ORIGINAL ARTICLE

Outcome in Survivors of Middle Cerebral Artery Territory Ischemic Stroke: Can it be Predicted?

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Abstract

Background: Stroke is the fourth leading cause of disability worldwide. The present study was designed to assess functional disability in middle cerebral artery (MCA) territory ischemic stroke patients by applying standard scales for stroke severity, cognitive impairment, disability, dependency and depression. We also wanted to study whether baseline assessment predicts outcome at 1 month.

Methodology: After institutional ethics committee approval, patients were enrolled from the inpatients of the Department of Medicine at Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai from July 2014 to December 2015. Various clinical parameters were recorded on admission. On day 5(±1) the National Institutes of health Stroke Scale (NIHSS), Mini Mental state examination (MMSE) were administered. On 1 month follow up, these were repeated along with Modified Rankin scale, Barthel's index (BI) and Hospital Anxiety and Depression Scale (HADS). Presence of certain risk factors for stroke were reviewed at 1 month.

Results: 75 patients were enrolled. There was a delay in reaching the hospital and therefore imaging, in a greater majority. Only 4% could be imaged within the first 3 hours. Mean NIHSS score at day-5 was 9 and at day-30 was 6. Thus it had significantly reduced over 1 month. The MMSE remain unchanged at day 5 and at day 30. Lower baseline MMSE scores correlated with poorer outcomes on NIHSS, BI and mRS at 1 month. Both BI and mRS at 1 month indicated that about 60% of the cases had poor outcome. Amongst 48 of the non-aphasic MCA strokes, 11(22.92%) had depression. An NIHSS score of 6 or above on day 5, predicted poor outcome at 1 month. Presence of aphasia, dominant lobe affection and female sex were associated with a higher disability at 1 month. Around 30% cases had at least 1 risk factor uncontrolled at 1 month follow-up.

Conclusions: Our findings show that disability assessment late in the first week after onset of stroke using NIHSS accurately forecast outcome at one month after onset of stroke. The MMSE too is not expected to change at 1 month. Those with aphasia are expected to have greater disability. Based on or study we recommend that stroke patients should be assessed with NIHSS and MMSE before discharge, to explain the prognosis of the patient. Also more intense counselling on controlling blood pressure and diabetes as well as abstinence from smoking should be undertaken routinely.

Introduction

Stroke is the second commonest cause of death and fourth leading cause of disability worldwide.[1] Dalal et al reported a prevalence of 90-222 per 100,000 in the Indian population.[2] Indian Council of Medical Research estimates in 2004 indicated that stroke contributed 41% of deaths and 72% of disability adjusted life years amongst the non-communicable diseases in India.[3] India may face a significant socioeconomic burden to meet the costs of managing stroke as life expectancy is projected to increase.[4]

In the last few decades, progressive reduction in stroke mortality has been observed, with subsequent increase of survivors, with residual impairments and disabilities. So there has been a growing interest in the factors that could interfere with functional outcome and quality of life.[5,6] Around 80% of all strokes are ischaemic in nature; of these a majority are of middle cerebral artery (MCA) territory.[4,7,8] The present study was designed to assess functional disability in middle cerebral artery (MCA) territory ischemic stroke patients by evaluating cognitive impairment, depression, disability and dependency, after stroke, using standard scales. Moreover, we have also evaluated risk factors of stroke in these patients and whether these risk factors are under control at one month follow up in stroke patients. We wanted to see whether the assessment in the first week after stroke, would predict the prognosis (cognition, functional disability, dependency and presence of depression) at one month follow-up.

