ORIGINAL ARTICLE

Retrospective Comparison of the Predictive Ability of SPAN-100 Index, Age, and the NIHSS Score on Acute Ischaemic Stroke 30-day Case Fatality Rate

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ABSTRACT

Background: Prognostication and risk prediction are important components of acute stroke management. Identification of acute stroke cases with an increased likelihood of adverse outcomes can promote the implementation of preventive strategies including intensified monitoring and pre-emptive interventions. The use of clinical parameters as predictors of outcome is of particular interest in our resource-limited setting.

Objectives: To determine the predictive ability of the Stroke Prognostication using Age and National Institutes of Health Stroke Scale/Score (SPAN-100) index on 30-day case fatality rate (CFR) in acute ischaemic stroke (AIS) and compare this to the predictive ability of the individual components of the index.

Methodology: This descriptive study retrospectively analysed data from the Lagos University Teaching Hospital Nigeria stroke database over a 30-month period. The cases were consecutive first-ever clinically overt, brain computed tomographically evident AIS, aged ≥18years, admitted within 7days of onset. The SPAN-100 index (sum of age and baseline NIHSS score) was characterized as SPAN-100 index positive (score ≥100) or negative (<100). The primary outcome of interest was 30-day all cause CFR.

Results: Four hundred and twenty-one AIS cases (220 males, 201 females; mean age 60.7±13.3years) satisfied the study criteria. Three hundred and ninety-six (94.1%) were SPAN-100 negative. The 30-day CFR was significantly greater in the SPAN-100 positive AIS cases (19/25 i.e. 76.6% v. 107/396 i.e. 27%) (*p=0.000; Odds ratio 8.55* (95% *CI 3.33–21.98*). The SPAN-100 index only fairly predicted 30-day CFR (AUC

0.74), while the NIHSS score was a good predictor of short-term outcome (AUC 0.85). Age had very poor predictive ability (AUC 0.52).

Conclusion: The NIHSS score is a better predictor of short-term outcome following AIS compared to either the SPAN-100 index or patient's age.

Keywords: *Lagos University Teaching Hospital, prognostication, short-term outcome, stroke*

INTRODUCTION

Stroke is the second leading cause of death globally and together with ischaemic heart disease accounts for >20% of all deaths.[1, 2] The current incidence of first-ever stroke in Nigeria (age adjusted to World Health Organization (WHO) population) is 54.0 per 100,000 annually, meaning that more than 92,000 new strokes occur yearly, excluding recurrent strokes.[3] The mortality and disability associated with stroke (stroke burden) is disproportionately higher in lower income countries than high income countries.[1,4] The estimated stroke mortality rate in Nigeria is 120–240 per 100,000 population (specifically 153/100,000) translating to a quarter of a million deaths annually. This is similar to the estimates for most of Eastern Europe and Sub-Saharan Africa.[3]

Of the 6.5million deaths that occurred globally from stroke in 2013, 51% were caused by ischaemic stroke, with a disproportionate high burden of these deaths in low and middle income countries.[2] Ischaemic stroke mortality rates were particularly higher in developing compared to developed countries in people >49years.[2] Factors contributing to the increasing stroke burden in developing countries, such as ours, may include patient characteristics, disease characteristics and issues relating to healthcare access, quality and standards.

Strategies directed at determining the predictors of stroke outcome are pertinent to improve identification and differentiation of patients at increased risk of adverse outcomes. Prediction models and stroke scores have several applications including prognostication, strategizing management, and increasing surveillance and monitoring. The end-points of interest include functional outcome (with or without thrombolysis), risk of haemorrhage (after thrombolysis), cognitive and bio-behavioural outcomes, quality of life, and risk of death.

The composition of risk scores includes demographic, historical, clinical, imaging or laboratory or a combination of any of these. Examples include the Stroke Thrombolytic Predictive Instrument (Stroke-TPI), Ischaemic Stroke Predictive Risk Score (iSCORE), ***D***ense Cerebral Artery Or Early Infarct Sign On CT, Modified ***R***ankin Scale Pre-stroke, ***A***ge, ***G***lucose Level On Admission, ***O***nset To Treatment Time and ***N***IHSS Score (DRAGON), Acute Stroke Registry And Analysis Of Lausanne (ASTRAL), Stroke Prognostication Using Age And NIHSS Score (SPAN-100), Post-thrombolysis Risk Score, Haemorrhage After Thrombolysis Score (HAT), Blood *S*ugar, Early Infarct Sign on admission CT head scan, Dense or hyperdense cerebral artery Sign on admission CT, Age, and *N*IHSS Score on admission (SEDAN), and Safe Implementation of Treatments in Stroke - symptomatic Intracerebral Haemorrhage risk score (SITS-ICH).[5-12]

The SPAN-100 score is a clinical score of the sum of age in years and the National Institutes of Health Stoke Scale (NIHSS) score on admission. Scores are dichotomized as SPAN-100 positive (sum ≥100) and negative (sum <100).[9] It has the advantage of simplicity and practicability by depending on two readily available parameters. The index, although initially designed and applied in the setting of acute strokes receiving thrombolysis, has been found to be useful in other scenarios.[9,13]

The objectives of this study were: to determine the ability of the SPAN-100 index to predict 30-day case fatality rate (CFR) following acute ischaemic stroke in our practice setting, and to compare this to the predictive ability of each of the component parameters (age and NIHSS score).

