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PROGNOSTICATION OF ISCHEMIC STROKE BASED ON THE STROKE VOLUME

Neurology

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ABSTRACT

Background and Purpose—Age and the National Institutes of Health Stroke Scale score (NIHSS) are established predictors of stroke. Ischemic stroke volume assessment plays a crucial role in its prognostication and final outcome. We studied outcome of acute ischemic stroke at 3 months and correlated it with the initial stroke volume.

Methods—Patients with acute ischemic stroke presenting within 7 days of onset constituted the study population. Stroke volume was assessed using ANALYZE. Stroke severity was assessed using NIHSS. Functional outcome was assessed after 3 months by using modified Rankin Scale (mRS) and Barthel Index (BI).

Results—Thirty patients were followed up for 3 months. Functional outcome and its correlation with age, NIHSS score, stroke volume at onset and other variables, was assessed. Only the NIHSS and stroke volume were robust predictors of the functional outcome. Stroke volume at onset correlated satisfactorily with stroke severity.

Conclusion—Both the NIHSS score and stroke volume within 7 days of acute ischemic stroke onset independently predicted the functional outcome and exhibited similar predictive strength.

KEYWORDS

Ischemic stroke; Stroke volume; NIHSS; Barthel Index, mRS

INTRODUCTION

Stroke is the second most common cause of mortality and the third most common cause of disability-adjusted life-years [1, 2]. India has a huge burden of stroke, with an incidence rate of 13–36 per 100,000 person-years and estimated age-adjusted prevalence rates of 84–262 per 100,000 persons in rural areas and 334–424 per 100,000 persons in urban areas [3-7]. The 30-day case fatality rate after the first-ever stroke ranges from 16% to 23%, and the 1-year survival rate is 77% [8]. According to a long-term follow-up of stroke survivors, 31% were dependent, 20% needed support for ambulation, and 71% had impaired vocational capacities.

The prognosis of stroke is extremely variable and difficult to predict at presentation because it is influenced by various factors including neurological, functional, and psychosocial factors [9-13]. Age and the National Institutes of Health Stroke Scale (NIHSS) score at baseline can be used to reliably predict the functional outcome; however, NIHSS certification and periodic recertification of the executor are necessary. Numerous studies with small sample sizes have suggested that the initial infarct size affects the clinical outcome. Infarct volume can be measured through magnetic resonance imaging (MRI, diffusion-weighted images [DWIs]) by using sophisticated software (e.g., ANALYZE). Very few studies have explored the added value of the MRI-measured stroke volume and clinical neurological variables in predicting clinical deterioration and functional outcomes [14]. Stroke volume assessment in patients with malignant middle cerebral artery infarct facilitates the identification of patients who are likely to experience early neurological deterioration and require early decompressive hemicraniectomy[15]. Furthermore, a large infarct volume and large vessel occlusion necessitate endovascular therapy rather than thrombolytic therapy. However, the validity of stroke volume as a measure of outcome has been questioned by many researchers because it does not provide information regarding the clinical condition. In this study, we evaluated whether the measurement of ischemic stroke volume and severity of stroke (as assessed using NIHSS score) can be used to accurately predict the functional outcome.

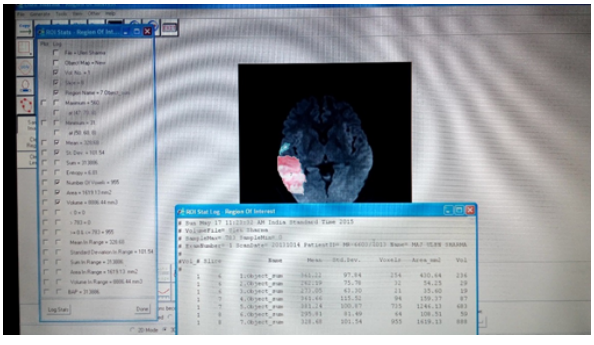
MATERIALS AND METHODS

This study was conducted at a single tertiary care armed forces hospital. The study population consisted of patients with ischemic stroke and infarcts in the anterior circulation territory. In total, 30 consecutive patients with anterior circulation ischemic stroke were evaluated and followed up for 90 days. The inclusion criteria were as follows: i) age, 18–80 years and ii) stroke onset within 7 days. The exclusion criteria were as follows: i) hemorrhagic stroke, ii) ischemic stroke in the posterior circulation territory, iii) pediatric stroke, iv) recurrent stroke, and v) venous stroke.

