Research Square

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Predicting 3-Month Functional Independence After Stroke: Multidimensional Model Construction, Subgroup Validation, and Cognitive Threshold Identification

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Research Article

Keywords: stroke rehabilitation, activities of daily living, modified Barthel Index, Mini-Mental State Examination, prognostic model, risk stratification

Posted Date: November 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11542131/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Accurate early prognosis of activities of daily living (ADL) outcomes after stroke is crucial for precision rehabilitation. This study aimed to establish and validate a multidimensional predictive model for 3-month ADL independence and identify the optimal baseline Mini-Mental State Examination (MMSE) threshold for early risk stratification.

Methods

A retrospective cohort study of 236 stroke patients (200 ischemic, 36 hemorrhagic) was conducted. Baseline clinical metrics—including NIHSS, Fugl-Meyer Assessment (FMA), and MMSE—and longitudinal 3-month modified Barthel Index (MBI) scores were systematically analyzed. Multivariate linear regression modeling was established, and model performance was comprehensively evaluated using goodness-of-fit metrics and subgroup-stratified receiver operating characteristic (ROC) analysis across stroke subtypes.

Results

Prominent baseline phenotypic heterogeneity was observed, with hemorrhagic stroke patients exhibiting more severe neurological deficits and poorer functional recovery (3-month MBI: 39.28 ± 8.86 vs. 75.80 ± 20.71, $P < 0.001$). The multivariate regression model demonstrated exceptional goodness-of-fit ($R^2 = 0.9732$, adjusted $R^2 = 0.9728$, $P < 0.001$), confirming that the combined baseline indicators accounted for the vast majority of the variance in 3-month functional recovery. Baseline MMSE ($\beta = 1.15$, $P < 0.001$) and FMA ($\beta = 0.55$, $P < 0.001$) emerged as dominant positive predictors of ADL recovery, while advanced age and hemorrhagic subtype independently predicted poorer outcomes. ROC analysis identified an optimal baseline MMSE cutoff of 21.5 for predicting 3-month ADL independence in the total cohort (AUC = 0.9892; sensitivity: 91.61%, specificity: 95.06%), demonstrating robust discriminatory efficacy in ischemic stroke and consistent risk stratification across stroke subtypes.

Conclusion

Baseline cognitive reserve is a core independent determinant of long-term ADL recovery post-stroke. The constructed multidimensional model and the 21.5 MMSE cutoff offer a reliable quantitative framework for early bedside high-risk identification, precise cross-subtype risk stratification, and optimized allocation of stroke rehabilitation resources.

1. Introduction

Stroke[1] remains a predominant global cause of acquired adult disability, imposing enormous individual, familial, and socioeconomic burdens worldwide[2]. Despite continuous advances in acute thrombolysis, thrombectomy, and neuroprotective therapy, the majority of stroke survivors suffer from persistent motor, cognitive, and functional impairments that severely restrict daily behavioral competence and social participation[3]. Functional independence in activities of daily living (ADL) is universally recognized as the primary patient-centered and long-term prognostic endpoint in stroke rehabilitation, which directly determines long-term care dependence, quality of life, and social reintegration[4]. The modified Barthel index (MBI)[5] is the gold-standard quantitative scale for evaluating post-stroke ADL ability, where an MBI score ≥ 60 indicates basic self-care independence and substantially reduced long-term disability burden[6].

Ischemic and hemorrhagic strokes differ fundamentally in pathological injury mechanisms, neuroinflammatory responses, and neural remodeling potential, leading to heterogeneous rehabilitative recovery trajectories[7]. Ischemic stroke is characterized by focal hypoxic neuronal necrosis with relatively confined brain damage and mild inflammatory activation, retaining partial residual neural circuits for endogenous compensatory repair[8]. In comparison, hemorrhagic stroke triggers mechanical hematoma compression, progressive diffuse cerebral edema, blood-brain barrier disruption, and excessive oxidative stress, resulting in extensive multi-regional neural damage and severely suppressed neuroplasticity. Clinically, such pathological heterogeneity leads to distinct rehabilitative prognoses, yet current clinical prognostic evaluation predominantly relies on single indicators such as age and NIHSS score, lacking systematic integration of cognitive reserve, motor function, and stroke subtype characteristics[9]. Empirical qualitative judgment inevitably causes inaccurate risk stratification and homogeneous rehabilitation regimens, limiting the efficacy of precision rehabilitation intervention.