Methodology

Study design

We designed a prospective observational hospital based study at Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai from July 2014 till December 2015. We decided to conduct this study on patients admitted in inpatient wards and following up in the Medicine OPD of Tertiary care teaching public hospital. The study commenced after getting approval from the Institutional Ethics committee. The study was done as per ICMR Schedule Y Guidelines for conduct of Human Research in India. After written informed consent, a designed proforma was used for data collection. A detailed clinical history of

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Received: 07.12.2016; Accepted: 30.12.2018

Table 1: Baseline characteristics of patients enrolled in the study and at 1 month FU

	At baseline	At 1 month FU
Total patients	75	
Age (mean±SD)	60.92 ± 11.14 years	
Males; Females	32; 43	
Previous medical history		
Diabetics at the time of enrollment: duration below:	30	15 uncontrolled
Less than 1 year	6	
1-5 years	11	
5-10 years	6	
More than 10 years	7	
Hypertension at the time of enrollment; duration below:	58	7 uncontrolled
Less than 1 year	23	
1-5 years	12	
5-10 years	9	
More than 10 years	14	
Hypertension with Diabetes mellitus at enrollment	28	2 uncontrolled HT
Dyslipidemia	13	
Ischemic Heart Disease	12	
H/o Transient ischemic attack	6	
Personal history		
Smokers at the time of enrollment	10	2 continued
Alcoholics at the time of enrollment	12	3 continued
Investigations		
Serum cholesterol (mg%)	175.14±41.62	Not reassessed
Serum triglycerides (mg%)	133.28±57.19	Not reassessed
ECG findings abnormal	23	
2-dimensional echocardiography abnormal	17	
Brain imaging (MRI/CT) showing infarct	67 (8-N CT brain)	
Physiotherapy	75	21 stopped PT

patients and a clinical examination was performed.

Patient were assessed on Day 5±1 of onset of symptoms with following scales: National Institutes of Health Stroke Scale[9] (NIHSS) (Refer Annexure 1 and 1a), Mini-Mental Status Examination[10] (MMSE) (Refer Annexure 2). Routine investigations and treatment, including physiotherapy which are standard of care for stroke patients were performed. None were

Table 2: Functional assessment in stroke patients included in the study

National Institutes of Health Stroke Scale (n=75)	Median score	Range of score
Day 5 (±1)	9	1-17
Day 30	6	1-15
Mini Mental Status examination (n=48)		
Day 5 (±1)	24	2-28
Day 30	24	2-28

thrombolysed. Patients were followed up after 1 month of presentation, during which assessments were done with following scales: NIHSS, MMSE, Modified Rankin Scale[11] (mRS) (Refer Annexure 3), Barthel Index[11,12] (BI) (Refer Annexure 4), Hospital Anxiety and Depression Scale[13] (HADS) (Refer Annexure 5). The control of risk factors such as hypertension, diabetes (by haemoglucotest), and abstinence from smoking and alcohol and compliance with physiotherapy were noted at the month 1 follow up. The lipid profile was not repeated.

Selection of cases

We included all patients who presented with stroke, with neuro-imaging suggestive of MCA territory infarct. We also included patients with normal computed tomography (CT) brain, but clinically consistent with MCA ischemic stroke. We excluded patients with present transient ischemic attack (TIA), those who lost to follow-up or those who expired during the first month after onset of stroke, those with head trauma, intracranial neoplasms, additional neurological disorders, those unwilling for consent or follow up, cardio embolic, vasculitic, tubercular stroke, those with history of past stroke, any young stroke (prior to the age forty-five years) and subarachnoid haemorrhage.

Data collection and analysis

National Institute of Health Stroke Scale (NIHSS), a standardized measure of neurological function was used to assess outcome and recovery of patients with acute ischemic stroke receiving conventional therapy. We used this scale to assess outcome. An increase or decrease in the stroke score by 4 or more points is a marker for clinically important change. Barthel Index (BI), that measured independence and Modified Rankin Scale (mRS), that measured disability, was also used to assess outcome with poor outcome defined as mRS >3 and BI <60. Using HADS, patients were diagnosed to have depression if the score is 8/21 or more. Association between qualitative variables was assessed by Chi- Square test and Fisher's exact test. Correlation between dichotomous variables and scores was analysed by Point- Bisferial Correlation Coefficient. Analysis of quantitative data was done using Wilcoxon Signed Rank test. Predictiveness of factors at 1st week for outcome at 1-month follow-up was assessed using linear regression analysis. SPSS Version 17 was used for analysis.

