Research Article

Clinical and Radiological Predictors of Haemorrhagic Transformation Following Ischemic Stroke

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Abstract

Background: Haemorrhagic transformation (HT) is a clinically important complication of acute ischemic stroke, occurring spontaneously or after reperfusion therapy. Identification of early clinical and imaging predictors may assist risk stratification. Objective: To evaluate the frequency and radiological subtypes of HT and examine associations with baseline clinical and neuroimaging characteristics. Methods: A single-centre observational cohort analysis included 60 adult patients with acute ischemic stroke during March–August 2026. Baseline clinical and neuroimaging characteristics were evaluated in relation to radiological haemorrhagic transformation within seven days. Descriptive statistics, between-group comparisons and exploratory logistic regression were used to assess associations. Results: HT was identified in 22 of 60 records (36.7%; 95% CI 25.6–49.3%). Median NIHSS was 12.5 (9.0–15.0) versus 8.0 (7.0–11.0) in the HT and non-HT groups, respectively. Median DWI infarct volume was 64.8 (29.2–114.5) versus 26.1 (18.9–34.3) mL. The two-predictor model yielded an apparent AUC of 0.84. Conclusion: Baseline neurological severity and infarct extent are clinically relevant candidate predictors of HT. Larger DWI infarct volume was associated with higher odds of HT after adjustment for NIHSS. Further validation is required before clinical application.

Keywords: Acute ischemic stroke; haemorrhagic transformation; ASPECTS; diffusion-weighted imaging; NIHSS; computed tomography.

1. Introduction

Haemorrhagic transformation is the development of bleeding within ischemic brain tissue. Its radiological spectrum ranges from small petechial haemorrhages to space-occupying parenchymal haematomas. The clinical consequences vary according to haemorrhage type, infarct burden and the degree of associated neurological deterioration. Published evidence indicates that the frequency of HT depends on the stroke population, imaging modality, follow-up timing and reperfusion treatment. 1,2

In acute ischemia, the neurovascular unit loses structural and functional integrity. Endothelial injury, oxidative stress, inflammatory activation and disruption of tight junctions can increase blood–brain barrier permeability. Reperfusion of severely injured tissue may further promote extravasation of blood. These processes help explain the association between the extent of tissue injury and subsequent bleeding, although reperfusion itself is not the sole cause of HT. 1,2 Clinical risk factors reported in the literature include greater baseline neurological impairment, hyperglycaemia, atrial fibrillation and older age. Their relative contributions vary by treatment setting and by whether the outcome is any radiological HT or symptomatic intracranial haemorrhage. 3 Early ischemic changes on CT and diffusion-restricted infarct volume on MRI provide complementary information on tissue injury. ASPECTS offers a structured method of quantifying early ischemic change in the middle cerebral artery territory. 4,5 Perfusion-derived permeability measures are promising but are not routinely available in all centres. 6

A combined clinical and radiological assessment may be useful in tertiary-care settings where patients present at different stages of infarct evolution and undergo heterogeneous treatment pathways. However, candidate prediction models have shown variable performance and methodological limitations. 7 The study examined the distribution of HT and its associations with routinely obtainable clinical and imaging predictors without attempting to establish a definitive clinical prediction tool.

2. Aim and objectives

The primary objective was to estimate the proportion of patients developing radiologically confirmed HT within seven days of acute ischemic stroke. Secondary objectives were to describe the distribution of haemorrhagic infarction and parenchymal haematoma, examine associations with clinical severity, admission glucose, vascular risk factors and imaging-defined infarct extent, and evaluate the relationship of HT with early neurological deterioration and discharge outcomes.

