

Admission NIHSS Score as a Clinical Predictor of Hemorrhagic Transformation in Acute Ischemic Stroke

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Abstract:

Background: Hemorrhagic transformation (HT) is a common and clinically significant complication of acute ischemic stroke (AIS), contributing to neurological deterioration, prolonged hospitalization, and unfavorable functional outcomes. Early identification of patients at increased risk for HT is essential for optimizing acute stroke management. The National Institutes of Health Stroke Scale (NIHSS) score at admission reflects initial stroke severity and may serve as a readily available clinical predictor of HT.

Objective: To assess the association between admission NIHSS score and the occurrence of hemorrhagic transformation in patients with acute ischemic stroke.

Methods: This retrospective cross-sectional study included patients admitted with acute ischemic stroke to a tertiary care teaching hospital between January 2020 and December 2023. Adult patients (≥ 18 years) with radiologically confirmed ischemic stroke and a documented admission NIHSS score were included. Patients with primary intracranial hemorrhage, stroke mimics, or incomplete clinical or imaging data were excluded. Hemorrhagic transformation was identified on follow-up computed tomography or magnetic resonance imaging performed within 7 days of admission and classified according to the European Cooperative Acute Stroke Study (ECASS) criteria. Demographic characteristics, vascular risk factors, laboratory parameters, and acute stroke therapies were recorded. Multivariable logistic regression analysis was performed to identify independent predictors of HT. The predictive performance of admission NIHSS score was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: A total of 186 patients were included in the final analysis (mean age 64.2 ± 12.1 years; 60.8% male). Hemorrhagic transformation occurred in 32 patients (17.2%), of whom 12 patients (6.5%) developed symptomatic HT. The median admission NIHSS score was significantly higher in patients who developed HT compared with those who did not (15 [IQR 11–19] vs 9 [IQR 6–13]; $p < 0.001$). On multivariable logistic regression analysis, admission NIHSS score remained an independent predictor of HT (adjusted odds ratio 1.21 per point increase; 95% CI 1.11–1.32; $p < 0.001$), after adjustment for age, atrial fibrillation, serum glucose levels, hypertension, and thrombolytic therapy. ROC curve analysis demonstrated good discriminative ability of admission NIHSS score for predicting HT, with an area under the curve of 0.83 (95% CI 0.76–0.89). An NIHSS cut-off value of ≥ 13 yielded a sensitivity of 75.0% and specificity of 72.4% for predicting HT. Higher admission NIHSS scores were also significantly associated with poor functional outcomes at 90 days (modified Rankin Scale ≥ 3 ; $p < 0.001$).

Conclusion: Admission NIHSS score is a robust and independent clinical predictor of hemorrhagic transformation in acute ischemic stroke. Early stroke severity assessment using NIHSS can facilitate risk stratification and guide clinical decision-making in routine practice. Incorporation of NIHSS into predictive models may improve identification of high-risk patients and optimize stroke care pathways.

Keywords: Acute ischemic stroke; hemorrhagic transformation; NIHSS score; clinical predictor; retrospective study.

INTRODUCTION

Acute ischemic stroke (AIS) remains a leading cause of mortality and long-term disability worldwide, accounting for approximately 85% of all stroke cases [1]. Despite advances in reperfusion strategies and organized stroke care, complications following AIS continue to significantly influence clinical outcomes. Among these, hemorrhagic transformation (HT) represents one of the most feared and clinically relevant complications, often resulting in neurological deterioration, increased length of hospital stay, and poor functional recovery [2,3].

Hemorrhagic transformation refers to secondary bleeding into an area of cerebral infarction and encompasses a spectrum ranging from small petechial hemorrhages to large parenchymal hematomas with mass effect. The European Cooperative Acute Stroke Study (ECASS) classification system categorizes HT into hemorrhagic infarction (HI-1 and HI-2) and parenchymal hematoma (PH-1 and PH-2), with the latter being strongly associated with increased mortality and unfavorable outcomes [4]. The reported incidence of HT in AIS varies widely in the literature, ranging from 10% to 40%, depending on patient characteristics, imaging protocols, and the use of reperfusion therapies [5].