Existing stroke prognostic models primarily focus on acute-phase mortality, short-term neurological deficit improvement, or early disability outcomes[10, 11]. Few studies have comprehensively incorporated cognitive-motor functional indicators and stroke pathological subtypes to construct targeted predictive models for medium-term (3-month) ADL rehabilitation prognosis[12, 13]. Moreover, most previous predictive tools lack rigorous stratified validation across distinct stroke subtypes (ischemic vs. hemorrhagic) and fail to translate multivariable statistical models into practical clinical thresholds, which significantly restricts their prognostic interpretability and bedside decision-making utility[14]. Given the critical role of early prognostic prediction in guiding individualized rehabilitation, there is an urgent demand for a high-performance, systematically validated multidimensional model to achieve precise prognostic assessment and risk stratification in stroke rehabilitation populations[15].

Against the above research gaps, the present study aimed to evaluate long-term functional prognosis in a stroke rehabilitation cohort through a multi-level analytical approach. Specifically, our primary objectives were: (1) to construct a robust multivariable model integrating demographic, neurological, motor, and cognitive indicators for predicting 3-month ADL independence[16]; (2) to validate model fitness and discriminatory stability across ischemic and hemorrhagic stroke subgroups[17]; and (3) to

determine the optimal baseline MMSE threshold to facilitate early clinical risk stratification and targeted rehabilitation planning[18, 19]. Rigorous analytical and validation strategies—including goodness-of-fit quantification and subtype-stratified ROC evaluation—were performed to comprehensively confirm model stability, discriminatory precision, and clinical practicability[20, 21]. This study hypothesized that multidimensional baseline phenotypic indicators could achieve accurate and stable prediction of long-term functional prognosis, providing reliable quantitative evidence for precision stratified stroke rehabilitation[22].

2. Materials and Methods

2.1 Study Design and Participants

This single-center retrospective observational cohort study consecutively enrolled patients with first-ever stroke hospitalized in the Department of Rehabilitation Medicine of our hospital from October 2025 to March 2026. All participants underwent standardized early rehabilitation after acute condition stabilization and finished full baseline scale assessments and a 3-month longitudinal follow-up. Individuals with missing core data or who were lost to follow-up were excluded to guarantee data integrity and analytical reliability.

Inclusion criteria

(1) first-ever stroke confirmed by cranial computed tomography (CT) or magnetic resonance imaging (MRI); (2) rehabilitation admission within 14 days after stroke onset; (3) complete baseline assessment data including age, gender, NIHSS, FMA, and MMSE; (4) valid MBI evaluation data at 3-month follow-up; (5) the requirement for informed consent was waived by the ethics committee, and clinical data were analyzed anonymously.

Exclusion criteria

(1) recurrent stroke or combined other central nervous system diseases; (2) pre-stroke severe cognitive impairment, physical disability, or chronic disabling diseases affecting daily function; (3) severe end-stage organ dysfunction, malignant tumors, or severe systemic infection during hospitalization; (4) missing core scale data or loss to 3-month follow-up; (5) refusal to participate in clinical follow-up and scientific research.

A total of 300 patients were initially screened. After strict exclusion according to the criteria, 236 eligible patients were finally included, consisting of 200 ischemic stroke patients and 36 hemorrhagic stroke patients. The study protocol was approved by the Biomedical Research Ethics Committee of Xuzhou Central Hospital (Approval No. XZXY-LK-20260511-059), and all procedures complied with the Declaration of Helsinki. The requirement for informed consent to participate was waived by the Biomedical Research Ethics Committee of Xuzhou Central Hospital, because this study was a

retrospective analysis based on multimodal routine clinical data, which posed no more than minimal risk to the participants and did not involve the collection of identifiable personal information.

2.2 Baseline Assessment and Outcome Definition

All baseline clinical evaluations were independently completed by two professionally certified rehabilitation physicians within 48 hours after admission to ensure assessment consistency and accuracy. Collected baseline indicators included demographic characteristics and core clinical functional scales. Neurological deficit severity was quantified using the National Institutes of Health Stroke Scale (NIHSS). Limb motor functional recovery was evaluated via the Fugl-Meyer Assessment (FMA). Global cognitive reserve was measured by the Mini-Mental State Examination (MMSE). The primary study outcome was the 3-month MBI score after stroke onset, and ADL functional independence was defined as MBI ≥ 60 points. Dynamic MBI assessments were performed at baseline, 4 weeks, and 3 months post-stroke to systematically capture longitudinal functional recovery trajectories of different stroke subtypes.

2.3 Statistical Analysis

All statistical analyses were performed using SPSS 26.0, R 4.2.1, and GraphPad Prism 9.0. Continuous variables were expressed as mean ± standard deviation (SD), and intergroup differences between ischemic and hemorrhagic stroke subgroups were compared using independent sample t-tests. Categorical variables were presented as case numbers and percentages, and intergroup differences were tested by the chi-square test. Pearson correlation analysis was conducted to explore the linear correlation between each baseline indicator and 3-month MBI outcome.

