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The influence of initial stroke severity on mortality, overall functional outcome and in-hospital placement at 90 days following acute ischemic stroke: A tertiary hospital stroke register study

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Abstract:

Background and Purpose: Epidemiological studies on the extent of the interaction and/or influence of stroke severity on clinical outcomes are important. The aim of the present study was to investigate the putative (and degree of) impact of initial stroke severity in predicting the overall functional outcome, in-hospital placement, and mortality in acute ischemic stroke (AIS) in comparison with age, admission to the stroke unit and thrombolytic treatment.

Materials and Methods: The John Hunter Hospital acute stroke register was used to collect a retrospective cohort of AIS patients being assessed for reperfusion therapy and admitted between January 2006 and December 2013. Univariate and multivariate logistic regression and receiver operating characteristics analyses were used to assess associations with functional outcome, in-hospital placement, and mortality at 90 days.

Results: 608 AIS patients with complete datasets were included in the study. On univariate analysis, initial stroke severity showed the strongest independent association to the risk of death within 90 days (Odds ratio (OR) =1.15; $P < 0.001$; 95% confidence interval (CI) = [1.11, 1.18]); age was a less significant independent influence (OR = 1.02; $P = 0.049$; 95% CI = [1.00, 1.03]). Multivariate logistic regression analysis demonstrated that initial stroke severity independently predicted the 90 day mortality (OR = 1.16; 95% CI = [1.12, 1.2]; $P < 0.0001$) and unfavorable outcome (OR = 1.16; 95% CI = [1.13, 1.2]; $P < 0.0001$). Higher National Institute of Health Stroke Scale at admission was significantly associated with longer in-hospital placement ($P < 0.0001$).

Conclusions: In this acute stroke cohort, initial stroke severity had a major impact on the likelihood of death following an AIS and appears to be the dominant influence on the overall stroke outcome and in-hospital placement.

Key Words:

Age, hospital assessment, mortality, NIHSS, prognosis, stroke, stroke severity

Key Message:

Baseline stroke severity has a dominant influence on the overall functional outcome, in-hospital placement, and post-stroke mortality. Analyses of stroke outcome that is not concomitantly assessing baseline stroke severity may be potentially misleading.

Stroke is a leading cause of death and disability worldwide.[1] According to the Australian Institute of Health and Welfare (AIHW 2012), Stroke is Australia's second biggest cause of death after coronary heart disease, and a leading cause of disability[2] (AIHW, 2012 #2). More than 65% of stroke survivors also suffer a disability that impedes their ability to carry out

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daily living activities unassisted.[3] Understanding of factors contributing to the progression of stroke and/or mortality may have an important impact on future stroke trials and patient management. The National Institute of Health Stroke Scale (NIHSS) is a commonly used stroke impairment scale and is well-validated across many hospitals around the globe.[4] NIHSS sums the scores from individual elements of the neurological examination to provide an overall stroke impairment score.[5] NIHSS has been used as an initial stroke severity assessment for a variety of purposes including prediction of progression of acute stroke[6] and patient outcomes.[4,7]

Predicting the clinical course of patients with acute stroke continues to be a prognostic challenge for stroke physicians.[8] Early risk stratification of acute stroke patients has contributed important clinical estimates of mortality risk using reliable and simple prognostic models.[9,10] At present, prognostic models of mortality are used in the economic and performance evaluation of stroke care centres. However, these models often lack appropriate case-mix adjustment of initial stroke severity. Initial severity of stroke and age are both recognized to influence the likelihood of an unfavorable functional outcome and/or mortality following an acute stroke. However, the extent of the interaction is uncertain. Therefore, epidemiological studies on the extent of the interaction and/or influence of stroke severity and age on mortality and overall functional outcomes are important. Performance evaluation and report cards on hospitals and physicians are increasingly utilized to judge, evaluate, and/or compare health-care provider performance in terms of various "outcome-determinants," including patient outcomes (such as mortality) and incurred costs.[10-26] Such analyses may use the available demographic data, including age, but not include relevant clinical data such as stroke severity. National stroke care guidelines now recommend the preferential triage of acute stroke to specialized tertiary care stroke units.[27,28] This results in specialized tertiary stroke units receiving different case-mixes compared to nonstroke unit hospitals. For instance, large hospital or university health care centres are more likely to encounter more severe cases including those that come as referrals from local small hospitals with severe morbidity. Based on the clinical experience, it may well be argued that there is anecdotal evidence that these facilities often receive patients who have greater morbidity, are in advanced stages of their illness, and are more likely to have severe comorbid health conditions.

