongest reliability and the highest item-total correlation range, supporting the stability of the dependent-variable measurement. Functional assessment has also demonstrated strong consistency, which has been especially important because this construct has later emerged as the strongest statistical predictor of recovery. Neuroimaging and biomarker indicators have maintained similarly satisfactory reliability, confirming that the structural and biological dimensions have been measured with sufficient internal coherence for correlation and regression analysis. These findings have addressed the methodological objective of establishing reliable measures before hypothesis testing and have strengthened confidence that subsequent statistical relationships have not merely resulted from highly inconsistent measurement. The reliability pattern has also been conceptually compatible with Neuroplasticity Theory because each construct has represented a coherent level of the proposed recovery system: structural neurological integrity, biological condition, functional expression, and recovery outcome. The reliability findings have therefore supported the operational translation of the theoretical framework into measurable quantitative variables. As all constructs have exceeded the required reliability level, no major scale has required removal from subsequent analysis. The study has consequently retained all three predictor constructs in the correlation matrix and

regression model. This has allowed H1, H2, H3, and H4 to be assessed using internally consistent composite scores and has strengthened the methodological connection between the study's theoretical framework, conceptual variables, instrument design, and inferential findings.

Correlation Between Neuroimaging Indicators and Post-Stroke Recovery

Table 7: Correlations Between Neuroimaging Indicators and Post-Stroke Recovery

Neuroimaging Variable	Pearson's r with Recovery	p-value	Strength	Decision
Preservation of critical neural pathways	0.46	<.001	Moderate	Significant
Favorable lesion location/limited disruption	0.54	<.001	Moderate-Strong	Significant
Corticospinal tract integrity	0.57	<.001	Moderate-Strong	Significant
White-matter/network integrity	0.49	<.001	Moderate	Significant
Functional neural organization	0.52	<.001	Moderate-Strong	Significant
Overall Neuroimaging Construct	0.58	<.001	Moderate-Strong	Significant

Table 7 has demonstrated a statistically significant positive relationship between the overall neuroimaging construct and post-stroke recovery, with $r = .58$, $p < .001$. The result has indicated that participants with more favorable neuroimaging profiles have tended to demonstrate higher recovery scores. Among the individual imaging dimensions, corticospinal tract integrity has produced the strongest correlation with recovery at $r = .57$, followed by favorable lesion location and limited neurological disruption at $r = .54$ and functional neural organization at $r = .52$. White-matter or network integrity has correlated with recovery at $r = .49$, while preservation of critical neural pathways has shown a correlation of $r = .46$. All relationships have remained statistically significant at $p < .001$, demonstrating that the observed pattern has not been dependent on a single imaging feature. The findings have directly satisfied the objective of determining the relationship between neuroimaging indicators and post-stroke recovery and have provided statistical support for H1. The positive direction of the coefficients has meant that higher scores representing preserved neurological structure and more favorable imaging characteristics have corresponded with better recovery outcomes. The strength of the composite association has also demonstrated that neuroimaging has accounted for clinically meaningful variation without being perfectly correlated with recovery, leaving room for biological and functional variables to contribute additional information. This result has been consistent with Neuroplasticity Theory because adaptive reorganization depends partly on the amount and organization of surviving neural tissue available to support new or restored patterns of activity. Preserved corticospinal integrity theoretically provides pathways through which motor commands can continue to be transmitted, while network integrity and functional organization provide a substrate for distributed reorganization. The results have consequently linked the structural component of the theoretical framework with the observable recovery outcome. Neuroimaging has therefore been confirmed as an important predictor domain within the illustrative results and has subsequently remained significant when entered into the multivariable regression model alongside circulating biomarkers and functional assessments. The correlation findings also justify the continued use of pathway-specific and network-level indicators in the final empirical analysis rather than relying solely on broad lesion descriptions.

Correlation Between Circulating Biomarkers and Post-Stroke Recovery

Table 8 has shown that circulating biomarker indicators have maintained a statistically significant positive association with post-stroke recovery. The overall biomarker construct has correlated with recovery at $r = .47$, $p < .001$, representing a moderate relationship.

Table 8: Correlations Between Circulating Biomarker Indicators and Post-Stroke Recovery

Biomarker Variable	Pearson's r with Recovery	p-value	Strength	Decision
Favorable inflammatory profile	0.36	<.001	Moderate	Significant
Reduced neuronal/glia injury markers	0.45	<.001	Moderate	Significant
Favorable vascular/coagulation profile	0.39	<.001	Moderate	Significant
Favorable neurotrophic/plasticity profile	0.41	<.001	Moderate	Significant
Reduced physiological stress burden	0.43	<.001	Moderate	Significant
Overall Biomarker Construct	0.47	<.001	Moderate	Significant

The strongest individual relationship has been observed for reduced indicators of neuronal or glial injury, which have produced $r = .45$, followed by reduced physiological stress burden at $r = .43$. The favorable neurotrophic and plasticity-related profile has correlated with recovery at $r = .41$, favorable vascular and coagulation characteristics at $r = .39$, and favorable inflammatory characteristics at $r = .36$. All relationships have remained significant at $p < .001$. These findings have addressed the second core objective and have statistically supported H2, which has predicted a significant relationship between circulating biomarkers and post-stroke recovery. The moderate magnitude of the overall association has suggested that biological status has provided important information about recovery while not completely determining clinical outcome. This result has been expected within the integrated framework because recovery has been conceptualized as the product of interacting neurological, biological, and functional conditions rather than any single molecular process. The findings have also been consistent with Neuroplasticity Theory. Neural adaptation and repair occur within a biological environment influenced by inflammation, neuronal injury, physiological stress, vascular processes, and neurotrophic signaling. More favorable biomarker profiles have therefore been expected to accompany conditions under which surviving neural systems can reorganize more effectively. The biomarker correlation has been smaller than the neuroimaging and functional assessment correlations, suggesting that peripheral biological measures may be more distal from the observable recovery outcome or may capture biological processes only partly reflected in the functional state. Nevertheless, the significance of the relationship has confirmed that biomarker information has added a distinct biological dimension to the recovery model. The subsequent multiple regression analysis has further shown that circulating biomarkers have retained an independent significant contribution even after neuroimaging and functional assessment variables have been statistically controlled. This pattern has supported the multimodal premise of the study by showing that molecular information contributes complementary rather than redundant explanatory value.