METHODOLOGY

This descriptive study used data from the Lagos University Teaching Hospital (LUTH) Stroke database. The database has approval from the LUTH Health Research Ethics Committee. The minimum data set included age, gender, admission blood pressures, admission NIHSS score, admission random blood glucose, and 30-day outcome (obtained either at admission if hospitalized up till day 30, or, at follow up out-patient attendance). The retrospective analysis utilized data over a 30-month period ending June 2013.

Inclusion criteria for this study were: first-ever clinically apparent ischaemic stroke, neuroimaging confirmation of stroke subtype – brain computed tomographic (CT) scan or magnetic resonance imaging (MRI), and presentation to our facility within 7days of stroke onset.

The SPAN-100 index (the sum of positive age and NIHSS score) was calculated, and cases were characterized as SPAN-100 index (score ≥100) or negative (<100). The primary outcome measure was the 30-day case fatality.

Data Analysis

Data was analysed using IBM Statistical Package for the Social Sciences (SPSS®) version 20.0. Baseline continuous variables are presented as mean ± SD and medians (ranges). Categorical variables are shown as frequencies (%). Categorical variables were compared using Yates corrected Chi square test while sensitivity analyses of the variables of interest (SPAN-100 index, age and admission NIHSS score) were conducted using Receiver Operating Characteristics (ROC) curves. Odds ratios and 95% confidence intervals (CI) for death were calculated. Predictive accuracy of the SPAN-100 index, age, NIHSS and ROC curves are reflected in the Area Under the Curve (AUC) with corresponding standard error, p values and 95% confidence intervals. The predictive ability from AUC is interpreted as follows: 0.9 –1.0 (excellent), 0.8–0.9 (good), 0.7–0.8 (fair), 0.6–0.7 (poor) and ≤0.5 (very poor, not useful, null). Statistical significance was set at $p<0.05$.

RESULTS

Four hundred and twenty-one (421) stroke cases fulfilled the study criteria for the period under review, and comprised of 220 males and 201 females. Demographic and clinical variables at admission are shown in Table 1.

Table 1. Baseline characteristics of the 421 acute ischemic stroke cases

Variable	**Mean ± SD**	**Median (Range)**
Age (years)	60.7 ± 13.3	62.0 (21 – 89)
NIHSS score	12.5 ± 9.9	9.0 (0 – 40)
SPAN index score	73.2 ± 16.6	73.0 (25 – 112)
Duration prior to presentation (hours)	53.1 ± 38.9	24.0 (22 – 169)
Admission Glasgow Coma Score	12.5 ± 3.6	15 (3 – 15)
Systolic blood pressure (BP) (mmHg)*	156.6 ± 30.0	160 (70 – 250)
Diastolic blood pressure (BP) (mmHg)*	93.7 ± 19.6	90 (50 – 150)
Random blood glucose (mg/dL)*	141.0 ± 68.8	123 (23 – 600)

**Admission values of variables*

The mean age (± SD) for the study population was 60.7 ± 13.3 years. The mean duration of stroke prior to presentation was 53.1 ± 38.9 hours. The median NIHSS score for the study population was 9, while the median GCS score was 15. Pre-existing hypertension was present in 319 (75.8%) of the study population while the mean admitting random blood glucose level was 141.0 ± 68.8 mg/dl.

The study population was divided into 2 groups based on the SPAN-100 index category.[9] Three hundred and ninety-six of the 421 cases (94.1%) were SPAN-100 negative while 25 of 421 (5.9%) cases were SPAN-100 positive. The comparison of baseline and clinical variables by SPAN-100 category is shown in Table 2.