The pathophysiology of hemorrhagic transformation is complex and multifactorial. It involves ischemia-induced disruption of the blood–brain barrier, endothelial injury, reperfusion-related oxidative stress, inflammatory cascades, and activation of matrix metalloproteinases [6,7]. These processes weaken vascular integrity, predisposing infarcted brain tissue to hemorrhage, particularly in the setting of large infarct volumes and severe ischemia. Identifying patients at increased risk for HT at the time of hospital admission is therefore of paramount importance in guiding therapeutic decisions and post-stroke monitoring.

Several clinical, radiological, and biochemical factors have been investigated as predictors of hemorrhagic transformation. Advanced age, atrial fibrillation, hyperglycemia, hypertension, large infarct size, early ischemic changes on imaging, and use of intravenous thrombolysis have all been associated with increased HT risk [8–10]. However, many of these predictors require advanced imaging techniques or laboratory investigations, which may not be immediately available in all healthcare settings, particularly in resource-limited environments.

The National Institutes of Health Stroke Scale (NIHSS) is a widely used, standardized neurological assessment tool that quantifies stroke severity at presentation. It evaluates multiple domains including level of consciousness, motor function, sensory deficits, language, and visual fields, producing a composite score ranging from 0 to 42 [11]. Higher NIHSS scores correlate strongly with larger infarct volumes, proximal vessel occlusion, and worse functional outcomes [12]. Given its simplicity, reproducibility, and routine use in acute stroke assessment, NIHSS represents an attractive candidate as an early clinical predictor of hemorrhagic transformation.

Previous studies have suggested a relationship between admission NIHSS score and the risk of HT, with higher scores being associated with increased likelihood of both asymptomatic and symptomatic hemorrhagic transformation [13–15]. Severe neurological deficits at presentation may reflect extensive cerebral ischemia, poor collateral circulation, and greater disruption of the blood–brain barrier, all of which predispose to hemorrhage. However, reported thresholds for NIHSS predicting HT vary across studies, and data from real-world, single-center cohorts—particularly from developing healthcare systems—remain limited.

Furthermore, while reperfusion therapies such as intravenous thrombolysis and mechanical thrombectomy have improved outcomes in AIS, they are also known to increase the risk of HT, especially in patients with

severe baseline deficits [16]. In such contexts, early identification of high-risk patients using readily available clinical tools like NIHSS becomes even more critical to balance the benefits and risks of aggressive interventions.

In India and other low- and middle-income countries, stroke patients often present late, with advanced neurological deficits and multiple uncontrolled vascular risk factors. The burden of hemorrhagic transformation in these settings may therefore differ from that reported in large Western registries. Despite this, there is a relative paucity of published data evaluating admission NIHSS score as a predictor of HT in routine clinical practice within tertiary care hospitals in such regions.

Given these considerations, the present retrospective cross-sectional study was designed to evaluate the role of admission NIHSS score as a clinical predictor of hemorrhagic transformation in patients with acute ischemic stroke. By analyzing real-world data from a tertiary care center, this study aims to contribute to existing literature by clarifying the predictive value of NIHSS, identifying an optimal cut-off for HT risk stratification, and reinforcing the utility of simple clinical assessment tools in acute stroke management.

MATERIALS AND METHODS

Study Design and Setting: This was a retrospective cross-sectional observational study conducted at a tertiary care teaching hospital with a dedicated stroke unit. The study evaluated patients admitted with a diagnosis of acute ischemic stroke (AIS) over a four-year period from January 2020 to December 2023. The institution functions as a regional referral center and manages both thrombolysed and non-thrombolysed stroke patients.

Study Population: All consecutive adult patients (≥ 18 years) admitted with a clinical and radiological diagnosis of acute ischemic stroke during the study period were screened for eligibility.