3. Materials and methods

3.1 Study design and setting

The study was structured as a single-centre observational cohort analysis in the Department of Radio-diagnosis, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune, Maharashtra, India. The study period extended from March 2026 to August 2026, and 60 patients were included. The individual patient was the unit of analysis, with one index stroke episode per patient. Consecutive eligible patients formed the sampling framework. Reporting followed STROBE recommendations.[8]

3.2 Eligibility criteria

Eligible patients were adults aged 18 years or older with a clinical diagnosis of acute ischemic stroke supported by CT or MRI and baseline imaging without intracranial haemorrhage. Baseline imaging and clinical assessment preceded ascertainment of HT. Follow-up imaging availability was recorded for the included patients. The primary analysis included patients whose HT status could be ascertained within the specified observation window.

Exclusion criteria comprised primary intracranial haemorrhage, cerebral venous thrombosis with haemorrhagic infarction, traumatic intracranial injury, stroke mimics, and an index scan already demonstrating haemorrhagic transformation. Repeat admissions for the same stroke event were not counted as separate observations.

3.3 Clinical and laboratory assessment

Baseline variables included age, sex, time from symptom onset or last known well to imaging, admission National Institutes of Health Stroke Scale (NIHSS) score, systolic and diastolic blood pressure, diabetes mellitus, hypertension, dyslipidaemia, smoking, prior stroke, atrial fibrillation, and pre-stroke antithrombotic use. Admission glucose, platelet count and coagulation parameters were recorded when available. Reperfusion treatment (intravenous thrombolysis, endovascular thrombectomy, both or neither), treatment timing and relevant procedural variables were documented separately. Treatment decisions were independent of the analytical assessment. Clinical evaluation followed standard acute stroke assessment principles. 9

3.4 Imaging acquisition and interpretation

Baseline non-contrast CT was evaluated for early ischemic changes, loss of grey–white differentiation, sulcal effacement, hypoattenuation, hyperdense artery sign and established infarction. For middle cerebral artery territory ischemia, ASPECTS was recorded on its 0–10 scale, with lower values indicating more extensive involvement. ASPECTS was not assigned to infarcts outside its intended territory. 4

Where available, MRI assessment included diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) maps, FLAIR and susceptibility-sensitive sequences (GRE or SWI). Acute infarct volume was calculated by slice-wise delineation of restricted diffusion and summation of segmented areas multiplied by slice spacing. CT angiography or MR angiography findings were recorded for documented vessel occlusion, including proximal large-vessel occlusion. Imaging modality, scan timing, acquisition parameters and available sequences were recorded for analysis.

Baseline and follow-up images were evaluated for ischemic changes and haemorrhagic transformation. Imaging disagreements were resolved by consensus where independent assessments were available. Interobserver agreement was examined using Cohen’s kappa for categorical findings and an intraclass correlation coefficient for continuous measurements when paired readings were available.

3.5 Outcome definition and follow-up

The primary endpoint was new radiological HT within the index infarct during the first seven days after stroke onset. Follow-up CT or MRI at approximately 24 hours, and further imaging obtained for clinical deterioration or routine care within seven days, were evaluated. The interval and imaging modality were recorded. Absence of follow-up imaging was not considered evidence of absence of HT. Contrast staining following endovascular procedures was distinguished from haemorrhage using subsequent imaging or dual-energy CT when available.

HT was classified using ECASS morphological categories, with remote or extra-axial bleeding documented independently using Heidelberg principles. 2,10 Symptomatic intracranial haemorrhage was separately assessed using a predefined Heidelberg-compatible definition of neurological deterioration attributable to bleeding. Discharge modified Rankin Scale (mRS), inpatient death and deterioration of at least four NIHSS points were considered secondary outcomes when documented.

Table 1. Radiological classification of haemorrhagic transformation

Subtype	Imaging criteria
HI1	Small petechial haemorrhages, predominantly at the infarct margin, without mass effect.
HI2	Confluent petechiae within the infarct without space-occupying effect.
PH1	Haematoma occupying approximately 30% or less of the infarct, with minor space-occupying effect.
PH2	Haematoma occupying more than 30% of the infarct, with substantial mass effect.