The purpose of this study was to investigate the putative (and degree of) impact of stroke severity in predicting the overall functional outcome, in-hospital placement, and death at 90 days, in comparison with age, admission to the stroke unit, and thrombolytic treatment. Our underlying hypothesis is that the NIHSS will be the dominant clinical determinant of stroke prognosis.

Materials and Methods

The John Hunter Hospital (JHH) is a tertiary referral hospital for the Hunter New England Local Health District (HNELHD). JHH acts as the regional thrombolysis referral centre servicing the great Newcastle, Hunter, and Manning region within the HNELHD. JHH acute stroke register was used to collect a retrospective cohort of acute stroke patients, who were being assessed for potential suitability for reperfusion therapy, admitted between January 2006 and December 2013. The JHH acute stroke registry collects all patients presenting with acute stroke being assessed for potential suitability for reperfusion therapy. The register prospectively documents covariates including age and baseline stroke severity (measured using the NIHSS) and 90-day functional outcome, as well as the patient demographics, medical comorbidities, risk factors, complications, treatment, and diagnostic procedures. Patients with intracerebral hemorrhage and subarachnoid hemorrhage were excluded from the final dataset. The database was then linked, to obtain 90-day mortality status, to HNELHD's Cardiac and Stroke Outcomes Unit database. HNELHD's Cardiac and Stroke Outcomes Unit tracks 90-day stroke mortality using medical records coding of all Hunter New England (HNE) stroke separations using International Statistical Classification of Diseases and Related Health Problems (ICD)-10 [Figure 1]. For the cohort identified through the JHH acute stroke register, mortality was tracked using the following criteria:

1. ICD10 code of I63 (cerebral infarction) or I64 (stroke, not specified as hemorrhage or infarction) in any of the first five diagnoses on discharge from any HNE hospital in a period of care
2. Admitted to JHH as part of a period of hospital care that occurred between 1 January 2006 and 31 December 2013
3. First admission to any hospital in the period of care classified as an emergency admission.

NIHSS score of >17 was classified as severe stroke, NIHSS <8 corresponded to a mild stroke, and NIHSS score of 8–16 was grouped in moderate stroke category, as used in other studies.[29,30] A score of 0–2 represented a good or favorable outcome, and a score of 3–6 a poor or unfavorable outcome. In-hospital placement or length of stay was defined as the total length of stay in the hospital during the various stages of the acute phase and post-acute rehabilitation treatment.

Statistical analysis

All statistical analysis was performed using STATA (Version 10, 2001; College Station, TX, USA). The principal analysis was the use of logistic regression to determine independent predictors of the 90-day mortality. The predictors of interest

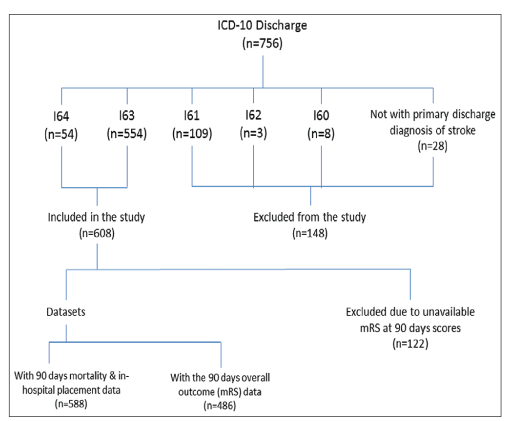

Figure 1: Inclusion and exclusion algorithm. 164 = stroke, not specified as hemorrhage or infarction, 163 = cerebral infarction, 162 = other nontraumatic intracranial hemorrhage, 161 = intracerebral hemorrhage, 160 = subarachnoid hemorrhage

