Analysis of Characteristics and Clinical Outcomes After Ischaemic Stroke by NIHSS in a Nationally Representative US Electronic Health Records Database

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Introduction

- About 75%[1] of the estimated 691,650 ischaemic strokes (IS) that occur in the United States each year[2] are classified as non-cardioembolic IS (NCIS).[1]
- Stroke severity can be classified using the 15-item National Institutes of Health Stroke Scale (NIHSS) into: ≤5: minor; 6–15: moderate; >15: severe.[3,4]
  - NIHSS scores are a strong predictor of stroke outcomes.[5,6]
- Risk of recurrent stroke or transient ischaemic attack (TIA) can be mitigated with appropriate secondary stroke prevention.[7,8]
  - American Heart Association/American Stroke Association guidelines recommend that patients with NCIS or TIA receive antiplatelet therapy in preference to an oral anticoagulant to reduce recurrent IS risk while minimising bleeding risk.[8]
  - Recommendations for patients with a NIHSS score ≤3 include dual antiplatelet therapy with aspirin + clopidogrel for 21 days, followed by single antiplatelet therapy.[8]

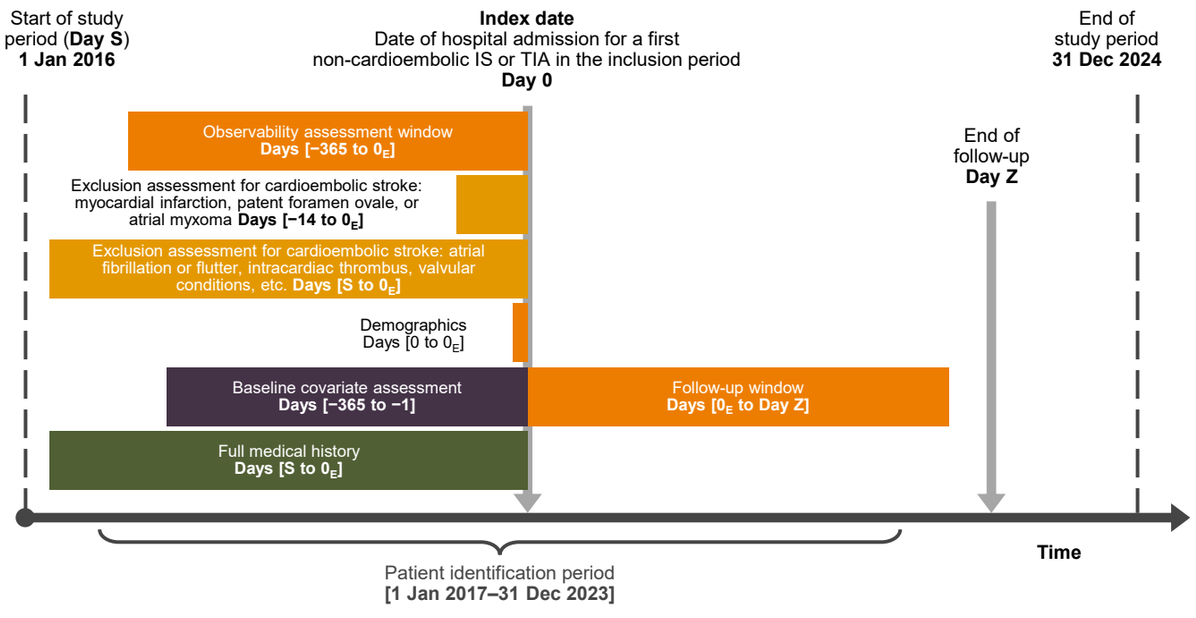
Objectives

- This sub-analysis of the US-based retrospective observational ALTEA study (Analysis of a Large naTionally representative US database on the BurdEn of disease and treatment pAtterns among stroke and TIA patients) assessed real-world patient characteristics and clinical outcomes among NCIS cases according to baseline NIHSS scores.

Methods

- ALTEA included adults (≥18 years of age) hospitalised for first NCIS or TIA (based on International Classification of Diseases, 10th Revision, Clinical Modification codes) between January 2017 and December 2023, as recorded in the Truveta electronic health record (EHR) database (**Figure 1**).

Figure 1. ALTEA study design.



Day 0_E, follow-up started from date of discharge from the index hospitalisation; Day S, start of study period; Day Z, the earliest of death, end of follow-up period or up to 365 days following hospitalisation for stroke/TIA.
IS, ischaemic stroke; TIA, transient ischaemic attack.

