The Egyptian Journal of Hospital Medicine (October 2021) Vol. 85 (1), Page 3284-3290

Diffusion Tensor Imaging (DTI) and Fractional Anisotropy (FA) for Arcuate Fasciculus in Predicting Post-Stroke Aphasia Outcome

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ABSTRACT
Background: In certain regions of the brain, aphasia arises from a lack of understanding and regulating language following damage. About 35–40 percent of the people receiving hospitalization after stroke are identified with aphasia. The recently developed imaging methods for the analysis of the impact of brain lesion sites and sizes on aphasia are the Diffusion Tensor Imaging (DTI) and Fractional Anisotropy (FA). In order to reflect micro-structural integrity DTI may give data on the damage level of the white matter of the brain and subcortical neural structure.
Objective: We examined the relationship between arcuate fasciculus (AF) and the prognosis of aphasia outcome after ischemic stroke utilizing DTI, and FA.
Patients and Methods: In this study, which included 34 patients with post stroke aphasia, we investigated DTI and FA of arcuate fasciculus in predicting post-stroke aphasia outcome.
Results: There was no significant association between the sex and Aphasia Handicap Scale (AHS) ($P>0.05$), while the age was significantly correlate with AHS ($P<0.05$). The vascular risk factors (hypertension, diabetes mellitus, smoking, dyslipidemia) were associated with poor aphasia outcome. In our study, we found that lesion size had significant effect on aphasia outcome. Also, the site of ischemic infarction site was important factor in determining aphasia outcome. In the Broca and Wernicke regions, AHS was greater than in the cortical injury, and in the insula and cortical injuries (1.92 ± 1.26) were the least common in patients.
Conclusion: The site and the size of ischemic infarction significantly predicted s aphasia outcome, also the extent and mechanism of AF injury, which can be detected in DTI and FA, stood as a significant indicator on aphasia severity for patients with ischemic stroke.
Keywords: AF, AHS, Aphasia, DTI, FA, Stroke.

INTRODUCTION
The most frequent debilitating effects of stroke were aphasia. At the beginning of the stroke, it is impossible to anticipate which patient exhibit significant language recovery and who have limited recovery or perhaps lifelong impairment [(1)]. In adults, aphasia which occurs as a result of stroke, represents 20% to 40% of symptoms in patients with acute stroke symptoms. Injury-relative variables such as the location, the lesion size and aphasia type may affect aphasia. Recovery may be affected by various variables such as age, sex, manhood and environment [(2)].

Many studies have shown a significant link between the location of a lesion in the arcuate fasciculus (AF), the integrity of right hemisphere white matter pathways, and the result of identifying and speech fluency in post stroke aphasia [(3)]. Newly developed methods such as diffusion tensor imaging (DTI), voxel-based lesion symptom mapping, and functional magnetic resonance imaging (MRI) have been utilized to investigate the impact of brain lesion sites and sizes on aphasia. DTI may offer useful information about the extent of injury and white matter structure by using water molecules diffusion inside the tissue to create pictures. By analyzing DT pictures, you may get several values like fractional anisotropy (FA), axial diffusivity, radial diffusivity, and mean diffusivity. It is now feasible to see white matter bundles via analytical tools. Because it represents microstructural integrity, FA is now one of the best indicators for assessing subcortical brain structures [(4)]. The AF is one of the most significant bundles of subcortical neurons involved in language function; it also connects the Broca and Wernicke regions of the brain. Many investigations have been conducted to compare the clinical characteristics of aphasia with AF damage [(5)].

DTI studies have shown variations in the asymmetry of fibre counts in AF of patients suffering ischemic stroke with and without aphasia. Patients who did not exhibit a left AF in DT tractography six months after their strokes suffered severer aphasia more than other patients [(6)]. The aim of this study was to examine the relationship between AF and the prognosis of aphasia outcome after ischemic stroke utilizing DTI, and FA.

PATIENTS AND METHODS
This was a cohort prospective study included 34 patients during a 12-month period.