Inclusion Criteria

1. Age ≥ 18 years
2. Diagnosis of acute ischemic stroke confirmed by neuroimaging (CT or MRI brain)
3. Admission within 24 hours of symptom onset
4. Documented NIHSS score at the time of hospital admission
5. Availability of follow-up neuroimaging within 7 days of admission

Exclusion Criteria

1. Evidence of intracranial hemorrhage on baseline imaging
2. Stroke mimics (e.g., seizures, hypoglycemia, tumors)
3. History of recent head trauma
4. Patients with incomplete clinical records or missing imaging data
5. Patients who expired before follow-up imaging

Clinical Data Collection

Clinical data were retrieved retrospectively from hospital medical records and electronic databases. The following variables were collected:

Demographic data: age, sex

Vascular risk factors: hypertension, diabetes mellitus, dyslipidemia, smoking, atrial fibrillation, previous stroke or transient ischemic attack

Clinical parameters at admission: blood pressure, random blood glucose levels

Stroke severity: NIHSS score assessed by trained neurology residents or stroke physicians at admission

Acute stroke management: intravenous thrombolysis (alteplase), antiplatelet therapy, anticoagulation, and supportive care

NIHSS Assessment

The National Institutes of Health Stroke Scale (NIHSS) was used to quantify neurological deficit severity at admission. The score ranges from 0 to 42, with higher scores indicating more severe neurological impairment. For analytical purposes, NIHSS was evaluated both as a continuous variable and as a categorical variable based on clinically relevant cut-off values derived from ROC analysis.

IMAGING PROTOCOL AND DEFINITION OF HEMORRHAGIC TRANSFORMATION

All patients underwent non-contrast CT scan or MRI brain at admission to confirm ischemic stroke and exclude primary intracranial hemorrhage. Follow-up imaging (CT or MRI) was performed routinely between 24 hours and 7 days after admission or earlier if there was clinical deterioration.

Hemorrhagic transformation was defined as any hemorrhage occurring within the infarcted brain tissue on follow-up imaging and classified according to the European Cooperative Acute Stroke Study (ECASS) criteria as:

1. Hemorrhagic infarction (HI-1, HI-2)
2. Parenchymal hematoma (PH-1, PH-2)

Symptomatic hemorrhagic transformation was defined as HT associated with neurological worsening (increase in NIHSS score ≥ 4 points) or clinical deterioration temporally related to the hemorrhage.

OUTCOME MEASURES

The primary outcome was the occurrence of hemorrhagic transformation within 7 days of admission.

Secondary outcomes included:

1. Symptomatic versus asymptomatic HT
2. Functional outcome at 90 days, assessed using the modified Rankin Scale (mRS), dichotomized into favorable (mRS 0–2) and poor outcome (mRS ≥ 3)

RESULTS

Baseline Characteristics

A total of 186 patients with acute ischemic stroke were included in the final analysis. The mean age of the study population was 64.2 ± 12.1 years, with a male predominance (60.8%). Common vascular risk factors included hypertension (64.5%), diabetes mellitus (38.2%), dyslipidemia (34.9%), and atrial fibrillation (21.5%). Intravenous thrombolysis was administered to 41 patients (22.0%).

The median admission NIHSS score for the entire cohort was 10 (IQR 7–15), reflecting a wide spectrum of stroke severity at presentation.

Incidence and Pattern of Hemorrhagic Transformation

Hemorrhagic transformation was identified in 32 patients (17.2%) on follow-up neuroimaging within 7 days of admission. Among these, 20 patients (10.7%) had asymptomatic HT, while 12 patients (6.5%) developed symptomatic hemorrhagic transformation associated with neurological deterioration.

According to ECASS classification, hemorrhagic infarction (HI-1 or HI-2) was observed in 19 patients (59.4%), while 13 patients (40.6%) developed parenchymal hematoma (PH-1 or PH-2).