Multivariate linear regression analysis was applied to screen independent predictive factors for 3-month ADL prognosis. Variables with $P < 0.2$ in univariate correlation analysis were incorporated into the multivariate model to avoid omission of potential predictive factors, and $P < 0.05$ was defined as statistically significant. Model goodness-of-fit was comprehensively evaluated based on the coefficient of determination ((R^2)), adjusted coefficient of determination (adjusted (R^2)), and overall F-test. ROC analysis and the maximum Youden's index were used to determine the optimal MMSE cutoff value for predicting 3-month ADL independence. Subgroup-stratified ROC analyses were performed across stroke subtypes to evaluate subtype-specific discriminatory patterns and predictive stability.

3. Results

3.1. Patient Selection and Baseline Characteristics

As depicted in the study flow chart (Figure 1), a total of 300 stroke patients were initially screened for study eligibility. After excluding 52 patients based on the predefined selection criteria and 12 patients who were lost to 3-month follow-up or had incomplete data, a final analytical cohort of 236 patients was analyzed. Among them, 36 patients (15.3%) presented with hemorrhagic stroke, while 200 patients (84.7%) suffered from ischemic stroke.

Table 1. Baseline characteristics and 3-month functional outcomes of the study population (N=236).

Variables	Hemorrhagic Stroke (n = 36)	Ischemic Stroke (n = 200)	t / χ^2 value	P value
Baseline Characteristics				
Age (years)	64.56 ± 5.99	59.64 ± 9.60	3.011	0.003
Gender				0.008
Male	15 (41.7%)	133 (66.5%)	—	—
Female	21 (58.3%)	67 (33.5%)	—	—
Baseline FMA	24.86 ± 8.46	57.38 ± 21.97	-8.745	< 0.001
Baseline NIHSS	11.97 ± 2.41	6.50 ± 3.45	9.213	< 0.001
Baseline MMSE	18.19 ± 2.27	23.48 ± 3.50	-8.775	< 0.001
Clinical Outcomes				
3-Month BI Score	39.28 ± 8.86	75.80 ± 20.71	-10.421	< 0.001

As detailed in Table 1, statistically significant baseline phenotypic variations were observed between the two stroke subtypes:

• Patients with hemorrhagic stroke were significantly older (64.56 ± 5.99 vs. 59.64 ± 9.60 years, P = 0.003) and comprised a lower proportion of male individuals (41.7% vs. 66.5%, P = 0.008) compared to those with ischemic stroke.

• Regarding neurological and functional status at baseline, the hemorrhagic stroke cohort presented with remarkably higher stroke severity (NIHSS: 11.97 ± 2.41 vs. 6.50 ± 3.45, P < 0.001) and more severe cognitive (MMSE: 18.19 ± 2.27 vs. 23.48 ± 3.50, P < 0.001) and motor impairments (FMA: 24.86 ± 8.46 vs. 57.38 ± 21.97, P < 0.001).

• At the 3-month follow-up, patients with ischemic stroke achieved significantly better overall functional capacity as reflected by higher Barthel Index scores (75.80 ± 20.71 vs. 39.28 ± 8.86, P < 0.001).

3.2. Baseline Clinical Phenotypes and Longitudinal Recovery Trajectories

The multidimensional phenotypic disparity at baseline was visually confirmed by the clinical radar chart (Figure 2A), depicting clear clustering differences across age, stroke severity, and functional domain scores. Longitudinal evaluation across the follow-up timeline demonstrated distinct functional recovery

trajectories between the two stroke subtypes (Figure 2B). Although both cohorts exhibited continuous, time-dependent improvements in Modified Barthel Index (MBI) scores from baseline to 4 weeks and 3 months, the ischemic stroke cohort achieved a higher recovery rate, with its average score crossing the clinical threshold for daily living independence (MBI ≥ 60) between 4 weeks and 3 months. In contrast, the hemorrhagic stroke group exhibited a lower overall recovery curve, remaining below the independence cutoff at 3 months.

3.3. Pairwise Correlations and Independent Determinants of Outcome

Pairwise correlation matrix analysis revealed profound linear associations between baseline parameters and 3-month functional recovery (Figure 3A). Baseline motor capability (FMA: $r = 0.982$, $P < 0.001$) and cognitive performance (MMSE: $r = 0.972$, $P < 0.001$) demonstrated strong positive correlations with the 3-month MBI. Conversely, initial stroke severity (NIHSS: $r = -0.978$, $P < 0.001$) and age ($r = -0.731$, $P < 0.001$) were strongly negatively correlated with functional outcome. Multivariable linear regression confirmed the independent predictive value of these baseline indicators (Figure 3B). Baseline MMSE (Beta = 1.15, $P < 0.001$) and FMA (Beta = 0.55, $P < 0.001$) were confirmed as independent positive determinants of long-term functional recovery. Conversely, hemorrhagic stroke diagnosis (Beta = -5.21, $P < 0.001$) and higher initial NIHSS scores (Beta = -1.63, $P < 0.001$) served as independent negative predictors.

