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Diffusion Tensor Imaging- Tractography In Subacute Stroke To Predict Motor Outcome

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Abstract

Background-

Diffusion Tensor Imaging (DTI) is an MRI technique that provides information about the orientation and structural organization of white major fibres, and, through tractography, the trajectories of cerebral white major tracts can be obtained. The DTI metric functional anisotropy (FA) is influenced by myelination, diameter, density, and orientation of axons. Anisotropy measurement helps in detecting the degree of fibre damage in stroke.

Aim- To assess whether anisotropy using Diffusion Tensor Imaging in the corticospinal tract correlates with motor outcome after stroke.

Materials And Methods-

We conducted a prospective observational study among 86 adults with new-onset, single anterior circulation stroke, after obtaining informed consent. DTI was done using a 1.5T MRI scanner between days 2-10 of stroke and FA, ADC, and voxels of the infarct and contralateral side and their ratios were derived. Clinical assessment was done by NIHSS at the time of the scan, and MRS and Barthel scores were obtained on days 7, 30, and 90 after stroke. Statistical analysis using Chi-square and ANOVA tests was done to determine the association of DTI-metrics with motor outcome and ROC curves were used to determine DTI-metric cut-offs to predict motor outcome.

Results-

rVoxels had a strong positive correlation with NIHSS score which was statistically significant. FA and rFA cut-off values, 0.356 and 0.465 respectively, were defined to predict moderate to severe disability and dependency post stroke.

Conclusions-

The number of fibres/ voxels and rVoxels correlated with severity of stroke at presentation. DTI metrics- FA and rFA can be a surrogate marker to predict long-term motor outcome in stroke patients.

Keywords: Diffusion tensor imaging tractography; Long term Prognosis of stroke; Voxels; ratio of fractional anisotropy; NIHSS

Introduction

Worldwide, stroke is an important cause of mortality and disability. In recent years, much interest is being focused on diffusion tensor imaging (DTI), a relatively novel MRI technique, for in vivo

quantification of microstructural damage to cerebral white matter following stroke. With the advent of DTI, the study of brain anatomy on a different scale is possible. Classical medical imaging techniques, such as conventional MRI or functional MRI are not capable of producing information on tracts and can only provide tissue information.

DTI is an MRI technique that captures the movement of particles that are subjected to Brownian movement within brain cells. These displacements give us further information about the orientation and structural organization of white matter fibers, and, through tractography, the trajectories of cerebral white matter tracts can be obtained. The information provided by DTI is oversimplified compared to the underlying neuroanatomy. Thus, this technique is an important tool to view anatomical structures since it allows in vivo identification of white matter regions, and provides newer insights into white matter integrity, and fiber connectivity, and thus helps in both patient diagnosis and prognosis.

DTI provides information on the direction and degree of tissue water diffusion. In the white matter, water diffuses faster lengthwise along the fibers and slower in a direction perpendicular to the fibers, resulting in anisotropic diffusion. The degree of anisotropy depends on the level of organization and integrity of the fibers forming the white matter tract and on the degree of freedom of water diffusion movements by oriented axonal membranes and myelin sheaths. DTI metrics, such as fractional anisotropy (FA), detects microstructural changes which are attributable to ischemic stroke.

We also investigated the potential of DTI in the corticospinal tract (CST) to predict motor outcome 90 days after stroke. CST is the projection fiber which constitutes the major efferent white matter tract that provides a connection from the motor cortex to the brain stem and spinal cord and thereby serves as the main conduit of information between the cortical structures and the voluntary musculature of the arms and legs. On their way to the lateral funiculus, the CST fibers converge into the corona radiata and through the posterior limb of the internal capsule (PLIC) to the cerebral peduncle.

One of the most prevalent outcomes of stroke is motor impairment, the severity of which is linked to functional disability and impaired quality of life[1]. The accurate prediction of motor deficit is important for management and rehabilitation[2]. Major clinical variables such as initial motor examination in the form of drifting and efforts against gravity measured with a neurologic deficit scale such as the National Institutes of Health Stroke Scale (NIHSS) have consistently been associated with functional outcome after stroke[3-5].

The integrity of CST is important for motor outcome[6-13]. DTI assesses the microstructural status of white matter quantitatively[14,15]. In DTI, regional FA values work as surrogate markers of motor deficit after stroke: lower values in affected fiber tracts correlate with worse motor function[13, 17-21].

After proximal axonal or cell body injury, anterograde degeneration of axons and their myelin sheaths occurs, and it is called Wallerian degeneration.[16]

Long-term limb motor deficiency can be compared to decreased anisotropy distal to the infarct on the damaged side of the CST, expressed as FA values assessed at the rostral pons. Tractography can detect acute stroke damage to specific CST regions, which can predict limb motor outcome[6-11, 22].

On directional DTI color maps, the internal capsule is a massive and compact fiber bundle that serves as a key conduit of white matter fibers to and from the cerebral cortex to the brain stem and spinal cord. The anterior limb of internal capsule is between the head of the caudate nucleus and the rostral aspect of the lentiform nucleus, while the posterior limb lies between the thalamus and the posterior aspect of the lentiform nucleus. The anterior limb routes projection fibers to and from the thalamus (thalamocortical projections) as well as frontopontine tracts, all of which are primarily anteroposteriorly oriented in contradistinction to the posterior limb, which routes the superior-inferiorly oriented fibers of the corticospinal, corticobulbar, and corticopontine tracts. This gives the anterior and posterior limbs distinctly different colors on directional DTI maps.

Although damage to the centrum semiovale and corona radiata was also associated with poor motor outcome, PLIC damage after stroke between days 2-7, was the best predictor of motor deficits and their severity. To our knowledge, no prospective studies have assessed DTI's ability to predict long-term

Volume 6, Issue 2; March-April 2023; Page No 235-261

motor outcome after stroke. We assessed whether FA values at specified stroke locations on DTI of the CST can predict motor outcome 90 days after stroke.

Our main contributions to clinical DTI research on stroke thus far support the notion that motor outcome is substantially dependent on lesion location and the degree to which acute stroke affects the CST[13, 22]. PLIC injury, in particular, could be used as an early imaging predictor of poor motor outcome[22].

Aims And Objectives

Aim-

To assess whether anisotropy using Diffusion Tensor Imaging in the corticospinal tract correlates with motor outcome after stroke.

Objectives-

1. Correlation of DTI metrics in early stroke with NIH stroke scale, at presentation, keeping it as the gold standard.
2. To predict clinical outcome by DTI metrics using MRS and Barthel score in early stroke.

Materials And Methods

Materials:

This was a hospital-based prospective observational study, conducted between September 2017 to August 2019 for 24 months in the Department of Radiology, at our Institute.

Institutional ethics committee approval was obtained **(IEC 737/2019).** Informed consent was taken from every patient.

Clinical Trials Registry- India (CTRI registration) obtained on 17/12/2019 **(CTRI Number CTRI/2019/12/022404)**.

Sample Size: 86 (Time-bound study)

Inclusion Criteria:

1. Age >18 years
2. Single anterior circulation stroke
3. No prior history of stroke or white matter pathology

Exclusion Criteria:

1. Patients with prior history of stroke
2. Patients with claustrophobia/ implants/ other contraindications for MRI scanning
3. Patient with intracranial hemorrhage
4. Patient with lobar/ global infarct involving most of brain parenchyma

In this study, we compared the DTI measures being FA, ADC values, and number of fibers (voxels) in stroke patients with clinical outcome measured by standard stroke scales being- the NIH stroke scale, Modified Rankin score, and Barthel index.

Study subjects: 86 patients with stroke, admitted to the Department of Neurology, with both radiological imaging and clinical follow-up were included in the study.

Instrumentation: Image acquisition was done using Magnetic Resonance Imaging: (model) - Philips Achieva 1.5 Tesla (using SENSE- NV- 16 coil).

The imaging parameters are as follows:

Sequences- FLAIR (axial sections) and DTI (med iso)

Parameters for DTI sequence- B factor of 1000s/mm^2 and TE of 100.

Radiological Assessment-

Diffusion Tensor imaging- MR Tractography and FLAIR sequence of the patients was acquired using Philips Achieva 1.5 Tesla, using SENSE- NV- 16 coil with B factor of 1000s/mm^2 and TE of 100.

Once acquired, the DTI data was transferred to a post-processing workstation to obtain the FA, ADC, and voxels.

DTI metrics were obtained from the region of interest (ROI) in the tract. Functional Anisotropy (FA) and Apparent diffusion coefficient (ADC) were measured in the ipsilateral and contralateral regions of interest.

Region of interest (ROI) size, however, was kept equivalent on the ipsilateral and contralateral sides.

Volume 6, Issue 2; March-April 2023; Page No 235-261

FA value between 0 (isotropic) and 1 (the most anisotropic).

The number of fibers in the region of interest was given in terms of voxels. This too was measured on the ipsilateral and contralateral sides.

The ratios of FA, and ADC on the infarct side: normal side was taken for further analysis.

Clinical Assessment-

NIH stroke scale was used to assess the patient at the time of presentation and Modified Rankin score and Barthel score were obtained on day 7, day 30, and 90 since stroke.

NIHSS includes the following parameters- level of consciousness, horizontal eye movement, visual field test, facial nerve, motor arm, motor leg, limb ataxia, sensory, language, speech, extinction, and inattention. Based on NIHSS, stroke is classified into no stroke, minor stroke, moderate stroke, moderate to severe stroke, and severe stroke. A score less than 6 indicates a strong possibility of a good recovery.

Modified Rankin score is used to measure the clinical outcome. The score varies from 0-6, 0 being perfectly healthy and 6 being death.

Barthel scale is an ordinal scale to measure performance in activities of daily life. It consists of 10 variables being presence or absence of fecal incontinence, presence or absence of urinary incontinence, help needed while grooming, help needed with feeding, help needed with toilet use, help needed with transfers, help needed with walking, help needed with dressing, help needed with climbing stairs and help needed with bathing.

Statistical analysis:

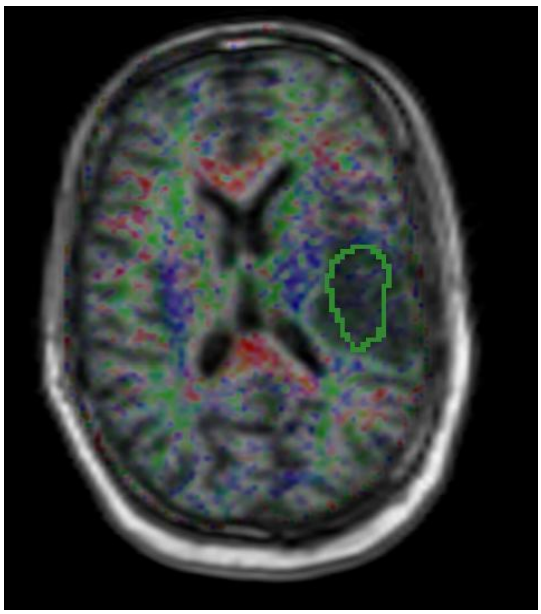
Data analysis was done using SPSS software version 23.0.

