Radiology Section

Original Article

Correlation of Diffusion-Weighted Magnetic Resonance Imaging Determined Infarct Volume with Clinically Assessed National Institutes of Health Stroke Scale in Patients of Acute Stroke: A Cross-sectional Study

BHAVYA KATARIA¹, SHIBANI MEHRA²

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ABSTRACT

Introduction: Infarct volume is an essential factor in predicting patient prognosis. National Institutes of Health Stroke Scale (NIHS) allows consistent reporting of neurological deficits in stroke patients. Limited studies have been done in the Indian population correlating the volume of infarct and the NIHS Scale.

Aim: To correlate the Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) assessed infarct volume with the clinically assessed NIHS to prognosticate clinical outcomes in patients of acute stroke.

Materials and Methods: This was a cross-sectional study comprising 36 patients of acute stroke with a study duration from November 2017 to April 2019. Diffusion-Weighted MRI was obtained on Siemens Magnetom 3 Tesla, and diffusion restriction on b=1000 image was measured with a Region of Interest (ROI) tool using manual contouring in each slice. Assessment of the neurological deficit was done by NIHS scale at the time of admission

and 7 days post admission for each patient. Correlation of the infarct volume with NIHS Scale was done with p<0.05 considered statistically significant. Receiver Operating Characteristic Curve (ROC) was used to predict cut-off of the volume of infarct and NIHS Scale to predict adverse patient outcome.

Results: Present study consisted of 36 patients of acute stroke with a mean age of 52.05 ± 18.53 years. The minimum age of the patient was one year, and the maximum age was 78 years. There was a statistically significant correlation between the volume of infarct and NIHS Scale at time of admission admission (p=0.001; r=0.807) and the NIHS Scale at one week (p=0.002; r=0.602).The Area Under the Curve (AUC) for a cut-off of 115 cc of the volume of infarct in predicting adverse patient outcomes was 0.931, whereas that for the NIHS scale of 20 was 0.998.

Conclusion: Volume of infarct of 115 cc and NIHS Scale of 20 are excellent as prognostic tools in predicting patient outcome and have comparable efficacy.

(SSS), NIHS scale, Barthel Index of Daily Living (BI), and modified

Keywords: Barthel index of daily living, Fluid attenuated inversion recovery sequence, Prognostic tools

INTRODUCTION

Stroke is a universal health problem with 20 million people in India suffering from stroke each year, out of which 5 million people do not survive [1]. DW-MRI sequences have a higher sensitivity than conventional MRI sequences in the detection of cerebral ischaemia in the hyperacute and acute phase of stroke and have become indispensable in stroke imaging protocols [2].

Diffusion-Weighted Imaging (DWI) analyses the molecular architecture of the cell by recognising cytotoxic oedema as early as 30 minutes of stroke onset which demonstrates as areas of diffusion restriction in the affected brain tissue on DWI and corresponding Apparent Diffusion Coefficient (ADC) maps. Diffusion-weighted MRI has a sensitivity and specificity of 88-100% and 86-100%, respectively, for demonstrating the cytotoxic oedema [3].

Diffusion-weighted MRI is also useful in the measurement of the size of the volume of the infarct and plays a significant role in predicting the utility of thrombolysis in acute stroke patients by characterising the ischaemia core (non salvageable brain tissue) and the penumbra (salvageable brain tissue) accurately. Patients with a small core and large penumbra form ideal candidates for reperfusion therapy [4].

Universal stroke assessment tools are essential in clinical practice and provide an objective insight into stroke progress and predict potential outcomes. The commonly used neurological assessment scales, particularly for stroke, are the Scandinavian Stroke Scale

Rankin Scale (mRS) [5]. The NIHS scale is an 11-item scale that standardises and quantifies the basic neurological examination, paying particular attention to those neurological aspects that are most pertinent to stroke. It is a straightforward clinical tool and takes around six minutes to perform. The scale includes an assessment of language, motor function, sensory loss, consciousness, visual fields, extraocular movements, coordination, neglect, and speech. It is scored from 0 (no impairment) to a maximum of 42. Baseline neurological status is classified as standard with a score of 0, minor stroke with a Score of 1-4, moderate stroke with a score of 5-15, moderately severe stroke with a score of 16-20 and severe stroke with a score of >20 [5].