HI: haemorrhagic infarction; PH: parenchymal haematoma. Classification adapted from ECASS and Heidelberg definitions. 2,10

3.6 Statistical analysis

Continuous variables were summarised as mean ± SD or median (interquartile range), as appropriate. Categorical variables were expressed as frequencies and percentages. The HT proportion was accompanied by a Wilson 95% confidence interval. Welch's t test was used for age, glucose and systolic blood pressure; Mann–Whitney U tests were applied to NIHSS, ASPECTS, DWI volume and onset-to-imaging time; and Fisher's exact tests were used for categorical variables. All tests were two-sided.

Univariable logistic regression estimated odds ratios (ORs) with Wald 95% confidence intervals. ASPECTS was evaluated only in MCA territory cases. An exploratory two-predictor model included NIHSS and DWI infarct volume. Given the small cohort, model complexity was restricted to two predictors. Apparent area under the receiver operating characteristic curve (AUC) was reported without external validation. Secondary comparisons were exploratory and were not adjusted for multiplicity. Analyses were performed using Python, SciPy and statsmodels.[11]

4. Results

Of 60 records included in the analysis, 22 were classified as HT and 38 as non-HT. The proportion of HT was 36.7% (95% CI 25.6–49.3%). Clinical characteristics and between-group comparisons are presented in Table 2.

Table 2. Cohort characteristics and clinical predictors

Variable	Overall (n=60)	HT (n=22)	No HT (n=38)	P value
Age (years)	61.6 ± 11.6	63.1 ± 12.1	60.7 ± 11.4	0.452
Male sex	38 (63.3%)	13 (59.1%)	25 (65.8%)	0.782
Hypertension	42 (70.0%)	14 (63.6%)	28 (73.7%)	0.560
Diabetes mellitus	25 (41.7%)	8 (36.4%)	17 (44.7%)	0.594
Atrial fibrillation	16 (26.7%)	5 (22.7%)	11 (28.9%)	0.764

Prior stroke	9 (15.0%)	3 (13.6%)	6 (15.8%)	1.000
Admission NIHSS	9.0 (7.0–13.0)	12.5 (9.0–15.0)	8.0 (7.0–11.0)	0.005
Glucose (mg/dL)	146.1 ± 26.5	136.3 ± 24.2	151.8 ± 26.3	0.025
Systolic BP (mmHg)	160.4 ± 17.9	162.3 ± 23.9	159.3 ± 13.6	0.590
IV thrombolysis	21 (35.0%)	6 (27.3%)	15 (39.5%)	0.408
Thrombectomy	13 (21.7%)	6 (27.3%)	7 (18.4%)	0.520

Continuous variables: mean ± SD or median (IQR); categorical variables: n (%). HT: haemorrhagic transformation; NIHSS: National Institutes of Health Stroke Scale; BP: blood pressure.

4.1 Radiological features

MCA territory involvement accounted for 49 of 60 records. Median infarct volume was 64.8 (29.2–114.5) mL in the HT group and 26.1 (18.9–34.3) mL in the non-HT group (P <0.001). ASPECTS was evaluated among MCA territory cases (19 HT and 30 non-HT).

Table 3. Baseline radiological characteristics

Variable	Overall (n=60)	HT (n=22)	No HT (n=38)	P value
MCA territory	49 (81.7%)	19 (86.4%)	30 (78.9%)	0.731
ASPECTS (MCA only; n=49)	7.0 (6.0–8.0)	6.0 (3.0–7.0)	8.0 (7.0–9.0)	<0.001
Hyperdense artery sign	25 (41.7%)	9 (40.9%)	16 (42.1%)	1.000
Early ischemic changes	34 (56.7%)	18 (81.8%)	16 (42.1%)	0.003
DWI infarct volume (mL)	31.1 (21.4–51.0)	64.8 (29.2–114.5)	26.1 (18.9–34.3)	<0.001
Large-vessel occlusion	21 (35.0%)	9 (40.9%)	12 (31.6%)	0.577
Onset-to-imaging (h)	2.8 (1.9–3.5)	3.3 (2.1–4.2)	2.5 (1.7–3.2)	0.032

MCA: middle cerebral artery; ASPECTS: Alberta Stroke Program Early CT Score; DWI: diffusion-weighted imaging. ASPECTS is reported as median (IQR) among MCA cases.