were gender, age, baseline stroke severity measured by NIHSS, and thrombolytic treatment. Each of these predictors was examined using a simple logistic regression model, and a selection of those with $P < 0.10$ were included in subsequent multiple logistic regression models. These models differed in terms of the particular predictors included. Univariate and multivariate logistic regression were used to assess associations with 90-day mortality. Finally, receiver–operator characteristic (ROC) curve was used to plot baseline stroke severity and age, each in relation to the 90 day mortality and unfavorable outcome, in order to investigate the extent of interactions of age and stroke severity with stroke mortality and overall outcome. We quantified the accuracy and independent effect of stroke severity and age by calculating the area under the curves (AUC) and odds ratio (based on the regression analysis). A P value of ≤ 0.05 was considered significant.

Logistic regression analysis was also performed to study the influence of stroke severity and age on the level of dependency or overall stroke outcome (modified Rankin score [mRS] at 90 days and in-hospital placement). The influence of stroke severity and age (as predictor variables) on in-hospital placement (or length of stay post-stroke) was studied using multivariate regression analysis. In addition, we performed correlation to study the extent of association of stroke severity on admission and age with the functional outcome (measured by mRS) at 90 days using pairwise Pearson's correlation coefficient (r). Significance level of the correlation coefficients for each variable was also tested.

Results

From the initial 957 patients entered in the register, 201 patients were excluded because of incomplete data on potentially important covariates. The exclusion and inclusion algorithm is shown in Figure 1. Overall, out of 756 patients who were discharged with ICD-10 diagnosis, 608 patients with complete datasets were included in the study after the exclusion of patients with intracerebral and subarachnoid hemorrhages. Dataset of 486 patients with available day 90 mRS scores were used to study the association of stroke severity and other covariates with the overall functional outcome. For the study on association of stroke severity and other covariates with in-hospital placement and mortality, the available dataset on 588 patients was used.

The demography of the population studied is shown in detail in Table 1. The average age of the study population was 75.3 (standard deviation [SD] =12.94, minimum = 24, maximum = 98) years. In addition, the average in-hospital placement or length of stay was 17.5 days (SD = 22.57, minimum = 1 day, maximum = 153) days. Females constituted 48% (n = 292) of the study population, and 81.9% of the admitted patients were 65 years or older. The distribution of patients based on their age category and stroke severity profile is shown in Figure 2. Patients aged 65 and above recorded moderate-to-severe stroke severity scores of 8 and above (70.7%). Patients with the NIHSS score of 17 and above accounted for 33.84% of the overall population. Thrombolytic treatment was given to 53.5% of patients. Patients aged 75 and above accounted for 60% of the overall study population. A total of 126 patients (126/608 = 20.7%) were dead at the end of the follow-up (90 days). Furthermore, 46% of the patients showed a good functional clinical outcome at

Table 1: Demographic and clinical characteristics of the study patients

	n=608
Gender	
Male	316 (52)
Female	292 (48)
Age (*n*=608); mean±SD	75.28±12.94
Age <55	49 (8.06)
55≤ Age ≤64	61 (10.03)
65≤ Age ≤74	135 (22.20)
Age ≥75	363 (59.70)
Treatment factors	
Thrombolytic treatment	325 (53.45)
Stroke unit admission	542 (89.14)
NIHSS at admission (*n*=588); median (IQR)	12 (13)
Mild (0≤ NIHSS ≤7)	185 (31.46)
Moderate (8≤ NIHSS ≤16)	204 (34.69)
Severe (17≤ NIHSS ≤44)	199 (33.84)
NIHSS at 24 h (*n*=426); median (IQR)	4 (12)
Length of hospital stay; median (IQR)	9 (15)
Dead at 90 days (*n*=608)	126 (20.72)
Day-90 mRS (*n*=504); median (IQR)	3 (4.5)
Good clinical outcome (mRS=0-2)	234 (46.43)
0	75 (14.88)
1	106 (21.03)
2	53 (10.52)
Bad clinical outcome (mRS=3-6)	270 (53.57)
3	51 (10.12)
4	42 (8.33)
5	51 (10.12)
6	126 (25)