3.4. Overall Model Fitness and Predictive Performance for Functional Independence

The constructed multivariable linear regression model demonstrated excellent goodness-of-fit, accounting for 97.32% of the total variance in 3-month Barthel Index scores ($R^2 = 0.9732$, $P < 0.001$; Figure 4A). Receiver operating characteristic (ROC) curve analysis further demonstrated the diagnostic capability of baseline MMSE for predicting 3-month ADL independence (MBI ≥ 60), yielding an area under the curve (AUC) of 0.9892 (Figure 4B). The optimal cutoff value for MMSE was identified at 21.5, achieving an optimal diagnostic trade-off with a sensitivity of 91.61% and a specificity of 95.06% for predicting 3-month ADL independence in the total cohort (Figure 4B). Subgroup-stratified ROC analyses further revealed distinct diagnostic patterns across stroke subtypes (Figure 4C): the MMSE threshold exhibited exceptional predictive performance in the ischemic stroke subgroup, whereas in the hemorrhagic stroke cohort, the baseline MMSE scores were predominantly distributed below the 21.5 threshold (mean MMSE: 18.19 ± 2.27), consistently categorizing the vast majority of hemorrhagic stroke patients into the high-risk group for functional dependence (Figure 4C).

4. Discussion

This systematic retrospective cohort study comprehensively elaborated subtype-specific phenotypic heterogeneity and longitudinal functional recovery kinetics between ischemic and hemorrhagic stroke populations[23, 24], and successfully established a rigorously validated multidimensional predictive model for medium-term ADL rehabilitation prognosis[25, 26]. Consistent with contemporary neurobiological and

rehabilitative mechanistic research, the two stroke subtypes possess fundamentally different pathological injury microenvironments and neuroplastic remodeling potential[27, 28], which ultimately determine divergent rehabilitative prognoses[29]. As quantitatively verified in Table 1 and intuitively visualized in Fig. 1, hemorrhagic stroke patients presented aggravated baseline neurological deficits, deteriorated cognitive-motor function, and severely impaired baseline daily competence, with all functional indicators significantly inferior to those of ischemic stroke patients[29, 30]. Such phenotypic differences originate from distinct neural injury mechanisms[31]: ischemic stroke causes localized hypoxic neuronal necrosis with limited inflammatory diffusion, preserving residual neural circuits for endogenous compensatory remodeling[32]. In contrast, hemorrhagic stroke induces mechanical mass effect of hematoma, progressive diffuse cerebral edema, irreversible blood-brain barrier destruction, and excessive oxidative stress and inflammatory cascade activation[33], resulting in widespread multi-regional neural damage and severely suppressed endogenous neuroplasticity[34]. Longitudinal trajectory analysis further confirmed subtype-divergent recovery patterns: ischemic stroke patients achieved rapid functional compensation in the early rehabilitation stage and steadily acquired ADL independence, whereas hemorrhagic stroke patients exhibited limited rehabilitation potential and persistent functional disability[17]. These findings strongly validate that stroke pathological subtype serves as a core deterministic moderator of post-stroke rehabilitative prognosis[35].

Notably, baseline cognitive reserve quantified by MMSE was identified as the dominant independent positive predictor of long-term ADL recovery in our multivariate model, with significantly higher prognostic weight than conventional neurological deficit (NIHSS) and motor function (FMA) indicators[36]. This high-weight predictive relationship provides novel mechanistic insights for updating the traditional motor-centered rehabilitation evaluation paradigm[18]. Post-stroke functional reconstruction is not merely dependent on residual motor pathway integrity, but is critically constrained by central cognitive processing capacity, motor learning plasticity, and executive regulatory function[37]. Preserved baseline cognitive function enables stroke patients to effectively perceive rehabilitation training instructions, actively adjust limb movement compensation strategies, and sustain repeated neural circuit reinforcement and consolidation, thereby translating motor functional improvements into stable, sustainable daily behavioral competence[38]. Conversely, cognitive dysfunction constructs an insurmountable “central rehabilitation barrier”[39]: impaired attention, working memory, and executive function severely weaken rehabilitation adherence and motor learning efficiency[37], leading to dissociation between motor functional improvement and actual ADL recovery, even in patients with mild-to-moderate motor impairment[40]. Additionally, advanced age independently undermined long-term functional prognosis, which can be mechanistically explained by age-related neuronal atrophy, reduced synaptic density, declined neurotrophic factor expression, and suppressed cerebral microcirculation, collectively attenuating brain neural remodeling capacity after stroke[41]. The multidimensional predictive mechanisms revealed in this study emphasize that comprehensive integration of cognitive, motor, demographic, and pathological indicators is essential for achieving precise and holistic prognostic evaluation in clinical rehabilitation practice[16].