Results

During the study period, 75 patients of MCA infarcts were included in the final analysis. The mean duration between the onset of stroke symptoms and the diagnosis of infarct on imaging was 28.4±33.2 hours. Only 20 of 75 (26.67%) completed neuro-imaging within 6 hours. Only 3(4%) of these did so within the first 3 hours. However none of these could afford thrombolysis. Refer to Table 1, for the baseline characteristics of our study subjects. Most common age group of the patients was 50-60 years. Of the 43 females, 40 were postmenopausal. On examination, raised blood pressure was noted in 43 patients. cranial nerve involvement was seen in 67 patients and aphasia was seen in 27 patients. Out of 73 patients 9 had mildly elevated creatinine. Deranged sugars were found in 24. Other relevant clinical information has been tabulated in Table 1.

The median range of the NIHSS score (range 0-42) in 75 patients at Day 5 was 9 (1-17) and at Day 30 was 6 (1-15) (Table 2). Using Wilcoxon matched pair signed ranked test, indicated that the NIHSS score at Day 30 was significantly lower than at Day 5 ($p<0.0001$). The NIHSS score showed major neurologic improvement in 2 (2.67%) patients while no patients were reported with major neurologic deterioration.

MMSE score was assessed in only 48(64%) of the 75 patients enrolled. It could not be assessed in 27 patients as they had aphasia. The median range of the MMSE score in 48 patients at Day 5 was 24 (2-28) and at Day 30 was 24 (2-28). Using Wilcoxon matched pair signed ranked test, it was indicated that there was no significant difference

Table 3: Association of National Institutes of Health Stroke Scale (NIHSS) at day 5 and variates

	NIHSS ≤ 6	NIHSS >6	p value
Diabetes mellitus			
Present	12	18	0.81
Absent	20	25	
Hypertension			
Present	24	34	0.78
Absent	8	9	
Aphasia			
Present	1	26	<0.0001
Absent	31	17	
Cranial nerve involvement			
Present	25	42	<0.001
Absent	7	1	
Depression			
Present	2	9	<0.001
Absent	29	8	
CT Head			
Abnormal	28	39	0.717
Normal	4	4	

in the MMSE score at Day 5 and Day 30 (p<0.0547). The MMSE of day 5, had a significant positive correlation between and the BI at 1 month and a significant negative correlation with NIHSS scores and mRS at 1 month.

The median modified Rankin Scale (mRS) score was 4 (range: 0 to 5). Of 75 patients, 43 (57.33%) had the mRS score of >3, indicating poor outcome.

The median Barthel Index (BI) was 35 (range: 15 to 100) in 75 patients. 45 (60%) of the patients had the BI<60, indicating poor outcome.

Out of the 75 patients, depression was assessed in 48 patients, while 27 patients could not be assessed due to aphasia. Out of 48 patients, only 11 (22.92%) patients had depression.

There was a significant high positive correlation between baseline NIHSS score and mRS score at 1 month (p<0.0001) and a significant high negative correlation between baseline NIHSS score and BI at 1 month (p<0.0001). Analysis of receiver operating characteristic curves using NIHSS score at day 5 after admission showed that the cut-off point of the 5th-day NIHSS score for predicting a poor outcome at 1 month after symptom onset was between 6 and 7, with a sensitivity of 95.2% and a specificity of 91%.

In our study we found statistically significant association of aphasia, cranial nerve involvement and depression, with NIHSS scores greater than 6. However, we found no statistical association between the findings of CT brain, presence of hypertension or diabetes with NIHSS>6 (Table 3).