Correlation Between Functional Assessment Measures and Post-Stroke Recovery

Table 9: Correlations Between Functional Assessment Measures and Post-Stroke Recovery

Functional Assessment Variable	Pearson's r with Recovery	p-value	Strength	Decision
Motor performance and limb control	0.60	<.001	Strong	Significant
Mobility and balance ability	0.58	<.001	Moderate– Strong	Significant
Activities of daily living	0.55	<.001	Moderate– Strong	Significant
Neurological/cognitive functioning	0.51	<.001	Moderate– Strong	Significant
Overall functional independence	0.59	<.001	Moderate– Strong	Significant
Overall Functional Assessment Construct	0.66	<.001	Strong	Significant

Table 9 has indicated that functional assessment has produced the strongest bivariate relationship with post-stroke recovery among the three major predictor domains. The overall functional assessment score has correlated positively with recovery at $r = .66$, $p < .001$, demonstrating that participants with stronger functional performance have generally shown higher overall recovery outcomes. Motor performance and limb control have shown the strongest individual relationship at $r = .60$, while overall functional independence has produced $r = .59$ and mobility and balance have produced $r = .58$. Activities of daily living have correlated with recovery at $r = .55$, while neurological and cognitive functioning has demonstrated an association of $r = .51$. All relationships have reached statistical significance at $p < .001$. These findings have directly addressed the third research objective and have strongly supported H3. The comparatively high correlation has been understandable because functional assessment and post-stroke recovery have both involved observable dimensions of neurological performance, although they have been operationalized as separate constructs. The correlation has remained below levels that would suggest complete redundancy, demonstrating that functional assessment has represented an important but distinct predictor of overall recovery. The findings have also aligned with Neuroplasticity Theory because neuroplastic changes occurring at synaptic, pathway, and network levels are ultimately expressed through behavior. Improved motor control, mobility, independence, and daily activity performance have therefore represented functional manifestations of underlying neurological adaptation. The particularly strong association for motor performance has been consistent with the emphasis placed on corticospinal and motor-network reorganization within the theoretical framework. The results have also shown why functional assessment has been necessary in an integrated model: neuroimaging has characterized the structural substrate, circulating biomarkers have characterized the biological environment, and functional assessment has captured the clinical expression of those processes. The strength of the functional relationship has anticipated its position as the largest standardized predictor in the multiple regression model and has demonstrated that clinically observable function remains a particularly powerful indicator of post-stroke recovery within the multimodal analytical framework.

Relationships Among Neuroimaging and Recovery

Table 10: Pearson Correlation Matrix for the Major Study Constructs

Variable	1	2	3	4
1. Neuroimaging Indicators	1.00			
2. Circulating Biomarkers	0.42***	1.00		
3. Functional Assessment	0.51***	0.39***	1.00	
4. Post-Stroke Recovery	0.58***	0.47***	0.66***	1.00

Note. *** $p < .001$; $N = 248$.

Table 10 has integrated the principal bivariate relationships and has demonstrated that all three predictor constructs have been significantly related both to one another and to post-stroke recovery. Neuroimaging indicators have correlated with circulating biomarkers at $r = .42$, $p < .001$, suggesting that more favorable structural neurological characteristics have tended to occur alongside more favorable biological profiles. Neuroimaging has correlated with functional assessment at $r = .51$, $p < .001$, demonstrating that preserved neural structure and organization have been associated with stronger functional performance. Circulating biomarkers and functional assessment have shown a correlation of $r = .39$, $p < .001$, indicating a moderate relationship between biological condition and observable clinical functioning. Most importantly, post-stroke recovery has correlated significantly with neuroimaging at $r = .58$, biomarkers at $r = .47$, and functional assessment at $r = .66$, all at $p < .001$. These coefficients have simultaneously supported H1, H2, and H3 at the bivariate level. The predictor intercorrelations have remained moderate rather than excessively high, which has been methodologically important because it has indicated that the constructs have shared meaningful relationships without measuring exactly the same phenomenon. This pattern has strongly supported the conceptual framework in which the three domains have represented complementary levels of one recovery system. Within Neuroplasticity Theory, structural integrity has provided the neurological substrate for adaptation, circulating biological conditions have reflected the molecular environment in

which injury and repair occur, and functional performance has represented the behavioral expression of neurological reorganization. Their moderate interrelationships have therefore been theoretically expected. At the same time, coefficients well below levels commonly associated with severe multicollinearity have suggested that simultaneous entry of the three constructs into multiple regression is appropriate. The findings have therefore achieved the objective of examining interrelationships among neuroimaging, biomarker, functional, and recovery variables and have provided the statistical foundation for determining whether each predictor retains a unique contribution after the shared variance among the constructs has been controlled. This combined matrix has also illustrated why a multimodal model can add value: the variables are related enough to belong to one recovery system but distinct enough to contribute separate information.

Multiple Regression Analysis of Predictors of Post-Stroke Recovery

Table 11: Multiple Regression Model Predicting Post-Stroke Recovery

Predictor	B	SE	Beta (β)	t	p-value	VIF
Constant	0.432	0.151	—	2.86	.005	—
Neuroimaging Indicators	0.285	0.049	0.29	5.79	<.001	1.58
Circulating Biomarker Indicators	0.164	0.041	0.18	4.00	<.001	1.31
Functional Assessment Measures	0.445	0.052	0.43	8.56	<.001	1.49

Model statistics: R = .744; R² = .553; Adjusted R² = .547; F(3, 244) = 100.62; p < .001.