Inclusion criteria: Patients presented with acute ischemic stroke (diagnosed by brain MRI or computed tomography (CT), aged less than 80 years. Their native language was Arabic.

The exclusion criteria consisted of patients with lesion did not affect AF like brainstem or cerebellar lesion, patients with traumatic brain lesions, a previous history of other neurological, psychiatric, or speech disorders which affected the language task.

All included patients were subjected to the following, history taking including the personal history and

Received: 3 /6 /2021
Accepted: 1 /8 /2021

comorbid conditions, full neurological and general clinical examinations.

Radiological imaging:

MRI: The size of the initial ischemic stroke lesion and its brain site were determined and assessed using MRI (GE, Sigma closed magnet, USA) mainly FLAIR and Diffusion weighted images using head coil.

DTI:

DTI was used in three-dimensional tracking reconstruction and detection of the path of the AF fiber track. DTI was performed approximately 26.66 ± 13.01 days after stroke onset.

***DTI MR Acquisition and Directional Mapping:**

Diffusion tensor MR images (DTI MRI) acquisition parameters were: single shot echo planar sequence of (4500/71.8/4 [TR/TE/excitations], field of view was 224 mm × 240 mm with slice sections of 2 mm of and only 2 slabs, each slap contain 20 sections, matrix was 128 ×128 zero filled to 256×256, the size of voxel 1.87×1.873.0 mm interpolated to 0.94 and flip angle, 90°.

The fibre tracking method was based on the fibre assignment by continuous tracking (FACT) technique, which used a fractional anisotropy threshold equivalent to 0.22 and a 60-degree angle threshold.

Two expert raters evaluated the reproducibility of the fibre structure in both hemispheres on all participants. Each fibre tract was obtained using two ROIs, and the fibres running through both ROIs were combined using a "AND" operation.

On all five patients, T1 weighted volumes were then co-registered with DTI-derived maps, allowing for a more accurate characterization of anatomic landmarks for ROI placement using FA-modulated or colour coded principal eigenvector maps.

Following the reconstruction of a fibre tract, the whole trajectory was checked slice by slice for conformity with anatomical biomarkers based upon an atlas of anatomy[7].

Outcome assessment:

Two weeks after stroke, Aphasia Handicap Scale (AHS), was used to assess aphasia. It is a modified scoring system of Rankin, which consists of 6 points that was used for handicap in vertebral communication[8].

Scale description:

0: was normal language.

1: Indicated slight language difficulties but without dysfunction (no effect on ordinary life).

2: Mild disability related to language (deprived of limitation in the autonomy of skills of daily verbal communication).

3: Moderate disability with limited verbal communication.

4: Advanced language-related disability.

5: Complete mutism.

Ethical consent:

An approval of the study was obtained from Tanta University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of sharing in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Demographic and clinical characteristics of included patients:

Thirty-four patients with post-stroke aphasia were included in this study, two weeks after ischemic stroke, They underwent language evaluations and evaluated during this study. Their age ranged from 35 to 79 years and the mean age was 55.45 ± 12.16 years. Majority of patients (53%) were males. Thirty-one patients were educated and 3 patients were illiterate. There was no significant association between the sex and AHS, while the age was significantly correlate with AHS. The vascular risk factors (hypertension, diabetes mellitus, smoking, dyslipidemia) were associated with poor aphasia outcome (table 1).

Table (1): Cerebrovascular risk factors in 34 patients with ischemic infarction and relation to Aphasia Handicap Scale (AHS)

	AHS												X^2	P-value
	Normal (n = 10)		1 (n = 12)		2 (n = 8)		3 (n = 18)		4 (n = 12)		5 (n = 8)			
	N	%	N	%	N	%	N	%	N	%	N	%		
Hypertension	0	0.00	0	0.00	2	25.00	2	11.11	12	100	4	66.67	46.474	**<0.001***
DM	0	0.00	0	0.00	0	0.00	10	55.56	12	100	6	100.00	49.973	**<0.001***
Smoking	0	0.00	0	0.00	0	0.00	10	55.56	12	100	4	66.67	44.146	**<0.001***
Cardiac	2	20.00	2	16.67	0	0.00	8	44.44	10	71.43	4	66.67	18.027	**0.003***
Dyslipidemia	0	0.00	0	0.00	2	25.00	8	44.44	12	83.33	6	100.00	43.483	**<0.001***

DM: diabetes mellitus *: significant difference.