To determine the association of variables with motor deficit severity, the chi-square test was used for categorical and ANOVA test for quantitative variables.

Receiver operating characteristic (ROC) curves were used to determine FA and rFA cut-offs for the infarct.

Univariate ordinal logistic regression was used to predict long-term motor outcome.

Fig A: ROI of size of infarct drawn at the level of infarct on DTI image with FLAIR image overlapped for better anatomical delineation.



Volume 6, Issue 2; March-April 2023; Page No 235-261

Fig B: ROI of size of infarct drawn above and below the level of infarct on DTI image with FLAIR image overlapped for better anatomical delineation.

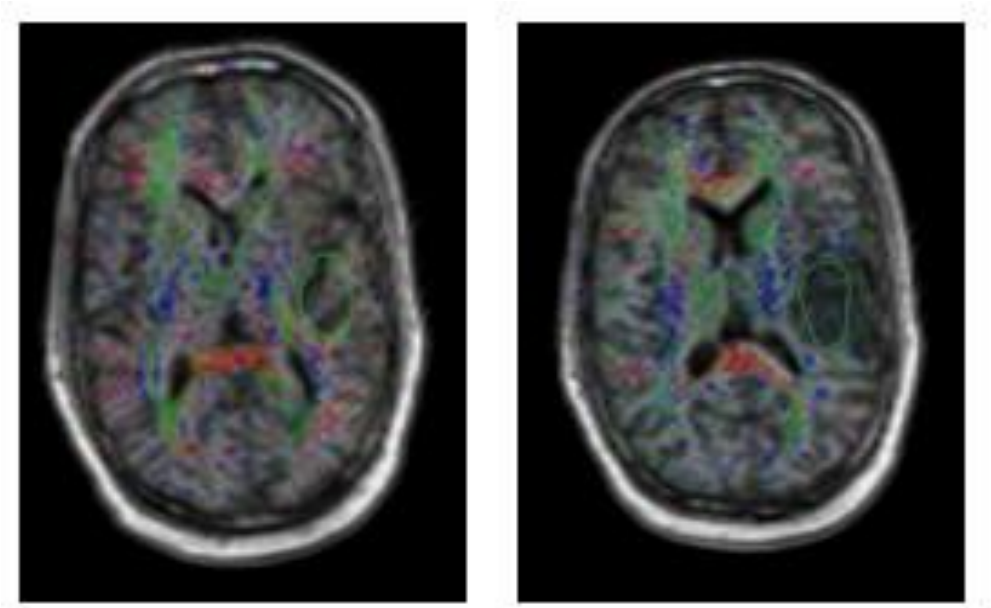
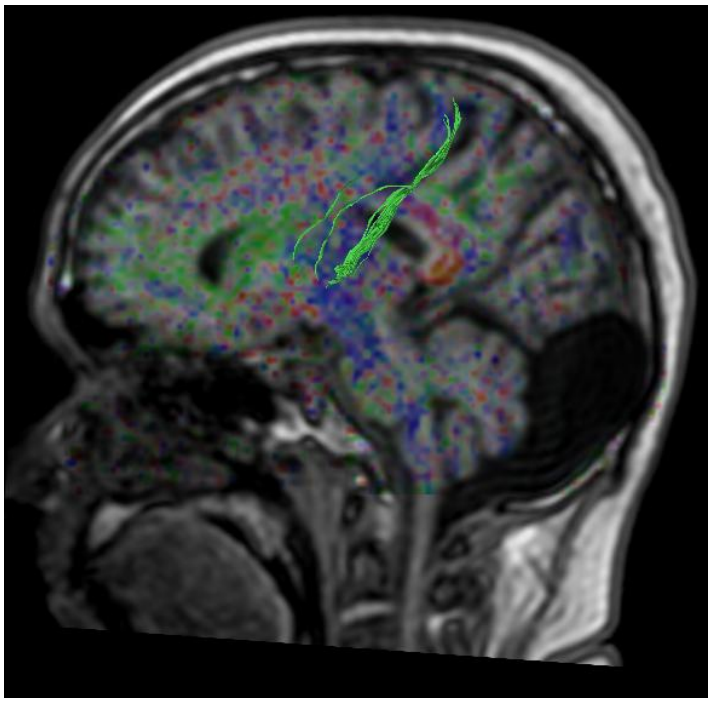


Fig C: Fibre tracking determines the number of voxels



Volume 6, Issue 2; March-April 2023; Page No 235-261

Fig D: Fibre tracking of contralateral normal side determines the number of voxels.

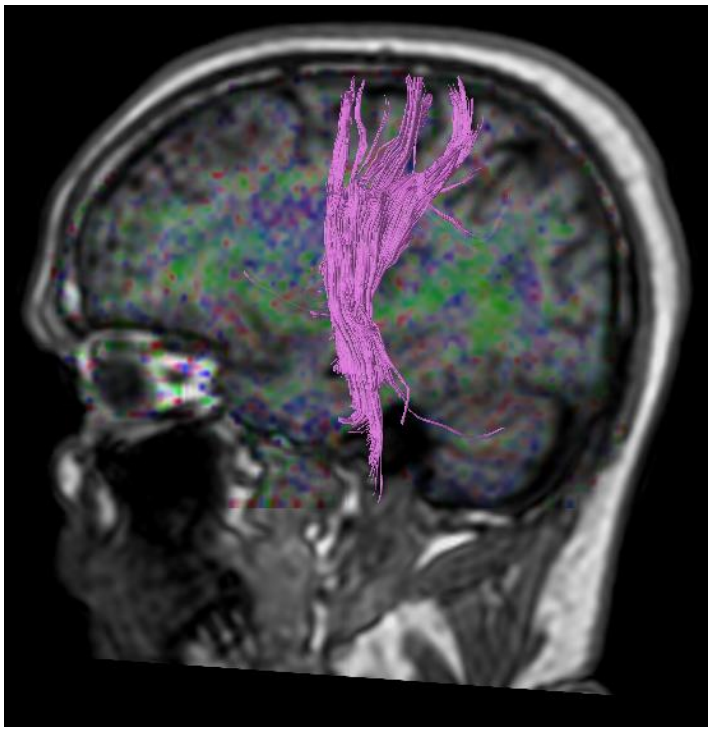
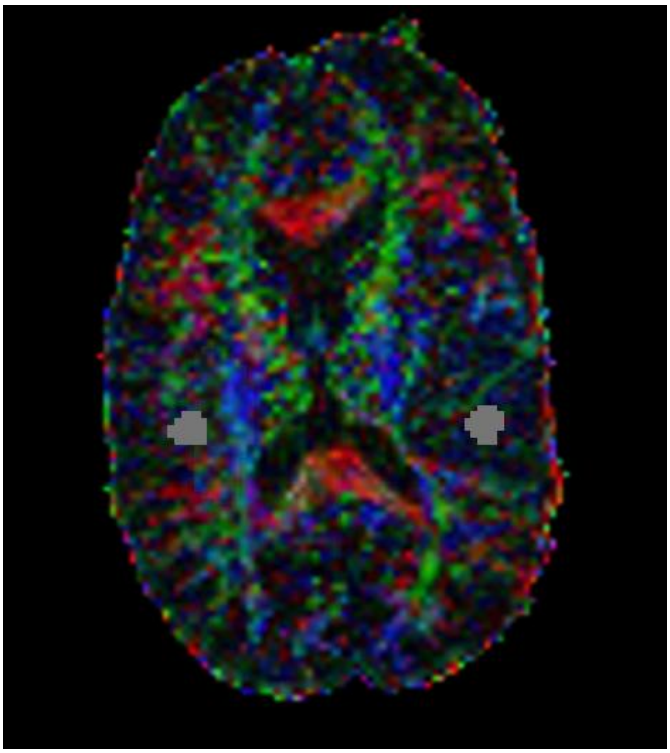


Fig E: ROI drawn to obtain FA and ADC values of the infarct and contralateral normal side.

Volume 6, Issue 2; March-April 2023; Page No 235-261



Infarct: FA= 0.167, ADC= 0.508, Voxels= 448

Normal: FA= 0.281, ADC= 0.795, Voxels= 1984

Ratios: rFA= 0.594 , rADC= 0.639, rVoxels= 0.225

Results

Among 86 patients, approximately 51%, 33% and 13% of patients had infarct in the left MCA, right MCA and right MCA and ACA territory respectively. Most of the patients (59%) had supracapsular infarct.

Approximately 45% and 44% of patients had small and moderate-sized infarcts, respectively.

Mean rFA of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.382, 0.596, 0.634, and 0.721 respectively.

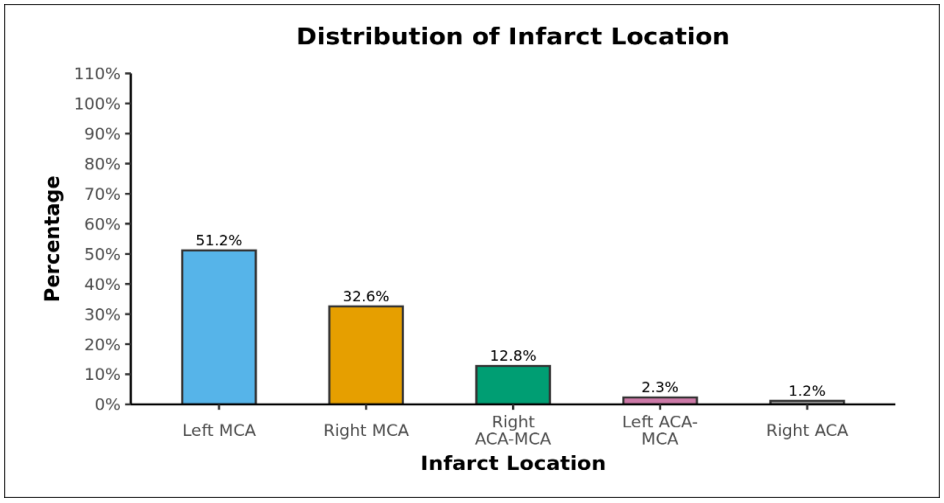
Mean rADC of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.396, 0.488, 0.621, and 0.712 respectively.

Mean rVoxels of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.391, 0.572, 0.638, and 0.692 respectively.