This study was approved by the institutional ethical committee, and written informed consent was obtained from all patients or their relatives. A sample of a feasible size, consisting of 30 patients, was selected and enrolled into this study. At entry into the study, stroke severity was assessed using the NIHSS score. At the entry point, stroke proforma was filled for each patient with the relevant details. Stroke volume on DWI sequences of MRI was assessed using ANALYZE.

The MRI scans of the patients were stored on a compact disc (CD) and were used to calculate stroke volume. A database of all patients was created in ANALYZE, and DWIs from the CD were transferred to the database. The area of restricted diffusion was the "region of interest" and was calculated according to the protocol provided by the software designer. All slices exhibiting restriction of diffusion were summed up to obtain the total infarct volume. The final volume (in cm^3) was considered while analyzing the data. A representative image of the assessment of stroke volume is shown in Fig. 1.

Fig.-1 Representative image of software used for stroke volume calculation



The stroke functional outcome was assessed by an independent observer every month using the modified Rankin scale (mRS) and Barthel Index (BI), and the 90-day mRS and BI scores were correlated with the initially calculated stroke volume.

All statistical analyses were performed using SPSS 20. The *t* test and chi-square test were used for the analysis of continuous and categorical variables, respectively. For comparison, the DeLong test was used to determine the correlation among NIHSS scores (ordinal variable), mRS scores, BI scores, and stroke volume. In univariate analysis, stroke volume was treated as a continuous variable.

RESULTS

Description of Data

Baseline Clinical and Imaging Characteristics

A total of 30 consecutive patients with ischemic stroke constituted the study population. The mean age was 57.8 years (standard deviation [SD], 14.04), and the age range was 32–80 years. Nine patients with stroke were younger than 45 years, and 12 patients were in the 60–70 years age group. The baseline characteristics of the patients are shown in Table 1.

Table-1: Baseline characteristics of the study population

Mean age in years (SD)	57.80 (SD 14.05)
Males (%)	22 (73.3%)
Female (%)	8 (26.7%)
Mean age of men in years (SD)	57.27 (14.492)
Mean age of women in years (SD)	59.25 (13.562)
Stroke in young patients (%)	9 (30%)
Left MCA territory infarct (%)	18 (60%)
Right MCA territory infarct (%)	12 (40%)
Hypertension (%)	16 (53.33%)
Diabetes mellitus (%)	6 (20%)
Coronary artery disease (%)	4 (13.33%)
Migraine	2 (6.7%)

According to NIHSS scores, 7, 18, and 5 patients, respectively, had mild (score 0–4), moderately severe (score 5–15), and severe (score 16–24) stroke.

Ischemic stroke volume on DWI sequences of MRI was calculated using ANALYZE. The stroke volume of the patients ranged from 3.57 to 241.4 cm^3. The overall mean stroke volume was 65.03 cm^3 (SD, 63.18). The values of the mean stroke volume were 67.5 cm^3 (SD, 66.66) and 55.5 cm^3 (SD, 55.35) in men and women, respectively. The ischemic stroke volume of men and women was not statistically different ($p = 0.627$). In total, 19 patients exhibited a stroke volume of <70 cm^3. The values of the mean stroke volume were 40.70, 48.65, and 133.69 cm^3 in patients with mild (NIHSS score 0–4), moderately severe (NIHSS score 5–15), and severe (NIHSS score 16–24) stroke, respectively. The values of the mean stroke volume were 45.46 and 75.68 cm^3 in young patients (n = 9) and elderly patients (age >70 years). In patients with hypertension (n = 16) and those without hypertension, the values of the mean stroke volume were 58.62 and 72.28 cm^3, respectively. The values of the mean stroke volume were 42.12 and 70 cm^3 in patients with diabetes mellitus (n = 6) and those without (n = 24) diabetes mellitus, respectively.