- To be included, patients had to have ≥12 months' EHR activity prior to the index date and, in the 12 months prior to the index date, to have received care documented in the EHR database from >1 provider. Patients with risk factors associated with cardioembolic stroke were excluded.
- Baseline patient characteristics according to baseline NIHSS score and clinical outcomes up to 1 year following hospitalisation for NCIS were calculated from structured data and unstructured clinical notes processed with Truveta's large language model.
- Clinical outcomes included recurrent IS, all-cause mortality, a composite outcome (recurrent stroke, myocardial infarction or death), International Society on Thrombosis and Haemostasis (ISTH) major bleeding and symptomatic intracranial haemorrhage.

Statistical analysis

- Time-to-event methods were used to study all outcomes. Cumulative risks were estimated using Kaplan–Meier methods. Patients were followed from the date of hospital admission until the earliest of death, end of follow-up period or up to 365 days following hospitalisation for IS/TIA.

Results

Study population

- Of 180,021 patients with NCIS, 67% (n=120,923) had estimable admission NIHSS scores, of which 78% were classed as NIHSS ≤5, 14% as NIHSS 6–15 and 8% as NIHSS >15.
  - Patients with both recorded or unknown NIHSS scores were predominantly White. Hypertension was the most common comorbidity, followed by hyperlipidaemia, diabetes, cerebrovascular disease and coronary artery disease.
- Compared with patients with NIHSS scores ≤5, patients with NIHSS scores >15 were older (mean age: 70 years vs 67 years, respectively), more likely to be female (51% vs 49%), and more frequently had large-artery atherosclerosis, cardioembolic or undetermined-combination TOAST (Trial of Org 10172 in Acute Stroke Treatment) stroke subtypes (**Table 1**).
- Final TOAST stroke subtype included 16% assessed to have had a cardioembolic stroke, which was unknown at the time of admission.

Table 1. Baseline characteristics by NIHSS score.