Values are expressed as number (percentages) unless otherwise indicated. *P<0.05 as threshold for statistical significance; mRS = Modified Rankin's scale; n = number; SD = Standard deviation; IQR = Interquartile range; NIHSS = National Institutes of Health Stroke Scale

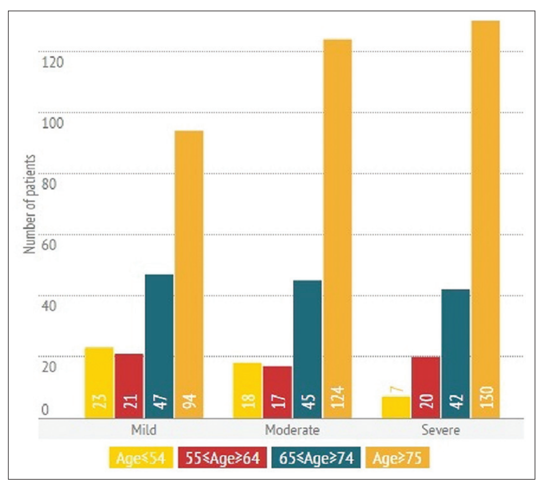

Figure 2: Chart showing the distribution of age profiles and corresponding stroke severity categories. Age categories: <55, 55–64, 65–74, and ≥75 years. Stroke severity categories: mild (NIHSS < 8), moderate (NIHSS: 8–16), and severe (NIHSS: 17 and above)

90 days. A majority of our patients (89%) were admitted to the specialized acute stroke unit.

Prediction of stroke mortality as well as favorable, and unfavorable outcome at 90 days

Univariate regression analysis showed that the stroke severity at admission, measured with NIHSS, was positively associated with the 90-day mortality (OR = 1.15; 95% CI = [1.11, 1.18]; $P < 0.001$) and unfavorable outcome (OR = 1.14; 95% CI = [1.10, 1.17]; $P \leq 0.0001$) in this study population. Age was less significantly associated with the 90-day mortality (OR = 1.02; 95% CI = [1.00, 1.02]; $P = 0.049$) and unfavorable outcome (OR = 1.03; 95% CI = [1.01, 1.04]; $P \leq 0.0001$) [Table 2]. Patients admitted to the stroke unit showed a positive association with the 90-day favorable outcome (OR = 2.85; 95% CI = [1.44, 5.61]; $P = 0.003$) and were negatively associated with an unfavorable outcome (OR = 0.35; 95% CI = [0.18, 0.69]; $P = 0.003$) and mortality (OR = 0.26; 95% CI = [0.15, 0.44]; $P \leq 0.0001$) at 90 days. Thrombolysis was not significantly associated with mortality and clinical outcome at 90 days. However, there was a tendency toward a favorable outcome in patients who received thrombolysis (OR = 1.33; 95% CI = [0.94, 1.9]; $P = 0.111$).

Multivariate analysis for the prediction of stroke mortality using stroke severity, age, admission to stroke unit, and thrombolysis as independent variables demonstrated that stroke severity was the strongest predictor of mortality (OR = 1.26; 95% CI = [1.12, 1.2]; $P \leq 0.0001$) [Table 2]. Age was no longer significantly associated with mortality (OR = 1.01; 95% CI = [0.99, 1.03]; $P = 0.303$). Admission to stroke unit (OR = 0.21; 95% CI = [0.10, 0.42]; $P \leq 0.0001$) and thrombolysis (OR = 0.58; 95% CI = [0.36, 0.95]; $P = 0.03$) were negatively associated with stroke mortality. In terms of unfavorable outcome, stroke severity was the dominant factor (OR = 1.16; 95% CI = [1.13, 1.2]; $P \leq 0.0001$), followed by age (OR = 1.03; 95% CI = [1.01, 1.05]; $P = 0.001$) while controlling for the effects of admission to stroke unit and thrombolysis.