All patients were followed up monthly, and the final outcome measures were assessed at 90 days. Follow-up was complete for all patients. None of the patients died during the follow-up period. An mRS score of 0–2 was considered to be a good outcome, whereas a score of >3 was considered to be a bad outcome. A total of 24 patients (80%) exhibited good outcomes (mRS score 0–2), and the remaining 20% exhibited bad outcomes. Ten patients (33.33%) exhibited complete functional recovery (i.e., an mRS score of 0). The mRS scores of male and female patients did not differ significantly ($p = 0.478$). The distribution of men and women was equal in the groups based on mRS scores. BI scores of >60 and ≤60 were considered to be good and bad outcomes, respectively. In total, the BI scores of 21 patients (70%) were >60 at 90 days. Twelve patients had BI scores of 100, thus indicating no functional disability at the end of three months.

Univariate logistic regression analysis revealed that the baseline stroke volume and NIHSS scores were statistically significantly correlated with the BI scores at 3 months ($p = 0.00569$ and $p = 0.019$, respectively). Fig. 2 depicts the correlation of the NIHSS score and infarct volume with the BI score. A comparison between these two variables using the DeLong test for the correlated receiver operating characteristic (ROC) curves revealed that both variables were equally and individually effective in predicting the BI score at 3 months (Fig. 3).

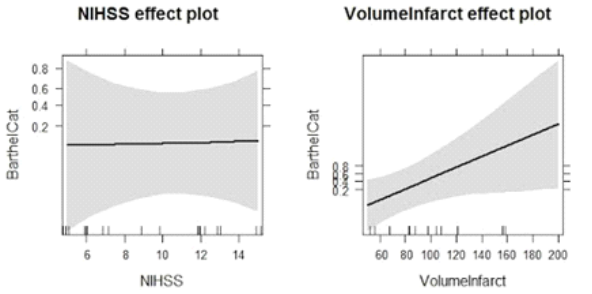


Fig. 2. NIHSS and volume infarct effect plot

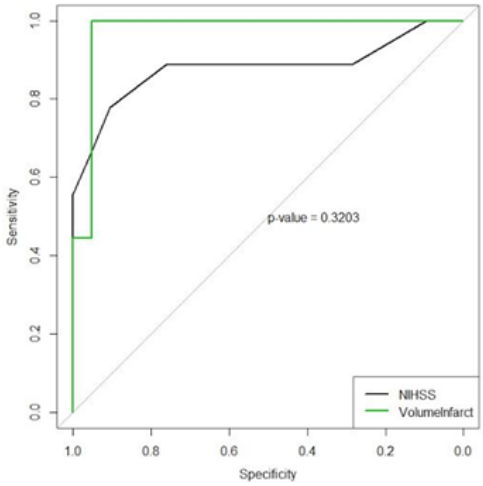


Fig. 3: DeLong test for correlation of NIHSS score and infarct volume for predicting the BI score

Similarly, in univariate regression analysis, both the NIHSS score and infarct volume were significantly accurate in predicting the mRS score at 3 months ($p = 0.0242$ and $p = 0.0418$, respectively), as shown in Fig. 4. A comparison of both variables by using the DeLong test for the correlated ROC curves indicated that both were variables equally effective in predicting the mRS score (Fig. 5).

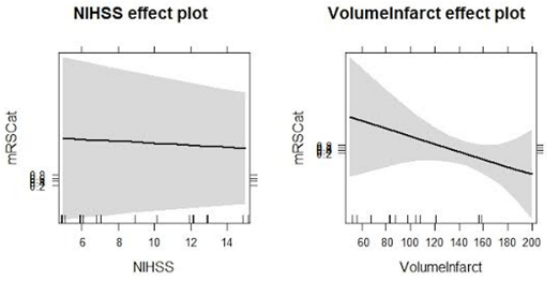


Fig. 4: NIHSS score and infarct volume effect plot for predicting the mRS score

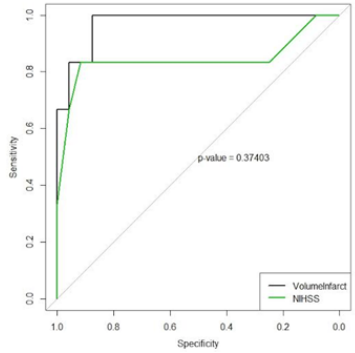


Fig. 5: DeLong test for correlation of NIHSS and infarct volume for predicting the mRS score