Relation between size of ischemic infarction and AHS:

In our study, we found that size of ischemic infarction had significant effect on aphasia outcome, complete middle cerebral artery (MCA) infarction had significant poor outcome in 3 patients (75%) who showed aphasia handicap score of 5 (4.28± 0.48) while score 5 was detected only in 1 patient (25%) with partial infarction (2.23± 1.41) and can't be detected in patient with lacunar infarction (1.50 ±1.04), $P < 0.001$) (Table 2, Figure1).

Table (2): Size of brain lesion and relation to Aphasia Handicap Scale (AHS)

Lesion size	AHS											
	Normal (n = 10)		1 (n = 12)		2 (n = 8)		3 (n = 18)		4 (n = 12)		5 (n = 8)	
	N	%	N	%	N	%	N	%	N	%	N	%
Partial (n = 38)	6	15.79	8	21.05	4	10.53	16	42.11	2	5.26	2	5.26
Complete (n = 16)	0	0	0	0	0	0	0	0	10	62.5	6	37.5
Lacunar (n = 14)	4	28.57	4	28.57	4	28.57	2	14.28	0	0	0	0

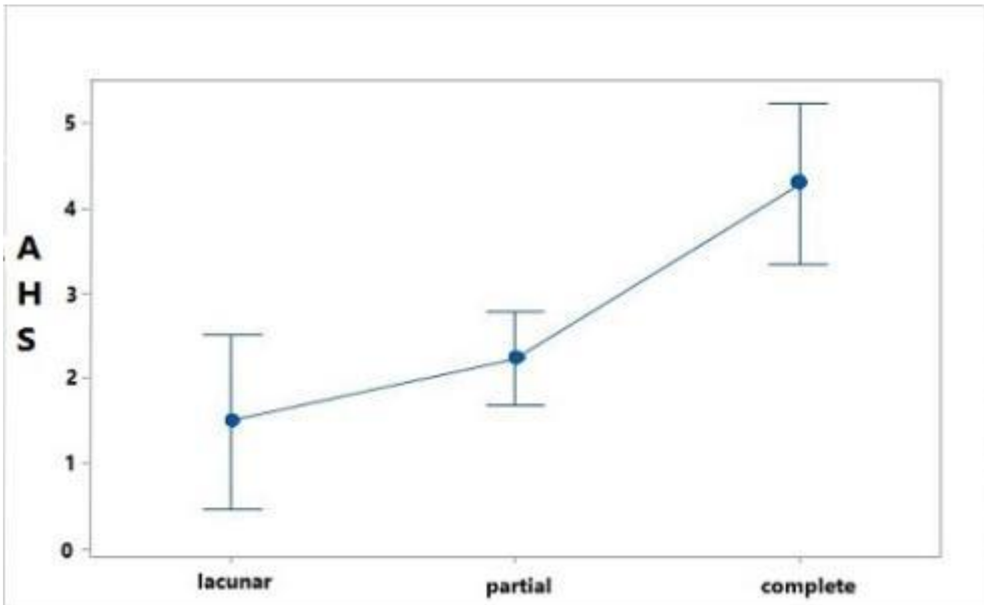

Figure (1): Relation between the size of infarction and AHS

Relation between site of ischemic infarction and AHS:

In this study, lesion site was important factor in determining aphasia outcome. AHS was severer in patients suffering subcortical and perisylvian lesions (4.00 ± 1.00) and in those suffering cortical lesions in the areas of Broca's and Wernicke (3.00± 0.70) and were the least in patients with insula (1.92 ± 1.26) and cortical lesions not detected in the areas of Broca or Wernicke (2.00 ± 1.85), (Figure 2).