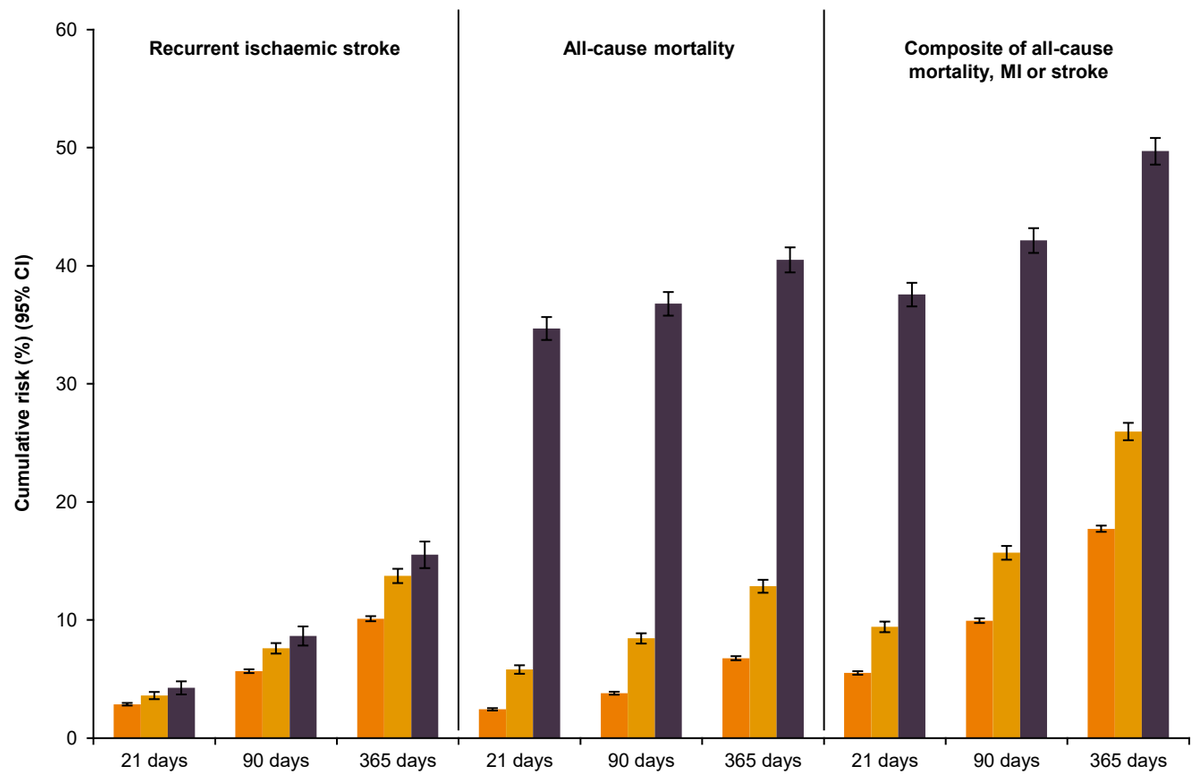
Characteristic	NCIS (N=180,021)	NIHSS ≤5 (n=94,069)	NIHSS 6–15 (n=17,218)	NIHSS >15 (n=9636)	NIHSS unknown (n=59,098)
Age, mean (SD), years	67.6 (14.5)	66.9 (14.3)	68.5 (14.6)	70.4 (14.8)	68.0 (14.6)
Sex, n (%)					
Female	88,752 (49.3)	45,635 (48.5)	8614 (50.0)	4918 (51.0)	29,585 (50.1)
Male	87,972 (48.9)	46,923 (49.9)	8269 (48.0)	4329 (44.9)	28,451 (48.1)
Other or unknown	3297 (1.8)	1511 (1.6)	335 (1.9)	389 (4.0)	1062 (1.8)
Ethnicity, n (%)					
White	122,933 (68.3)	64,512 (68.6)	11,143 (64.7)	5791 (60.1)	41,487 (70.2)
Black or African American	24,285 (13.5)	12,973 (13.8)	2365 (13.7)	945 (9.8)	8002 (13.5)
Asian	4446 (2.5)	2742 (2.9)	516 (3.0)	220 (2.3)	968 (1.6)
Other†	8268 (4.6)	4922 (5.2)	992 (5.8)	368 (3.8)	1986 (3.4)
Unknown	20,089 (11.2)	8920 (9.5)	2202 (12.8)	2312 (24.0)	6655 (11.3)
Comorbidities‡, n (%)					
Hypertension	128,762 (71.5)	67,063 (71.3)	11,763 (68.3)	6211 (64.5)	43,725 (74.0)
Hyperlipidaemia	69,140 (38.4)	36,770 (39.1)	5952 (34.6)	3084 (32.0)	23,334 (39.5)
Diabetes	47,857 (26.6)	24,229 (25.8)	4462 (25.9)	2222 (23.1)	16,944 (28.7)
Cerebrovascular disease	35,077 (19.5)	16,982 (18.1)	3715 (21.6)	1922 (19.9)	12,458 (21.1)
Coronary artery disease	31,407 (17.4)	15,706 (16.7)	2733 (15.9)	1470 (15.3)	11,498 (19.5)
Prior therapies, n (%)					
High blood pressure medications	98,757 (54.9)	52,808 (56.1)	9593 (55.7)	5243 (54.4)	31,113 (52.6)
Cholesterol-lowering medications	70,703 (39.3)	37,954 (40.3)	6703 (38.9)	3618 (37.5)	22,428 (38.0)
Anti-diabetic medications	31,796 (17.7)	18,103 (19.2)	3215 (18.7)	1591 (16.5)	8887 (15.0)
Anti-obesity medications	5485 (3.0)	3309 (3.5)	525 (3.0)	206 (2.1)	1445 (2.4)
NSAID	61,073 (33.9)	31,523 (33.5)	5512 (32.0)	2755 (28.6)	21,283 (36.0)
Prior antiplatelet therapy	39,564 (22.0)	19,071 (20.3)	3730 (21.7)	1882 (19.5)	14,881 (25.2)
Prior parenteral ACT	68,197 (37.9)	36,268 (38.6)	6598 (38.3)	3632 (37.7)	21,699 (36.7)
Prior oral ACT	11702 (6.5)	5402 (5.7)	1202 (7.0)	787 (8.2)	4311 (7.3)
Thrombolytic therapy	1901 (1.1)	946 (1.0)	227 (1.3)	128 (1.3)	600 (1.0)
Thrombectomy	182 (0.1)	85 (<0.1)	41 (0.2)	42 (0.4)	14 (<0.1)
	NCIS (N=29,816)§	**NIHSS ≤5 (n=20,116)§**	**NIHSS 6–15 (n=4773)§**	**NIHSS >15 (n=2837)§**	**NIHSS unknown (n=2090)§**
Final TOAST stroke subtype, n (%)					
Large-artery atherosclerosis	6473 (21.7)	4223 (21.0)	1207 (25.3)	795 (28.0)	248 (11.9)
Small-vessel occlusion	8990 (30.2)	6612 (32.9)	1101 (23.1)	210 (7.4)	1067 (51.1)
Cardioembolism‖	4641 (15.6)	2945 (14.6)	766 (16.0)	664 (23.4)	266 (12.7)
SODA	845 (2.8)	560 (2.8)	141 (3.0)	103 (3.6)	41 (2.0)
Stroke of undetermined aetiology	6846 (23.0)	4623 (23.0)	1092 (22.9)	721 (25.4)	410 (19.6)
Undetermined-Combination	2021 (6.8)	1153 (5.7)	466 (9.8)	344 (12.1)	58 (2.8)
Unknown¶	150,205 (83.4)	73,953 (78.6)	12,445 (72.3)	6799 (70.6)	57,008 (96.5)