Receiver–operator characteristic analysis

The ROC analyses revealed that the model with stroke severity and age, while controlling for the effects of stroke unit admission and thrombolysis, demonstrated a higher predictive ability for mortality (ROC area = 0.80; specificity = 97%; overall rate of correct classification = 81%; positive predictive value = 61%) versus an overall unfavorable outcome (ROC area = 0.78;

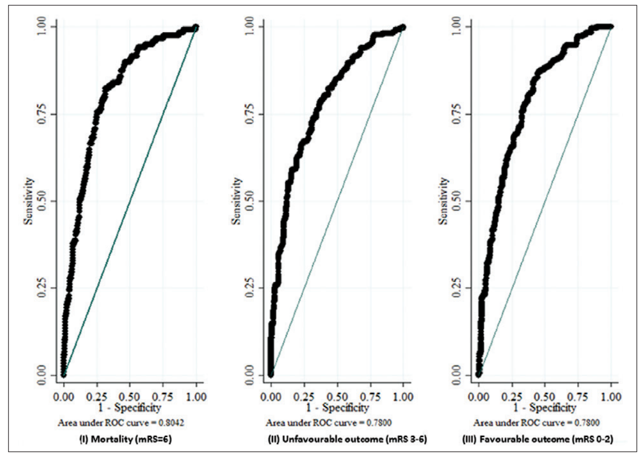

Figure 3: Receiver operating characteristic (ROC) curves for mortality (a), favorable outcome (b), and unfavorable outcome (c). Area under the curve (AUC) is a measure of the discriminatory power of the risk model

Table 2: Odds ratios (95% confidence intervals) for prediction of the 90-day mortality (Model I), the favorable outcome at 90 days (Model II), and unfavorable outcome at 90 days (Model III)

Variable	Mortality (*n*=588)		Favorable outcome (mRS 0-2) [*n*=486]		Unfavourable outcome (mRS 3-6) [*n*=486]	
	Simple OR (95% CI); *P*>|*z*|	Mixed OR (95% CI); *P*>|*z*|	Simple OR (95% CI); *P*>|*z*|	Mixed OR (95% CI); *P*>|*z*|	Simple OR (95% CI); *P*>|*z*|	Mixed OR (95% CI); *P*>|*z*|
NIHSS at admission	1.15 (1.11-1.18); *P*<0.0001*	1.16 (1.12-1.2); *P*≤0.0001*	0.88 (0.85-0.91); *P*<0.0001*	0.86 (0.83-0.89); *P*<0.0001*	1.14 (1.10-1.17); *P*≤0.0001*	1.16 (1.13-1.2); *P*<0.0001*
Age	1.02 (1.00-1.02); *P*=0.049*	1.01 (0.99-1.03); *P*=0.303	0.97 (0.96-0.99); *P*<0.0001*	0.97 (0.96-0.99); *P*=0.001*	1.03 (1.01-1.04); *P*≤0.0001*	1.03 (1.01-1.05); *P*=0.001*
Admission to stroke unit	0.26 (0.15-0.44); *P*<0.0001*	0.21 (0.10-0.42); *P*<0.0001*	2.85 (1.44-5.61); *P*=0.003*	4.17 (1.74-10); *P*=0.001*	0.35 (0.18-0.69); P=0.003*	0.24 (0.1-0.57); *P*=0.001*
Thrombolysis	0.77 (0.52-1.15); *P*=0.203	0.58 (0.36-0.95); *P*=0.03*	1.33 (0.94-1.9); *P*=0.111	2.12 (1.33-3.34); *P*=0.001*	0.75 (0.53-1.07); *P*=0.111	0.11 (0.03-0.50); *P*=0.004*

OR = Odds ratio; CI = Confidence interval; NIHSS = National Institutes of Health Stroke Scale; * = Significant value

Table 3: Sensitivity and specificity analysis for age and stroke severity controlling for the effects of thrombolysis and admission to a stroke unit, as a test for prediction of the 90-day mortality (Model I), the favorable outcome at 90 days (Model II), and unfavorable outcome at 90 days (Model III)