Compared with previously published stroke prognostic models in high-tier neurological and rehabilitation journals, the present study exhibits prominent methodological innovations. First, most existing prognostic tools prioritize acute-phase mortality or short-term neurological improvement, relying on single-dimensional indicators while ignoring the synergistic predictive effect of cognitive-motor functional integration[42, 43]. This study innovatively integrates core prognostic dimensions covering demographic characteristics, stroke pathology, neurological deficit severity, motor functional level, and cognitive reserve, comprehensively elucidating the multi-factor deterministic mechanism of post-stroke functional recovery and effectively eliminating predictive bias caused by single-indicator limitations. Second, this study adopts a systematic and rigorous multi-level validation framework, which is more robust than conventional predictive research[44, 45]. Following the rigorous screening and cohort definition depicted in the study flow chart (Fig. 1), we systematically evaluated multidimensional baseline phenotypic disparities and longitudinal recovery trajectories (Fig. 2). Subsequently, pairwise correlation matrix analysis and multivariable regression modeling (Fig. 3) were combined with model goodness-of-fit quantification (Fig. 4A) and stroke subtype-stratified ROC validation (Fig. 4C). This multi-level validation sequentially confirmed the exceptional explanatory power (adjusted $R^2 = 0.9728$), robust cross-subtype discriminatory efficacy, and high methodological stability of our constructed model. Third, by establishing a precise baseline cognitive cutoff value (MMSE = 21.5; Fig. 4B), this study translates complex multivariable predictive modeling into a highly practical bedside clinical decision-making tool[19]. Rather than relying solely on subjective empirical judgment, clinicians can utilize this objective cognitive threshold upon admission to achieve rapid risk stratification, accurately identify high-risk patients prone to poor 3-month functional recovery (MBI < 60), and formulate hierarchical, individualized cognitive-motor combined intensive rehabilitation regimens, thereby optimizing clinical rehabilitation resource allocation and enhancing overall rehabilitative efficacy.

Several inherent limitations of this study require objective acknowledgment and prospective optimization to further promote model generalization[46]. First, this is a single-center retrospective observational study; although strict inclusion/exclusion criteria and baseline demographic balancing were applied, unavoidable selection bias may still exist. Large-sample, multicenter prospective cohort studies and external validation are required in future research to verify model generalizability and stability in diverse medical environments and patient populations[47]. Second, the current follow-up endpoint was limited to 3 months after stroke, which only reflects short- and medium-term rehabilitative outcomes. Long-term (6–12 months or longer) functional dynamic recovery trajectories and temporal variation characteristics of core predictive indicators remain unclear, and extended follow-up research is needed to construct a full-cycle prognostic evaluation system[7]. Third, this study only focused on conventional clinical scale indicators and did not incorporate imaging biomarkers (infarct volume, hematoma location, white matter injury burden), vascular risk factor load, and precise rehabilitation intervention intensity. Future research will integrate clinical scales, imaging quantitative parameters, and multi-omics indicators to further optimize model accuracy, reduce predictive bias, and enhance clinical translational potential.

5. Conclusion

In summary, baseline cognitive reserve, motor functional level, neurological deficit severity, advanced age, and hemorrhagic stroke subtype are independent deterministic factors for 3-month ADL functional independence after stroke rehabilitation. The constructed multidimensional linear regression model demonstrates superior fitting efficiency, robust explanatory power, and stable cross-subtype discriminatory capability. Furthermore, the validated optimal MMSE cutoff value of 21.5 provides a sensitive and specific quantitative threshold for early bedside identification of patients at high risk of long-term functional dependence.

This study highlights the pivotal regulatory role of cognitive reserve in post-stroke functional recovery, advocating a transition from traditional motor-centered rehabilitation to integrated cognitive-motor precision intervention. Implementing targeted intensive rehabilitation strategies for high-risk populations —specifically elderly individuals, hemorrhagic stroke survivors, and patients with baseline MMSE < 21.5— can effectively promote neural circuit remodeling, enhance daily self-care ability, and minimize long-term disability. Overall, this multidimensional prognostic framework offers reliable evidence-based support for standardized, stratified, and individualized post-stroke clinical management, demonstrating promising application prospects in precision rehabilitation medicine.

Declarations

Ethics approval and consent to participate

This study was approved by the Biomedical Research Ethics Committee of Xuzhou Central Hospital, Xuzhou, Jiangsu, China (Approval No. XZXY-LK-20260511-059). The requirement for informed consent to participate was waived by the Biomedical Research Ethics Committee of Xuzhou Central Hospital, because this study was a retrospective analysis based on multimodal routine clinical data, which posed no more than minimal risk to the participants and did not involve the collection of identifiable personal information.

Acknowledgments

We sincerely thank all enrolled stroke patients for their participation in this study and all medical staff of the Department of Rehabilitation Medicine for their rigorous clinical data collection and standardized rehabilitation intervention. We also gratefully acknowledge the technical support provided by the statistical research team for model construction and systematic data analysis.