Distribution of infarct location

Graph No 1: Distribution of patients w.r.t infarct location n=86

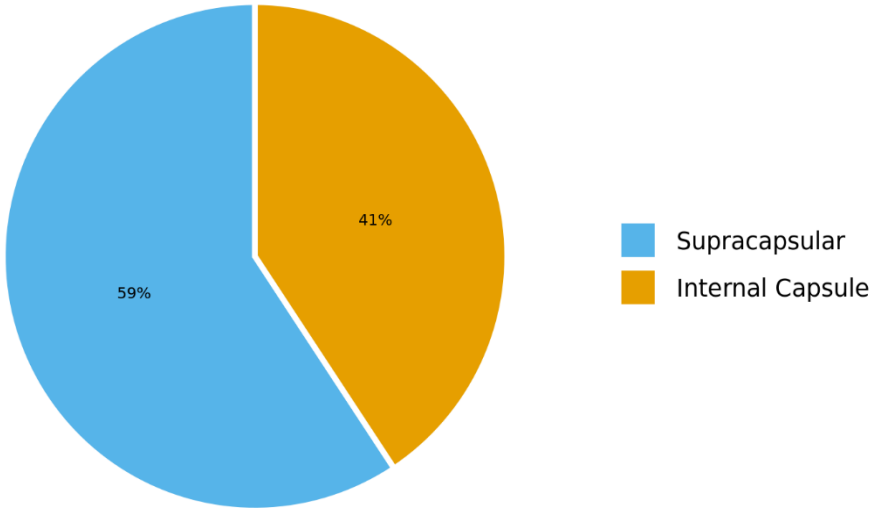
Volume 6, Issue 2; March-April 2023; Page No 235-261



Approximately 51%, 33% and 13% of patients had infarct in the left MCA, right MCA and right MCA and ACA territory respectively.

Distribution of patients w.r.t infarct location

Graph No 2: Distribution of patients w.r.t infarct location n=86

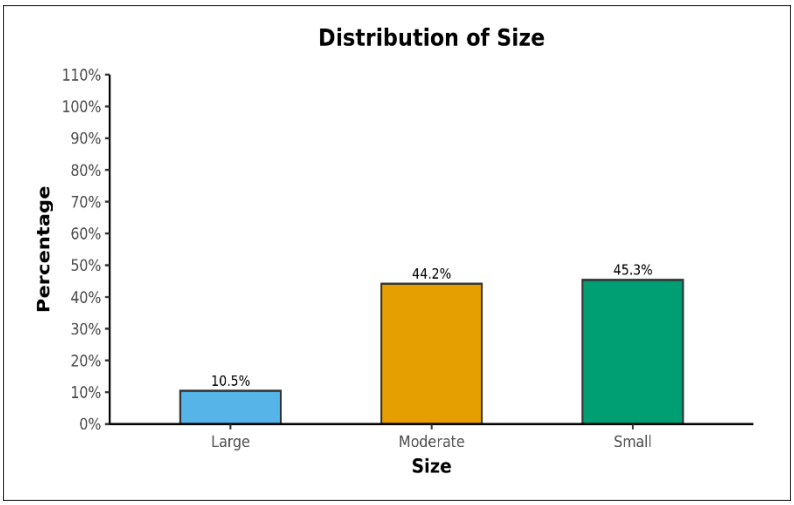


Most of the patients (59%) had supracapsular infarct.

Distribution in terms of size

Graph No 3: Distribution of patients w.r.t infarct size n=86

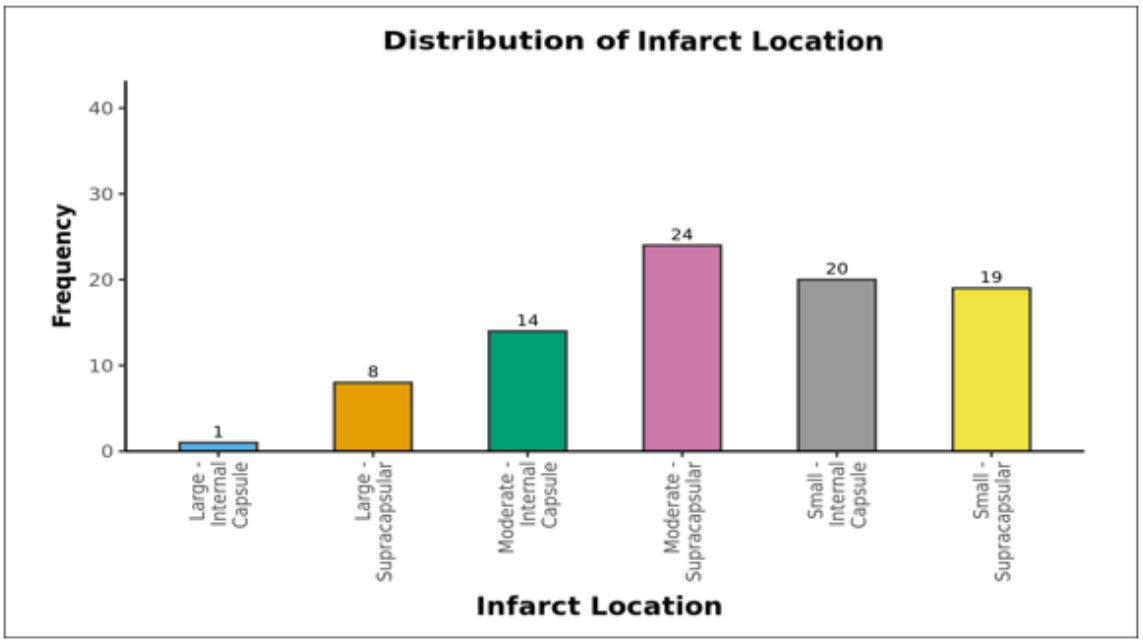
Volume 6, Issue 2; March-April 2023; Page No 235-261



Approximately 45% and 44% of patients had small and moderate-sized infarcts, respectively.

Distribution of participants in terms of infarct location

Graph No 4: Distribution of Patients W.R.T Infarct Location N=86

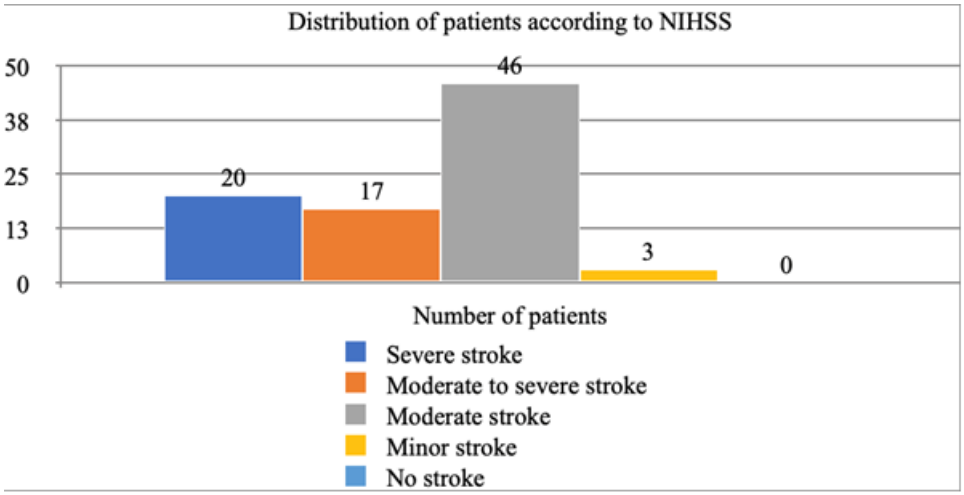


Approximately 28%, 23% and 22% of patients had infarcts of moderate size in the supracapsular region, small size in the internal capsule and small size in supracapsular region, respectively.

Distribution of patients according to NIHS

Graph No 5: Distribution of patients w.r.t infarct location and size n=86

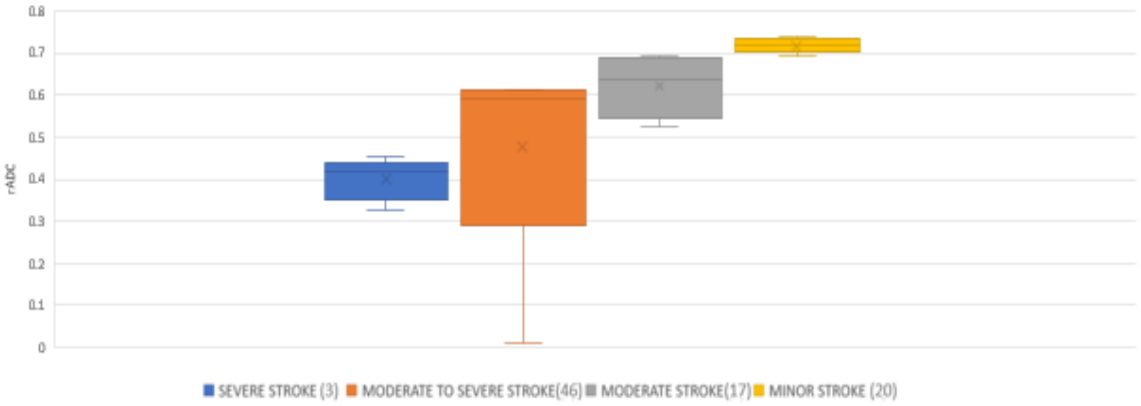
Volume 6, Issue 2; March-April 2023; Page No 235-261



Mean rFA of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.382, 0.596, 0.634, and 0.721 respectively.

Comparison of NIHSS at baseline with rADC

Graph No 7: Severity of stroke by NIHSS vs rADC n=86

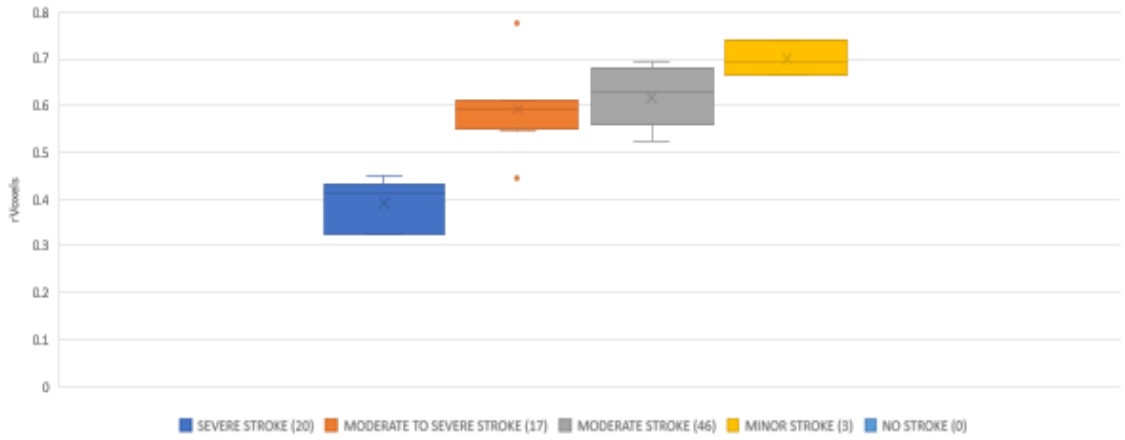


Mean rADC of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.396, 0.488, 0.621, and 0.712 respectively.

