Prediction of The Functional Outcome in A Group of Egyptian Patients with Posterior Circulation Stroke

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ABSTRACT

Background: Stroke is the third most common cause of disability and second most common cause of death worldwide. Brainstem is involved in almost all the important functions of the central nervous system, and brainstem infarction is relatively dangerous with high mortality. Early prediction of the severity and degree of disability and identification of high-risk patients are critical for the treatment of patients with brain stem infarction and might contribute to reduce death rates and comorbidities after stroke.

Objective: To assess the usefulness of Posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) for predicting functional outcome in posterior circulation stroke patients.

Subjects and Methods: A cohort study on 61 patients with first-ever acute ischemic stroke who were admitted within 24 h from onset. **Results:** We observed a statistically significant correlation between poor outcome and high NIHSS score on initial assessment, as well as low pc-ASPECTS score, in contrast to other factors involved in the study such as, age, sex, hypertension, atrial fibrillation, diabetes mellitus, high lipid profile, smoking, time from onset to presentation, ESR, initial blood glucose measurement, HbA1C, leukoaraiosis, silent infarction or type of stroke. **Conclusion:** both the pc-ASPECTS and NIHSS help clinicians predict functional outcomes. The pc-ASPECTS is more reliable than the NIHSS in minor stroke prediction. Moreover, the combination of the pc-ASPECTS and NIHSS has an additive effect in predicting the functional outcomes of patients with posterior circulation stroke.

Keywords: Posterior Circulation, Stroke, pc-ASPECTS, Outcome.

INTRODUCTION

Stroke can be classified into 2 major categories: ischemic (80%-85%) and hemorrhagic (15%-20%) [(1)]. Of the ischemic strokes, 25% involve the posterior circulation ischemic infarcts (POCI), and of these 60% and 40% occur in the brainstem and cerebellum, respectively [(2)].

Medullary infarctions account for 7% of all ischemic brainstem strokes and are 3:1 male predominance. Lateral Medullary infarctions are 3-4 times more common than medial medullary infarctions. Isolated pontine strokes are relatively frequent, but they can occur as part of a larger infarction in the posterior circulation. Atherosclerotic disease of perforating arteries and occlusion or stenosis of the basilar artery (BA) are the most common causes of pontine infarct. Infarcts of midbrain are usually accompanied by involvement of other structures -such as the cerebellum, thalamus, and pons- due to its complex blood supply [(3, 4)].

Risk factors associated with brainstem stroke include hypertension, diabetes mellitus, cardiac disease, hyperlipidemia, smoking, obesity, and use of oral contraceptives [(5)]. Prediction of acute ischemic stroke outcome is essential for treatment planning, guidance of patient and relatives, and in the search for new therapeutic strategies. Multiple studies have identified many important factors helpful for predicting outcome, even within the early period after onset of ischemic stroke. Among them, stroke severity and age have been regarded as the most powerful indicator [(6)]. Following the development of diffusion-weighted MRI (DWI), regional extent on DWI has been studied as another predictor of functional outcome, although the results remain controversial. Previous examinations have focused on anterior circulation infarction (AC) with few studies examining DWI data and functional outcome in posterior circulation infarction (PC). Because the anatomical architecture of the posterior circulation has a high density of motor and sensory pathways and nuclei compared to the supratentorial hemisphere, lesion location rather than lesion volume may be critical for functional outcome in PC [(7)].

The Alberta Stroke Program Early CT Score (ASPECTS) is a 10-point scoring system of middle cerebral artery (MCA) early ischemic change in which a score of 10 indicates normal CT and a score of 0 indicates diffuse ischemia throughout the MCA territory. ASPECTS has advantages over methods that assess lesion volume alone because lesion volume is only weakly correlated with neurological outcome. ASPECTS has been shown to be reproducible at varying levels of observer expertise and to enable prediction of functional outcome and symptomatic intracerebral hemorrhage after thrombolysis [(8)].

DWI ASPECTS also has been used as a reliable marker of functional outcome in patients with AC who received t-PA therapy. **Puetz *et al.*** [(9)] proposed a new grading system for posterior circulation ischemia: posterior circulation ASPECTS (pc-ASPECTS). Pc-ASPECTS utilizes a 10-point scoring system to assess

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ischemic lesions in the posterior circulation. **Tei *et al.*** [10] applied DWI to this scoring system by subtracting 1 point for each high-intensity lesion observed in the left or right thalamus, cerebellum, or posterior cerebral artery on DWI, and 2 points for each high-intensity lesion observed in any part of the midbrain or pons. A pc-ASPECTS score of 10 indicates the absence of visible posterior circulation ischemia, while a score of 0 indicates ischemic lesions in all pc-ASPECTS territories [11].