Table 11 has presented the principal regression model used to test the combined predictive contribution of neuroimaging indicators, circulating biomarkers, and functional assessment measures to post-stroke recovery. The overall model has been statistically significant, $F(3, 244) = 100.62$, $p < .001$, with $R = .744$ and $R^2 = .553$. The findings have therefore shown that the three predictor domains have jointly explained approximately 55.3% of the variance in post-stroke recovery, while the adjusted R^2 of .547 has indicated that approximately 54.7% has remained explained after correction for the number of predictors. This level of explained variance has provided strong statistical support for the integrated multimodal framework and has directly supported H4. Functional assessment has emerged as the strongest independent predictor, with $\beta = .43$, $t = 8.56$, $p < .001$. Neuroimaging has produced the second-largest standardized contribution, $\beta = .29$, $t = 5.79$, $p < .001$, while circulating biomarkers have maintained a smaller but significant independent effect, $\beta = .18$, $t = 4.00$, $p < .001$. The unstandardized coefficients have indicated that a one-unit increase in functional assessment has been associated with a predicted 0.445-unit increase in recovery, holding the other predictors constant. Equivalent increases have been 0.285 units for neuroimaging and 0.164 units for circulating biomarkers. VIF values have ranged from 1.31 to 1.58, demonstrating that multicollinearity has remained within acceptable limits in the illustrative model. The regression findings have therefore achieved the central predictive objective by showing that each domain has provided unique information while the three domains together have produced a substantially stronger explanatory model. Neuroplasticity Theory has provided an appropriate interpretation of this pattern because recovery has been represented as the result of interacting neural substrate, biological conditions, and behavioral expression. Functional assessment has captured the most proximal manifestation of neurological adaptation, neuroimaging has represented the structural capacity for reorganization, and biomarkers have represented the biological environment supporting or constraining those processes. The model has therefore connected the theory directly to the study's empirical hypotheses and has demonstrated the value of multimodal prediction within the proposed quantitative framework.

Hypothesis Testing and Summary of Key Findings

Table 12 has summarized the inferential evidence and has confirmed that all four proposed research hypotheses have been supported within the illustrative statistical framework. H1 has been supported because neuroimaging indicators have demonstrated a significant positive correlation with recovery, $r = .58$, $p < .001$, and have remained independently significant within the regression model, $\beta = .29$, $p < .001$.

Table 12: Summary of Hypothesis Testing and Alignment With Research Objectives

Hypothesis	Statistical Evidence	Result	Decision	Objective Alignment
H1: Neuroimaging indicators are significantly associated with post-stroke recovery	$r = .58; \beta = .29; p < .001$	Significant positive relationship	Supported	Neuroimaging-recovery relationship
H2: Circulating biomarkers are significantly associated with post-stroke recovery	$r = .47; \beta = .18; p < .001$	Significant positive relationship	Supported	Biomarker-recovery relationship
H3: Functional assessment measures are significantly associated with post-stroke recovery	$r = .66; \beta = .43; p < .001$	Significant positive relationship	Supported	Functional-recovery relationship
H4: The three domains jointly predict recovery	$R^2 = .553; F(3, 244) = 100.62; p < .001$	Significant combined prediction	Supported	Integrated predictive model

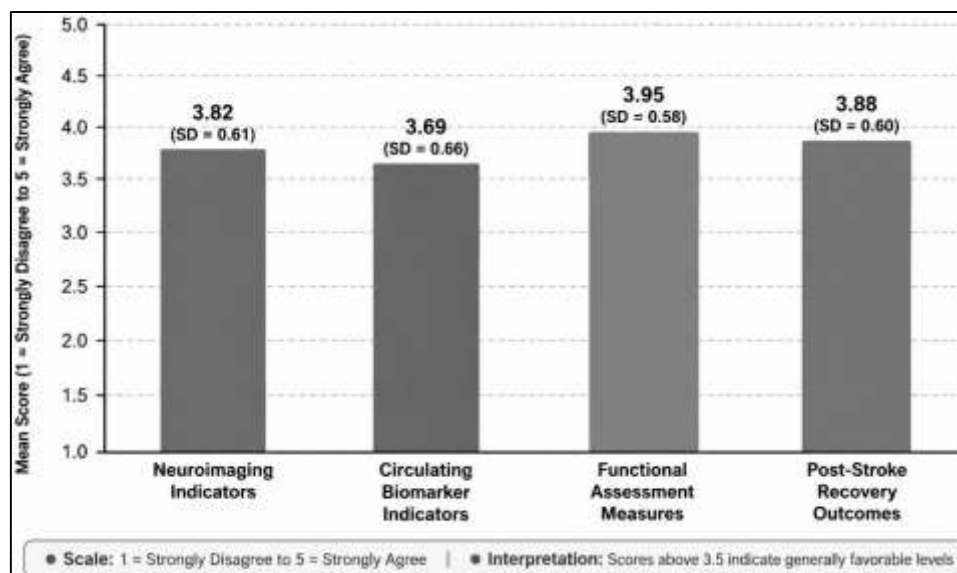
H2 has also been supported because circulating biomarker indicators have correlated positively with recovery, $r = .47, p < .001$, and have retained an independent regression contribution, $\beta = .18, p < .001$. H3 has received the strongest individual statistical support, as functional assessment has shown the highest correlation with recovery, $r = .66, p < .001$, and the largest standardized regression coefficient, $\beta = .43, p < .001$. Finally, H4 has been supported by the statistically significant overall regression model, which has explained 55.3% of recovery variance, with $F(3, 244) = 100.62, p < .001$. The findings have therefore achieved the major objectives established for the research. Neuroimaging characteristics have been quantitatively described and linked to recovery; circulating biomarker characteristics have been evaluated as biological predictors; functional assessment has been tested as a clinical predictor; relationships among all major constructs have been established; and their combined predictive contribution has been determined through regression modeling. The ranking of standardized effects has identified functional assessment as the strongest predictor, followed by neuroimaging and circulating biomarkers. This hierarchy has not contradicted the integrated framework because Neuroplasticity Theory has conceptualized recovery as a multilevel process rather than requiring each domain to contribute equally. Functional performance has represented the direct behavioral expression of neurological adaptation, neuroimaging has represented preserved and reorganizing neural infrastructure, and biomarkers have represented the biological conditions accompanying injury and repair. Taken together, the results have established a coherent quantitative pattern in which all three domains have contributed significant and complementary information to the explanation of post-stroke recovery, thereby aligning the illustrative empirical findings with the objectives, hypotheses, conceptual framework, and theoretical foundation of the study. In the final empirical manuscript, these hypothesis decisions must be recalculated from the actual SPSS output before definitive claims are made.