Comparison of NIHSS at baseline with rVoxels

Graph No 8: Severity of stroke by NIHSS vs rVoxels n=86

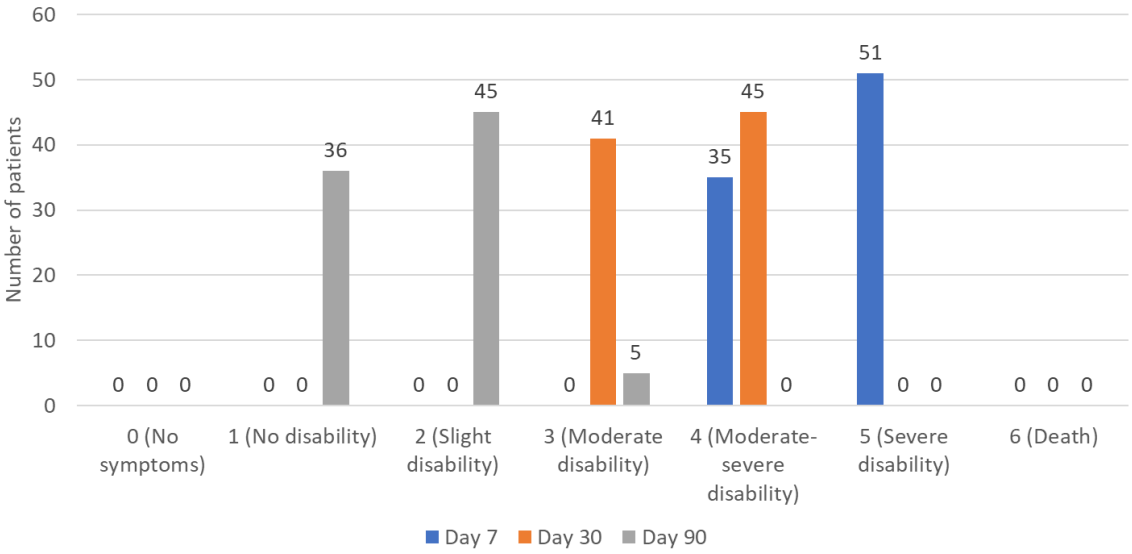
Volume 6, Issue 2; March-April 2023; Page No 235-261



Mean rVoxels of patients with severe stroke, moderate to severe stroke, moderate stroke and minor stroke were 0.391, 0.572, 0.638, and 0.692 respectively.

Distribution of patients according to MRS on days 7, 30 & 90

Graph No 9: Distribution of patients according to MRS at days 7, 30 and 90 n=86



On day 7, 60% of patients had severe disability and 40% had moderate to severe disability.

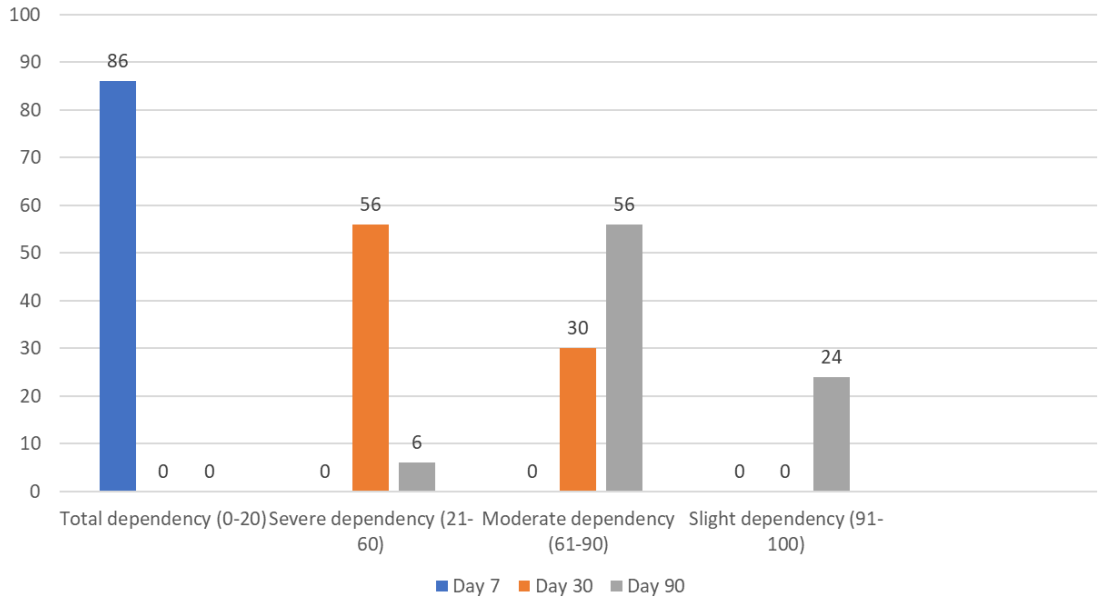
On day 30, 52% had moderate to severe disability and 48% had moderate disability.

On day 90, 6% had moderate disability, whereas 52% and 42% had slight and no disability respectively.

Distribution of patients according to Barthel score at days 7, 30 & 90

Graph No 10: Distribution of patients according to Barthel score at day 7, 30 and 90 n=86

Volume 6, Issue 2; March-April 2023; Page No 235-261



On day 7, all patients were totally dependent.

On day 30, 65% had severe dependency and 35% had moderate dependency.

On day 90, 7% had severe dependency, whereas 65% and 28% had moderate and slight dependency respectively.

Comparison of large supracapsular infarct and small capsular infarct with various parameters

Table No 1: Comparison of large supracapsular infarct and small capsular infarct with various parameters

Parameters	Large supracapsular (n=8)	Small capsular (n=20)
FA (infarct)	0.36	0.37
ADC (infarct)	0.58	0.54
Voxels (infarct)	1338±792	970±476
rFA	0.49	0.45
rADC	0.66	0.66
rVoxels	0.59	0.46
NIHSS (≥16)	4 (50%)	12 (60%)
MRS day 7 (≥4)	8 (100%)	20 (100%)
MRS day 30 (≥4)	3 (38%)	13 (65%)
Barthel day 7 (≤60)	8 (100%)	20 (100%)
Barthel day 30 (≤60)	4 (50%)	15 (75%)

About 23% of patients had small capsular infarct and 9% had large supracapsular infarct.

Volume 6, Issue 2; March-April 2023; Page No 235-261

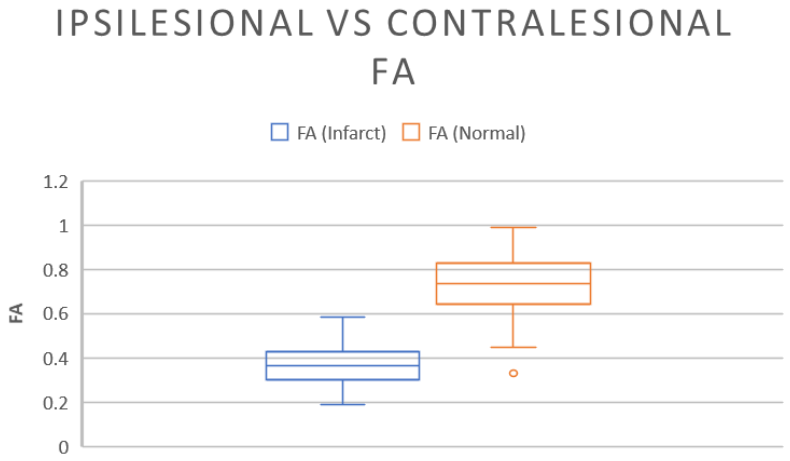
The patients with small capsular infarct had slightly lesser rFA and rVoxels.

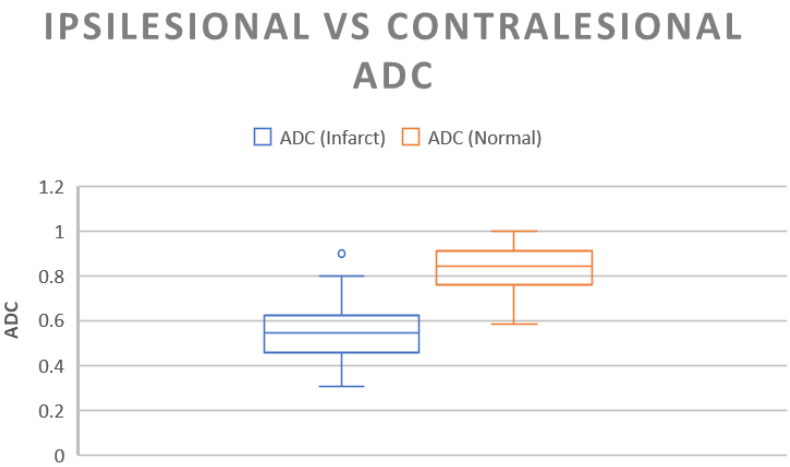
Though about 60% and 50% of patients with small capsular and large supracapsular infarct respectively had moderate to severe stroke, 65% and 75% of patients with small infarct had poor motor outcome on day 30.

Comparison of ipsilesional (infarct) and contralesional FA, ADC and Voxels n=86

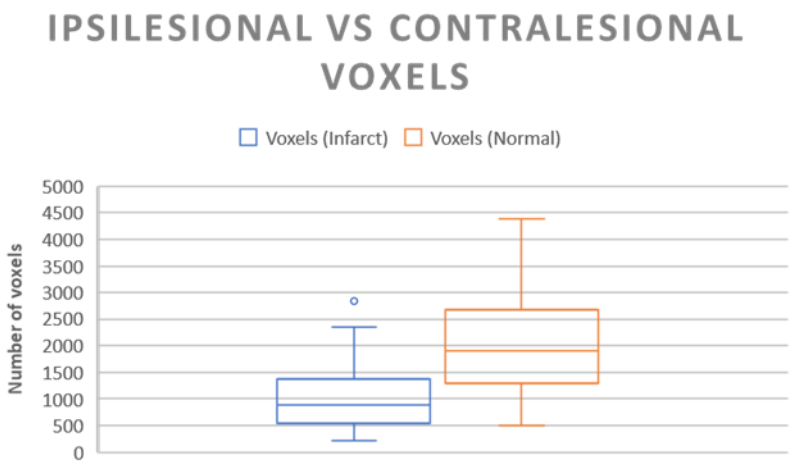
Graph No 11,12,13: Ipsilesional v/s Contralesional FA, ADC and Voxels n=86

FA, ADC and Voxels was lesser in the region of infarct.