	Model I (90-day mortality [mRS=6]; *n*=588	Model II (favorable outcome [mRS=0-2] at 90 days); *n*=486	Model III (unfavorable outcome [mRS=3-6] at 90 days); *n*=486
Sensitivity	21.01%	69.60%	70.66%
Specificity	96.59%	70.66%	69.60%
PPV	60.98%	67.52%	72.62%
NPV	82.82%	72.62%	67.52%
Overall rate of correct classification	81.29%	70.16%	70.16%
Area under the ROC curve	0.80	0.78	0.78

NPV = Negative predictive value; PPV = Positive predictive value; ROC = Receiver-operating characteristic; *n* = Number; mRS = modified Rankin scale

specificity = 71%; Overall rate of correct classification = 70%; positive predictive value = 67%%) at 90 days [Table 3]. Figure 3 shows the ROC (sensitivity vs. 1-specificity) analyses curves for the prediction of mortality and overall clinical outcomes at 90 days.

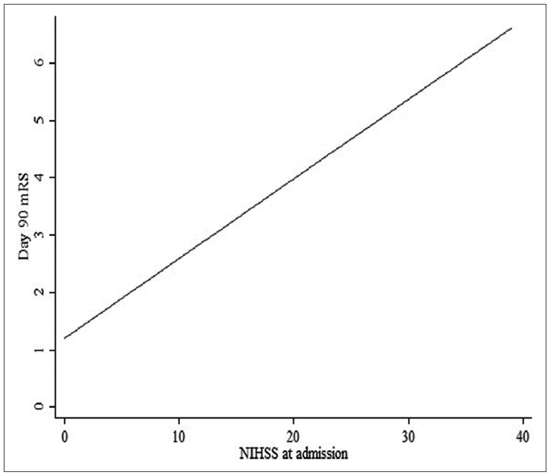

Figure 4: Correlation of the presenting NIHSS score and the modified Rankin score (at 90 days). The baseline NIHSS score was predictive of the overall functional outcome at 90 days. The regression line is obtained by plotting the fitted values of 90-day mRS scores and the NIHSS at admission

Influence on stroke outcome and in-hospital placement

Moderate positive correlation was observed between NIHSS score at admission and mRS scores at 90 days (r = 0.47; P < 0.001) [Figure 4]. However, no correlation was observed between age and mRS at 90 days (r = 0.15, P = 0.0006).

Severe (OR = 16, 95% CI = [7.6, 35], $P \leq$ 0.0001) and moderate (OR = 4.8; 95% CI = [2.13, 10.7]; $P \leq$ 0.0001) strokes were significantly associated with mortality at 90 days [Table 4]. Patients aged 75 and above were two times more likely to be associated with mortality at 90 days. However, the association was not statistically significant (P = 0.153). In terms of an unfavorable outcome, severe stroke (OR = 12; 95% CI = [6.7, 21.6]) had a dominant effect in comparison to that of age ≥75 (OR = 4; 95% CI = [1.75, 10.55]), as evident from higher odds ratios of 12 vs. 4.

The influence of NIHSS at admission and age on the length of hospital stay or in-hospital placement is shown in Table 5. Multivariate regression analysis revealed that increasing NIHSS at admission was significantly associated with a longer in-hospital placement (P < 0.0001). Severe strokes were more likely to have a longer in-hospital placement (P < 0.0001).

Table 4: Multivariate analysis with stratified stroke severity and age groups showing odds ratios (95% confidence intervals) for the prediction of 90-day mortality (Model I), the favorable outcome at 90 days (Model II), and the unfavorable outcome at 90 days (Model III)

