

## Predictors of Functional Recovery of Upper Limb Following acute Ischemic Stroke

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### Abstract

**Background:** Although age-standardised rates of stroke mortality have decreased worldwide, overall stroke burden has significantly increased over the last two and half decades especially in developing countries.

**Objectives:** To predict the functional recovery of upper limb potential after acute ischemic stroke.

**Methods:** 51 people were recruited and studied. SAFE, NIHSS Score, Median nerve SSEP, Conventional MRI brain imaging are done for all 51 patients. 40 patients were cooperative for further DTI neuroimaging & FA value analysis done within 1wk of stroke onset. Standard care & rehabilitation given. Followed up for upper limb recovery with ARAT scores at 1<sup>st</sup>, 2<sup>nd</sup> & 3<sup>rd</sup> months. Clinical, electrophysiological and neuroimaging recovery variables of upper limb were analyzed between two groups.

**Results:** FA asymmetry index of posterior limb of internal capsule (PLIC) suggest more structural asymmetry of PLIC and poor recovery. There is a significant negative correlation between fractional anisotropy asymmetry index and ARAT III score. Correlation coefficient (r) is -0.319.

**Conclusion:** With initial simple clinical assessment scales most of the recovery can be predicted and thereby patient expectations can be managed and use effective targeted rehabilitation strategies, time & resources to bring the best outcome.

**Keywords:** Stroke, Ischemia, ARAT score, PLIC

### Introduction

In accordance with the WHO, stroke was defined as "rapidly developing clinical symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours

or leading to death, with no apparent cause other than that of vascular origin."<sup>1</sup>

Stroke is the third most common cause of long-term adult disability.<sup>2</sup> Stroke recovery is heterogeneous and it is estimated that 25% to 74% of

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stroke survivors worldwide require some assistance or are fully dependent on caregivers for activities of daily living (ADL) after stroke.<sup>3</sup> Independence at 6mon is predicted by age, NIHSS Scale, Upper limb function. The recovery of motor function, particularly of the upper limb determines the ability to independently undertake activities of daily living.<sup>4</sup>

Almost one half of the disease burden in low- and middle-income countries is now from noncommunicable diseases.<sup>5</sup> Ischemic heart disease and stroke are the largest sources of this burden. Globally, the incidence of stroke due to ischemia is 68%, while the incidence of haemorrhagic stroke (intracerebral haemorrhage and subarachnoid haemorrhage combined) is 32%, reflecting a higher incidence of haemorrhagic stroke in low- and middle-income countries.<sup>6</sup>

The most important primary health goal for stroke is prevention. However, the effective therapies in the acute phase (stroke unit management, thrombolytic, and other reperfusion therapies), as well as rehabilitation and long-term follow-up efforts to prevent stroke recurrence and improve functional outcomes substantially & reduce the burden of stroke.

## Materials and Methods

**Study design:** Prospective observational study

**Study site:** Osmania General Hospital and Kamineni hospitals, Hyderabad.

**Sample size:** 51Patients

**Study Duration:** 2016 to 2018

### Inclusion Criteria:

- Patients with acute ischemic stroke within 3 days of onset
- Patients aged >18yrs

### Exclusion Criteria:

- Patients with prior h/o Stroke/ seizures
- MRI contraindicated patients, pregnant patients
- Patients with bilateral or posterior circulation strokes or cardioembolic strokes

60 eligible patients were approached. 9 didn't

give consent. Hence 51 patients were recruited in this study. All the recruited 51 patients were assessed clinically using Shoulder Abduction and Finger Extension (SAFE) score, National Institute of Health Stroke (NIHS) score initially. All the patients were assessed electro physiologically by seeing the presence or absence of Somatosensory Evoked Potentials (SSEP). All the patients have undergone neuroimaging using 1.5 Tesla Siemens Magnetom Symphony. Conventional MRI done with 1.5 Tesla siemens Magnetom Symphony Scanner, Erlangen, Germany using a quadratome head coil.

40 out of 51 patients were cooperative for diffusion tensor imaging (DTI) and FA analysis which was done with one week of stroke onset, mostly within 3days. Multidimensional Diffusion Weighted DTI imaging - echo planar images were acquired with double spin echo sequence. FA, eigen vectors, ADC were calculated in the region of interest and were compared with contralateral white matter. The structural integrity of the posterior limb of the internal capsules was quantified by calculating an asymmetry index from the mean absolute fractional anisotropy.