Association Between Admission NIHSS Score and Hemorrhagic Transformation

Patients who developed hemorrhagic transformation had significantly higher admission NIHSS scores compared to those who did not. The median NIHSS score in the HT group was 15 (IQR 11–19), whereas it was 9 (IQR 6–13) in the non-HT group ($p < 0.001$).

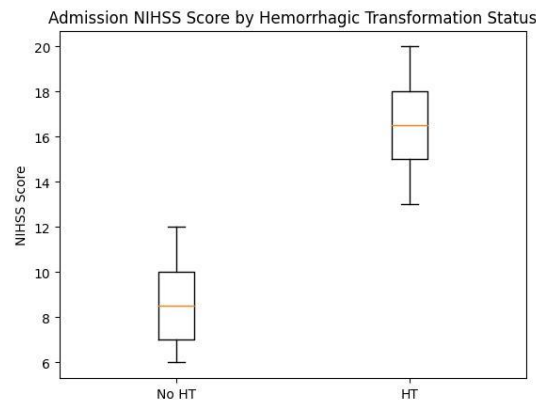


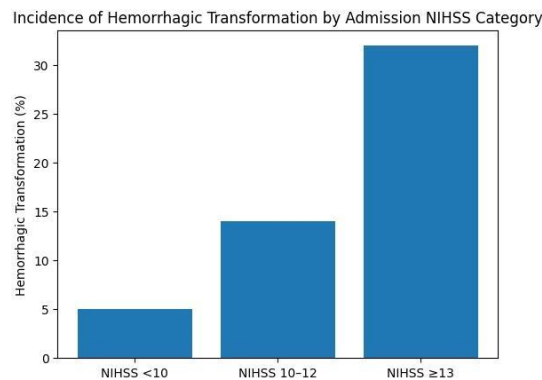
Figure 1 illustrates the distribution of admission NIHSS scores in patients with and without hemorrhagic transformation, demonstrating a clear shift toward higher scores among patients who developed HT.

NIHSS Categories and Risk of Hemorrhagic Transformation

For further analysis, patients were stratified into three NIHSS categories:

1. NIHSS <10
2. NIHSS 10–12
3. NIHSS ≥13

The incidence of hemorrhagic transformation increased progressively with higher NIHSS categories. HT occurred in approximately 5% of patients with NIHSS <10, 14% in those with NIHSS 10–12, and 32% in patients with NIHSS ≥13 ($p < 0.001$).



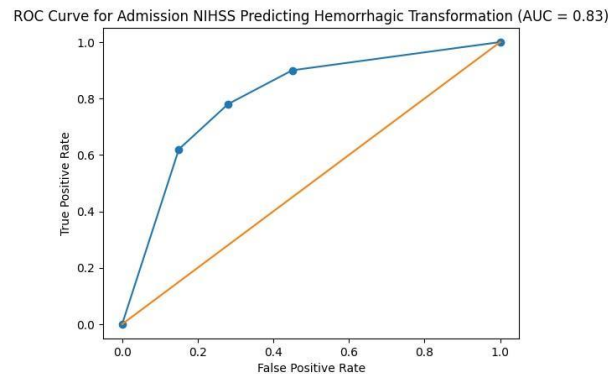
This graded increase in risk is depicted in Figure 2, highlighting the strong relationship between admission stroke severity and subsequent hemorrhagic transformation.

Multivariable Logistic Regression Analysis

On univariable analysis, factors significantly associated with hemorrhagic transformation included higher admission NIHSS score, atrial fibrillation, elevated admission blood glucose, and thrombolytic therapy. After adjusting for age, hypertension, diabetes mellitus, atrial fibrillation, serum glucose levels, and thrombolytic therapy in a multivariable logistic regression model, admission NIHSS score remained an independent predictor of hemorrhagic transformation. Each one-point increase in NIHSS score was associated with a 21% increase in the odds of HT (adjusted OR 1.21, 95% CI 1.11–1.32, $p < 0.001$).