†Includes categories of 'Other' and Native American, Alaskan, Hawaiian or Pacific Islander.
‡Top five most prevalent comorbidities in all patients with NCIS.
§TOAST stroke subtype classification was available for a subset of the full analytical cohort, as these data were extracted from unstructured notes. Unstructured notes were available in a limited number of health systems that provide data to Truveta.
‖Patients classified as having a cardioembolic source for the current admission but no prior history or risk factors for cardiometabolic stroke.
¶Percentages of total patients (n=94,069 for NIHSS ≤5, n=17,218 for NIHSS 6–15, n=9636 for NIHSS >15, n=59,098 for NIHSS unknown).
ACT, anticoagulant therapy; NCIS, non-cardioembolic ischaemic stroke; NIHSS, National Institutes of Health Stroke Scale; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SODA, stroke of other determined aetiology; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Clinical outcomes

- The risk of recurrent IS, all-cause mortality and composite outcome (all-cause mortality, myocardial infarction or stroke) increased with higher NIHSS score categories across all time points up to 1 year (**Figure 2**).
  - The cumulative risk for the composite outcome at 1 year was almost 50% for patients with NIHSS scores >15 compared with only 18% for patients with NIHSS scores ≤5.

Figure 2. Clinical outcomes by NIHSS score: Recurrent ischaemic stroke, all-cause mortality and composite.