Volume 6, Issue 2; March-April 2023; Page No 235-261



Comparison of number of patients with poor outcome

Table No 2: Comparison of number of patients with poor outcome.

		Number of patients	Percentage
NIHSS (≥16)		37	43%
MRS (≥4)	**7**	86	100%
	30	45	52%
	90	8	9%
Barthel (≤60)	**7**	86	100%
	30	30	35%
	90	10	12%

43% of patients had moderate to severe stroke according to NIHSS.

Among them, 9% and 12% had poor motor outcome according to MRS and Barthel scores at day 90 respectively.

Volume 6, Issue 2; March-April 2023; Page No 235-261

Description of variables in patients with poor outcome

Table No 3: Various parameters in patients with poor outcome

NIHSS ≥ 16	**(Number of patients)**	**37**
Mean age in years		65.8
Location of infarct	**Supracapsular**	21 (57%)
	Capsular	16 (43%)
Infarct type	**Moderate supracapsular**	30%
	Small capsular	22%
DTI metrics	**FA**	0.36
	ADC	0.54
	Voxels	675 ± 412
	rFA	0.5
	rADC	0.67
	rVoxels	0.5
MRS ≥ 4	**Day 7**	37 (100%)
	Day 30	19 (51%)
	Day 90	8 (9%)
Barthel score ≤ 60	**Day 7**	37 (100%)
	Day 30	22 (60%)
	Day 90	10 (12%)

Among the 43% of patients with severe stroke according to NIHSS, 30% had moderate supracapsular stroke.

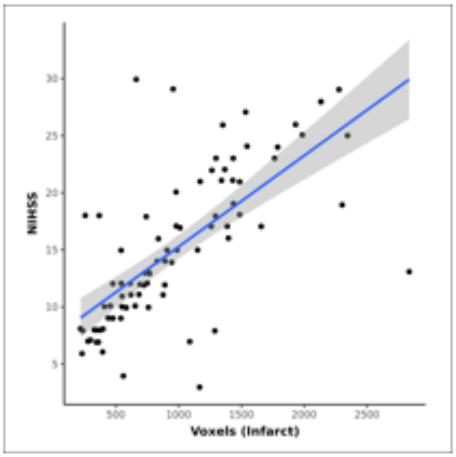
Their mean FA, ADC, and Voxels were 0.36, 0.54, and 675+ 412 respectively.

Their mean rFA, rADC, and rVoxels were 0.5, 0.67, and 0.5 respectively.

Volume 6, Issue 2; March-April 2023; Page No 235-261

Correlation of NIHSS with DTI metrics

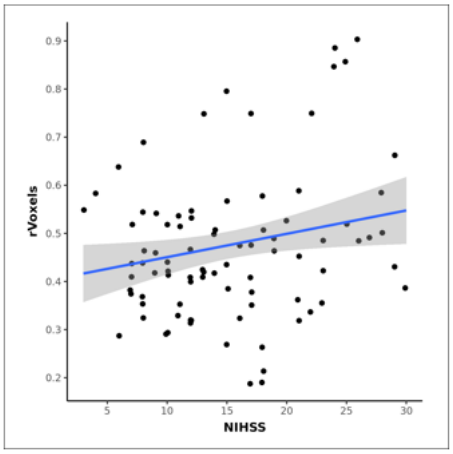
Graph No 14: Correlation between NIHSS vs voxels of infarct n=86



There was a strong positive correlation between NIHSS and Voxels (Infarct), and this correlation was statistically significant (rho = 0.75, p = <0.001).

Correlation of rVoxels with clinical scores

Graph No 15: Correlation of rVoxels with NIHSS at baseline n=86.

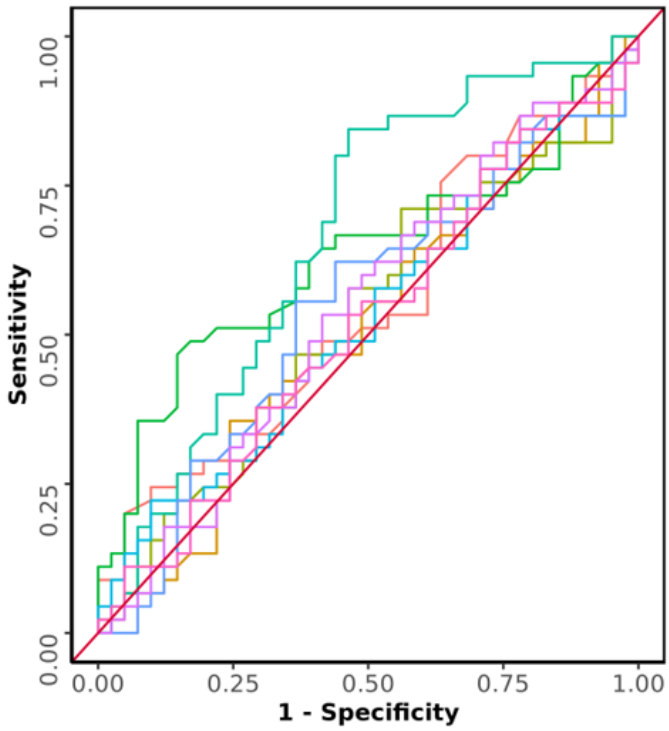


There was a strong positive correlation between rVoxels and NIHSS, and this correlation was statistically significant (rho = 0.75, p = <0.001).

Volume 6, Issue 2; March-April 2023; Page No 235-261

Comparison of diagnostic performance of various predictors in predicting MRS >4 and Barthel score of <60 on day 30

Graph No 16: Comparison of diagnostic performance of various predictors in predicting MRS >4 and Barthel score of <60 on day 30

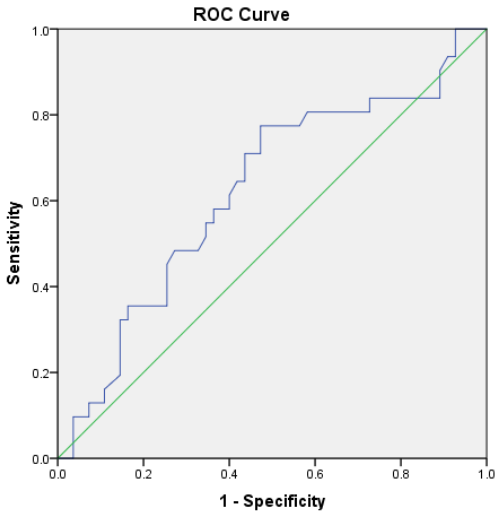


Among the various parameters, all parameters had AUC ~0.5, except FA and rFA with AUC > 0.6.

No specific cut-off value could be generated with ADC, rADC, voxels, and rVoxels to predict poor outcome, with good sensitivity and specificity.

FA cut-off by ROC curve

Graph No 17: Comparison of diagnostic performance of FA in predicting MRS >4 and Barthel score of <60 on day 30



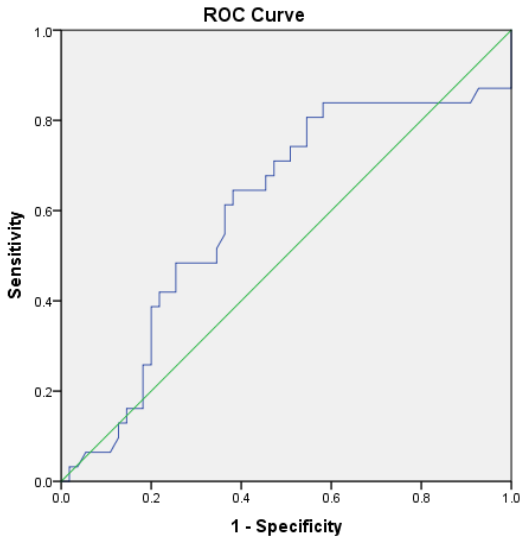
Volume 6, Issue 2; March-April 2023; Page No 235-261

AUC= 0.652, n=86

FA cut-off value for poor outcome i.e., MRS >4 and Barthel score of <60 on day 30 with a sensitivity of 90% and specificity of 92% is 0.356.

rFA cut-off by ROC curve

Graph No 18: Comparison of diagnostic performance of FA in predicting MRS ≥4 and Barthel score of ≤60 on day 30



AUC= 0.623, n=86

rFA cut-off value for poor outcome i.e., MRS >4 and Barthel score of <60 on day 30 with a sensitivity of 91% and specificity of 92% is 0.465.

Image Gallery

Cases 1-6 (examples of different cases based on infarct size, location, and their calculations).

Case No 1:

Volume 6, Issue 2; March-April 2023; Page No 235-261

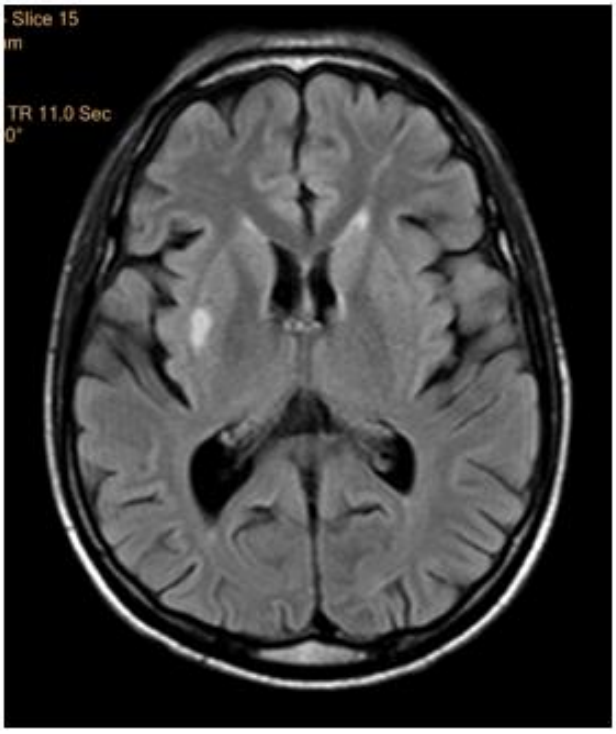


Fig A

Infarct: FA= 0.344, ADC= 0.478 Voxels= 1368
Normal: FA= 0.668, ADC= 0.794 Voxels= 1986
Ratios: rFA= 0.514, rADC= 0.602, rVoxels= 0.688

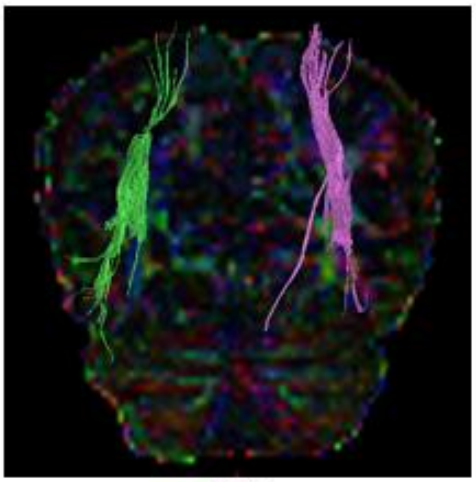


Fig B

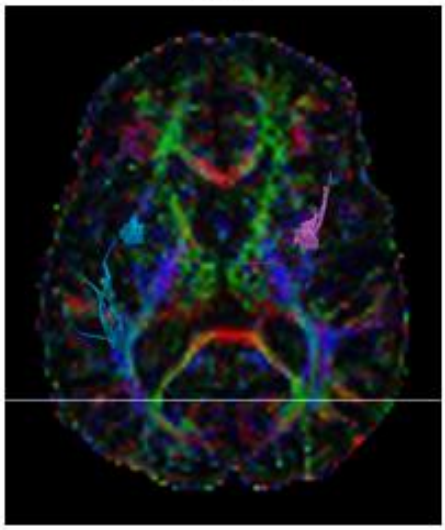


Fig C

Fig 1A: FLAIR axial image shows hyperintensity in the right lentiform nucleus

Fig 1B and 1C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 52-year-old male presented with left-sided- weakness for 1 day.