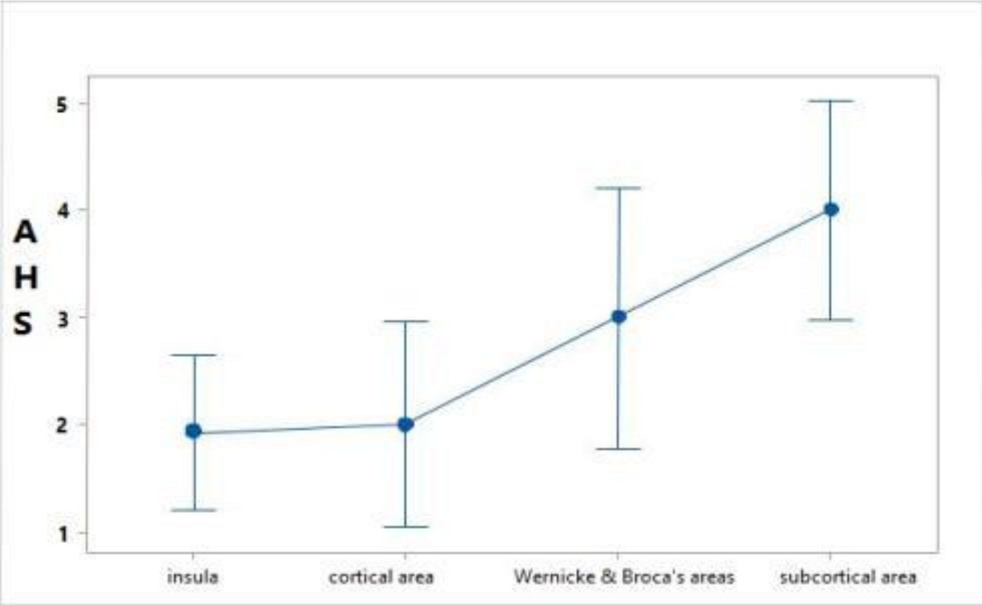

Figure (2): Relation between the site of infarction and AHS

Relation between reconstruction of AF and AHS:

In DTI, patients who showed evidence of reconstruction of the AF fiber had better aphasia outcome (1.07 ± 0.91) than those with no reconstruction (3.55 ± 0.88) (Figures 3).