A study have been done in the Indian population assessing the prognostic significance of volume of infarct and the NIHS scale; lacunae in the cited study being absence of follow-up for the patient outcome and merely establishing a statistical correlation between the variables [6]. Hence, present study aimed to establish correlation between the DW-MRI assessed infarct volume and the clinically assessed NIHS as well as prognosticate clinical outcomes in patients of acute stroke.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Radiodiagnosis at PGIMER and Dr. RML Hospital for a duration of two years from November 2017 to April 2019 in a total of 36 patients of acute stroke referred from all Clinical Departments. Informed consent was taken from all patients in the study; parental consent was taken for minor subjects in the study. The Institutional Ethics Committee (IEC) approval for the study was obtained in 2018. (F.No.TP(MD/MS (103/2017)/IEC/PGIMER/ RMLH/311/18).

Acute stroke was defined as patients presenting with neurological deficit within seven days of symptom onset.

Inclusion criteria: Acute stroke patients irrespective of the vascular territory involved and lacunar strokes were included in the study.

Exclusion criteria: The patients with general contradictions to MRI scanning and those with haemorrhagic stroke without an obvious infarct were excluded from the study.

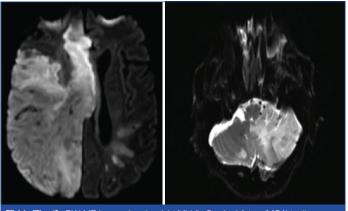
Sample size calculation: The sample size was calculated using the statistical formula:

$$N = \frac{Z^{\alpha 2} \times p(1-p)}{d^2}$$

where Z^{α} is 1.96 at a confidence level of 95%; d=(1-p/2) and p is the prevalence. The average prevalence was taken to be 70% according to a study taken into consideration [7]. The minimum sample size thus calculated was approximately 35.8 (~36).

All 36 patients were taken up for Diffusion-weighted MRI within 48 hours of admission. MRI was acquired using the Siemens 3 Tesla Magnetom Skyra machine at b values of 0,500 and 1000 along with routine T1, T2, and Fluid Attenuated Inversion Recovery (FLAIR) sequences. A Time of Flight (TOF) MR Angiography sequence was performed in all patients to detect additional information about the aetiology of stroke.

The infarct was identified as an area of bright signal intensity on DWI with a corresponding dark region on the ADC map [Table/Fig-1,2]. The area of infarct was measured with a free hand ROI tool using commercial automatic software Syngo MR D13A by manual contouring in each DWI slice with a b value of 1000, and the sum of the value so obtained was multiplied by the total slice thickness [Table/Fig-3].

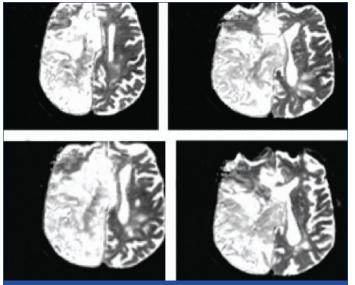


[Table/Fig-1]: DW-MR image showing right Middle Cerebral Artery (MCA) territory acute infract; [Table/Fig-2]: Diffusion MR image in patients with acute cerebellar infarct. (Image from left to right)

The formula used for infarct volume was: Volume (cm³)=(Area×slice thickness).

In each patient, the degree of neurological deficit related to the stroke was assessed by calculating the NIHS scale by the neurologist at the time of admission. The patients were followed-up to 1 week (discharge), and amongst those who survived at the end of 1 week, NIHS scale was assessed again to evaluate a change in the scale calculated at the time of admission [5].

The volume of infarct was correlated with the NIHS scale at admission and discharge. The prognostic efficacy of the two was also calculated in predicting patient outcome.