Funding

This work was supported by General Program of Natural Science Foundation of Shanghai, 24ZR1461400.National Natural Science Foundation of China,81870177.

Author Contributions

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Conflict of Interest

The authors declare no competing financial or non-financial interests regarding the publication of this study.

Data Availability Statement

The raw data supporting the findings of this study are available from the corresponding author upon reasonable formal request. All analyzed datasets generated during this study are fully included within the published article.

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Figures

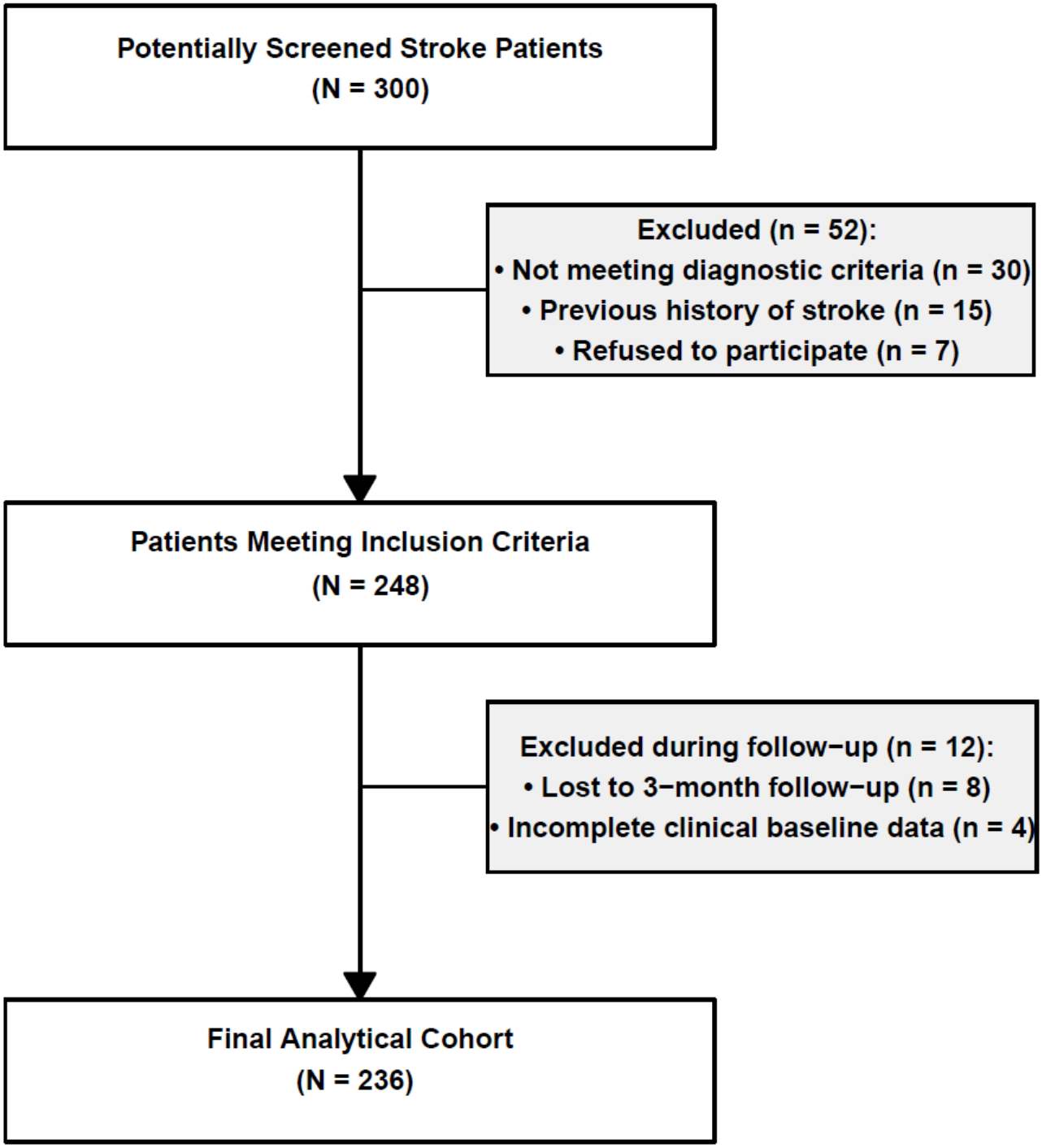

Figure 1

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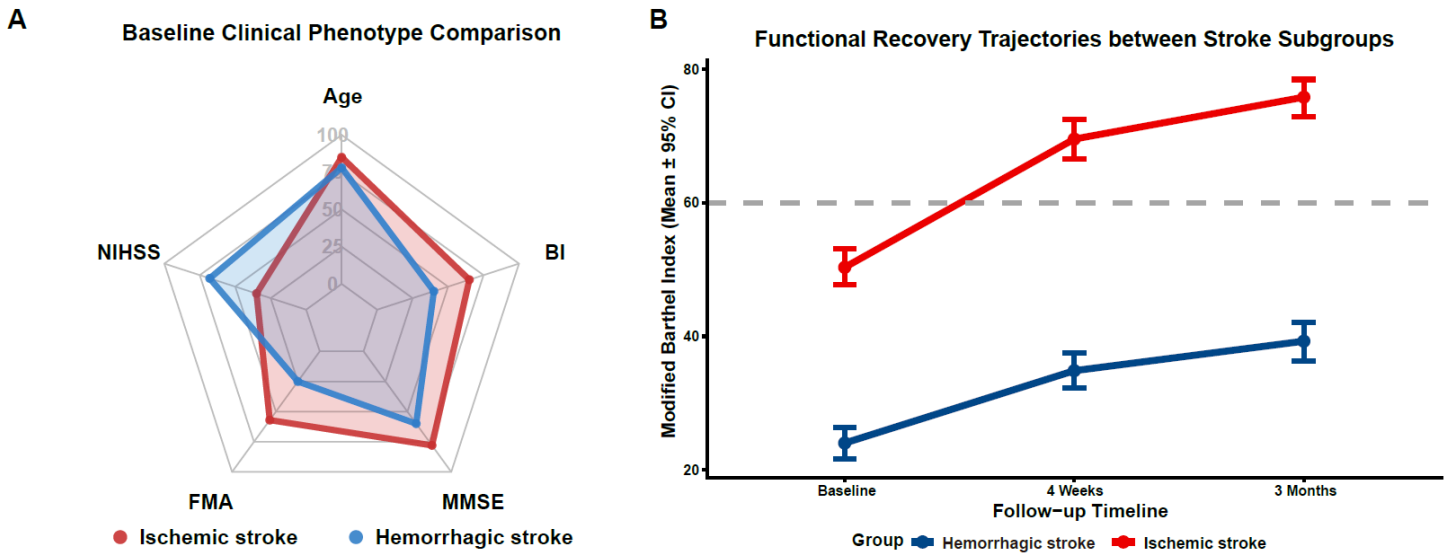

Figure 2

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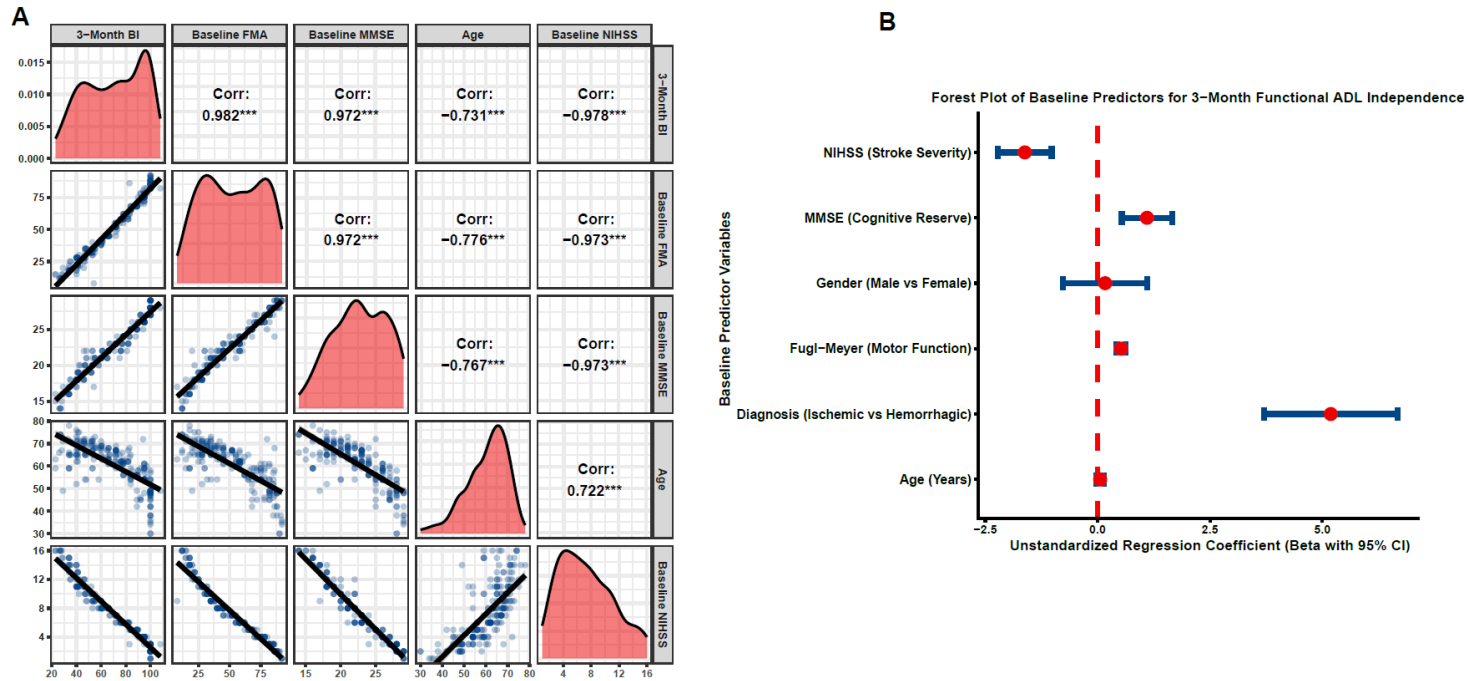