Table 4: Point-bisferial correlation of certain dichotomous variables and various scores

	NIHSS-baseline		NIHSS-1 month		mRS-1 month		BI-1 month	
Binary variables (n)	rpb	p value	rpb	p value	rpb	p value	rpb	p value
Female (43)	-0.21	0.074	-0.26	0.024	-0.28	0.014	(+)0.24	0.035
Male (32)	Female strokes were associated mildly with higher NIHSS, higher mRS and lower BI at 1 month.							
Dominant (45)	-0.42	0.0002	-0.48	<0.0001	-0.32	0.005	(+)0.32	0.005
Non-dominant (30)	The affection of the dominant lobe was moderately associates with higher NIHSS scores at baseline and 1 month, and higher mRS and lower BI at 1 month.							
Aphasic	-0.76	<0.0001	-0.81	<0.0001	-0.58	<0.0001	(+)0.36	0.001
Non-aphasic	The presence of Aphasia is strongly associated with higher NIHSS scores both at baseline and 1 month; moderately with higher mRS; mildly with lower BI at 1mt.							
CT abnormal (67)	-0.02	0.85	0	0.976	0.05	0.69	-0.05	0.661
CT normal (8)	There is no significant relation between CT being normal or abnormal, with NIHSS scores, mRS and BI.							
Risk factors not controlled at 1 month	-	-	0.01	0.952	-0.01	0.921	-0.02	0.881
Controlled at 1 month	There is no significant relation between risk factors being controlled or not, with NIHSS scores, mRS and BI.							
PT discontinued	-	-	-0.02	0.881	0.07	0.55	-0.04	0.742
PT continued	There is no significant relation between physiotherapy being continued or not, with NIHSS scores, mRS and BI.							

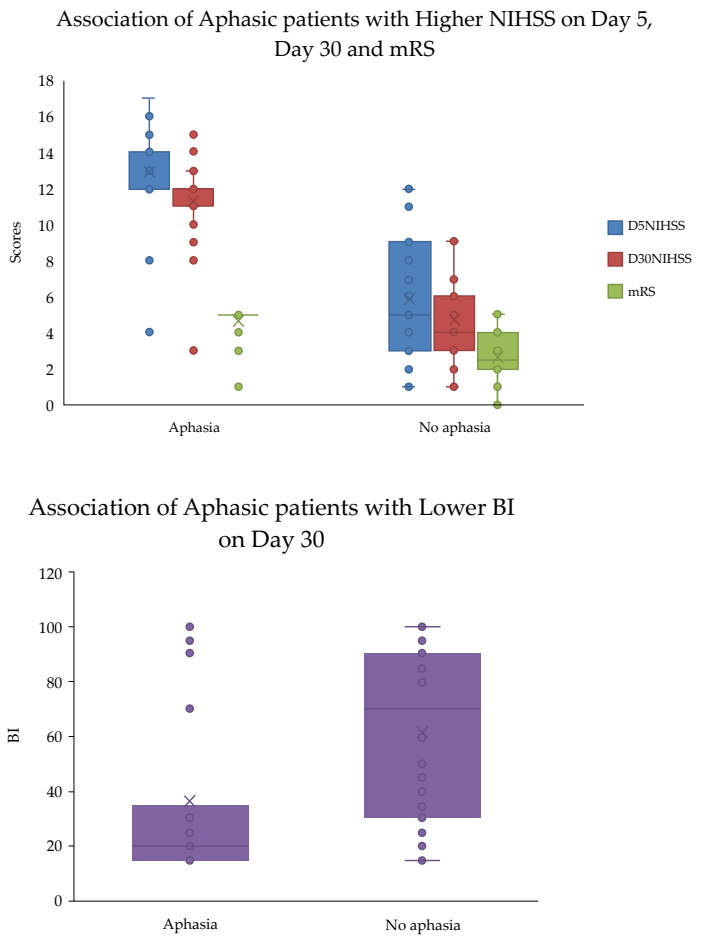

Fig. 1: Point bisferial correlation: aphasia and scores

We also found by Bisferial correlation, that those with aphasia, dominant lobe affection or female sex had higher stroke severity and functional disability; Aphasia having the strongest association (Table 4) (Figure 1).