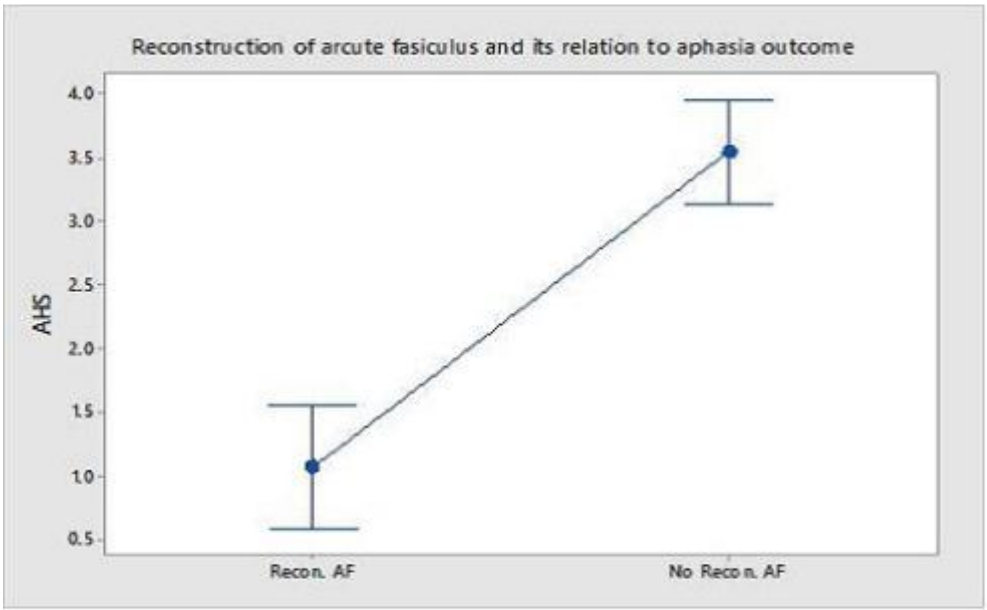

Figure (3): Relation between AF reconstruction and AHS

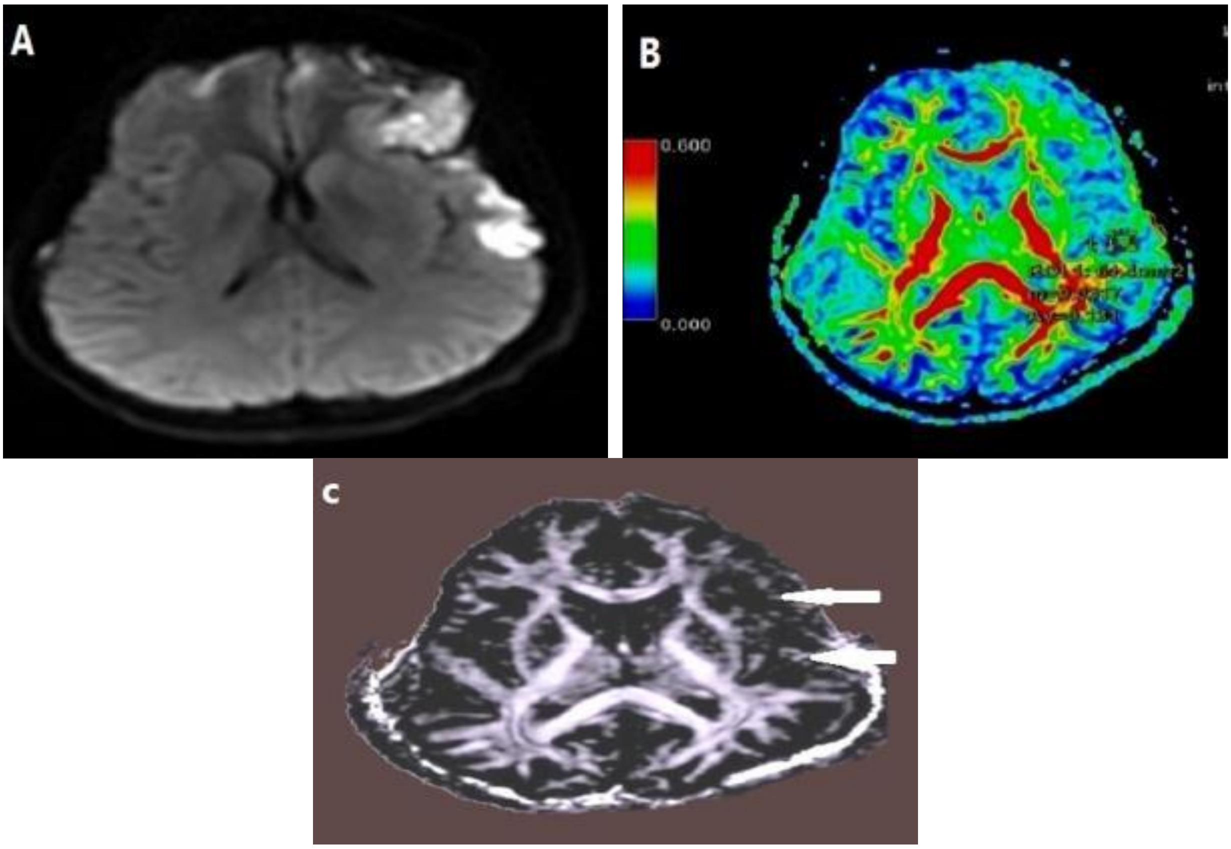

Figure (4): A male patient aged 57 years, there was a medical history of hypertension and diabetes, the patient was presented with right side weakness and aphasia. (A) and (B) large infarction lesion was seen in the left Broca's area, area of restricted diffusion in (DWI) and color ADC map. (C) Fractional anisotropy (FA) map showed: disruption of the left FA fibers (Left arrows) in comparison to right side, this patient had AHS of 3.55.