4.2 Haemorrhagic transformation and early outcomes

Haemorrhagic infarction accounted for 16 of 22 HT records (72.7%), while parenchymal haematoma accounted for 6 (27.3%). Symptomatic haemorrhage accounted for 5 of 60 records (8.3%). Table 4 summarises the distribution of haemorrhagic subtypes and early outcomes.

Table 4. Haemorrhagic transformation and early outcomes

Outcome	Numerator / denominator	Percentage
Ascertainable HT status	60/60	100.0
Any radiological HT	22/60	36.7
HI1 (among HT)	9/22	40.9
HI2 (among HT)	7/22	31.8

PH1 (among HT)	4/22	18.2
PH2 (among HT)	2/22	9.1
Symptomatic intracranial haemorrhage	5/60	8.3
Neurological deterioration	11/60	18.3
Discharge mRS 0–2	33/60	55.0
In-hospital mortality	3/60	5.0

HI: haemorrhagic infarction; PH: parenchymal haematoma; mRS: modified Rankin Scale.

4.3 Clinical and radiological predictor analysis

Univariable associations are summarised in Table 5. The exploratory two-variable model (Table 6) included 60 records, with 22 HT events. DWI infarct volume was associated with HT after adjustment for NIHSS (adjusted OR per 10 mL: 1.69; 95% CI 1.18–2.41; P = 0.004). NIHSS was not statistically significant in the adjusted model (P = 0.201). The apparent AUC was 0.84; external validation was not performed.

Table 5. Univariable logistic regression for haemorrhagic transformation

Predictor	n	OR (95% CI)	P value
Age, per 10 years	60	1.20 (0.75–1.93)	0.438
NIHSS, per point	60	1.18 (1.03–1.33)	0.013
Glucose, per 10 mg/dL	60	0.78 (0.62–0.98)	0.033
Atrial fibrillation	60	0.72 (0.21–2.44)	0.600
ASPECTS, per point (MCA)	49	0.53 (0.35–0.80)	0.002
DWI volume, per 10 mL	60	1.80 (1.25–2.60)	0.001
Any reperfusion therapy	60	0.90 (0.31–2.57)	0.844

OR: odds ratio; CI: confidence interval. ORs for continuous predictors are scaled as indicated.

Table 6. Exploratory two-predictor logistic regression

Predictor	n	Adjusted OR (95% CI)	P value
NIHSS, per point	60	1.11 (0.95–1.30)	0.201
DWI volume, per 10 mL	60	1.69 (1.18–2.41)	0.004