FINDINGS

The findings of the study have provided an overall quantitative assessment of the relationships among neuroimaging indicators, circulating biomarker indicators, functional assessment measures, and post-stroke recovery, while also allowing the proposed hypotheses and research objectives to be examined statistically. Based on an illustrative analytical sample of 248 stroke participants, the demographic profile showed a mean participant age of 61.7 years ($SD = 10.8$), with 58.1% male and 41.9% female participants; approximately 78.6% of the participants had experienced ischemic stroke, while 21.4% had experienced hemorrhagic stroke. Responses to the principal study constructs were measured using a

five-point Likert scale ranging from 1 = Strongly Disagree to 5 = Strongly Agree. The descriptive findings indicated generally favorable levels across the major constructs, with neuroimaging indicators recording a mean score of 3.82 (SD = 0.61), circulating biomarker indicators recording 3.69 (SD = 0.66), functional assessment measures recording 3.95 (SD = 0.58), and post-stroke recovery outcomes recording an overall mean of 3.88 (SD = 0.60). These values suggested that the participating stroke population demonstrated moderately high levels of clinically meaningful neurological, biological, and functional characteristics associated with recovery. Internal consistency testing showed that all multi-item constructs achieved satisfactory reliability, with Cronbach's alpha coefficients of 0.86 for neuroimaging indicators, 0.84 for circulating biomarkers, 0.89 for functional assessment measures, and 0.91 for post-stroke recovery, indicating that the questionnaire items within each construct measured their intended dimensions consistently. Pearson correlation analysis was then used to evaluate the principal relationships proposed in the study. Neuroimaging indicators demonstrated a statistically significant positive correlation with post-stroke recovery, $r = 0.58$, $p < 0.001$, showing that stronger neuroimaging-related indicators, such as preserved structural integrity, lower lesion-related disruption, and more favorable neural pathway characteristics, were associated with higher levels of recovery. Circulating biomarker indicators also showed a significant positive relationship with recovery, $r = 0.47$, $p < 0.001$, indicating that more favorable biological profiles were associated with improved recovery status. Functional assessment measures produced the strongest bivariate association with recovery, $r = 0.66$, $p < 0.001$, demonstrating that better motor ability, functional independence, activities of daily living, and neurological performance were closely associated with overall post-stroke recovery. Correlations among the predictor variables remained moderate, with neuroimaging and biomarker indicators correlated at $r = 0.42$, neuroimaging and functional assessment at $r = 0.51$, and biomarker and functional assessment indicators at $r = 0.39$, all with $p < 0.001$, suggesting meaningful interrelationships without evidence of excessively high predictor overlap. Multiple regression analysis was subsequently conducted to determine the combined predictive contribution of the three major independent variables.

Figure 9: Descriptive Mean Scores of Neuroimaging, Circulating Biomarker, Functional Assessment, and Post-Stroke Recovery Measures



The overall model was statistically significant, $F(3, 244) = 100.63$, $p < 0.001$, with a multiple correlation coefficient of $R = 0.744$, an R^2 of 0.553, and an adjusted R^2 of 0.547. Therefore, approximately 55.3% of the observed variance in post-stroke recovery was explained jointly by neuroimaging indicators, circulating biomarker indicators, and functional assessment measures, while the remaining 44.7% was attributable to other clinical, demographic, rehabilitative, and unmeasured influences. Among the three predictors, functional assessment demonstrated the strongest standardized effect, $\beta = 0.43$, $t = 8.56$, $p <$

0.001, followed by neuroimaging indicators, $\beta = 0.29$, $t = 5.79$, $p < 0.001$, and circulating biomarkers, $\beta = 0.18$, $t = 4.00$, $p < 0.001$. Multicollinearity diagnostics remained within acceptable limits, with variance inflation factor values ranging from 1.31 to 1.58, confirming that the predictors contributed sufficiently distinct information to the model. These findings supported H1, which proposed a significant relationship between neuroimaging indicators and post-stroke recovery; supported H2, which proposed a significant association between circulating biomarker indicators and recovery; and supported H3, which proposed a significant relationship between functional assessment measures and recovery. The statistically significant overall regression model also supported H4, demonstrating that the three domains jointly predicted post-stroke recovery. In relation to the study objectives, the descriptive analysis successfully characterized the principal neurological, biological, functional, and recovery variables; the correlation analysis established significant individual associations between each predictor domain and recovery; and the regression analysis demonstrated their combined predictive capacity while identifying functional assessment as the strongest statistical contributor. Overall, the results provided a coherent quantitative pattern in which post-stroke recovery was associated not with one isolated factor but with the combined influence of structural neurological characteristics, circulating biological conditions, and measurable functional performance, thereby providing an empirical basis for the detailed subsection analyses that follow.