[Table/Fig-3]: Measurement of area of infract in multiple slices in a patient with MCA territory infract.

STATISTICAL ANALYSIS

For statistical analysis, a categorical variable was presented in number and percentage (%), and continuous variables were presented as mean±Standard Deviation (SD) and median. The normality of data was tested by the Kolmogorov-Smirnov test. A diagnostic test was used to find out sensitivity, specificity, negative predictive value, and positive predictive value. The ROC curve was used to find cut off points of the NIHS scale and volume of infarct for predicting patient outcome. Quantitative variables were compared using the Independent Student t-test between the two groups. Qualitative variables like patient outcome were assessed using the Chi-square test. Analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0, with a p-value <0.05 considered statistically significant.

RESULTS

Present study consisted of 36 patients of acute stroke with a mean age of 52.05 ± 18.53 years. The minimum age of the patient was one year, and the maximum age was 78 years. Two patients were below 21 years, three patients between 21-30 years, four patients between 31-40 years age group, eight patients between 41-50 years age group, eight patients between 51-60 years age group, eight patients between 61-70 years and three patients were more than 71 years.

Out of 36 patients, 24 patients were males (66.7%) while 12 patients were females (33.3%). Hemiparesis was found in 27 patients amongst which 14 patients (38.88%) had right-sided hemiparesis and 13 patients (36.11%) had left-sided hemiparesis.

Infarcts were seen involving a single vascular territory in 27 (75%) patients and multiple vascular territories in 9 (25%) patients. Out of these, 29 (80.55%) patients had involvement of MCA territory, 5 (15.1%) patients were involved of PCA territory, 3 (8.3%) patients had involvement of ACA territory and 8 (22.22%) patients involved vertebrobasilar territory of which two patients had brainstem infarcts and six patients had cerebellar infarcts [Table/Fig-4a,b].

Vascular territory involved	Number of patients	Percentage (%)		
Single	27	75		
Multiple	9	25		
[Table/Fig-4a]: Vascular territory involved by infarct (single/multiple) in the study population.				

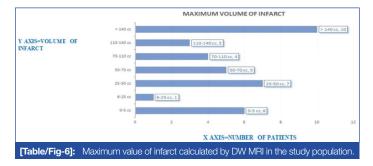
Of the total 36 patients included in the study, 27 presented with hemiparesis (75%), 28 with altered sensorium (77.77%) [Table/ Fig-5]. The maximum volume of infarct was 487 cc, whereas the minimum volume of infarct was 1.68 cc. It was found that infarct volume was less than 5 cc in six patients, 6-25 cc in one patient,

Territory of infarct infarct/infarcts	Number of patients	Percentage (%)			
MCA territory	29	80.55			
PCA territory	5	13.88			
ACA territory	3	8.3			
Vertebrobasilar territory	8	22.22			
[Table/Fig-4b]: Distribution of vascular territory of infarcts in the study population. MCA: Middle cerebral artery; PCA: Posterior cerebral artery; ACA: Anterior cerebral artery; The numbers mentioned for separate vascular territories are not adding upto 36 as they include the ones with involvement of multiple territories					

25-50 cc in seven patients, 50-70 cc in five patients, 70-110 cc in four patients, 110-140 cc in three patients and more than 140 cc in 10 patients [Table/Fig-6].

Clinical symptom	Number of patients	Percentage (%)			
Hemiparesis	27	75			
Altered sensorium	28	77.77			
Visual abnormality	11	30.55			
Facial paralysis	20	55.55			
Sensory loss	27	75			
Cerebellar signs	3	8.33			
Dysarthria/aphasia	31	86.11			
[Table/Fig-5]. Clinical presentation of stroke in the study population					

[Table/Fig-5]: Clinical presentation of stroke in the study population.