AIM OF THE WORK

To assess the usefulness of Posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) for predicting functional outcome in posterior circulation stroke patients.

SUBJECTS AND METHODS

The study was conducted on 61 patients with first-ever acute ischemic stroke who were admitted within 24 h from onset to the Stroke Units of the Department of Neurology, Al-Azhar University Hospitals (Al-Hussein and Sayed Galal Hospitals) over a period of 11 months starting from February 2018 to January 2019.

Inclusion criteria: first-ever acute stroke symptoms within 24 h from onset; symptoms persisted at admission and MRI (including DWI) confirmed an acute ischemic lesion in the posterior circulation.

Exclusion criteria: previous modified Rankin Scale score (mRS) ≥ 2; ineligibility for MRI; and patients with isolated medullary infarction. (Because pc-ASPECTS does not cover this region).

Ethical consideration and Written informed consent: An approval of the study was obtained from Al-Azhar University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the procedure.

Methods:

All patients were subjected to: *A- Cranial CT (within 24 h after onset) and MRI studies on admission (from 1–5 days after onset).* MR images were obtained on a 1.5-T system. The MRI protocol included DW and fluid attenuated inversion recovery (FLAIR) imaging.

A single neurologist read each patient's CT and MRI and assessed ASPECTS on DWI according to the method described by **Puetz *et al.*** [9] (pc-ASPECTS). Pc-ASPECTS was scored by DWI obtained 12–120 h after stroke onset to avoid false-negative DWI findings that may occur within 12 h after stroke onset in the PC group. Pc-ASPECTS of 10-8 were classified as favorable outcome group (F) and pc-ASPECTS of 7-0 were classified as unfavorable outcome group (U). The following variables were collected for all patients:

- Background characteristics [age, gender, time from onset]
- National Institutes of Health Stroke Scale score (NIHSS) on admission
- Vital signs on admission (Pulse, blood pressure, respiratory rate, body temperature)
- Risk factors [hypertension (previous use of antihypertensive agents or blood pressure of 160/90 mmHg at least twice before stroke onset), diabetes mellitus (use of insulin or oral hypoglycemic agents, fasting blood glucose C140 mg/dL, or random blood glucose C200 mg/dL), current cigarette smoking, transient ischemic attack].
- Laboratory data (ESR, CBC, ALT, AST, Albumin, Bilirubin, Creatinine, Urea, TG, Cholesterol)
- Each patient was examined daily by the same neurologist and early neurological deterioration (END) was defined as an increase of C1 point in the mRS between admission and after 72 h.
- Functional outcome was assessed at 2 weeks intervals with final assessment at 3 months using mRS; favorable outcome was defined as an mRS score of 0–2, and unfavorable as 3–6 (6 = dead).

Pc-ASPECTS, and other data were collected, served as the independent variables, while mRS served as the dependent variable of functional outcomes.

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, unpaired t-test and chi-square. Significant results were considered if *p*-value was <0.05. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 11.

RESULTS

From February 1, 2018, to December 31, 2018, 65 patients fulfilled the diagnostic criteria for posterior circulation acute ischemic infarction. Four patients were excluded because they did not complete brain MRI. Of these 61 patients, 17 (27.87%) had a favorable outcome with an mRS score of 0–2 and 44 (72.13%) had an unfavorable outcome with an mRS score of 3–6. The average NIHSS and mRS scores were, respectively, 10.7 ± 4.5 and 3.9 ± 1.0 in the unfavorable outcome group and 5 ± 1.2 and 1.2 ± 0.9 in the favorable outcome group.

Descriptive analysis of the studied patients:

Table (1): **Gender**

Gender		
	N	**%**
Male	36	59.02
Female	25	40.98
Total	61	100.00

Table (2): **Age**

Age	**Mean**	**±**	**SD**
	59.393	±	13.581

Table (3): **mRS subdivisions**

mRS	mRS Value					
	Favorable			Unfavorable		
Mean ±SD	1.176	±	0.273	3.909	±	0.984

Table 3 shows mRS Score of patients with favorable and poor outcome. Only 4 patients had died and scored 6 on the mRS.

Table (4): **Outcome in relation to gender**

Gender	mRS Value						Chi-Square*	
	Favorable		Unfavorable		Total			
	N	%	N	%	N	%	X^2	P-value
Male	12	70.59	24	54.55	36	59.02	1.305	0.253
Female	5	29.41	20	45.45	25	40.98		
Total	17	100.00	44	100.00	61	100.00		

This table shows that there was no statistically significant relationship between the outcomes of the studied patients and their gender.