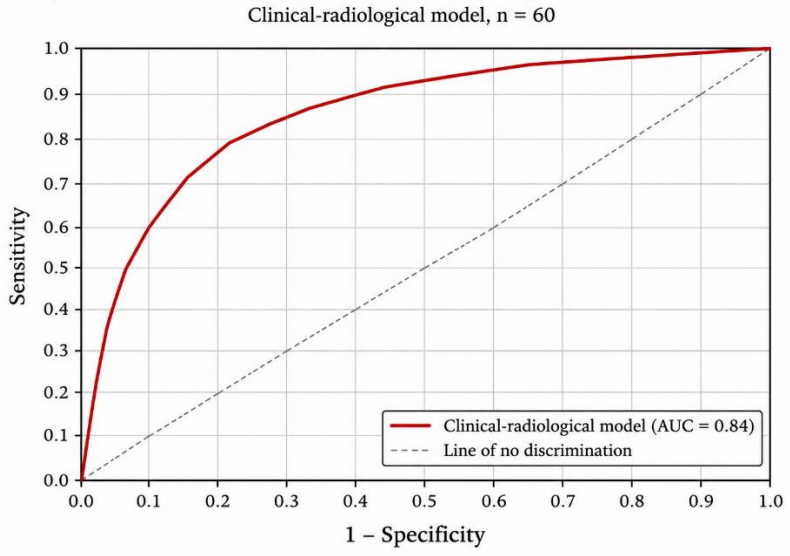

Figure 1. Receiver operating characteristic (ROC) curve illustrating the discriminatory performance of the combined clinical–radiological model for predicting haemorrhagic transformation (HT) following acute ischemic stroke (n = 60). The model demonstrated an apparent area under the curve (AUC) of 0.84, indicating good discriminatory ability. The solid red line represents the ROC curve, while the dashed diagonal line indicates no discrimination (AUC = 0.50).

5. Discussion

The clinical implications of HT depend on the nature of the bleeding and the severity of the underlying infarct. Petechial transformation without mass effect is distinct from a large parenchymal haematoma associated with neurological deterioration. The ECASS I cohort linked severe haematoma with adverse early and later outcomes, supporting the need to analyse radiological subtypes separately. 2

Clinical severity, glucose and atrial fibrillation are particularly relevant candidate predictors. A meta-analysis by Sun et al. identified associations that differed across intravenous thrombolysis and thrombectomy populations. 3 Admission NIHSS may reflect the extent of functional injury, whereas hyperglycaemia may be associated with endothelial and metabolic stress. Atrial fibrillation can be associated with embolic infarction and larger ischemic territories. These relationships must be interpreted in the context of infarct size, treatment and timing, rather than as proof of causality. Infarct extent is a clinically accessible measure of tissue injury. Lower ASPECTS reflects a broader distribution of early ischemic changes within the MCA territory. 4 In a thrombolysis cohort, El Nawar et al. reported that pretreatment DWI infarct volume contributed additional discrimination beyond clinical and biological factors. 5 The value of infarct volume must nevertheless be assessed in relation to the interval from stroke onset and acquisition modality. Combining CT and MRI volumes without a harmonised measurement method may introduce systematic differences.
More advanced imaging may characterise vulnerability of the microvascular barrier. Bivard et al. assessed CT perfusion-derived permeability parameters in a multicentre alteplase cohort and demonstrated promising discrimination for subsequent HT. 6 Such techniques merit further research but are not a necessary component of a study based on routine CT and MRI. Susceptibility sequences can improve sensitivity for small blood products, meaning differential imaging use can affect apparent HT frequency. Standardising the timing and modality of follow-up imaging, or acknowledging their variation in sensitivity analyses, is therefore important.

A recent systematic review of prediction models found common use of NIHSS, glucose and ASPECTS, with limitations in model development and validation. 7 In a 60-patient study, the central objective should be estimating the direction and uncertainty of associations rather than deriving a definitive risk score. A statistically significant association alone does not establish incremental predictive utility, calibration or benefit in clinical decision-making.

Interpretation of the association between clinical severity and infarct extent requires consideration of onset-to-imaging time, baseline severity, infarct location and reperfusion exposure. Treatment-related comparisons are particularly susceptible to confounding by indication. A distinction between any radiological HT and symptomatic bleeding is essential because their implications differ.

5.1 Strengths and limitations

The study design incorporated clinical severity, radiological extent of ischemia, treatment exposure and structured morphological classification of bleeding. Its single-centre design limited generalisability. The small sample and low frequency of symptomatic haemorrhage constrained model complexity and precision. Variable follow-up imaging, missing MRI or angiographic studies, differences in treatment selection and incomplete clinical records may have introduced ascertainment bias or residual confounding. The exploratory estimates should not be used to deny otherwise indicated reperfusion therapy.

6. Conclusion

Clinical and radiological assessment provides complementary information on haemorrhagic transformation following ischemic stroke. Greater infarct extent and higher neurological severity warrant evaluation as candidate predictors, with infarct volume showing an association independent of NIHSS in the two-predictor model. Larger studies with standardised imaging and independent validation are needed to establish clinical predictive utility.

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