Total 14 patients (38.89%) had a NIHS scale between 5 to 15 at the time of admission (moderate stroke), nine patients (25%) had a NIHS scale between 16 to 20 at admission (moderately severe stroke), and 13 patients (36.11%) had a NIHS scale of more than 20 at admission (severe stroke).

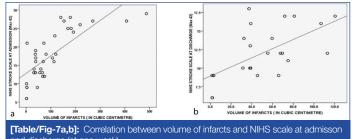
All 36 patients of acute stroke in this study were evaluated for the outcome at the end of one-week (at discharge). Out of these, 12 (33.3%) patients died within a week of onset of a stroke while 24 (66.7%) survived. Amongst the 24 patients who survived, 17 patients (70.83%) had a NIHS scale between 5 to 15 (moderate stroke), and seven patients (29.17%) had a NIHS scale between 16 to 20 (moderately severe stroke). None of the patients who survived had a NIHS scale of more than 20.

On statistical analysis by student t-test, the volume of infarcts measured was found to correlate positively with NIHS scale evaluated at the time of admission with a correlation coefficient of 0.807. The p-value was found to be statistically significant for this correlation and was less than 0.001 [Table/Fig-7a].

Further, the results of this study also show that diffusion-Weighted MRI calculated infarct volume correlates positively with the NIHS scale evaluated at one week after onset of stroke (time of discharge) with a correlation coefficient of 0.602. The correlation was statistically significant, with a p-value of 0.002 [Table/Fig-7b].

The statistical analysis by student t-test revealed that the diffusionweighted MRI calculated infarct volume was highly significant in predicting the clinical outcome in all the patients with a p-value of less than 0.001 [Table/Fig-8].

In this study, DWI measured infarct volume greater than 115 cc was associated with a higher NIHS scale and an adverse clinical outcome in the form of death whereas DW measured infarct volume



and discharge (at one week).

		Patient outcome				
Volume of infarcts (in cubic	Death		Survival			
centimetre)	Frequency	%	Frequency	%	p-value	
0-5	1	8.3	5	20.8		
6-25	0	0	1	4.2		
25-50	0	0	7	29.2		
51-70	0	0	5	20.8	0.001	
71-110	0	0	4	16.7	<0.001	
110-140	1	8.3	2	8.3		
>140	10	83.3	0	0		
Total	12	100	24	100		
[Table/Fig-8]: Association between volume of infarcts and patient outcome. Student t-test was used						

less than 115 cc was associated with a better clinical outcome in terms of survival or functional improvement [Table/Fig-9].

Volume of infarct (in cc)	NIHS scale at admission	NIHS scale at one week	Patient outcome
487.25	29	Death before one week	Death
406.6	27	Death before one week	Death
270.1	27	Death before one week	Death
218.93	26	Death before one week	Death
191.76	24	Death before one week	Death
182.5	25	Death before one week	Death
178.88	28	Death before one week	Death
169.34	25	Death before one week	Death
153.41	27	Death before one week	Death
140.4	28	Death before one week	Death
120.54	18	17	Survived
116.26	23	Death before one week	Death
113.05	16	12	Survived
106.91	17	16	Survived
81.1	18	17	Survived
75.12	12	11	Survived
71.9	21	17	Survived
69.54	16	12	Survived
67.7	12	12	Survived
66	13	9	Survived
59.63	14	14	Survived
55.5	13	12	Survived
45.55	9	9	Survived
39.05	17	16	Survived
38.93	16	10	Survived
38.53	19	13	Survived
38.2	13	10	Survived
37.38	18	18	Survived
32.44	14	14	Survived
31.48	13	10	Survived
4	21	Death before one week	Death
3.22	9	9	Survived

3.16	6	9	Survived		
1.75	6	6	Survived		
1.68 10 9 Survived					
[Table/Fig-9]: Association of volume of infarct, NIHS scale and patient outcome.					

Using the ROC curve, the Area Under the Curve (AUC) for cut-off 115 cc as infarct volume to predict patient outcome was 0.931 {Cl:95% (0.805-1.056), sensitivity: 91.7%, specificity: 95.8%, PPV: 91.7%, NPV: 95.8%, accuracy: 94.4%} [Table/Fig-10,11].