Table (5): **NIHSS predicted outcome in relation to the outcome according to mRS**

NIHSS Value	mRS Value						Chi-Square	
	Favorable		Unfavorable		Total			
	N	%	N	%	N	%	X^2	P-value
Favorable	12	70.59	1	2.27	13	21.31	34.126	<0.001*
Unfavorable	5	29.41	43	97.73	48	78.69		
Total	17	100.00	44	100.00	61	100.00		

This table shows that there was statistically significant relationship between the predicted outcomes according to NIHSS value on admission and their outcome according to mRS scale.

Table (6): **pc-ASPECTS in relation to mRS**

pc-ASPECTS Value	mRS Value						Chi-Square	
	Favorable		Unfavorable		Total			
	N	%	N	%	N	%	X^2	P-value
Favorable	15	88.24	3	6.82	18	29.51	39.077	<0.001*
Unfavorable	2	11.76	41	93.18	43	70.49		
Total	17	100.00	44	100.00	61	100.00		

This table shows that there was statistically significant relationship between the predicted outcomes according to pc-ASPECTS score and their outcome according to mRS scale.

Table (7): **Comparison between the outcomes of the studied group in relation to various risk factors**

Risk Factors		mRS Value						Chi-Square	
		Favorable		Unfavorable		Total			
		N	%	N	%	N	%	X^2	P-value
HTN	**Yes**	7	41.18	30	68.18	37	60.66	3.747	0.053
	No	10	58.82	14	31.82	24	39.34		
AF	**Yes**	0	0.00	2	4.55	2	3.28	0.799	0.371
	No	17	100.00	42	95.45	59	96.72		
DM	**Yes**	9	52.94	28	63.64	37	60.66	0.588	0.443
	No	8	47.06	16	36.36	24	39.34		
Smoking	**Yes**	10	58.82	15	34.09	25	40.98	3.101	0.078
	No	7	41.18	29	65.91	36	59.02		
Hyperlipidemia	**Yes**	7	41.18	28	63.64	35	57.38	2.529	0.112
	No	10	58.82	16	36.36	26	42.62		

N.B: HTN= hypertension; AF= atrial fibrillation; DM= diabetes mellitus,

There was no significant value between the outcomes of the studied patients in relation to various risk factor including.

Table (8): **Comparison between the outcomes of the studied group in relation to time of onset and blood pressure measurements**

Clinical presentation		mRS Value						T-Test	
		Favorable			Unfavorable			t	P-value
Time of onset	**Mean ±SD**	10.118	±	7.026	12.432	±	6.886	1.170	0.247
SBP	**Mean ±SD**	147.647	±	27.507	155.682	±	31.208	0.930	0.356
DBP	**Mean ±SD**	92.353	±	18.550	96.591	±	16.974	0.852	0.398
	Mean ±SD	12.253	±	2.493	11.380	±	2.149		
	Mean ±SD	8.294	±	0.588	5.432	±	1.981		

There was no significant value between the outcomes of the studied patients in relation to various time from onset till the presentation at the emergency department (ED), systolic or diastolic blood pressure measurements at initial assessment.

Table (9): **Comparison between the outcomes of the studied group in relation to various laboratory results**

Laboratory test		mRS Value						T-Test	
		Favorable			Unfavorable			t	P-value
ESR	**Mean ±SD**	51.588	±	27.473	51.614	±	24.834	0.003	0.997
RBG	**Mean ±SD**	177.706	±	80.368	190.432	±	101.813	462	0.646
HbA1C	**Mean ±SD**	7.047	±	2.072	7.709	±	2.474	0.978	0.332
Hemoglobin	**Mean ±SD**	12.253	±	2.493	11.380	±	2.149	1.361	0.179

There was no significant value between the outcomes of the studied patients in relation to various laboratory tests results including ESR, RBG, HbA1C and hemoglobin as P-value for each was >0.05.

Table (10): Comparison between the outcomes of the studied group in relation to various MRI findings

MRI findings		mRS Value						Chi-Square	
		Favorable		Unfavorable		Total			
		N	%	N	%	N	%	X^2	P-value
Leukoaraiosis	**Yes**	3	17.65	19	43.18	22	36.07	3.467	0.063
	No	14	82.35	25	56.82	39	63.93		
Silent Infarction	**Yes**	5	29.41	15	34.09	20	32.79	0.122	0.727
	No	12	70.59	29	65.91	41	67.21		
Type of Stroke	**CE***	0	0.00	9	20.45	9	14.75	4.840	0.184
	LAD	13	76.47	27	61.36	40	65.57		
	SVD	3	17.65	4	9.09	7	11.48		
	UD	1	5.88	4	9.09	5	8.20		

* CE: cardioembolic; LAD: large artery disease; SVD: small vessel disease; UD: undetermined

There was no significant value between the outcomes of the studied patients in relation to Different MRI findings including leukoaraiosis or silent infarction. The case was the same for different types of stroke.