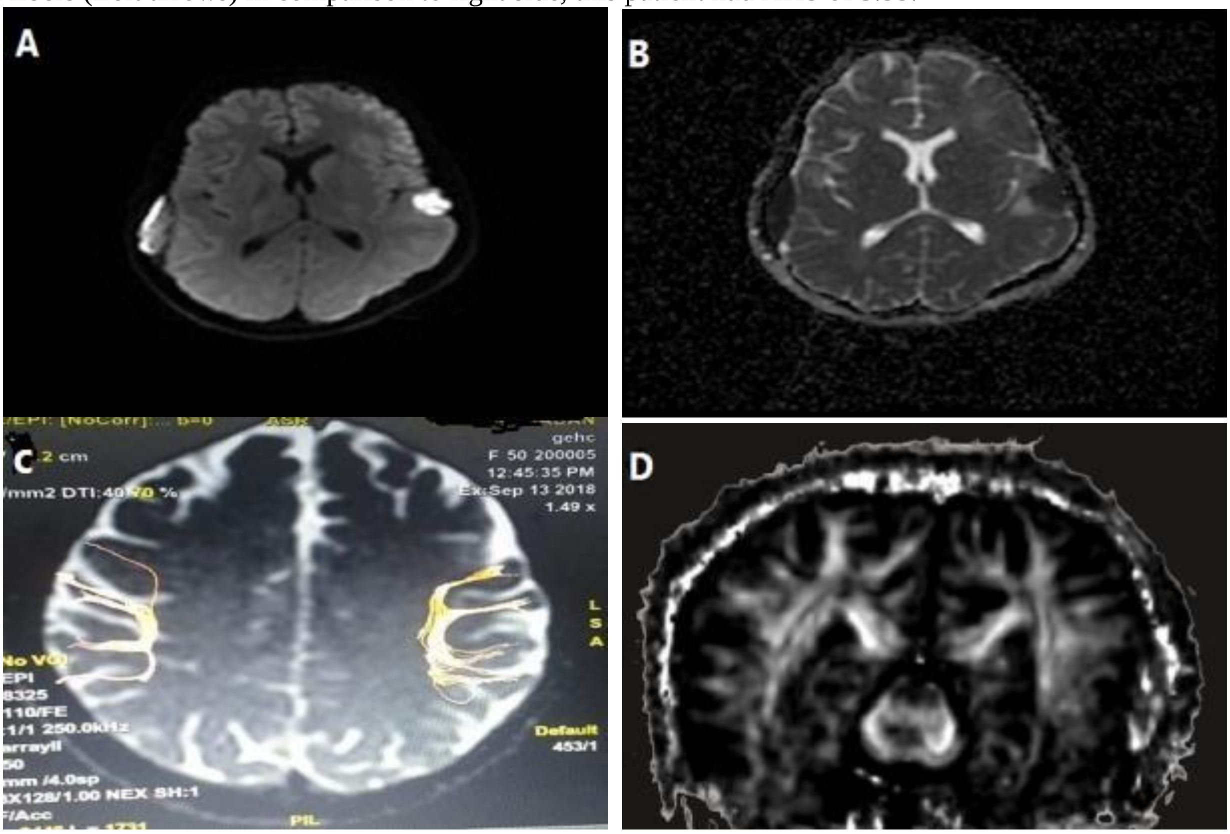

Figure (5): Female patient aged 50 years, there was no medical history of hypertension or diabetes, the patient was presented with global aphasia. (A) and (B) DWI and ADC map showed: Bilateral cortical areas of recent infarction were seen in parietal regions. (C) Diffusion tensor tractography showed: reconstruction of the FA fibers in both sides. (D) Fractional anisotropy (FA) map showed: reconstruction of the FA fibers in both sides, this patient had AHS of 1.92.