Variables	Mortality at 90 days (*n*=588)		Unfavorable outcome (*n*=486)		Favourable outcome (*n*=486)	
	Dead vs. alive at 90 days, *n* (%); *P*	Mixed OR (95% CI); *P*>|*z*|	90-day unfavorable vs. favorable outcomes, *n* (%); *P*	Mixed OR (95% CI); *P*>|*z*|	90-day favourable vs. unfavourable outcomes, *n* (%); *P*	Mixed OR (95% CI); *P*>|*z*|
NIHSS at admission		*P*≤0.00001*		*P*≤0.00001*		*P*≤0.00001*
Mild (0≤ NIHSS ≤7)	10 (8.4) vs. 175 (27.31); *P*≤0.0001*	1	35 (13.5) vs. 94 (41.4); *P*≤0.0001*	1	94 (41.41) vs. 35 (13.51); *P*≤0.0001*	1
Moderate (8≤ NIHSS ≤16)	30 (25.21) vs. 174 (37.10); *P*=0.017*	4.77 (2.13-10.68); *P*≤0.0001*	85 (32.82) vs. 91 (40.1); *P*=0.108	3.8 (2.18-6.64); <0.0001*	91 (40.09) vs. 85 (32.82); *P*=0.108	0.26 (0.15-0.46); *P*≤0.0001*
Severe (17≤ NIHSS ≤44)	79 (66.39) vs. 120 (25.59); *P*=0.0001*	16.44 (7.63-35.42); *P*≤0.0001*	139 (53.67) vs. 42 (18.5); *P*≤0.0001*	11.99 (6.66-21.6); <0.0001*	42 (18.50) vs. 139 (53.67); *P*≤0.0001*	0.08 (0.05-0.15); *P*≤0.0001*
Age		*P*=0.3833		*P*=0.0058*		*P*=0.0058*
Age <55	4 (3.17) vs. 45 (9.34); *P*=0.026*	1	8 (2.96) vs. 27 (11.54); *P*≤0.0001*	1	27 (11.54) vs. 8 (2.96); *P*≤0.0001*	1
55≤ Age ≤64	14 (11.11) vs. 47 (9.75); *P*=0.621	2.01 (0.54-7.4); *P*=0.296	31 (11.48) vs. 21 (8.97); *P*=0.381	4.69 (1.59-13.79); *P*=0.005*	21 (8.97) vs. 31 (11.48); *P*=0.381	0.21 (0.07-0.63); *P*=0.005*
65≤ Age ≤74	22 (17.46) vs. 113 (23.44); *P*=0.185	1.63 (0.48-5.52); *P*=0.429	49 (18.15) vs. 58 (24.79); *P*=0.081	2.76 (1.06-7.22); *P*=0.039*	58 (24.79) vs. 49 (18.15); *P*=0.081	0.36 (0.14-0.95); *P*=0.039*
Age ≥75	86 (68.25) vs. 277 (57.47); *P*=0.032*	2.3 (0.73-7.2); *P*=0.153	182 (67.41) vs. 128 (54.7); *P*=0.004*	4.3 (1.75-10.55); *P*=0.001*	128 (54.70) vs. 182 (67.41); *P*=0.004*	0.23 (0.09-0.57); *P*=0.001*
Stroke unit admission	96 (76.19) vs. 446 (92.53); *P*=0.0001*	0.21 (0.11-0.42); *P*≤0.0001*	234 (86.67) vs. 222 (94.87); *P*=0.002*	0.29 (0.12-0.68); *P*=0.005*	222 (94.87) vs. 234 (86.67); *P*=0.002*	3.49 (1.47-8.27); *P*=0.005*
Thrombolysis	61 (48.41) vs. 264 (54.77); *P*=0.229	0.58 (0.36-0.94); *P*=0.028*	146 (54.07) vs. 143 (61.1); *P*=0.125	0.49 (0.31-0.78); *P*=0.003*	143 (61.11) vs. 146 (54.07); *P*=0.125	2.03 (1.28-3.21); *P*=0.003*

NIHSS = National Institutes of Health Stroke Scale; * = Significant

Table 5: Multivariate linear regression analysis for prediction of in-hospital placement or length of hospital stay