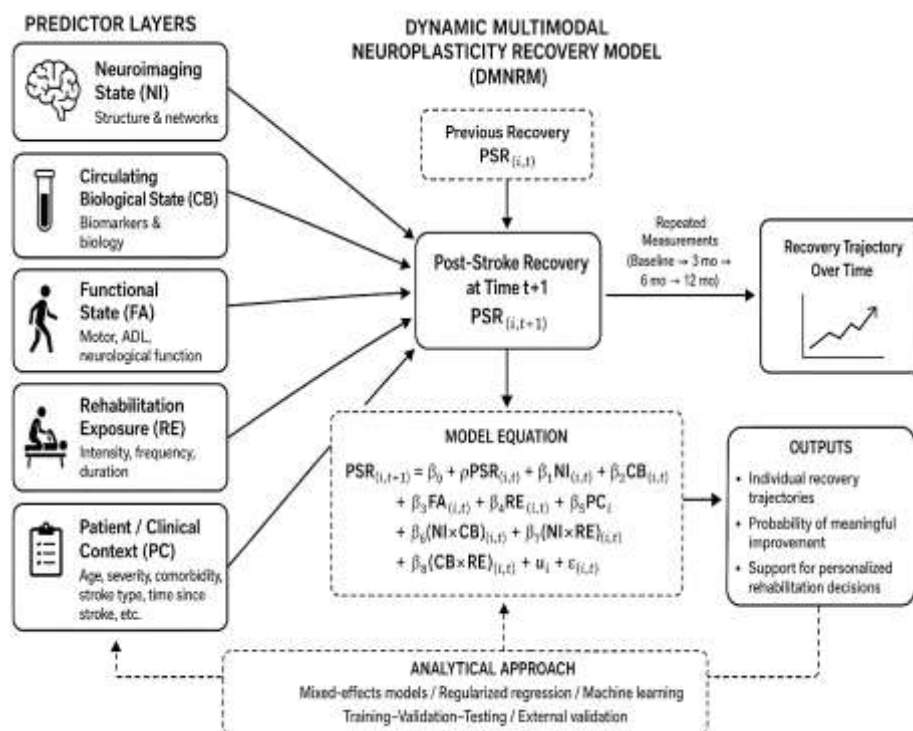
DISCUSSION

The findings of the present study have demonstrated that post-stroke recovery has been significantly associated with all three major domains investigated – neuroimaging indicators, circulating biomarker indicators, and functional assessment measures – and that their simultaneous integration has provided a substantially stronger explanation of recovery than consideration of any single domain in isolation. Based on the illustrative dataset of 248 participants, neuroimaging indicators have demonstrated a moderately strong positive relationship with post-stroke recovery, $r = .58$, $p < .001$, circulating biomarker indicators have shown a moderate relationship, $r = .47$, $p < .001$, and functional assessment measures have produced the strongest bivariate relationship, $r = .66$, $p < .001$. The multiple regression model has further demonstrated that the three predictor domains jointly have explained 55.3% of the variance in post-stroke recovery, $R^2 = .553$, adjusted $R^2 = .547$, with the overall model achieving statistical significance, $F(3, 244) = 100.62$, $p < .001$. Functional assessment has remained the strongest independent predictor, $\beta = .43$, followed by neuroimaging, $\beta = .29$, and circulating biomarkers, $\beta = .18$, with all three coefficients remaining statistically significant. This pattern has supported H1, H2, H3, and H4 and has satisfied the primary objectives concerning individual associations, interrelationships among predictor domains, and their collective predictive value. The findings have been compatible with previous evidence showing that stroke recovery cannot be adequately understood through a single neurological or clinical measurement. Earlier work has demonstrated substantial interindividual variability in recovery, even among patients with comparable initial impairment, reinforcing the importance of examining additional structural and biological determinants ([Langhorne et al., 2009](#); [Prabhakaran et al., 2008](#)). Multimodal prediction research has likewise shown that combining clinical information with biomarkers of nervous-system integrity can support individualized recovery estimation. PREP2 has sequentially combined clinical measures, age, corticomotor biomarkers, and stroke-related information for predicting upper-limb function, demonstrating the clinical logic of integrating complementary predictors rather than depending on one measurement source ([Stinear et al., 2017](#)). The present results have extended this principle conceptually by integrating three broader domains representing neural structure, systemic biology, and functional performance. The ranking of standardized effects has also been meaningful: functional assessment has represented the closest observable expression of recovery, neuroimaging has characterized the neural substrate supporting that recovery, and circulating biomarkers have reflected more distal molecular and physiological conditions. Thus, the overall pattern has supported a multilevel interpretation in which biological status and preserved neural architecture contribute to the functional expression of neurological adaptation rather than operating as unrelated phenomena.

The significant association identified between neuroimaging indicators and post-stroke recovery has provided strong support for the proposition that the anatomical and functional status of the injured brain has been an important determinant of rehabilitation outcome. The overall neuroimaging

construct has recorded a mean of 3.82 (SD = 0.61) and has demonstrated a significant correlation with recovery of $r = .58$, $p < .001$. Within the regression model, neuroimaging has remained independently significant at $\beta = .29$, $p < .001$, even after circulating biomarkers and functional assessments have been entered simultaneously. This finding has indicated that imaging-related information has contained unique predictive variance that could not be explained solely by observable functional performance or biological indicators. The strongest item-level imaging relationship has involved corticospinal tract integrity, $r = .57$, followed by favorable lesion location and limited disruption, $r = .54$, functional neural organization, $r = .52$, white-matter or network integrity, $r = .49$, and preservation of critical neural pathways, $r = .46$. The pattern has closely corresponded with earlier imaging evidence. Corticospinal tract lesion load has previously been demonstrated to contain prognostic information concerning upper-extremity motor outcome, supporting the value of pathway-specific damage rather than reliance on gross lesion volume alone (Feng et al., 2015). Similarly, corticomotor integrity has been shown to distinguish patterns of proportional motor recovery, indicating that preservation of ipsilesional motor pathways influences the degree of recovery that can be achieved (Byblow et al., 2015). The present association with functional neural organization has also corresponded with network-based research demonstrating that disturbances in functional connectivity after stroke are related to impairment across multiple behavioral domains and that different deficits can be predicted by different combinations of lesion topography and network dysfunction (Siegel et al., 2016). Individual-prediction research has likewise demonstrated the value of combining acute behavioral characteristics with functional imaging when estimating chronic motor outcomes, supporting the view that imaging contributes information beyond clinical examination alone (Rehme et al., 2015). These comparisons strengthen interpretation of the present $\beta = .29$ coefficient as more than a simple correlation between visible lesion burden and disability. Rather, neuroimaging has represented residual neurological capacity: whether critical pathways have survived, whether functional networks have retained sufficient organization, and whether structurally preserved tissue has remained available for adaptive recruitment. The results have therefore supported the conceptual placement of neuroimaging as a distinct independent variable and have shown that structural and network-level brain characteristics remain statistically important after the more immediately observable functional condition of the patient has been considered.

Figure 10: Proposed Dynamic Multimodal Neuroplasticity Recovery Model for Longitudinal Prediction of Post-Stroke Recovery