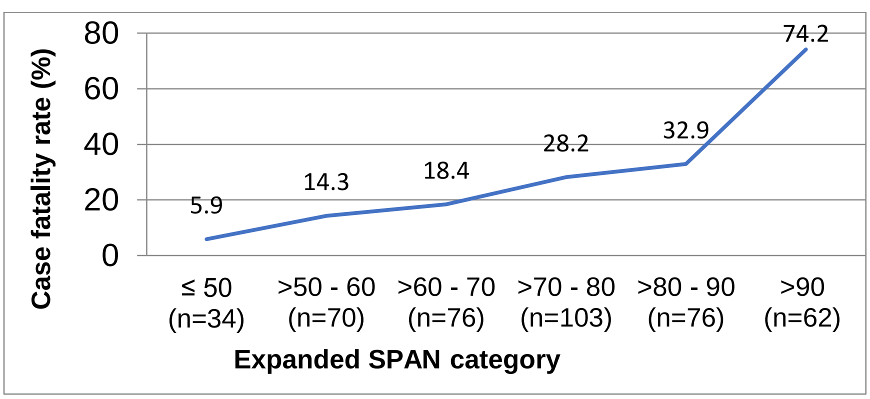
Table 2. Comparison of baseline variables in SPAN-100 positive and negative acute ischemic stroke cases

Variable	SPAN 100 positive n = 25	SPAN 100 negative n = 396	Statistics (p value)
Female (n, %): Male (n, %):	12 (48%): 13 (52%)	189 (47.7%): 207 (52.3%)	0.98
Age (mean ± SD, years)	74.1 ± 7.9	59.5 ± 13.10	0.000
GC Score (mean ± SD, median)	6.44 ± 2.9 (7)	12.87 ± 3.3 (15)	0.000
NIHSS Score (mean ± SD, median)	31.4 ± 7.64(36)	11.26 ± 8.7(9)	0.000
RBS (mg/dL) (mean ± SD, median)	171.1 ± 99.7	139.1 ± 66.1	0.03
Case fatality rate (n, %)	19 (76.6)	107 (27)	0.000

RBS – Random Blood Sugar *GC - Glasgow Coma*

Overall, 126 of 421 cases died within 30 days of ischaemic stroke onset, giving a 30-day CFR of 29.9%. The CFR was similar in the age categories above and below 60years (70/288, 30.7% vs 56/193, 29%) (*p=0.71; OR 0.9, 95%CI 0.61–1.40*). Employing the NIHSS cut-off for severe stroke, CFR was significantly higher in the category of stroke patients with NIHSS ≥ 16 (severe stroke) (85/111, 76.6%) compared to the category of cases with NIHSS <16 (mild – moderately severe stroke) (41/310, 13.2%) (*p=0.000; OR 21.45, 95%CI 12.39–37.12*).[14] Applying the SPAN-100 index, CFR was 76.6% (19/25) in the SPAN-100 positive category and this was significantly worse than the CFR of 27% (107/396) in the SPAN-100 negative category (*p=0.000*). The OR for death in the SPAN-100 positive compared to SPAN-100 negative subgroups was 8.55 (*95% CI 3.33–21.98*).

Figure 1. Case fatality rates in relation to expanded SPAN categories

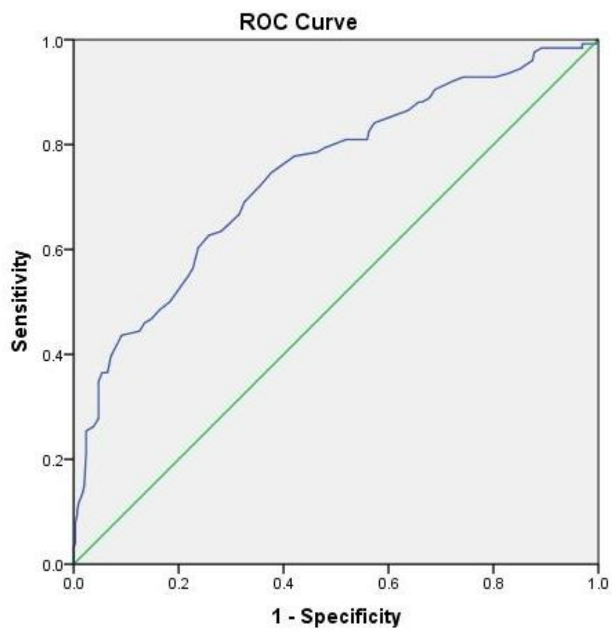


SPAN categories indicate ranges of scores for sum of age and NIHSS score

Table 3. Area Under the Curve (AUC), and related statistical parameters for the SPAN index, NIHSS score and age

Variable	AUC	Performance	Standard error	P value	95% CI
SPAN 100 index	0.74	Fair	0.03	<0.0001	0.69 – 0.80
NIHSS score	0.85	Good	0.023	<0.0001	0.81 – 0.90
Age (years)	0.52	Very poor	0.03	0.41	0.46 – 0.59

Figure 2. ROC curve for sensitivity analysis of SPAN index



The 30-day CFR was further compared against expanded SPAN index categories as shown in Figure 1.[13] The receiver operating curve (ROC) for the SPAN-100 index is shown in Figure 1, while, the area under the curve (AUC), standard error, *p-value* and 95% confidence intervals of the three variables of interest are compared in Table 3.