MRI stroke protocol revealed a small acute infarct in the right capsuloganglionic region with FA value of 0.344, ADC of 0.478, and voxels of 1368.

NIHSS score was 14 (moderate stroke).

Day 7

MRS score: 5 (severe disability)

Barthel score: 15 (total dependency)

Day 30

MRS score: 4 (moderate to severe disability)

Barthel score: 65 (moderate dependency)

Volume 6, Issue 2; March-April 2023; Page No 235-261

Day 90

MRS score: 2 (slight disability)

Barthel score: 95 (slight dependency)

A small-sized infarct in the capsuloganglionic region showed reduced FA, ADC, and voxels. The patient had a moderate stroke (according to NIHSS) with a baseline FA value of 0.344. However, by day 90, he had a slight disability and dependency. However, on day 30, he showed moderate to severe disability and moderate dependency, owing to the region of the infarct i.e. capsuloganglionic region, rather than the size of the infarct.

Case No 2:

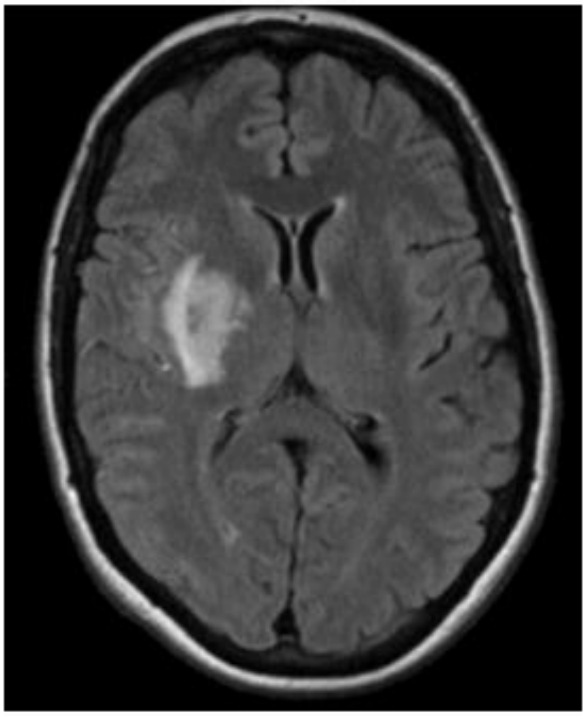


Fig A

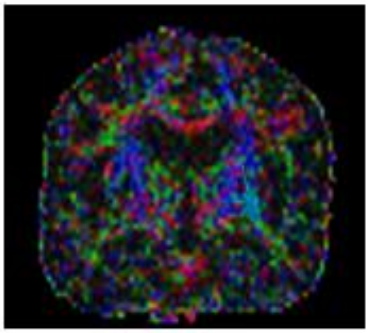


Fig B

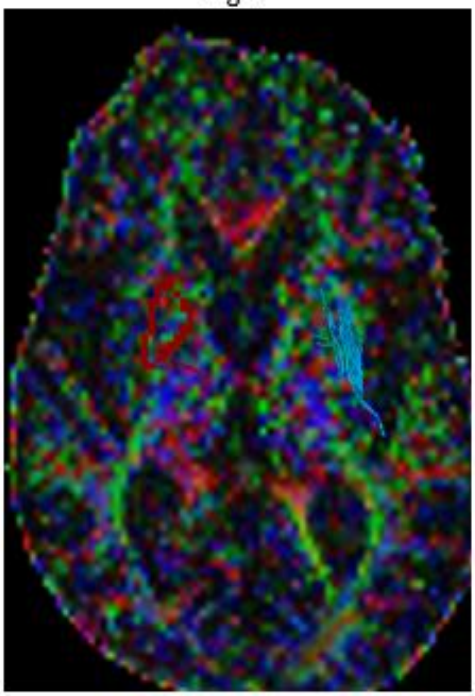


Fig C

Infarct: FA= 0.322, ADC= 0.621 Voxels= 1311
Normal: FA= 0.694, ADC= 0.716 Voxels= 2696
Ratios: rFA= 0.463 , rADC= 0.867, rVoxels= 0.486

Fig 2A: FLAIR axial image shows hyperintensity in the right capsuloganglionic region.

Fig 2B and 2C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 68-year-old male presented with left-sided- weakness for 1 day.

MRI stroke protocol revealed moderate acute infarct in the right capsuloganglionic region with FA value of 0.322, ADC of 0.621, and voxels of 1311.

NIHSS score was 18 (severe stroke).

Volume 6, Issue 2; March-April 2023; Page No 235-261

Day 7

MRS score: 5 (severe disability)

Barthel score: 10 (total dependency)

Day 30

MRS score: 4 (moderate to severe disability)

Barthel score: 30 (severe dependency)

Day 90

MRS score: 2 (slight disability)

Barthel score: 85 (moderate dependency)

A moderate sized infarct in the capsuloganglionic region showed reduced FA, ADC, and voxels. The patient had a severe stroke (according to NIHSS) with a baseline FA value of 0.322. However, by day 90, he had a slight disability and moderate dependency. However, on day 30, he showed moderate to severe disability and severe dependency, owing to the region of the infarct i.e. capsuloganglionic region, the and size of the infarct.

Case No 3

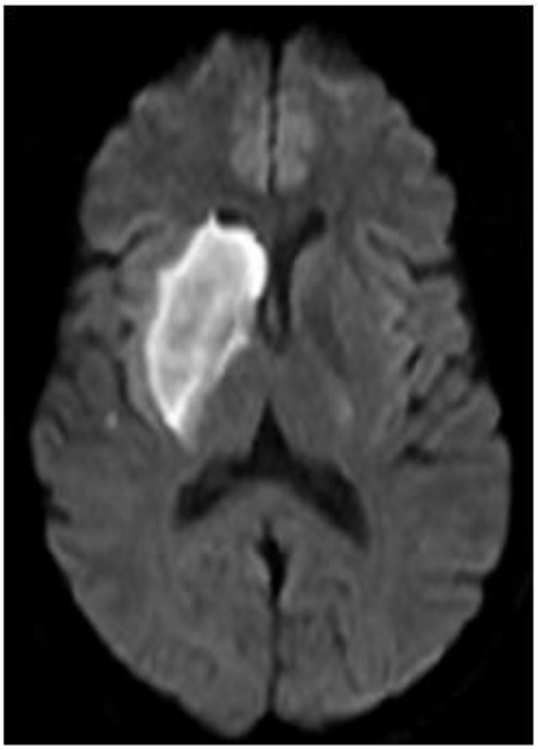


Fig A

Infarct: FA= 0.457, ADC= 0.731 Voxels= 2609
Normal: FA= 0.768, ADC= 0.766 Voxels= 4418
Ratios: rFA= 0.595, rADC= 0.954, rVoxels= 0.590

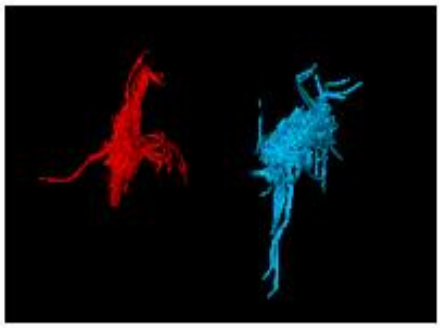


Fig B

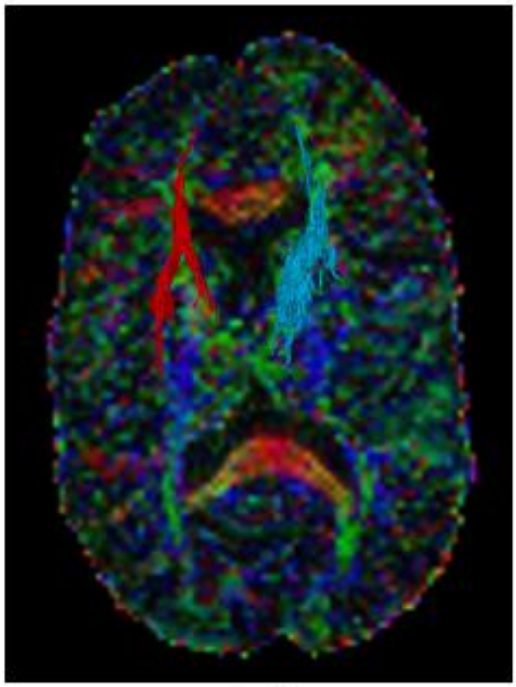


Fig C

Volume 6, Issue 2; March-April 2023; Page No 235-261

Fig 3A: DWI axial image shows hyperintensity in the right capsuloganglionic region.

Fig 3B and 3C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 54-year-old male presented with left-sided- weakness for a day.

MRI stroke protocol revealed a large acute infarct in the right capsuloganglionic region with FA value of 0.457, ADC of 0.731, and voxels of 2609.

NIHSS score was 22 (severe stroke).

Day 7

MRS score: 5 (severe disability)

Barthel score: 10 (total dependency)

Day 30

MRS score: 5 (severe disability)

Barthel score: 55 (severe dependency)

Day 90

MRS score: 3 (moderate disability)

Barthel score: 25 (severe dependency)

A large-sized infarct in the capsuloganglionic region showed reduced FA, ADC, and voxels. The patient had a severe stroke (according to NIHSS) with a baseline FA value of 0.457. By day 90, he had a moderate disability and severe dependency. On day 30, he showed severe disability and dependency, owing to the region of the infarct i.e. capsuloganglionic region, and the size of the infarct.