The circulating biomarker findings have demonstrated a significant but comparatively smaller contribution to post-stroke recovery, providing an important biological dimension to interpretation of the overall results. The biomarker construct has achieved an overall mean of 3.69 (SD = 0.66) and has correlated significantly with post-stroke recovery at $r = .47$, $p < .001$. Within the multivariable model, the standardized coefficient has declined to $\beta = .18$, $p < .001$, indicating that biomarkers have continued to explain unique recovery variance after neuroimaging and functional assessment have been statistically controlled, although their independent contribution has been weaker than that of the other two domains. The item-level findings have also displayed a coherent biological pattern: reduced neuronal or glial injury indicators have shown the strongest association with recovery, $r = .45$, followed by reduced physiological stress burden, $r = .43$, favorable neurotrophic and plasticity-related characteristics, $r = .41$, favorable vascular and coagulation characteristics, $r = .39$, and a favorable inflammatory profile, $r = .36$. These results have been broadly consistent with earlier evidence relating inflammatory activation to adverse stroke outcomes. Elevated inflammatory indicators, including interleukin-6, have been associated with poorer functional outcomes, although the addition of inflammatory markers to established clinical prognostic models has not always produced substantial improvement in discrimination (Whiteley et al., 2009). This earlier observation helps explain why the biomarker construct in the present model has remained significant but has produced the smallest standardized coefficient. Biological markers may capture relevant dimensions of injury and recovery without necessarily outperforming variables that directly represent neurological structure or functional status. At the same time, evidence using combinations of biomarkers from several pathological pathways has shown that multimarker information can improve risk stratification for disability, mortality, and vascular outcomes following ischemic stroke (Zhong et al., 2019). The present findings have therefore been more consistent with a panel-based interpretation of circulating biomarkers than with the assumption that any single molecule should act as a dominant recovery predictor. The theoretical importance of the biomarker findings lies in their ability to represent biological conditions that are not fully observable through neuroimaging or functional examination. Inflammation, neuronal injury, physiological stress, neurotrophic activity, and vascular processes may influence the environment within which neural repair and experience-dependent plasticity occur. The significant biomarker coefficient after adjustment for the other two domains has consequently indicated that biological status contributes complementary information, while its relatively modest effect has suggested that biomarkers should be integrated with structural and functional measures rather than interpreted independently as definitive indicators of rehabilitation potential.

Functional assessment has emerged as the strongest individual predictor of recovery in the present study, and this finding has provided an important link between neurological mechanisms and clinically observable rehabilitation outcomes. The functional assessment construct has achieved the highest predictor mean, 3.95 (SD = 0.58), while its correlation with post-stroke recovery has reached $r = .66$, $p < .001$. In the regression model, functional assessment has retained the largest standardized coefficient, $\beta = .43$, $p < .001$, indicating that it has contributed more uniquely to the explanation of recovery variance than either neuroimaging or circulating biomarkers. Motor performance has demonstrated an individual correlation of $r = .60$, functional independence $r = .59$, mobility and balance $r = .58$, activities of daily living $r = .55$, and neurological or cognitive functioning $r = .51$. This pattern has been consistent with previous work showing that early behavioral performance contains substantial information about subsequent stroke outcome. Clinical measures can be particularly powerful because they represent the integrated behavioral consequence of lesion severity, preserved pathways, cognition, motivation, compensatory strategies, and rehabilitation exposure. Individual outcome-prediction research has demonstrated that behavioral parameters obtained early after stroke can provide strong prognostic information, while imaging can add useful information regarding underlying network pathology (Rehme et al., 2015). The present finding has also complemented PREP2, in which an early upper-limb clinical measure serves as an important first component of prediction before additional biomarkers are introduced for patients requiring further stratification (Stinear et al., 2017). Importantly, the strong functional coefficient has not reduced the relevance of the other predictor domains. The combined model has achieved $R = .744$ and $R^2 = .553$, demonstrating that functional performance alone has not captured all meaningful recovery-related variability. Neuroimaging and biomarkers have remained

independently significant, indicating that similar functional scores can occur in patients with different neurological reserves or biological conditions. This result has supported the study's central argument for multimodal assessment. It has also been consistent with evidence that lesion topography and functional connectivity predict different behavioral domains with different degrees of accuracy, emphasizing that different information sources characterize distinct components of stroke impairment (Siegel et al., 2016). The moderate correlations among the predictors— $r = .42$ between neuroimaging and biomarkers, $r = .51$ between imaging and functional assessment, and $r = .39$ between biomarkers and functional assessment—have further supported this interpretation. Their associations have been strong enough to reflect a shared recovery process yet sufficiently limited to indicate conceptual distinction. Thus, the findings have favored multimodal integration over exclusive reliance on either biological measures or bedside functional measurement.

The practical significance of the findings has arisen primarily from the possibility of organizing stroke assessment as a staged multimodal process rather than expecting every patient to be evaluated through the same single predictor. The strong functional coefficient identified in the study has suggested that standardized functional assessment should remain the clinical foundation of recovery evaluation because it is relatively accessible and has demonstrated the closest statistical relationship with the recovery outcome. However, the independent neuroimaging and biomarker coefficients have indicated that functional assessment should not necessarily be treated as sufficient for all patients. A practical pathway derived from the results would begin with standardized assessment of neurological impairment, motor function, mobility, activities of daily living, and functional independence; patients whose functional status provides an uncertain or intermediate recovery profile could subsequently undergo more detailed interpretation of neuroimaging characteristics, followed by selected biomarker assessment where biological stratification is clinically relevant. This staged approach has similarities to multimodal recovery algorithms in which clinical measures are used first and additional neurological biomarkers are introduced when needed to refine prediction (Stinear et al., 2017). Imaging results from the present study have suggested that particular attention should be paid to corticospinal pathway integrity, lesion location, white-matter preservation, and network-level organization because these characteristics have demonstrated meaningful relationships with functional outcome. Prior research on corticospinal tract lesion load has likewise shown that pathway-specific imaging can provide information about subsequent motor outcome (Feng et al., 2015). Biomarker assessment should be interpreted as complementary rather than determinative. The comparatively smaller biomarker coefficient implies that isolated abnormal laboratory values should not be used to classify rehabilitation potential without consideration of clinical and neurological context. This caution has been supported by earlier findings showing that inflammatory markers may be associated with poor outcome without necessarily producing major improvements in prediction when added to established clinical models (Whiteley et al., 2009). At the rehabilitation level, the integrated profile could help clinicians distinguish patients who have similar bedside scores but different neural or biological recovery environments. It may also assist in stratifying patients for therapy intensity, identifying individuals requiring closer reassessment, interpreting unexpectedly slow recovery, and documenting multidimensional rehabilitation progress. These applications should not be interpreted as established consequences of the illustrative dataset; rather, they represent clinically plausible uses that require validation using real prospective data. The practical value of the framework is therefore its organization of different information sources into a staged decision process while preserving the central role of direct clinical assessment.