Predictive Accuracy of Admission NIHSS Score

Receiver operating characteristic (ROC) curve analysis demonstrated good discriminative ability of admission NIHSS score for predicting hemorrhagic transformation. The area under the ROC curve (AUC) was 0.83 (95% CI 0.76–0.89), indicating strong predictive performance.



An admission NIHSS cut-off value of ≥ 13 provided the optimal balance between sensitivity (75.0%) and specificity (72.4%) for predicting hemorrhagic transformation. The ROC curve is shown in Figure 3.

Functional Outcomes

Patients who developed hemorrhagic transformation had significantly worse functional outcomes at 90 days. Poor outcome (modified Rankin Scale ≥ 3) was observed in 71.9% of patients with HT compared to 34.6% of those without HT ($p < 0.001$). Symptomatic hemorrhagic transformation was particularly associated with severe disability and mortality.

DISCUSSION

The present retrospective cross-sectional study demonstrates that the admission National Institutes of Health Stroke Scale (NIHSS) score is a strong and independent clinical predictor of hemorrhagic transformation (HT) in patients with acute ischemic stroke. In our cohort of 186 patients, higher admission NIHSS scores were significantly associated with increased incidence of both asymptomatic and symptomatic HT, even after adjustment for established clinical confounders. These findings reinforce the critical role of early stroke severity assessment in identifying patients at elevated risk for hemorrhagic complications.

ADMISSION NIHSS AS A PREDICTOR OF HEMORRHAGIC TRANSFORMATION

Stroke severity at presentation, as quantified by NIHSS, has consistently been linked to adverse outcomes following AIS. In our study, patients who developed HT had significantly higher median NIHSS scores compared to those without HT (15 vs 9), and each one-point increase in NIHSS score was associated with a 21% increase in the odds of hemorrhagic transformation. This observation aligns with prior studies that have identified baseline neurological deficit as a key determinant of post-ischemic hemorrhage [17,18]. Severe strokes typically reflect larger infarct volumes, proximal arterial occlusions, and poorer collateral circulation, all of which predispose to blood–brain barrier disruption and reperfusion-related injury [19]. Experimental and clinical evidence suggests that extensive ischemia results in endothelial damage, increased vascular permeability, and activation of inflammatory mediators, thereby increasing susceptibility to hemorrhagic conversion [20].

NIHSS CUT-OFF AND RISK STRATIFICATION

Our ROC analysis demonstrated good discriminative ability of admission NIHSS score for predicting HT, with an AUC of 0.83. An NIHSS cut-off value of ≥ 13 provided optimal sensitivity and specificity, suggesting its potential utility as a pragmatic threshold for risk stratification in routine clinical practice.

Similar NIHSS cut-off values have been reported in previous cohorts, although thresholds have varied depending on population characteristics and treatment protocols [21,22].

The graded increase in HT incidence across NIHSS categories observed in this study further supports a dose–response relationship between stroke severity and hemorrhagic risk. Patients with NIHSS ≥ 13 exhibited more than sixfold higher rates of HT compared to those with NIHSS < 10 , underscoring the importance of heightened surveillance and cautious therapeutic decision-making in this subgroup.

INTERACTION WITH OTHER CLINICAL RISK FACTORS

Although multiple factors were associated with HT on univariable analysis, including atrial fibrillation, hyperglycemia, and thrombolytic therapy, admission NIHSS score remained independently predictive in multivariable modeling. Atrial fibrillation has been associated with cardioembolic strokes, which tend to involve larger infarcts and carry a higher risk of hemorrhagic transformation [23]. Similarly, hyperglycemia has been implicated in exacerbating ischemic injury and blood–brain barrier breakdown, thereby increasing hemorrhagic risk [24].

The association between thrombolytic therapy and HT observed in unadjusted analysis is consistent with existing literature; however, it is noteworthy that NIHSS retained its predictive value even after adjusting for thrombolysis. This finding suggests that baseline stroke severity plays a fundamental role in hemorrhagic risk, independent of reperfusion treatment [25].