Case No 4

Volume 6, Issue 2; March-April 2023; Page No 235-261

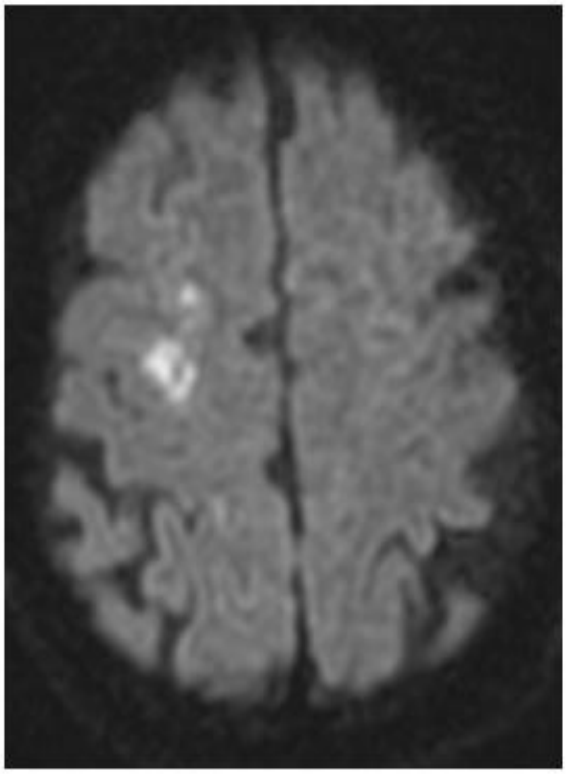


Fig A

Infarct: FA= 0.418, ADC= 0.665 Voxels= 949
Normal: FA= 0.694, ADC= 0.758 Voxels= 1588
Ratios: rFA= 0.602 , rADC= 0.877, rVoxels= 0.597

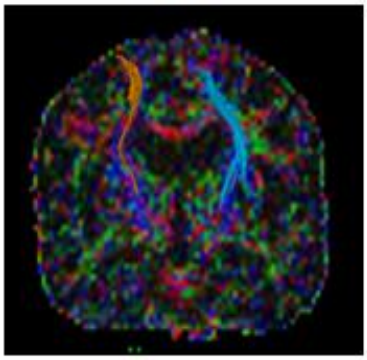


Fig B

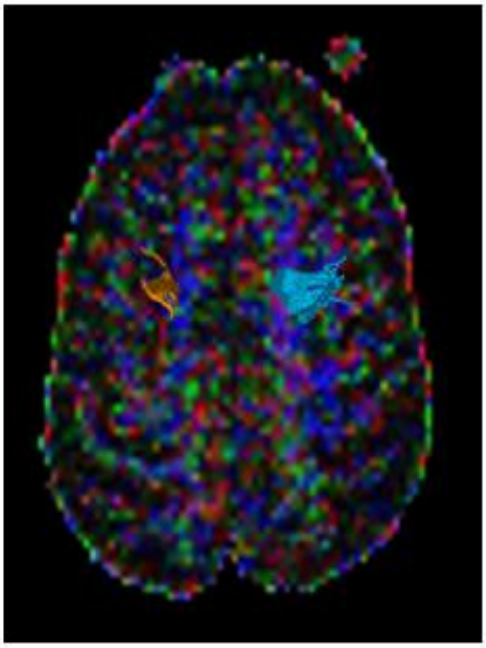


Fig C

Fig 4A: FLAIR axial image shows hyperintensity in the right frontal lobe.

Fig 4B and 4C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 71-year-old female presented with left-sided- weakness for 2 days.

MRI stroke protocol revealed a large acute infarct in the right supracapsular region with FA value of 0.418, ADC of 0.665, and voxels of 949.

NIHSS score was 6 (moderate stroke).

MRS score: 4 (moderate to severe disability)

Barthel score: 15 (total dependency)

Day 30

MRS score: 3 (moderate disability)

Barthel score: 70 (moderate dependency)

Day 90

MRS score: 1 (no disability)

Volume 6, Issue 2; March-April 2023; Page No 235-261

Barthel score: 95 (slight dependency)

A small-sized infarct in the supracapsular region showed reduced FA, ADC, and voxels. The patient had a moderate stroke (according to NIHSS) with a baseline FA value of 0.418. On day 30, he showed moderate disability and dependency, however, by day 90, he had no disability and slight dependency, owing to the region of infarct i.e. supracapsular region, and size of the infarct i.e. small size.

Case No 5

Fig A

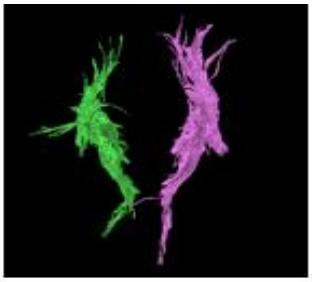


Fig B

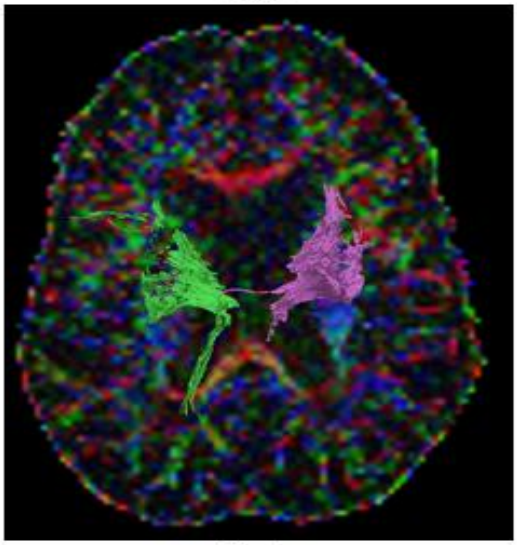


Fig C

Infarct: FA= 0.457, ADC= 0.731 Voxels= 2609
Normal: FA= 0.768, ADC= 0.766 Voxels= 4418
Ratios: rFA= 0.595, rADC= 0.954, rVoxels= 0.590

Fig 5A: FLAIR axial image shows hyperintensity in the right centrum semiovale, corona radiata.

Fig 5B and 5C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 50-year-old male presented with left-sided- weakness for 1 day.

MRI stroke protocol revealed moderate acute infarct in the right supracapsular region with FA value of 0.457, ADC of 0.731, and voxels of 2609.

NIHSS score was 13 (moderate stroke).

Day 7

MRS score: 4 (moderate to severe disability)

Barthel score: 10 (total dependency)

Day 30

MRS score: 3 (moderate disability)

Barthel score: 50 (severe dependency)

Day 90

Volume 6, Issue 2; March-April 2023; Page No 235-261

MRS score: 2 (slight disability)

Barthel score: 85 (moderate dependency)

A moderate sized infarct in the supracapsular region showed reduced FA, ADC, and voxels. The patient had a moderate stroke (according to NIHSS) with a baseline FA value of 0.457. On day 30, he showed moderate disability and severe dependency, however, by day 90, he had a slight disability and moderate dependency, owing to the region of infarct i.e. supracapsular region, and size of the infarct i.e. moderate size.

Case No 6

Fig A

Infarct: FA= 0.316, ADC= 0.678 Voxels= 2418
Normal: FA= 0.664, ADC= 0.842 Voxels= 3881
Ratios: rFA= 0.475, rADC= 0.805, rVoxels= 0.623

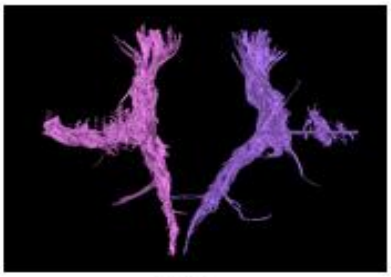


Fig B

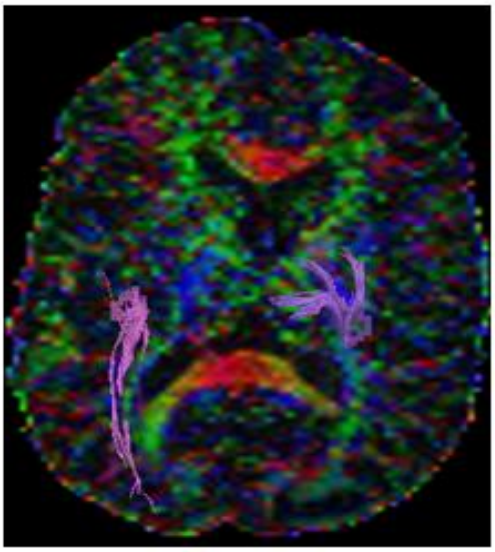


Fig C

Fig 6A: FLAIR axial image shows hyperintensity in the right frontotemporal lobe and insular cortex.

Fig 6B and 6C: ROI-based analysis of DTI metrics of the infarct and tracts (voxels).

A 64-year-old male presented with right-sided- weakness for 1 day.

MRI stroke protocol revealed a large acute infarct in the left supracapsular region with FA value of 0.316, ADC of 0.678, and voxels of 2418.

NIHSS score was 22 (severe stroke).

Day 7

MRS score: 5 (severe disability)

Barthel score: 10 (total dependency)

Day 30

MRS score: 4 (moderate to severe disability)

Volume 6, Issue 2; March-April 2023; Page No 235-261

Barthel score: 55 (severe dependency)

Day 90

MRS score: 2 (slight disability)

Barthel score: 85 (moderate dependency).

A large-sized infarct in the supracapsular region showed reduced FA, ADC, and voxels. The patient had a severe stroke (according to NIHSS) with a baseline FA value of 0.316. By day 90, he had a slight disability and moderate dependency. On day 30, he showed moderate to severe disability and severe dependency, owing to the region of the infarct i.e. supracapsular region, and size of the infarct i.e., large size.

Discussion

Cerebrovascular stroke is one of the leading causes of death worldwide. Imaging with conventional MR techniques cannot provide reliable information concerning the integrity of the white matter tracts and therefore limiting its ability to predict the clinical outcome. The role of imaging with conventional MRI and DWI is limited to the early diagnosis of the infarcted tissue, while diffusion tensor imaging has shown promising results in the evaluation of pathological microstructural changes in ischemic tissues and prediction of the clinical outcome.

Motor deficit on admission, infarct volume and location, and CST involvement are all proposed predictors of motor outcome. Although greater initial motor impairment indeed predicts poorer motor recovery, the relationship varies greatly between subjects, making accurate prognosis difficult.

Prediction of the motor outcome becomes more crucial for determining the specific rehabilitation strategies and final clinical outcomes. Diffusion tensor MR imaging in patients with acute ischemic stroke works as a prognostic imaging modality to predict the clinical outcome.

Our findings showed that both infarct size and location are important to predict motor recovery. Large infarct sizes do not necessarily predict poor outcome because it is related to critical motor areas in the brain.