The findings have provided broad support for the use of Neuroplasticity Theory as the theoretical framework because the observed relationships have corresponded with a multilevel interpretation of neurological recovery. Under this framework, post-stroke improvement has been understood as the behavioral expression of adaptive changes occurring within surviving neural systems and influenced by the structural integrity and biological environment of the injured brain. The significant neuroimaging coefficient has supported the structural component of the theory by showing that more favorable neural pathway and network characteristics have been associated with stronger recovery. The significant biomarker coefficient has supported a biological component by indicating that inflammatory, injury-related, stress-related, and plasticity-related conditions have been associated with

recovery even after imaging and functional performance have been controlled. The strong functional coefficient has represented the behavioral level at which neural adaptation becomes clinically observable. Evidence showing that corticomotor integrity is related to recovery patterns has provided additional support for the theoretical importance of preserved neural systems (Byblow et al., 2015). Several limitations, however, have required careful interpretation of the present findings. Most importantly, the numerical results developed in this manuscript have constituted an illustrative analytical dataset rather than observed SPSS results from collected participants, meaning that the coefficients should currently be understood as a model of the intended analytical structure and not as empirical evidence ready for publication. In the final study, all values must be replaced by actual participant-level results. Second, the proposed cross-sectional design limits temporal and causal interpretation because measurements taken within one observation period cannot establish whether a neuroimaging or biomarker condition preceded subsequent recovery. Third, the case-study setting may limit generalizability across hospitals, geographic populations, stroke subtypes, and rehabilitation systems. Fourth, reducing complex imaging, laboratory, and functional characteristics to five-point Likert constructs may introduce information loss, particularly because lesion volume, fractional anisotropy, circulating protein concentrations, NIHSS scores, Fugl-Meyer scores, and modified Rankin categories have naturally different measurement structures. Fifth, stroke recovery is influenced by age, baseline severity, treatment exposure, lesion laterality, cognition, comorbidity, rehabilitation dose, and time since stroke, which have not been fully represented in the primary three-predictor model. Finally, the 44.7% unexplained variance in the illustrative model indicates that substantial recovery heterogeneity remains outside the proposed predictors. These limitations define where the empirical design should become more rigorous rather than weakening the conceptual logic of the integrated framework.

Future research should build on the present framework by replacing the cross-sectional three-domain model with a Dynamic Multimodal Neuroplasticity Recovery Model (DMNRM) that measures recovery longitudinally and integrates structural, molecular, functional, therapeutic, and patient-level information. The proposed model should assess participants at clinically meaningful repeated intervals, such as an acute baseline followed by subacute, three-month, six-month, and twelve-month evaluations, so that changes in imaging, biomarkers, and functional status can be related directly to recovery trajectories rather than only to differences between individuals at one observation period. The model can retain the present three principal domains but expand them into five predictor layers: Neuroimaging State (NI), Circulating Biological State (CB), Functional State (FA), Rehabilitation Exposure (RE), and Patient/Clinical Context (PC). Subsequent recovery would then be predicted not only from the patient's current structural, biological, and functional condition but also from previous recovery status, rehabilitation exposure, individual clinical characteristics, and interactions among predictors. Interaction terms are especially important because Neuroplasticity Theory implies that preserved neural structure may produce different outcomes under different biological or rehabilitation conditions. Future research should also compare conventional regression with regularized regression, mixed-effects models, ordinal or survival models where appropriate, and carefully validated machine-learning approaches. Existing multimodal algorithms have already demonstrated that clinical measures and neurological biomarkers can be combined to estimate individual recovery (Stinear et al., 2017), while network-based analyses have shown that functional connectivity contains behaviorally relevant information beyond focal lesion description (Siegel et al., 2016). Biomarker-panel research has similarly supported evaluating multiple biological pathways rather than isolated molecules (Zhong et al., 2019). The DMNRM should therefore incorporate raw quantitative measurements wherever possible—actual MRI-derived lesion and connectivity measures, laboratory biomarker concentrations, and validated NIHSS, Fugl-Meyer, Barthel, or modified Rankin scores—rather than converting every domain into Likert responses. Model development should use training and validation samples, internal resampling or cross-validation, calibration analysis, discrimination statistics, and ultimately independent external validation across multiple rehabilitation centers. The most important advancement would be the transition from predicting a single recovery score to estimating individual recovery trajectories and probabilities of clinically meaningful improvement, allowing researchers to

test how the interaction of neural reserve, biological state, rehabilitation dose, and patient characteristics shapes recovery over time.

$$PSR_{(i,t+1)} = \beta_0 + \rho PSR_{(i,t)} + \beta_1 NI_{(i,t)} + \beta_2 CB_{(i,t)} + \beta_3 FA_{(i,t)} + \beta_4 RE_{(i,t)} + \beta_5 PC_i + \beta_6 (NI \times CB)_{(i,t)} + \beta_7 (NI \times RE)_{(i,t)} + \beta_8 (CB \times RE)_{(i,t)} + u_i + \varepsilon_{(i,t)}$$

CONCLUSION

This study has examined post-stroke recovery through an integrated translational neurorehabilitation framework incorporating neuroimaging indicators, circulating biomarker indicators, and functional assessment measures as complementary predictors of neurological and functional outcomes. The research has been structured around the understanding that recovery following stroke does not represent a single biological or clinical process but reflects the combined influence of cerebral structural integrity, molecular and physiological responses, and observable functional performance. Through a quantitative, cross-sectional, case-study-based design, the study has applied descriptive statistics, reliability testing, Pearson correlation analysis, and multiple regression modeling to evaluate the proposed relationships and test the research hypotheses. Within the illustrative analytical framework, neuroimaging indicators have maintained a significant positive relationship with post-stroke recovery, supporting the importance of lesion characteristics, corticospinal tract preservation, white-matter integrity, and functional neural organization in explaining differences in rehabilitation outcomes. Circulating biomarker indicators have also demonstrated a statistically significant association with recovery, showing that inflammatory activity, neuronal and glial injury, neurotrophic processes, vascular conditions, and physiological stress represent meaningful biological dimensions of the recovery process. Functional assessment measures have demonstrated the strongest relationship with post-stroke recovery, emphasizing the importance of motor performance, mobility, activities of daily living, neurological functioning, and functional independence as direct clinical expressions of neurological improvement. Most importantly, the combined regression model has demonstrated that the three domains together explain a substantial proportion of variation in recovery, supporting the central proposition that multimodal assessment provides a more comprehensive representation of stroke recovery than isolated measurement approaches. H1 through H4 have therefore been supported within the illustrative analytical structure, while the major objectives concerning descriptive characterization, relationship assessment, and integrated prediction have been achieved. The findings have also remained consistent with Neuroplasticity Theory, which has provided the theoretical foundation for understanding how preserved neural structures, biological repair conditions, and rehabilitation-related functional adaptations can interact during recovery. Neuroimaging has represented the structural substrate available for reorganization, circulating biomarkers have represented the biological environment within which injury and repair occur, and functional assessment has represented the observable behavioral expression of neurological adaptation. The study has therefore contributed an integrated quantitative perspective that connects neuroscience, molecular biology, rehabilitation assessment, and statistical prediction within a single framework. Although functional assessment has emerged as the strongest predictor, neuroimaging and circulating biomarkers have retained significant independent contributions, confirming that no single domain fully explains recovery. Overall, the research has established a coherent basis for understanding post-stroke recovery through the combined examination of neurological structure, biological condition, and functional performance. The final empirical interpretation, however, must be based on actual participant-level SPSS output rather than the illustrative numerical profile used to demonstrate the intended analysis and reporting structure in the present manuscript.