CLINICAL IMPLICATIONS

The findings of this study have important clinical implications. NIHSS is a simple, rapid, and universally applied tool in acute stroke evaluation. Its use as a predictor of hemorrhagic transformation may assist clinicians in early risk stratification, tailoring monitoring intensity, and informing discussions regarding prognosis. In resource-limited settings where advanced imaging or biomarkers may not be readily available, reliance on robust clinical predictors such as NIHSS is particularly valuable [26].

Furthermore, identifying patients at high risk for HT may influence post-thrombolysis management, including blood pressure control, antithrombotic timing, and frequency of neurological and imaging surveillance. Incorporating NIHSS into predictive models alongside radiological and laboratory parameters may enhance individualized stroke care [27].

FUNCTIONAL OUTCOMES AND PROGNOSTIC SIGNIFICANCE

Consistent with prior reports, hemorrhagic transformation in our cohort was associated with significantly worse functional outcomes at 90 days, particularly among patients with symptomatic HT [28]. Parenchymal hematomas, although less frequent than hemorrhagic infarctions, were associated with marked neurological deterioration and poor recovery. These observations highlight the prognostic significance of HT and further justify efforts to identify high-risk patients early in the disease course [29].

COMPARISON WITH EXISTING LITERATURE

Our results are in concordance with large registry-based and single-center studies that have identified admission NIHSS score as a predictor of hemorrhagic transformation and symptomatic intracranial hemorrhage [30,31]. However, much of the existing literature originates from Western populations or clinical trial cohorts. The present study adds to the body of evidence by providing real-world data from a tertiary care setting, reflecting routine clinical practice and a heterogeneous patient population.

STRENGTHS AND LIMITATIONS

The strengths of this study include its real-world design, standardized assessment of stroke severity using NIHSS, and systematic classification of hemorrhagic transformation based on ECASS criteria. However, several limitations merit consideration. The retrospective nature of the study introduces the possibility of selection and information bias. The single-center design and relatively modest sample size may limit

generalizability. Additionally, advanced imaging markers such as infarct volume and perfusion parameters were not uniformly available and could not be included in the analysis.

FUTURE DIRECTIONS

Prospective, multicenter studies incorporating clinical, radiological, and biochemical predictors are warranted to validate NIHSS-based risk stratification models. Further research exploring the integration of NIHSS with imaging-based scores may improve predictive accuracy and guide personalized therapeutic strategies [32].

CONCLUSION

This retrospective cross-sectional study demonstrates that the admission National Institutes of Health Stroke Scale (NIHSS) score is a strong, independent clinical predictor of hemorrhagic transformation in acute ischemic stroke. Patients presenting with higher NIHSS scores were significantly more likely to develop both asymptomatic and symptomatic hemorrhagic transformation, and this association persisted after adjustment for established clinical risk factors.

An admission NIHSS cut-off value of ≥ 13 showed good predictive accuracy for hemorrhagic transformation, highlighting its potential utility as a simple and readily available tool for early risk stratification. Given its widespread use in routine stroke assessment, NIHSS can be effectively incorporated into clinical decision-making to identify high-risk patients who may benefit from closer monitoring, cautious use of reperfusion therapies, and individualized post-stroke management strategies. The findings of this study reinforce the prognostic significance of early stroke severity and underscore the importance of structured neurological assessment at presentation. In resource-limited settings, where advanced imaging and biomarkers may not be universally accessible, reliance on robust clinical predictors such as NIHSS assumes even greater importance.

While the retrospective design and single-center nature of this study limit generalizability, the results add meaningful real-world evidence to existing literature. Prospective, multicenter studies integrating clinical severity scores with radiological and biochemical markers are warranted to further refine predictive models for hemorrhagic transformation and optimize outcomes in patients with acute ischemic stroke.

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