None of the other variables were significantly correlated with the functional outcome, individually. Multivariate logistic regression analysis showed that only infarct volume was significantly correlated with the BI score ($p = 0.0348$). The NIHSS score was not significantly correlated with the BI score. When the mRS score was the outcome measure evaluated in multivariate regression analysis, none of the parameters were significantly correlated with it.

The NIHSS score and infarct volume were linearly correlated ($p = 0.000143$). The adjusted R-square was 0.3875, which indicates that nearly 39% variation in the NIHSS score can be explained by variation in the infarct volume (Fig. 6).

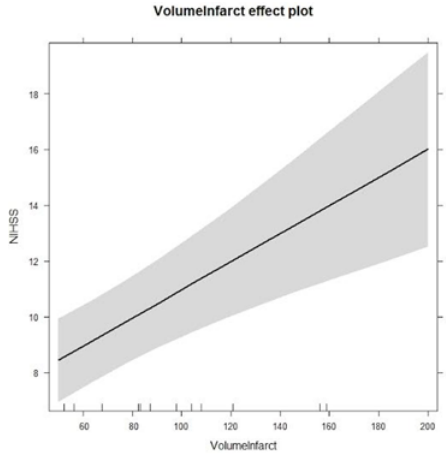


Fig. 6: Correlation between the NIHSS scores and infarct volume

DISCUSSION

This single-center observational study was conducted to correlate the initial ischemic stroke volume and NIHSS score with the functional outcome at 90 days (mRS and BI scores). In this small and heterogeneous cohort, we showed that the ischemic stroke volume and NIHSS score at baseline were strongly correlated with and were strong predictors of the clinical outcomes at 90 days.

NIHSS scores on admission significantly affected the outcome at 90 days. In this study, high NIHSS scores were strongly associated with high mRS scores at 90 days. Eighty six percent of patients with NIHSS scores of 0–4 achieved a good functional outcome (mRS score 0–2). Of the five patients with NIHSS scores >16, only one patient achieved a good functional outcome, whereas the remaining four patients exhibited mRS scores >3. Similar results were observed when the BI score was considered as an outcome measure. Eighty five percent of patients with mild stroke (NIHSS score 0–4) and eighty three percent of patients with moderately severe stroke (NIHSS score 5–15) at admission had BI scores of >60 at 3 months. This finding corroborates the available evidence that the stroke severity, assessed using NIHSS, at the time of admission is reliable predictor of outcomes, either individually or in combination with other predictors [16,17].

This study also showed a strong correlation between the NIHSS score at admission and the initial ischemic stroke volume. The stroke volume of patients with lower NIHSS scores was <70 cm^3. A previous study by Scheimank et al, involving 94 patients, also revealed a strong correlation between the NIHSS score at admission and the lesion volume [18]. In another study, a combination of clinical (the NIHSS score) and imaging parameters (lesion volume) was used for accurate outcome prediction [19].

This study showed that ischemic stroke volume on the DWI sequences of MRI measured within 7 days of onset reliably predicted patient outcomes. The ischemic stroke volume was significantly correlated with the functional outcome at 90 days. Similar results have been observed in earlier studies, wherein stroke volume has been reported to reliably predict outcomes [20]. In one study, a stroke volume of >89 cm^3 was shown to reliably predict early neurological deterioration [21]. The BI score at 90 days was predicted reliably using initial ischemic stroke volume. All patients with an initial stroke volume of <70 cm^3 exhibited good functional recovery (BI > 60); however, only 18.18% of patients with an initial stroke volume of >70 cm^3 exhibited a good outcome.