			Asymptotic 95% confidence interval		
Area	Std. Error	p-value	Lower bound	Upper bound	
0.931	0.064	<0.001	0.805 1.056		
[Table/Fig-10]: Reciever operating characteristics curve for analysis of volume of infarct in predicting patient outcome.					

Chi-square test was used, p-value <0.05 considered statistically significant

Volume	Death		Surviv	Survival	
(cc)	Frequency	%	Frequency	%	p-value
<115	1	8.3	23	95.8	
≥115	11	91.7	1	4.2	<0.001
Total	12	100	24	100	
[Table/Fig-11]: Prognostic significance of volume of infarct cut-off by ROC curve. Chi-square test used, p-value <0.05 considered statistically significant					

Using the ROC curve, the AUC for a cut-off value of 20 of NIHS scale at the time of hospital admission to predict patient outcome in this study population was 0.998 {CI:95% (0.991-1.005), sensitivity: 100%, specificity: 95.8%, PPV: 92.3%, NPV: 100%, accuracy: 97.2%} [Table/Fig-12,13].

			Asymptotic 95% confidence interval			
Area	Std. Error	p-value	Lower bound	Upper bound		
0.998	0.004	<0.001	0.991	1.005		
[Table/Fi	[Table/Fig.12]: Receiver Operating Characteristics (ROC) curve for analysis of					

NIHS scale at admission in predicting patient outcome. Chi-square test was used, p-value <0.05 considered statistically significant

NIHSS at	Death Survival				
admission	Frequency	%	Frequency	%	p-value
<20	0	0	23	95.8	
≥20	12	100	1	4.2	<0.001
Total	12	100	24	100	
[Table/Fig-13]: Prognostic significance of NIHS scale cut-off by ROC curve.					

DISCUSSION

Diffusion sequences help characterise penumbra and ischaemic core for identifying patients for reperfusion therapy. Patients showing large penumbras and small core infarct volumes are good candidates for reperfusion therapy even beyond the 4.5 hour therapeutic window [8,9].

Greater the infarct volume, the greater is the neurological deficit in the patient, and worse is the prognosis. The NIHS scale can also be used to prognosticate the patient outcome [10]. Zaidi SF et al., found a significant correlation between infarct volume and patient outcome and concluded that infarct volume more than 111.8 cc was associated with unfavourable outcomes (p<0.01) [11].Saunders DE et al., found that patients with an initial infarct volume of fewer than 80 cm³ were found to have a better outcome than those with larger infarct volumes [12].

Sablot D et al., found that NIHS scale <5 was predictive of functional outcome whereas NIHS scale >22 was predictive of

physical dependency or death, thus concluding that low and high NIHS scale cut-off points are effective positive predictive values for good and poor outcomes [13]. Yaghi S et al., concluded that the NIHS scale on admission is associated with stroke severity and functional outcome. The accuracy of the NIHS scale in predicting the outcome is most reliable in the first nine days after stroke for determining patient prognosis. A score of more than or equal to 16 predicted a high probability of death or severe disability, and the score below six predicted good recovery [14]. Thijs VN et al., found that the NIHSS score at admission and the volume of infarct measured on DW-MRI correlated significantly with a spearman rank correlation coefficient of 0.454 and a p-value of less than 0.01 [15]. The findings of present study were in agreement with the above mentioned studies [11-15].

The results of present study show that all patients who had lower than 15 NIHS scale at admission survived and showed some amount of functional improvement at one week with the improvement of NIHS scale. Out of the seven patients who had a moderately severe stroke and NIHS scale of 16 to 20 at the time of admission, three patients showed an improved NIHS scale at one week corresponding to improvement in clinical symptoms. The NIHS scale improved from 21 to 17 in one patient, whereas the other two patients with significant improvement showed a change of NIHSS at one week from 16 to 10 and 19 to 13, respectively. The significant improvement was noted in the level of sensorium.