On discharge, 21 out of 75(28%) discontinued physiotherapy (PT) on

discharge. At 1 month, 23 of 75(30.67%) cases had at least a single risk factor for stroke that was not under control. They were: uncontrolled hypertension(7), uncontrolled diabetes(15), continuation of smoking(2) and alcohol intake(3) (Table 1).

Discussion

The main purpose of this study was to prognosticate patients with an ischaemic stroke so that the close relatives may be counselled.

Reason for selection of MCA ischaemic stroke

A greater majority of strokes consist of MCA territory ischaemic infarcts[4,7,8] . Other catagories such as intra-cranial bleed, posterior circulation strokes, lacunar infarcts, etc. have a different clinical course and recovery. Hence to maintain a certain uniformity, we chose to study MCA territory infarcts.

Reasons for baseline assessment on day 5±1

Major patho-physiologic changes are known to occur in the initial few days after a stroke. Some may cause worsening such as cerebral oedema, herniation, seizures, electrolyte imbalance, progression of the clot, accelerated hypertension, deranged sugars, etc. Some that may cause improvement are fragmentation of clot, distal movement of embolus, spontaneous recanalisation and reperfusion, collateral supply, reduction of cerebral edema by mannitol, early thrombolysis, etc. These changes tend to stabilise within 4-5 days. In a majority of cases, this timing was usually just before discharge from the hospital. This would be the best time the explain the prognosis to the patient and family. The study by Bang O, et al,[14] discussed below also supported our decision.

Various scales used

1. NIHSS is a tool used to objectively quantify the impairment caused by a stroke. The NIHSS is composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed in order to calculate a patient's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0.
2. The MMSE or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. Higher scores indicate better cognition.

   Both these assessments were done at baseline and at 1 month. In addition, the following were assessed at 1 month:
3. mRS is a commonly used scale for measuring the degree of disability or dependence in the daily activities of people . The scale runs from 0-6, running from perfect health without symptoms to death.
4. BI is an ordinal scale used to measure performance in activities of daily living (ADL). It uses ten variables describing ADL and mobility(maximum score 100). Higher the score, greater is the independence.
5. HADS This is a questionnaire with 7 questions (maximum 3 points each) that can screen for depression. A score of 8 or above out 21 indicates presence of depression.

Our findings compared to other studies

Dalal, et al, in a population-based study[4] of all kinds of stroke, in a Mumbai ward, found mild disability in 43.33% and moderate to severe disability in 56.77% of 310 stroke survivors at day 28. Our figures for the same were 33.33% and 66.66% of 75 respectively. This difference may be due to the heterogenicity of the stroke types included by Dalal, whereas we included only MCA territory infarcts. Both studies used mRS for this outcome.

Prediction of outcome of stroke

Bang O, et al (Korea)[14] conducted a similar study on MCA infarcts, not thrombolysed, however excluded lacunar infarcts and followed up to 6 months. The NIHSS, BI and mRS were checked serially in these 437 patients at 0,1,3,7 and 14 days after admission. Poor outcome was defined as any of these end-points: death, mRS>3 or BI<60. They found that the 7th day NIHSS score, age and diffusion-weighted imaging lesion volume and past stroke were independently associated with poor outcome. An NIHSS score of 6 or more on day 7 of admission, predicted a poor outcome at 6 months after symptom onset. None of the other scores done along with NIHSS could improve this prediction. Our study analysed a cut-off score of NIHSS score on day 5 of at least between 6 and 7, to predict a poor outcome at 1 month. In our study NIHSS Score at 5±1 day after onset of stroke was a good predictor of outcome as it significantly correlated with mRS score and BI at 1 month after onset of stroke.

We found that higher the cognitive impairment, worse is the functional disability lower independence and stroke severity at one month, consistent with the study by Tatemichi, et al.[15] Also the cognitive impairment on day 5 and 1 month did not change significantly. Thus it would be expected that the cognitive level at 1month would be similar to that around day 5.