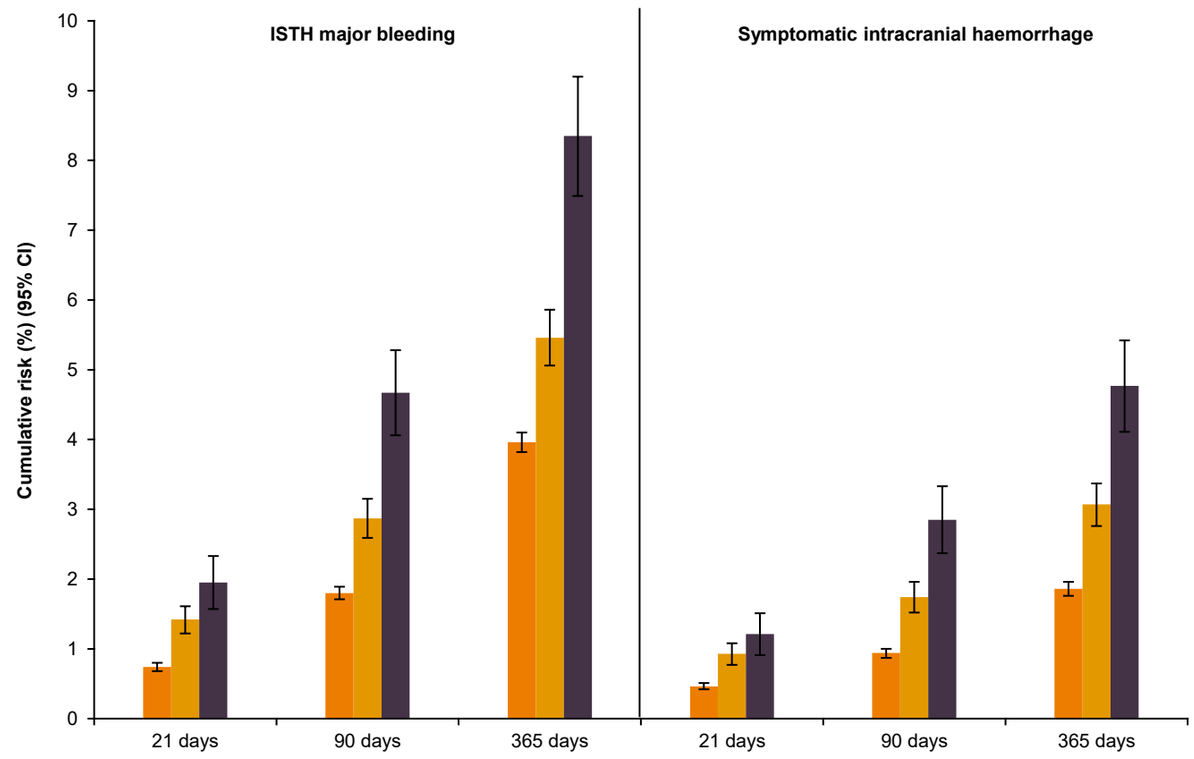


Cumulative risk (%) (95% CI)†	Recurrent ischaemic stroke			All-cause mortality			Composite of all-cause mortality, MI or stroke		
	21 days	90 days	365 days	21 days	90 days	365 days	21 days	90 days	365 days
NIHSS ≤5	**2.9** (2.76–2.98)	**5.7** (5.51–5.83)	**10.1** (9.9–10.33)	**2.4** (2.34–2.54)	**3.8** (3.68–3.93)	**6.8** (6.60–6.94)	**5.5** (5.37–5.67)	**10.0** (9.75–10.15)	**17.7** (17.47–18.00)
NIHSS 6–15	**3.6** (3.30–3.91)	**7.6** (7.16–8.05)	**13.7** (13.13–14.34)	**5.8** (5.45–6.17)	**8.5** (8.01–8.88)	**12.9** (12.31–13.41)	**9.4** (8.97–9.87)	**15.7** (15.11–16.28)	**26.0** (25.23–26.70)
NIHSS >15	**4.3** (3.70–4.81)	**8.7** (7.84–9.46)	**15.5** (14.40–16.65)	**34.7** (33.72–35.66)	**36.8** (35.78–37.78)	**40.5** (39.44–41.56)	**37.6** (36.56–38.56)	**42.2** (41.09–43.19)	**49.7** (48.57–50.83)

†Cumulative risk (%) and 95% CIs were estimated using time-to-event methods, accounting for censoring. Reported cumulative risks represent the probability of experiencing the outcome by the end of the specified time point, regardless of interval-specific event counts.
CI, confidence interval; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale.

- The risk of ISTH major bleeding and symptomatic intracranial haemorrhage also increased with higher NIHSS score categories across all time points up to 1 year (**Figure 3**).

Figure 3. Clinical outcomes by NIHSS score: ISTH major bleeding and symptomatic intracranial haemorrhage.



Cumulative risk (%) (95% CI)†	ISTH major bleeding			Symptomatic intracranial haemorrhage		
	21 days	90 days	365 days	21 days	90 days	365 days
NIHSS ≤5	**0.7** (0.68–0.80)	**1.8** (1.71–1.89)	**4.0** (3.82–4.10)	**0.5** (0.42–0.51)	**0.9** (0.87–1.00)	**1.9** (1.76–1.96)
NIHSS 6–15	**1.4** (1.22–1.61)	**2.9** (2.59–3.15)	**5.5** (5.06–5.86)	**0.9** (0.77–1.08)	**1.7** (1.52–1.96)	**3.1** (2.76–3.37)
NIHSS >15	**2.0** (1.57–2.33)	**4.7** (4.06–5.28)	**8.4** (7.49–9.20)	**1.2** (0.91–1.51)	**2.9** (2.37–3.33)	**4.8** (4.11–5.42)

†Cumulative risk (%) and 95% CIs were estimated using time-to-event methods, accounting for censoring. Reported cumulative risks represent the probability of experiencing the outcome by the end of the specified time point, regardless of interval-specific event counts.
CI, confidence interval; ISTH, International Society on Thrombosis and Haemostasis; NIHSS, National Institutes of Health Stroke Scale.

Conclusions

- In people with NCIS, analysis of ALTEA data showed that all clinical outcomes (including recurrent IS, all-cause mortality, composite outcome and major bleeding) were worse among those with higher baseline NIHSS scores. The 1-year event rate for the composite outcome of recurrent stroke, myocardial infarction or death was almost 50% for those with severe stroke (NIHSS >15).
- Limitations of these data include the high number of patients with unknown NIHSS (33%) and uncertainty about the classification of NCIS (vs cardioembolic stroke) for the index admission.

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