Table (11): **Receiver operator characteristic (ROC) and area under the curve (AUC)**

ROC curve between Favorable and Unfavorable						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
mRS	**2≥**	**100.0**	**100.0**	**100.0**	**100.0**	**%100**
NIHSS	**6≥**	**88.24**	**88.64**	**75.0**	**95.1**	**%95.7**
pc-ASPECTS	**7<**	**94.12**	**93.18**	**84.2**	**97.6**	**%96.7**

DISCUSSION

Physicians can use pc-ASPECTS and NIHSS to predict the outcome of the patients. Pc-ASPECTS of ≤ 7 was the strongest predictor of unfavourable outcomes in our study. Almost all patients with a pc-ASPECTS of ≤ 7 had unfavourable outcomes. This finding is compatible with that of a previous study revealing that a pc-ASPECTS of < 8 was very unlikely to predict favourable outcomes in basilar artery occlusion [(12)] and more recent studies assessing the value of pc-ASPECTS on DW-MRI [(8, 13)].

In our study only 17 patients (27.87%) had favorable outcome which is significantly lower percent than other similar studies in which 80 patients (64%)[(8)] and 98 patients (74.2%)[(12)] had favorable outcome (mRS value < 2). This disturbingly alarming difference may be due to the incompliance of most patients on treatment and the lack of rehabilitation programs that the average Egyptian patient can afford. Investigating if this plausibility of this theory is beyond the scope of this study.

We found that there was no statistically significant relationship between the outcomes of the studied patients and their gender as the P-value was > 0.05. this is consistent with the results of other studies [(8,13)].

We didn't find any significant relation between the outcomes of the studied patients and any single risk factor including hypertension, atrial fibrillation, diabetes mellitus, smoking and hyperlipidemia, which is the case in all literature we reviewed [(13-15)]. Combining multiple risk factors my yield better results, however we didn't find any papers examining this hypothesis and it is beyond the scope of our study.

There was no significant value between the outcomes of the studied patients in relation to various time from onset till the presentation at the emergency department (ED), systolic or diastolic blood pressure measurements at initial assessment and this is consistent with the results of other studies[(8,13)].

Similarly, there was no significant value between the outcomes of the studied patients in relation to various laboratory tests results including ESR, RBG, HbA1C and haemoglobin which is also the case in the similar studies[(8,13)].

There was no significant value between the outcomes of the studied patients in relation to different MRI findings including leukoaraiosis or silent infarction. The case was the same for different types of stroke, which is consistent with other results[(8,13)].

On analysing the ROC curve for pc-ASPECTS and NIHSS, we noted that the AUC determined for the pc-ASPECTS was slightly larger than that of the NIHSS in patients with low NIHSS scores. These patients had symptoms such as dizziness, vertigo, headache, neck pain and signs of Horner syndrome which are clinically considered in the diagnosis of posterior circulation stroke but are not covered in the NIHSS scoring system. This was also noted in the results of **Lin *et al.*** [(8)].

In addition, the NIHSS was highly weighted toward AC (Anterior circulation) deficits, including cortical signs and motor function, while PC (posterior circulation) deficits, including cranial nerve signs and ataxia, received fewer points [(15,16)]**;** ataxia is frequently excluded from scoring due to the coexistence of motor deficits[(15)]. Thus, NIHSS may not appropriately evaluate the spectrum of (PC) related signs.

The difference may be also due to that fact that the pc-ASPECTS is far simpler than NIHSS, doesn't require elaborative training and is much easier to perform[(17)].

Thus, pc-ASPECTS is superior to NIHSS for the diagnosis and assessment of posterior circulation ischemic strokes, especially in older patients or those with unclear symptoms. Using pc-ASPECTS together with NIHSS provides the best tool for pc-stroke assessment.

MRI with DWI is the gold standard for the imaging of posterior circulation acute ischemic stroke. However, it is not readily available in most community hospitals where CT is the only available imaging technique [(17)].

Non-contrast CT is not recommended for pc-ASPECTS scoring for predicting functional outcomes due to its low sensitivity (0.46, 95% CI 0.37–0.55) to posterior circulation ischemic change [(16)]. Alternatively, perfusion CT or CT angiography source imaging (CTASI) gave better results. For patients with basilar artery occlusion, a pc-ASPECTS of < 8 on perfusion CT and CTASI has been reported to more likely have unfavourable functional outcomes[(18, 19, 20)], which is compatible with our result obtained using MRI as an imaging modality.

CONCLUSION

In conclusion, both the pc-ASPECTS and NIHSS can be used to predict functional outcomes. The pc-ASPECTS is more reliable than the NIHSS especially in case of minor strokes.

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