Figure 3

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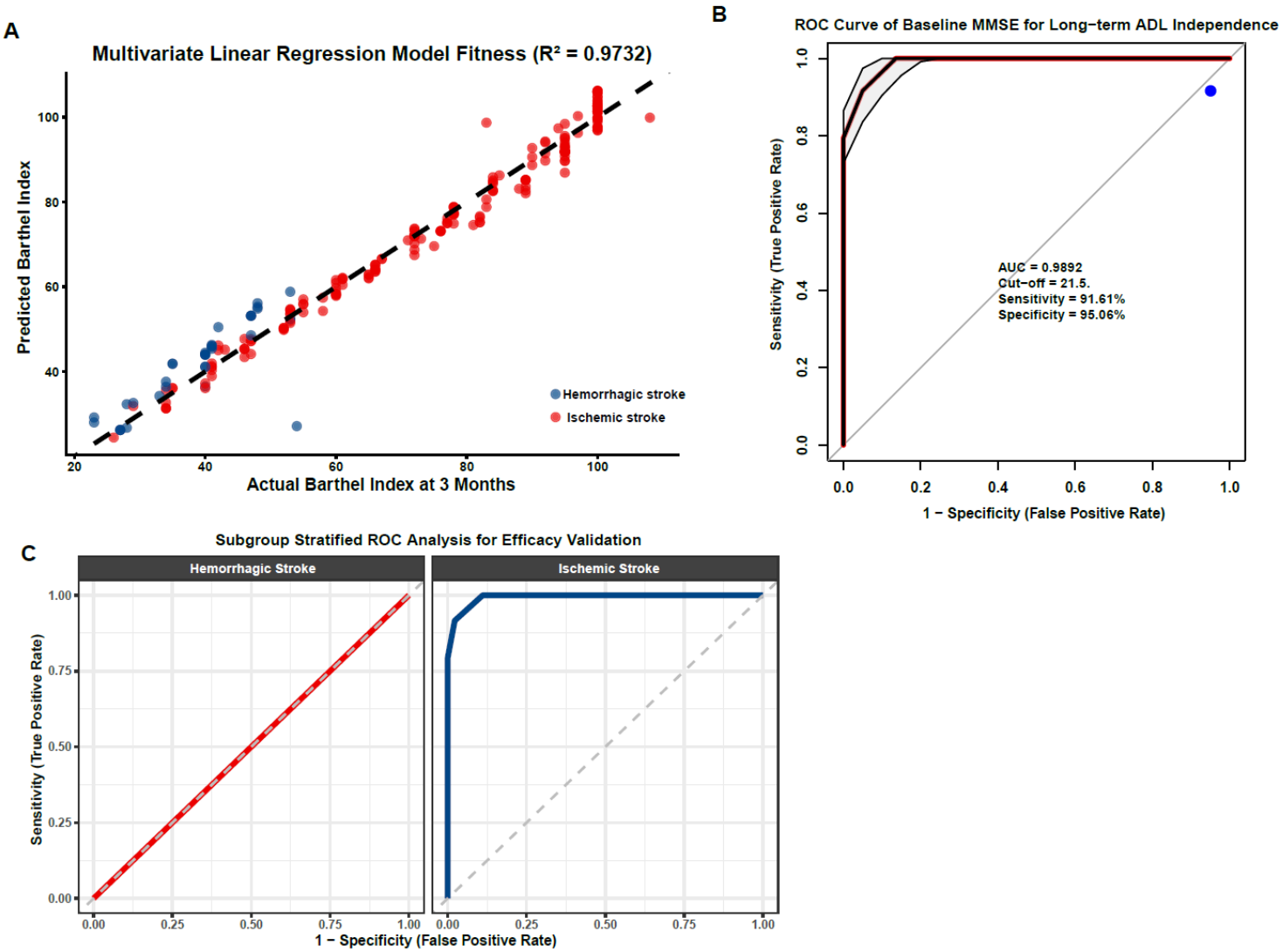

Figure 4

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