DISCUSSION

Aphasia means impairment of comprehension or speech task, verbal communication skills as well as the capacity to read or write due to cerebral damage. Aphasia due to cerebral stroke is the most common type of aphasia [(9)].

The use of both methods of structural and functional neuroimaging on post-stroke patients has aided in a better understanding of the anatomical and metabolic variables that influence aphasia rehabilitation. The (FA) fraction anisotropy is a perfect frequently utilized DTI measures for assessing the degree of AF damage and diagnosing aphasia [(10)]. A mixture of lesion area, severity of initial aphasia, as well as age, and FA of long segment of right AF are good predictors of language improvement after stroke[(11)].

This study investigated DTI and tractography of AF in predicting post-stroke aphasia outcome in the period of time of the first 2 weeks post ischemic stroke onset.

In the present study, our findings were that lesion size had significant effect on aphasia outcome, complete MCA infarction had significant poor outcome in 3 patients (75%) who showed aphasia handicap score of 5 (4.28± 0.48), while score 5 was detected only in 1 patient (25%) with partial infarction (2.23± 1.41) and can't be detected in patient with lacunar infarction (1.50 ±1.04). **Bahrainwala *et al.*** [(12)] in their study, which included a sequence of 206 patients with acute ischemic right-hemispheric stroke, they considered lesion size to be an important predictor of recovery and partial or lacunar infarction had better prognosis regarding aphasia outcome.

Lesions in the superior temporal gyrus (STG); that mostly occur in large infarctions and perisylvian area result in a severer global aphasia that's linked to weak aphasia recovery. According to other research, cortical lesions cause more severe aphasia than subcortical lesions, while subcortically situated aphasias have a better prognosis [(13)]. In a sample of 102 patients suffering ischemic stroke in addition to chronic aphasia, **Henseler *et al.*** [(14)] linked patholinguistic profiles of aphasic patients to matching lesion locations, and they proposed a new classification of aphasia based on the location of the brain lesion. Another research found that patients with subcortical brain lesions had higher AQ scores than those with cortical lesions affecting the Broca and Wernicke regions, and that patients suffering insular and cortical lesions away from the areas of Broca or Wernicke had the lowest AQ scores [(15)].

In the current research, lesion site was important factor in determining aphasia outcome, AHS were severer for patients suffering subcortical and perisylvian lesions (4.00 ± 1.00) and in subjects suffering cortical lesions in the areas of Broca's and Wernicke (3.00 ± 0.70) and were the least in patients with insula (1.92 ± 1.26) and cortical lesions not detected in the Broca or Wernicke areas (2.00 ± 1.85). Patients with stroke whose left arcuate fasciculus (AF) could not be rebuilt owing to significant damage had a poorer prognosis; patients suffering stroke whose left AF could be reconstructed, regardless of the left AF's integrity, had a better prognosis, which was totally going with this study as all the patients who had reconstruction of the AF had better prognosis while those who didn't, had the worst prognosis. This explains the importance of the DTI in delineating the language tracts on the acute stage of ischemic stroke hence it can predict aphasia outcome [(16)].

Lee *et al.* [(17)] in their study, which included 68 post stroke patients who underwent language evaluations, they concluded that FA was significantly correlated with the outcome of aphasia 2 weeks post hemorrhagic stroke. They claimed that both ischemic and hemorrhagic strokes had different degrees and mechanisms of AF damage. These variations may have a role in the severity of aphasia.

CONCLUSION

Aphasia outcome is affected by patient linked factors like age, vascular risk factors (hypertension, diabetes mellitus, smoking, dyslipidemia) and lesion connected factors like area and position. In fact, the size and site of ischemic infarction significantly predicted s aphasia outcome, also the extent and mechanism of AF injury, which can be detected in DTI and FA was a significant indicator on aphasia severity for patients with ischemic stroke.

Sponsors and funding sources: Nil
Conflict of interests: Nil
Acknowledgement: Nil

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