DTI metrics FA and rFA have been proven to be predictors of motor outcome after stroke with cut-off values defined to predict moderate to severe disability and dependency at day 30 than day 90 in our study.

While NIHSS correlated with the severity of stroke initially, it does not predict the long-term disability and dependency of the patient.

Since we studied mostly patients with moderate stroke, only 9-12% of patients had moderate to severe dependency or disability by day 90, however, 50-61% of the patients had moderate to severe dependency or disability.

Not many studies have proved the predictive features of DTI fiber tractography in stroke in the past. We studied the number of fibers or voxels in the region of infarct which correlated with the severity of stroke at baseline (p-value <0.001).

Cut-off values of FA and rFA were also obtained with good sensitivity and specificity to predict poor outcome MRS $\geq$4 and Barthel score of $\leq$60 on day 30 i.e., FA cut-off value with a sensitivity of 90% and specificity of 92% is 0.356 and rFA cut off value with a sensitivity of 91% and specificity of 92% is 0.465.

Puig et all[13] in their study- Decrease corticospinal tract fractional anisotropy predicts long-term motor outcome after stroke- evaluated 70 patients with stroke to correlate rFA with the degree of motor deficit at 2 years comparing with the Motricity index which is classified as no deficit (score 100), slight to moderate (50-99) and severe (<50). The median FA value of infarct in Puig et all's study is 0.38 and our study is 0.36 and rFA is 0.59 and 0.51 respectively.

The motoricity index is a measure of limb strength to assess motor impairment after stroke. It includes measurement of arm, and leg movement and trunk control score. While the Modified Rankin score and Barthel score are measures of disability and dependency. Hence, rFA cut-off for severe deficit is

Volume 6, Issue 2; March-April 2023; Page No 235-261

lower in our study as we used MRS and Barthel index.

Thomalla et all[12] in their study- Diffusion tensor imaging detects early Wallerian degeneration of pyramidal tract after ischemic stroke- used DTI to assess Wallerian degeneration of corticospinal tract within 14 days after ischemic stroke and whether it correlated with NIHSS and Motoricity index at the time of MRI scan and at day 90.

Chunshui et all[23] in their study- A longitudinal diffusion tensor imaging study on Wallerian degeneration of corticospinal tract after motor pathway stroke- evaluated 9 patients with motor pathway subacute infarct using NIHSS and Motoricity index, radiologically and clinically at 5 different time points within 1 week, at 2 weeks, at 1 month, at 3 months and at 1 year. rFA of CST monotonously decreased during the first 3 months and then relatively remained unchanged. Therefore, Chunshui et all[23] found that changes in rFA within the first two weeks correlated with clinical (NIHSS) and motor (MI) outcome after 1 year. Moreover, other stroke measures like rMD, rλ1, and rλ23 of CST at any time and rFA at other times did not correlate with clinical scales after 1 year.

In our study, however, we radiologically assessed the patients at one time i.e., between days 2-10 of stroke, and correlated with disability and dependency indices at days 7, 30, and 90.

DTI metrics, FA, and rFA in our study showed weak positive correlation at different times. This predictive ability may contribute to determining optimal strategies for stroke treatment and rehabilitation at the early post-stroke stage. Further, it has also been studied by Polders et all, that average FA in high field strength magnets like 3T and 7T machines remained relatively constant.

Limitations

1. Follow-up DTI imaging at 3 months and 6 months to study the trend of FA during the course of Wallerian degeneration was not done.
2. 30-day and 90-day follow-ups of MRS and Barthel scores were obtained by telephonic conversation.
3. The number of patients receiving rehabilitation facilities which could be one of the confounding factors was not documented or assessed in our study.
4. Further, higher field strength MRI machine (3T), would provide a better signal-to-noise ratio.

Declarations

This study was not funded.

Ethical approval: Obtained. IEC (IEC 737/2019). Informed consent was taken from every patient.

CTRI registration: Obtained on 17/12/2019 (CTRI Number CTRI/2019/12/022404).

Conclusions

1. NIHSS is a well-known clinical indicator to classify the severity of stroke. However, not a good predictor of long-term motor outcome.
2. FA, ADC, and voxels of the infarct and their ratios with the normal contralateral side, were reduced.
3. The number of fibers/ voxels and rVoxels positively correlated with NIHSS score (statistically significant), thus associating to severity of stroke at presentation. However, no specific cut-off value with good sensitivity and specificity could be derived which predicted the motor outcome of the patient.
4. Location and size of the infarct along the corticospinal tract also affected the motor outcome of patients i.e., patients with small infarct in the internal capsule had a poor motor outcome.
5. DTI metrics- FA and rFA is a surrogate marker to predict long-term motor outcome in stroke patients.

List Of Abbreviations

CST- corticospinal tract

PLIC- posterior limb of internal capsule

DTI- Diffusion Tensor Imaging

MRI- Magnetic resonance imaging

FA- Functional anisotropy

rFA- ratio of functional anisotropy

ADC- apparent diffusion coefficient

rADC- ratio of apparent diffusion coefficient

Volume 6, Issue 2; March-April 2023; Page No 235-261

rVoxels- ratio of voxels

rMD- ratio of mean diffusivity

Dav- average mean diffusivity

NIHSS- National Institutes of health stroke scale

MRS- Modified Rankin score

ROI- Region of Interest

References

1. Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke: outcome assessment and sample size requirements. Stroke 1992;23:1084–1089.

2. Coupar F, Pollock A, Rowe P, Weir C, Langhorne P. Predictors of upper limb recovery after stroke: a systematic review and meta-analysis. Clin Rehabil. 2012; 26:291–313.

3. Hendricks HT, van Limbeek J, Geurts AC, Zwarts MJ. Motor recovery after stroke: a systematic review of the literature. Arch Phys Med Rehabil 2002; 83:1629–1637.

4. Prabhakaran S, Zarahn E, Riley C, Speizer A, Chong JY, Lazar RM, Marshall RS, Krakauer JW. Inter-individual variability in the capacity for motor recovery after ischemic stroke. Neurorehabil Neural Repair 2008; 22:64–71.

5. Schiemanck SK, Kwakkel G, Post MW, Kappelle LJ, Prevo AJ. Impact of internal capsule lesions on outcome of motor hand function at one year post-stroke. J Rehabil Med 2008; 40:96–101.

6. Nelles M, Gieseke J, Flacke S, et al. Diffusion tensor pyramidal tractography in patients with anterior choroidal artery infarcts. AJNR Am J Neuroradiol 2008; 29:488–493.

7. Nelles M, Gieseke J, Flacke S, et al. Diffusion tensor pyramidal tractography in patients with anterior choroidal artery infarcts. AJNR Am J Neuroradiol 2008; 29:488–493.

8. Jang SH, Bai D, Son SM, et al. Motor outcome prediction using diffusion tensor tractography in pontine infarct. Ann Neurol 2008; 64:460–465.

9. Cho SH, Kim DG, Kim DS, et al. Motor outcome according to the integrity of the corticospinal tract determined by diffusion tensor tractography in the early stage of corona radiata infarct. Neurosci Lett 2007; 426:123–127.

10. Konishi J, Yamada K, Kizu O, et al. MR tractography for the evaluation of functional recovery from lenticulostriate infarcts. Neurology 2005; 64:108–113.

11. Lee JS, Han MK, Kim SH, et al. Fiber tracking by diffusion tensor imaging in corticospinal tract stroke: Topographical correlation with clinical symptoms. Neuroimage 2005; 26:771–76

12. Thomalla G, Glauche V, Weiller C, et al. Time course of Wallerian degeneration after ischaemic stroke revealed by diffusion tensor imaging. J Neurol Neurosurg Psychiatry 2005; 76:266–68

13. Puig J, Blasco G, Schlaug G, Stinear CM, Daunis-I-Estadella P, Biarnes C, Figueras J, Serena J, Hernández-Pérez M, Alberich-Bayarri A, Castellanos M, Liebeskind DS, Demchuk AM, Menon BK, Thomalla G, Nael K, Wintermark M, Pedraza S. Diffusion tensor imaging as a prognostic biomarker for motor recovery and rehabilitation after stroke. Neuroradiology. 2017 Apr;59(4):343-351. doi: 10.1007/s00234-017-1816-0. Epub 2017 Mar 14. PMID: 28293701.

14. Nucifora PG, Verma R, Lee SK, et al. Diffusion-tensor MR imaging and tractography: exploring brain microstructure and connectivity. Radiology 2007; 245:367-384

15. Chung HW, Chou MC, Chen CY. Principles and limitations of computational algorithms in clinical diffusion tensor MR tractography. AJNR Am J Neuroradiol 2011; 32:3-13.

16. Møller M, Frandsen J, Andersen G, et al. Dynamic changes in corticospinal tracts after stroke detected by fiber tracking. J Neurol Neurosurg Psychiatry 2007; 78:587–92. 35.

17. Ludeman NA, Berman JI, Wu YW, et al. Diffusion tensor imaging of the corticospinal tracts in infants with motor dysfunction. Neurology 2008; 71: 1676–1682.

18. Liang Z, Zeng J, Zhang C, et al. Longitudinal investigations on the anterograde and retrograde degeneration in the corticospinal tract following

Volume 6, Issue 2; March-April 2023; Page No 235-261

pontine infarction with diffusion tensor imaging. Cerebrovasc Dis 2008; 25:209–216.

19. Khong PL, Zhou LJ, Ooi GC, et al. The evaluation of Wallerian degeneration in chronic pediatric middle cerebral artery infarction using diffusion tensor MR imaging. Cerebrovasc Dis 2004;18:240–247.

20. Liang Z, Zeng J, Liu S, et al. A prospective study of secondary degeneration following subcortical infarction using diffusion tensor imaging. J Neurol Neurosurg Psychiatry 2007; 78:581–586.

21. Watanabe T, Honda Y, Fujii Y, et al. Three-dimensional anisotropy contrast resonance axonography to predict the prognosis for motor function in patients suffering from stroke. J Neurosurg 2001; 94:955–960.

22. Puig J, Pedraza S, Blasco G, Daunis-I-Estadella J, Prados F, Remollo S, Prats-Galino A, Soria G, Boada I, Castellanos M, Serena J. Acute damage to the posterior limb of the internal capsule on diffusion tensor tractography as an early imaging predictor of motor outcome after stroke. AJNR Am J Neuroradiol. 2011; 32:857-863.

23. Yu C, Zhu C, Zhang Y, Chen H, Qin W, Wang M, Li K. A longitudinal diffusion tensor imaging study on Wallerian degeneration of corticospinal tract after motor pathway stroke. Neuroimage. 2009 Aug 15;47(2):451-8. doi: 10.1016/j.neuroimage.2009.04.066. Epub 2009 May 3. PMID: 19409500.

Volume 6, Issue 2; March-April 2023; Page No 235-261