Univariate analysis revealed that both stroke volume and NIHSS scores at baseline were crucial predictors of the functional outcome. When the mRS score was the outcome measure evaluated in multivariate regression analysis, stroke volume was not an independent predictor ($p = 0.9$) after adjustment for the NIHSS score at the baseline, age, hypertension, history of coronary artery disease, diabetes mellitus, and smoking status. When the BI score was the outcome measure, stroke volume was an independent predictor of the functional outcome even after adjustment for the NIHSS score at baseline, age, smoking status, diabetes mellitus, and coronary artery disease. However, with such a small sample size, the multivariate model is unstable (not reproducible); hence, the results from the analysis should be interpreted with caution. Numerous studies have already examined the potential predictivity of the baseline lesion volume for clinical outcomes. Most of these studies have included a small number of patients (between 10 and 102) and have used various statistical methods and different outcome scales. Baird et al reported that the volume on DWI obtained within 48 hours of ischemic stroke onset was an independent predictor of outcome in addition to age, the NIHSS score, and the delay between symptom onset and MRI [22]. Saunders et al reported that the infarct volume determined 72 hours after symptom onset was predictive of the functional outcome in a univariate analysis of 23 patients with stroke in the middle cerebral artery territory [20]. In a study of 63 patients, Thijs et al reported that the baseline NIHSS score, age, and lesion volume significantly affect the functional outcome, and they incorporated these items into a statistical model [23]. In the same study, univariate analysis revealed that patients with independent outcomes were younger, had low baseline NIHSS scores, and had small lesion volumes on DWI. In a logistic regression model, stroke volume on DWI was an independent predictor of the outcome in addition to age and the NIHSS score. For the first time, this study implicitly stated that ischemic stroke volume contributes independently from the NIHSS score to the clinical outcome of ischemic stroke.

The largest study till date is a retrospective analysis of the VISTA database, which includes >1800 patients [17]. In this analysis, the initial lesion volume was found to be a strong and independent predictor of the stroke outcome in a statistical regression model that also accounted for age and the NIHSS score at the baseline ($p < 0.0001$). However, in this large cohort, both computed tomography and MRI were used for volume analysis (calculated using the ABC/2 method), and all types of stroke (including hemorrhagic strokes) were included in the analysis.

Previous studies have shown that age is one of the most critical and nonmodifiable risk factors and the prognostic marker for ischemic stroke. The risk of ischemic stroke increases with age, and the functional outcome is poor [24-26]. Age is a consistent variable used in most models for ischemic stroke outcome prediction. However, in our study, the age was not a significant predictor of the outcome. Age exerted no statistically significant effects on the functional outcome, measured as mRS and BI scores. This result may be attributed to the small size of the sample and the substantial number (n = 9) of young patients with stroke (age <45 years). Of all variables studied, the NIHSS score and initial ischemic stroke volume at the time of admission were found to have a high predictive value. The other variables, such as hypertension, diabetes mellitus, coronary artery disease, migraine, smoking status, and, blood glucose at admission and lipid profile, did not show a significant correlation with the outcome.

In this study, we confirmed the results of earlier studies in a small and heterogeneous patient population and established the significance of stroke volume at the baseline for outcome prediction. According to our knowledge, such a study has not been reported in the Indian population. Our study had some limitations. First, the sample size was small, and the population was heterogeneous. The sample size (30 patients) was based on the patient load at the tertiary care center, where the study was conducted. This small sample size may have biased the results. The functional outcomes may have been affected by the age distribution in our group because the young population with stroke constituted a large percentage of our study population. Second, only anterior circulation stroke was considered for the lesion volume analysis and outcome prediction. The exact role of stroke volume estimation in the posterior circulation territory or in the infratentorial region has also not been evaluated in most of the available studies. This needs to be addressed in future studies because even a small stroke in this territory can produce more significant disability than that in the anterior territory. Third, the side of the stroke, dominant or

nondominant, was not considered in the final analysis because of the small sample size.

We conclude from our analysis that the stroke volume and NIHSS scores at baseline are predictors of the functional outcome, even in a small-sample-size study. Other clinical variables are not as robust as the NIHSS scores and stroke volume. However, a large multicentric study is recommended to confirm the findings of this study.

DISCLOSURES

None

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