Picking up associated depression, a treatable co-morbidity

In a North Indian hospital based study by Raju, et al,[8] all categories of stroke were assessed at varying durations greater than a month (1-180 months) post-stroke. In addition to NIHSS, mRS and HADS, they used Functional Independence Measure. Depression was found in 60 of 162 (37%) of strokes after excluding those with aphasias. They found that presence of anxiety, depression and functional dependence were associated with impaired quality of life. Our study found depression in 11 (22.92%) of the 48 MCA ischaemic strokes without aphasia, at 1 month post-stroke. Perhaps one should be vigilant to detect depression in more number of strokes as the duration of follow-up increases, as in the above study. Treating this co-morbidity would improve the quality of life.

Though we excluded aphasia, for detection of depression, a greater attempt needs to be made in this subset to diagnose this co-morbidity. The simple 10-question Montgomery-Åsberg Depression Rating Scale (MADRS) may be feasible in at least two third of aphasic strokes in the acute phase and over a period of 6 months post-stroke the feasibility increases to 100%, as per the study by Laska C, et al.[16] They could diagnose depression in 24% of 87 cases of stroke over the period of 6 months.

Challenges faced while managing stroke

Delayed presentation: What if they could be thrombolysed?

Our study showed that patients who presented late, so were imaged late and received delayed treatment, were not more disabled as compared to patients who presented early and received early treatment. This should be interpreted cautiously because we excluded patients who died within one month of stroke onset. Also none of our patients were thrombolysed due to late presentation and non-affordability, thus missing an opportunity for a better outcome. Nandigam K, et al[17] have conducted a detailed study on hurdles to thrombolytic therapy in a rural setup; despite being in the urban setup, we face similar hurdles.

In a Cochrane review of 2016,[18] a meta-analysis of 27 randomised trials of any thrombolytic agent, compared with control in people with definite ischaemic stroke, was done. They concluded that thrombolytic therapy given up to six hours after stroke, reduces the proportion of dead or dependent people (mRS: 3-6). Those treated within the first three hours derive substantially more benefit than with later treatment. This overall benefit was apparent despite an increase in symptomatic intracranial haemorrhage, deaths at seven to 10 days, and deaths at final follow-up (except for trials testing rt-PA, which had no effect on death at final follow-up). Thus after missing the window of opportunity to administer thrombolysis, the delay in diagnosis of ischaemic stroke and hence in any form of treatment, does not affect the outcome at 1 month.

Risk factors still present at 1 month

Though only partly studied, we found a gap between recommended secondary preventive measures and their implementation in subjects. Nearly a third of the cases had at least a single risk factor for atherosclerosis. This calls for more intense counselling of stroke patients before they are discharged from the hospital. Li C, et al[19] did a population based, 7.5 year follow-up study of life-style risk factors in cases of stroke. Compared to subjects without a history of stroke, the risk of cardiovascular event or recurrent stroke were found significantly higher in stroke survivors. Simple control of hypertension would have prevented a substantial proportion of them.

Limitations of the study

A small sample size, a bias of selecting better outcome strokes, as deaths within the first month were excluded, not analysing depression in aphasics are the limitations of this study. A single observer administering the various scoring scales was an advantage. And so was maintaining uniformity, by assessing only MCA territory ischaemic strokes.

Conclusion

Majority of the patients suffering from stroke present to the hospital late, making imaging not available before 3 hours of onset. This, in additional to financial constraints, makes administration of potentially disability-limiting thrombolysis virtually impossible. Depression is found in about one fifth of non-aphasic strokes. Special efforts need to be taken to detect the same in aphasic strokes. Presence of aphasia, dominant lobe affection and female sex were associated with higher disability. Our study shows that disability assessment late in the first week after onset of stroke using NIHSS successfully forecast outcome at one month after onset of stroke. Cognitive impairment is not expected to change. Hence we recommend assessment of patients with NIHSS and MMSE before discharge from hospital to predict prognosis at follow-up. Online calculators or mobile applications can simplify calculating NIHSS score.[20] A more intense counselling on how to prevent a recurrent stroke or cardiovascular event, by controlling risk factors such as hypertension, diabetes and smoking, must be undertaken.

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