Variable (n=588)	Coefficients (95% confidence interval)	$P>\|t\|$
Model A		
NIHSS at admission	0.49 (0.24, 0.74)	<0.0001*
Age	−0.17 (−0.31, −0.03)	0.018*
Stroke unit admission	7.84 (1.71, 13.96)	0.012*
Thrombolysis	0.16 (−3.74, 4.05)	0.936
Model B		
NIHSS at admission		<0.00001*
Mild (0≤ NIHSS ≤7)	1	
Moderate (8≤ NIHSS ≤16)	8.96 (4.34, 13.59)	<0.0001*
Severe (17≤ NIHSS ≤44)	11.08 (6.41, 15.74)	<0.0001*
Age		0.001*
Age <55	1	
55≤ Age ≤64	8.26 (−0.27, 16.79)	0.058
65≤ Age ≤74	−0.44 (−7.79, 6.91)	0.907
Age ≥75	−4.14 (10.91, 2.63)	0.230
Stroke unit admission	7.96 (1.85, 14.07)	0.011*
Thrombolysis	−0.44 (−0.43, 3.45)	0.825

NIHSS = National Institutes of Health Stroke Scale; * = Significant

Discussion

This study aimed to compare the independent influence of both initial stroke severity and age on the likelihood of an unfavorable clinical outcome and death within 90 days of an acute ischemic stroke. We found that the initial stroke severity showed the strongest independent association to the risk of death and unfavorable outcome within 90 days. Previous studies have also indicated that stroke severity is an important determinant of patient outcome in stroke.[31-33] Initial stroke severity is also a significant predictor of responses to treatment in ischemic stroke.[34-38] Our results indicate that it is important to measure stroke severity and make an adjustment for stroke severity when reporting for both functional outcome and mortality rates. At present, in most of the administrative datasets, stroke severity measurements are not available. This is pertinent because there is an increasing number of administrative dataset publications reporting stroke mortality rates where adjustment for stroke severity is absent or limited.[10,39] Indeed, studies have shown that if the severity of stroke case-mix is not taken into account, it can lead to skewed or even misleading mortality estimates, which in turn may have implications for funding and health-care policy. A recent study in the United States by Fonarow *et al.*,[10] has generated interest in the practice of performance evaluation for acute stroke services. The authors noted that risk-models potentially used to measure a hospital's performance, which discount initial stroke severity, can be misleading and could lead to misalignment of incentives. The authors re-evaluated rankings of hospitals with the post-stroke severity adjustment in place and found that a significant proportion of hospitals initially ranked as mortality rate outliers fell within the specified boundaries post-adjustment. Therefore, stroke risk models using either administrative data or clinical data that do not include severity have inferior discrimination, substantial unaccounted-for variance, and can result in the misclassification of the hospital's performance.

Our findings also suggest that stroke severity is an independent predictor of overall functional outcome. We found a positive correlation between increasing admission NIHSS score and the unfavorable modified Rankin scale score at 90 days. This further establishes the need for appropriate case-mix adjustment in the comparison of functional outcome performance across hospitals.[40,41] We also found that increasing stroke severity was associated with longer in-hospital placement. At present, most administrative datasets do not contain many of the key covariates necessary to perform appropriate case-mix adjustment. Our study also showed that the length of in-hospital placement was significantly influenced by the stroke severity. This is in agreement with the findings reported elsewhere.[42]

Our study has several limitations and we acknowledge that bias could have been introduced. First, the retrospective nature of our study limits acquisition of some data elements; and, the tertiary hospital–based acute stroke program under assessment for reperfusion therapy sampling frame has led to a collection of hyperacute and severe stroke case-mix. Higher rates of thrombolysis implementation in our cohort are an indicator of this selection bias. Importantly, however, intravenous tissue plasminogen activator or alteplase does not significantly alter ischemic stroke mortality rates.[43,44] Bias could also have been introduced due to the kind of treatment regimen or the treatment pathway the patient was on.

In conclusion, this study shows that baseline stroke severity is a dominant influence on the overall functional outcome, in-hospital placement, and mortality post-stroke. Stroke severity was independently associated with the likelihood of death following an acute stroke. Baseline stroke severity is an essential covariate in any analysis of stroke outcome. Reliable prognostic modelling in acute stroke requires the use of a valid adjustment of the baseline stroke severity. Our results are an addition to the evidence base for clinicians and researchers to use stroke severity for early risk-stratification. Analyses of stroke outcome not including baseline stroke severity should be considered inadequate and potentially misleading.

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Conflicts of interest

There are no conflicts of interest.

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