DISCUSSION

Prognostication is an integral aspect of medical treatment (acute stroke management inclusive), that, when formally conducted, serves to predict outcomes for individual patients.[15] Outcomes of interest include treatment response (to specific interventions), probability of development of complications and adverse outcomes, and identification of specific subsets of patients requiring additional monitoring and intervention on account of increased predicted risk.

The present study retrospectively explored the utility of the SPAN-100 index as a predictor of short-term (30 day) case fatality following acute ischaemic stroke using our institutional database. The parameters required for the model are clinical variables routinely obtainable at admission, thus, making the index an appropriate and practical tool for our practice setting.

This study found that the SPAN-100 index performed fairly (AUC 0.74) in predicting short-term case fatality. Specifically, using the conventional SPAN dichotomization (SPAN

100 positive i.e. score ≥100 or negative <100), CFR (76%) was significantly higher in the SPAN-100 positive group. Despite haven been developed in the context of patients receiving thrombolysis, the utility of the SPAN-100 index in the general stroke population has also been explored with similar conclusions as in this study.

Researchers using the Chinese National Stroke Registry found 4% (479 of 11,894 ischaemic strokes) to be SPAN-100 positive (similar to the 6% of our database). A significantly higher number of SPAN-100 positive patients had poor functional outcomes at 3 and 12 months.[16]

Also, with a further subdivision of the SPAN-100 index as suggested by the CHIMES (Chinese Medicine NeuroAid Efficacy on Stroke Recovery Study) investigators there was a clear trend of increasing CFR with incremental rise in the SPAN score, and a steep increase (more than double) in CFR beyond a SPAN score of 90 and above.[13] This finding is not unexpected as the SPAN incorporates two clinical parameters that reflect patient vulnerability (age) and stroke severity (NIHSS).

Although there is no consensus on the independent influence of age on stroke outcome, age may impart its effect on stroke severity or outcome through age-dependent burden of co-morbidities, the presence of multiple vascular risk factors, and a decline in the integrity of collateral circulation.[17,18,19] The NIHSS has previously been shown to strongly predict the likelihood of recovery after an ischaemic stroke and a score of ≥16 predicts a high probability of death.[14] The NIHSS correlates closely with the severity of the underlying pathological substrate causing the clinical features.

Fischer, *et al*, reported a significant association of NIHSS scores with the presence and location of vessel occlusion, with scores being higher in basilar, internal carotid, middle cerebral artery M1 and M2 segment occlusions.[20]

The NIHSS scores obtained 24hours post-stroke onset, also, correlated strongly with perfusion- and diffusion-weighted brain magnetic resonance imaging (MRI) conducted early (within 6.5hours) after stroke onset.[21]

One of the observed limitations of the SPAN-100 index is that, based on the score limits of the NIHSS (maximum of 42), patients aged below 58, regardless of stroke severity, cannot be classified as SPAN-100 positive.[13] Vice-versa, older patients (e.g. above 85 years), with milder stroke (based on NIHSS score), will inadvertently be classified as SPAN-100 positive.

On this basis, we also, examined the effect of the individual components of the SPAN-100 index and found that the NIHSS score was a better predictor of CFR (AUC 0.85 – good performance) than the SPAN-100 index (AUC 0.74 – fair) and also, age alone (AUC 0.52 – very poor).

In a retrospective study of ischaemic strokes conducted in a Brazilian population over a period of 2years, authors compared 4 prognostic scores in the prediction of in-hospital mortality and functional outcome – the NIHSS, SPAN-100, ASTRAL and Total Health Risk In Vascular Events (THRIVE) scores.[22] Of the 206 ischaemic strokes included, the authors reported poorer outcome in older cases, who also had a significantly higher percentage with NIHSS score >16.

The present study included a robust sample size and stroke cases managed within the same institution utilizing similar non-thrombolytic treatment protocol across board. As such, this would limit variability in outcomes related to specific interventions and be representative of the practice scenario in our locality.

Although the analysis was retrospective, the database routinely collects stroke related characteristics utilized in this study at presentation of all strokes, thus, limiting recall bias and incompleteness of data.

CONCLUSION

On the basis of our findings, we would recommend that although age may have an impact on stroke outcome, the more important effect following acute ischaemic stroke is that related to stroke severity, and the NIHSS should be incorporated as part of the routine admission evaluations at all centres admitting stroke cases in this country and the Sub-Saharan region. The NIHSS is a well-standardized clinical tool for which training and certification are freely available online (nihstrokescale.org) to ensure standardization in its application by both neurologists and non-neurologists.

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