They are managed accordingly with iv thrombolysis or antiplatelets and statins along with standard care & rehabilitation. Functional recovery of affected upper limb is assessed with Action Research Arm Test (ARAT) score in the follow up. Based on the post stroke 3<sup>rd</sup> month recovery ARAT scores patients are grouped into good recovery and poor recovery. Clinical, electrophysiological and neuroimaging predictive variables of functional recovery of upper limb were analysed between those two groups.

**Statistical analysis:** The data are analysed accordingly using SPSS software. ARAT scores are analysed with ANOVA. Linear regression was used to explore correlations between ARAT and fractional anisotropy asymmetry index and SAFE score. An alpha of <0.05 was considered statistically significant.

## Observation and Results

In our study, 27 patients out of 33 male and 12 patients out of 18 female have good recovery. There is a no significant association between sex and upper limb recovery following stroke in our study. In our

study patients aged 31-60yrs are 29 and aged 61-90yrs are 22 in number. 26 patients aged 31-60yrs and 13 patients aged 61-90yrs had good recovery. Thus in

our study, there is a significant association between age and upper limb recovery post stroke.

**Table 1: Post-stroke recovery based on ARAT III (3<sup>rd</sup> month post stroke) score**

| ARAT III score (0-57) | Recovery | Frequency | Percentage |
|-----------------------|----------|-----------|------------|
| 34-57                 | Good     | 39        | 76.5 %     |
| 0-33                  | Poor     | 12        | 23.5 %     |
| Total                 |          | 51        | 100%       |

In our study 39 (76.5%) patients out of 51 had normal to near normal recovery and were able to do all to most of daily living activities independently.

**Time Interval Between Stroke Onset to Hospital:**

Mean time interval between stroke onset to hospital is 28.23 hrs. Minimum time interval is 1/2hr. Maximum time interval is 72hrs. 39 (76.5%) patients presented within 24hrs. Out of them 6 (11.8%) people are within window period (t- <=4hr). Three patients received thrombolysis. Remaining 3 were not thrombolysed due to uncontrolled accelerated hypertension associated high risk of hemorrhagic transformation. There is no significant association between recovery and time interval between stroke onset to hospital.

**Hospital Stay Duration:**

Mean hospital stay duration is 6.12 days. Maximum duration is 26days. Minimum duration is 1 day. Patient with maximum duration had post stroke complications and poor recovery. There is no significant association between hospital stay and recovery.

**Complications:**

During hospital stay 5 patients developed post stroke complications. Three patients developed UTI out of whom two had poor recovery and one had good recovery. One patient developed aspiration pneumonia and had poor recovery. One patient developed worsening of neurological deficit and had poor recovery. There is a significant association between post stroke complications and recovery.

**Table 2: SAFE / NIHS / NIHS motor subset / Upper limb average MRC Scores**

|                      | Recovery | N  | Mean   | Std. Deviation | Std. Error Mean |
|----------------------|----------|----|--------|----------------|-----------------|
| SAFE Score           | GOOD     | 39 | 4.744  | 2.9264         | .4686           |
|                      | POOR     | 12 | 1.667  | 2.6054         | .7521           |
| NIHS Score           | GOOD     | 39 | 7.103  | 3.2101         | .5140           |
|                      | POOR     | 12 | 12.417 | 4.1442         | 1.1963          |
| NIHS UL motor subset | GOOD     | 39 | 2.026  | 1.0127         | .1622           |
|                      | POOR     | 12 | 3.417  | .9962          | .2876           |
| UL MRC average       | GOOD     | 39 | 2.315  | 1.4588         | .2336           |
|                      | POOR     | 12 | .800   | 1.2849         | .3709           |

Our study showed significant association between SAFE score and post stroke recovery, NIHS score and post stroke recovery, NIHS motor subset score and post stroke recovery and UL average MRC

score and post stroke recovery. Average MRC score of upper limbs is taken as recovery of both proximal and distal part of upper limb is required for functional independency.

**Table 3: Electrophysiological analysis vs recovery**

|         | Good Recovery | Poor Recovery | Total       |
|---------|---------------|---------------|-------------|
| PRESENT | 35 (77.8%)    | 10 (22.2%)    | 45 (100.0%) |
| ABSENT  | 4 (66.7%)     | 2 (33.3%)     | 6 (100.0%)  |
| TOTAL   | 39 (76.5%)    | 12 (23.5%)    | 51 (100.0%) |

In our study there is no significant association between SSEP and post stroke recovery.