The statistical analysis showed that the volume of infarct correlates positively in a statistically significant manner with NIHS scale at discharge (one week) with a correlation coefficient of 0.602 and a p-value of 0.002. The NIHS scale at discharge was less than 20 in all patients, along with a lower volume of infarct as measured on DW MR (less than 115 cc). Schiemanck SK et al., in a study also concluded that there was a strong correlation between the volume of infarct measured on DWI and NIHS scale measured at two weeks of symptom onset with a correlation coefficient of 0.61 and a p-value of 0.001 [16].

Laredo C et al., found that the AUC of the volume of infarct in predicting mortality was 0.89, whereas the AUC of NIHS scale at admission was 0.73. The results of their study showed the MR assessed volume of the infarct is a better diagnostic tool in predicting patient outcome than the NIHS scale [17]. The results of present study are similar to those conducted by Laredo C et al., as the AUC of the volume of infarct was seen to be (0.931), whereas that for NIHS scale at admission was (0.998), indicating that the two have comparable efficacy as a prognostic tool in predicting the outcome [17].

One patient in present study with multiple infarcts in bilateral deep gray matter distribution (bilateral thalami and left side of the midbrain) with a maximum volume of infarct 4 cc had a poor prognosis and died within one week of onset of stroke. There was non visualisation of the proximal left vertebral artery on 3D TOF MR angiography, indicating the possibility of thrombotic occlusion. The NIHS scale in this patient calculated at the time of admission was 21 (severe stroke category). Author feel that the reason for the poor NIHS scale at admission and the poor outcome seems to be the presence of multiple infarcts involving the thalamus and midbrain, both of which contain important decussation pathways for motor tracts. Moreover, acute total thrombotic occlusion of the left vertebral artery, as shown by 3D TOF MR angiography, could have precipitated death in this patient.

One patient who had an infarct volume greater than 115 cc survived. The NIHS scale at the time of admission was 18 and at one week (time of discharge) was 17. The infarct was found involving the ipsilateral MCA and PCA territory. The cortical grey and white matter were involved without the involvement of the deep grey matter. Author feel that the better prognosis in this patient could be explained by the involvement of two vascular territories and the border zone with a likelihood of more effective collateralisation.

One patient with NIHS scale at the admission of 21 (severe stroke) survived. The NIHS scale at discharge was 17. The improvement in patient outcome could be explained by the smaller volume of infarct (71.9 cc) in this patient.

The patients with symptom onset less than 4.5 hours in duration and those without haemorrhagic transformation were taken for thrombolysis irrespective of the infarct volume. However, amongst those in which intervention was performed, no change in outcome was seen. Patients with infarct volume >115 cc had succumbed to death, whereas those with infarct volume <115 cc showed improvement in symptoms.

Limitation(s)

Small sample size and the usage of manual contouring for measuring volume of infarct with existence of the possibility of human error for the same are few limitations.

CONCLUSION(S)

Clinical outcomes in stroke patients can be predicted from initial infarct volume quantified by DW-MRI and NIHS scale. The cut-off value of 115 cc of infarct volume and NIHS scale of 20 suggest the two being comparable and excellent as prognostic tools in predicting the patient outcome. Both the parameters have high sensitivity and specificity in predicting the clinical outcome. It is thus recommended that the infarct volume ought to be measured using Diffusion-Weighted MRI in all patients of acute stroke. The infarct volume obtained on Diffusion-Weighted MR must be correlated with the NIHS scale at admission and at the time of discharge (one week) in order to predict patient outcome.

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PARTICULARS OF CONTRIBUTORS:

- 1. Senior Resident, Department of Radiodiagnosis, RML Hospital, New Delhi, India.
- 2. Professor, Department of Radiodiagnosis, RML Hospital, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR: Bhavya Kataria,

D-12, Tower-1, Type-4, East Kidwai Nagar, New Delhi, India. E-mail: nono_5333@yahoo.co.in

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