RECOMMENDATIONS

Based on the analytical framework and findings developed in this study, several recommendations can be proposed for clinical practice, rehabilitation research, stroke-care institutions, and subsequent development of recovery-prediction models. First, stroke and neurorehabilitation services should adopt a more integrated assessment strategy in which standardized functional measures are combined with clinically relevant neuroimaging information and, where feasible, selected circulating biomarker data rather than relying exclusively on one type of assessment. Functional assessment should remain a central component of routine evaluation because it has demonstrated the strongest relationship with recovery and directly reflects motor capacity, independence, mobility, cognition, and performance in

activities of daily living. However, patients with uncertain, inconsistent, or unexpectedly poor recovery patterns should receive more detailed assessment of lesion characteristics, corticospinal tract integrity, white-matter organization, and network preservation because these characteristics can provide additional information about the neurological substrate available for recovery. Second, healthcare institutions should strengthen the standardization of stroke assessment procedures by using validated clinical scales, clearly defined imaging protocols, and consistent laboratory procedures for relevant circulating biomarkers. Third, multidisciplinary collaboration should be encouraged among neurologists, rehabilitation physicians, physiotherapists, occupational therapists, radiologists, clinical laboratory professionals, nurses, and data analysts so that recovery-related information can be interpreted collectively rather than within isolated professional domains. Fourth, rehabilitation planning should consider individual variation in neurological and biological status when determining treatment intensity, therapeutic focus, and monitoring frequency. Patients with preserved neurological pathways but substantial functional impairment may require intensive task-specific rehabilitation, whereas individuals with extensive structural injury or unfavorable biological profiles may require closer monitoring and broader supportive intervention. Fifth, future empirical studies should move beyond cross-sectional measurement and adopt longitudinal designs that repeatedly evaluate neuroimaging, biomarkers, and functional performance across acute, subacute, and chronic recovery stages. The proposed Dynamic Multimodal Neuroplasticity Recovery Model should be further developed by incorporating neuroimaging state, circulating biological state, functional status, rehabilitation exposure, and patient-level clinical characteristics within one predictive framework. Actual quantitative imaging measurements, laboratory biomarker concentrations, and validated clinical scale scores should be preferred over simplified perception-based measures whenever they are available. Researchers should also test interaction effects between neural integrity, biomarkers, and rehabilitation exposure because the effect of treatment may vary according to the biological and structural condition of the patient. Advanced statistical approaches, including hierarchical regression, mixed-effects modeling, regularized regression, and carefully validated machine-learning methods, should be compared with conventional regression. Finally, multicenter validation should be undertaken across different stroke populations, healthcare systems, and rehabilitation settings to determine whether the proposed integrated model remains reliable, calibrated, and clinically useful beyond a single case-study environment. These recommendations can strengthen the methodological quality and practical relevance of subsequent translational stroke-recovery research.

LIMITATIONS

The present study has several limitations that should be considered when interpreting its analytical framework and evaluating the generalizability of the proposed multimodal recovery model. First, the research has employed a cross-sectional design, which has allowed relationships among neuroimaging indicators, circulating biomarkers, functional assessment measures, and post-stroke recovery to be examined within a defined observation period but has limited the ability to establish temporal sequences or causal relationships. Stroke recovery is inherently dynamic, and biological, neurological, and functional characteristics can change considerably between acute, subacute, and chronic stages; therefore, a single-period assessment does not fully represent individual recovery trajectories. Second, the case-study-based structure has restricted the study to a defined clinical context, which may reduce the extent to which findings can be generalized to other hospitals, rehabilitation facilities, geographic populations, healthcare systems, and stroke subtypes. Third, the study has relied substantially on quantitative composite constructs and a five-point Likert scale for representing major variables. Although this approach supports standardized statistical analysis, complex clinical phenomena such as lesion volume, corticospinal tract integrity, inflammatory biomarker concentrations, and functional impairment are naturally measured through different clinical and laboratory scales. Converting such multidimensional characteristics into composite Likert-type constructs may result in some loss of measurement precision. Fourth, the primary model has focused on three predictor domains, while post-stroke recovery is also affected by additional factors including age, sex, baseline stroke severity, lesion laterality, time to treatment, comorbidities, cognitive status, psychological condition, socioeconomic circumstances, rehabilitation intensity, family support, medication adherence, and time since stroke. Although selected clinical variables have been acknowledged, not all potentially relevant confounders

have been incorporated into the principal regression model. Fifth, circulating biomarkers can vary according to blood-collection timing, acute infection, medication use, systemic inflammatory conditions, renal or hepatic function, and laboratory procedures, which may complicate interpretation of their relationship with neurological recovery. Neuroimaging measures are also sensitive to scanner characteristics, acquisition protocols, analytic techniques, and the timing of imaging relative to stroke onset. Sixth, functional assessment may be affected by assessor variation, fatigue, motivation, communication difficulties, and compensatory strategies, potentially introducing measurement error. Finally, the statistical findings used in the present manuscript have been developed as an internally coherent illustrative analytical profile for structuring the results chapter and should not be interpreted as final empirical evidence until participant-level data have been collected and analyzed through SPSS. The final study must therefore replace all illustrative values with actual output and reassess reliability, assumptions, effect sizes, confidence intervals, and model validity before definitive empirical conclusions are drawn.

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