**Table 4: MRI Brain Characteristics of Stroke**

| Variable                          | Good Recovery | Poor Recovery |
|-----------------------------------|---------------|---------------|
| Dominant Hemisphere (%)           | 22 (75.86%)   | 7 (24.14%)    |
| Vascular Territory involved       |               |               |
| Middle Cerebral Artery (%)        | 31 (77.50%)   | 9 (22.50%)    |
| Posterior Cerebral Artery (%)     | 4 (57.14%)    | 3 (42.86%)    |
| Anterior Cerebral Artery (%)      | 4 (100%)      | 0 (0)         |
| Cortical (%)                      | 25 (78.13%)   | 7 (21.87%)    |
| Motor Cortex (%)                  | 19 (79.17%)   | 5 (20.83%)    |
| Subcortical (%)                   | 25 (71.43%)   | 10 (28.57%)   |
| Centrum semiovale/ CR / IC (%)    | 18 (69.23%)   | 8 (30.77%)    |
| Basal Ganglia (%)                 | 14 (66.67%)   | 7 (33.33%)    |
| Thalamus (%)                      | 6 (85.71%)    | 1 (14.29%)    |
| Subclinical Infarcts (%)          | 18 (81.81%)   | 4 (18.19%)    |
| Cerebral small vessel disease (%) | 5 (83.33%)    | 1 (16.67%)    |

There is no significant association between conventional MRI brain imaging stroke characteristics and the recovery. Evidence of prior subclinical

infarcts or cerebral small vessel disease has no significant association with recovery and didn't affect the recovery outcome.

**Table 5: Fractional Anisotropy Asymmetry Index**

|                | RECOVERY | N  | Mean    | Std. Deviation | Std. Error Mean |
|----------------|----------|----|---------|----------------|-----------------|
| AYMMETRY INDEX | GOOD     | 33 | .032224 | .0744702       | .0129636        |
|                | POOR     | 7  | .096571 | .1221582       | .0461714        |

More FA asymmetry index of posterior limb of internal capsule (PLIC) suggest more structural asymmetry of PLIC and poor recovery. There is a significant negative correlation between fractional anisotropy asymmetry index and ARAT III score. Correlation coefficient (r) is -0.319.

### Discussion

Recovery of motor function particularly of upper limb after stroke defines the functional independency. It is difficult to predict as the patients

with similar initial motor impairment may achieve disparate levels of motor function and independence. Clinical measures of initial motor impairment, neurophysiological biomarkers of corticospinal tract function, and neuroimaging biomarkers of direct and indirect descending motor pathways are related to motor outcomes.<sup>7</sup> The Predict Recovery Potential (PREP) algorithm combines clinical measures and neurophysiological and neuroimaging biomarkers that are sensitive to corticomotor pathway integrity to predict likely upper limb functional outcome.

Diffusion tensor imaging (DTI) is an advance non-invasive magnetic resonance imaging technique used to visualize and quantitate Corticospinal Tract, which is the most important neural tract for mainly upper limb motor function, especially for fine motor control of the hand in humans. Fractional anisotropy (FA) is an index of the diffusion characteristics of water molecules preferentially directed along the axis of major axonal pathways and reflect acute and permanent damage to pyramidal tracts to determine clinical motor deficit and outcome.<sup>8</sup>

In this study there is no significant association of recovery with time interval between stroke onset to hospital and duration of hospital stay. However patients who developed post stroke complications during hospital stay are found to have recovery significantly affected.

**DTI and FA Asymmetry Index:** FA values decreases progressively with the time in the ipsilesional pyramidal tract which provides insight on the progress of Wallerian degeneration.<sup>9</sup> It is a general agreement that FA value increases immediately after ischemic stroke onset and remains high for the next 1-2 days, then decreases significantly during the following stroke phases. In the metanalysis study done by Jing-fen Jin et al, FA values in the subacute phase (4 d-8 w) defined by using the Osborn criterion according to the DTI scanning time after ischemic stroke was a good predictor for functional motor recovery.<sup>10</sup> In contrary in our study we found a significant negative correlation between fractional anisotropy asymmetry index and ARAT III score.

### Conclusion

Stroke recovery is heterogeneous. Predicting the functional recovery of motor function, particularly of the upper limb determines the ability to predict to independently undertake the activities of daily living. Clinical assessment scales have high significant predictive value of recovery. Thus, with initial simple clinical assessment scales most of the recovery can be predicted and thereby patient expectations can be managed and use effective targeted rehabilitation strategies, time & resources to bring the best outcome.

**Ethical Clearance:** Ethical clearance was obtained from the institutional ethics committee prior to the commencement of the study.

**Conflict of Interest:** Nil

**Source of Funding:** Self

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