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Prediction of stroke outcome in relation to Alberta Stroke Program Early CT Score (ASPECTS) at admission in acute ischemic stroke: A prospective study from tertiary care hospital in north India

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Abstract

Objective: To evaluate correlation of Alberta Stroke Program Early CT Score (ASPECTS) and early and delay outcome measures among acute anterior ischemic stroke patients who presented within 48 hours of stroke onset. *Methods:* In a prospective cohort study, we recruited consecutive patients with acute middle cerebral artery (MCA) ischemic stroke who presented within 48 hours of stroke onset. All the patients were evaluated at admission (Glasgow Coma Scale - GCS and National Institute of Health Stroke Scale - NIHSS) at discharge (GCS, NIHSS, Barthel Index - BI and modified Rankin Scale - mRS) and at 3 months (BI and mRS). CT ASPECTS was calculated by two observers independently. We divided patients in to two groups with 'Better' and 'Worse' ASPECTS with score of 8-10 and 0-7 respectively and compared the primary and secondary stroke outcome measures. *Results:* Among 100 patients with acute MCA infarction (median age 55 yrs, 62 males), median ASPECTS scores had inter-rater reliability of 0.82. The mortality, GCS and NIHSS at discharge, and mRS and BI at 3 months are significantly better among patients with 'Better' compared to 'Worse' APSECTS. The hospital stay was shorter in patients with Better ASPCTS.
Conclusion: In the setting of acute ischemic stroke, ASPECTS has good correlation with severity of stroke, and is strong predictor of early and delayed outcome in acute ischemic stroke.

INTRODUCTION

Computed tomography (CT) is currently the modality of first choice for imaging patients with acute stroke. Although MRI has uncovered considerable information on the process of ischemic infarction, most patients with a stroke present to community hospitals without readily available MRI.[1] Previous study has reported that a simple, valid, reliable, sensitive and inexpensive tool to accurately measure patient outcome in stroke clinical trials would be highly valued.[2]

Alberta Stroke Program Early CT score (ASPECTS) is a valid, robust and reliable method to judge degree of early ischaemic changes (EIC) (focal parenchymal hypo-attenuation, loss of gray-white differentiation, and sulcal effacement) on CT scan in patients with acute ischemic stroke.[3] ASPECTS has been shown to have modest prognostic value for determining clinical outcome after intravenous tissue plasminogen activator (i.v. tPA) in management of acute ischaemic stroke. ASPECTS has shown good correlation in predicting intracranial haemorrhage (ICH) following i.v. tPA and it has also shown to be well correlated with other advanced modality of imaging in stroke like CT angiography source images (CTA-SI), perfusion CT (CTP), multimodal magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) and perfusion imaging (PI).[4]

Most studies using ASPECTS is done in the setting of acute stroke with i.v. tPA (recombinant tissue plasminogen activator) use only, while only 1% of population with acute ischemic stroke received i.v. tPA.[5] Hence, it might not translate the real association of ASPECTS with other variable in patients presented after the standard window period.

Hence, we aim to study correlation of ASPECTS with mortality and early and late morbidity among the patients with acute anterior ischemic stroke who presented within 48 hours of stroke onset, but not necessarily within the window period.

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METHODS

This is a prospective cohort study, conducted at the Department of Neurology, All India Institute of Medical Sciences (AIIMS), New Delhi, India, from June 1, 2009 to May 31, 2011. This study was approved by the Institutional ethics committee of AIIMS.

We recruited consecutive patients with Acute Ischemic stroke who had presented to either Emergency Department or Outpatient Department of the institute. The patients with first episode of acute middle cerebral artery (MCA) territory infarction who presented to hospital within 48 hours duration and age more than 18 years were included in study. The exclusion criteria of the study were associated anterior or posterior cerebral artery infarction, posterior circulation infarction, infarction due to cortical venous thrombosis and past history of stroke.

After an informed consent, all the patients were assessed at presentation, at time of discharge and at the end of 3 months. A detailed history of all subjects including personal details, risk factors, details of onset of stroke (time, activity while onset and date), reporting time at hospital and time of CT scan, and presenting symptoms was noted.

All the subjects were examined in terms of vital signs, carotid bruit and detailed nervous system and other systemic examination. Glasgow Coma Scale (GCS) and National Institute of Health Stroke Scale (NIHSS) were assessed at time of presentation.

All the patients underwent routine blood investigation, lipid profile, electrocardiogram and CT scan. Some patients underwent echocardiography, carotid Doppler, MRI and CT/MR angiography. Time and date of CT scan were noted and ASPECTS was calculated by two observers independently in the absence of clinical information of the recruited patients. If patients were hospitalized, then inpatient treatment, need for decompressive surgery, inpatient complications and hospital stay was noted. All the patients were treated as per the discretion of the treating neurologist, with aim of best medical and/or surgical treatment. At time of discharge, all patients were assessed in terms of GCS, NIHSS, modified Rankin Scale (mRS) and Barthel Index (BI).

At the end of three months, patients were again assessed in terms of mRS and BI; either on their routine follow up visit or by telephone.

Outcome measures

The primary outcome measures included death and morbidity at time of discharge (by comparing admission ASPECTS with GCS and NIHSS at discharge) or 3 months (by comparing admission ASPECTS with BI and MRS).

The secondary outcome measures included assessment of severity of stroke (comparison of admission ASPECTS with admission GCS and admission NIHSS), length of hospital stay, and development of complication during hospitalization.

Image

Standard non contrast CT was performed with a multislice CT scanner (Siemen Systems) using 110 kV, 280 mA, 1-second scan time, and 3-mm slice thickness, which was reconstructed at 9 mm. Coverage, was from skull base to vertex with contiguous axial slices parallel to the inferior orbitomeatal line.

Image analysis

ASPECTS scoring to each patient's image were performed independently by a neuroradiologist (AG) and a stroke neurologist (PZ). All images were reviewed digitally at workstation with a large high-resolution monitor. Care was taken to use optimal width and level settings during CT image review to maximize the contrast produced by the small attenuation difference between normal and hypodense brain parenchyma (Figure 1).[6] Non contrast CT images were evaluated for evidence of focal parenchymal low attenuation, loss of gray-white differentiation, and sulcal effacement using ASPECTS as previously described.[7]

Ischemic stroke parameters: ASPECTS, GCS, NIHSS, mRS, BI

The Alberta Stroke Program Early CT Score (ASPECTS) gives a means of quantitatively assessing acute ischemia on CT images by using a 10-point topographic (M1–M6, I = insula, IC = internal capsule, L = lenticular, and C = caudate), each of which accounts for one point in the total score (Figure 2). The normal CT scan is assigned a total score of 10. For each area involved in stroke on the unenhanced CT images, one point is deducted from that score. Hence, a score of 0 translates into a finding of diffuse ischemic involvement throughout the MCA territory. ASPECTS system is a systematic and practical method that is applicable to axial images acquired

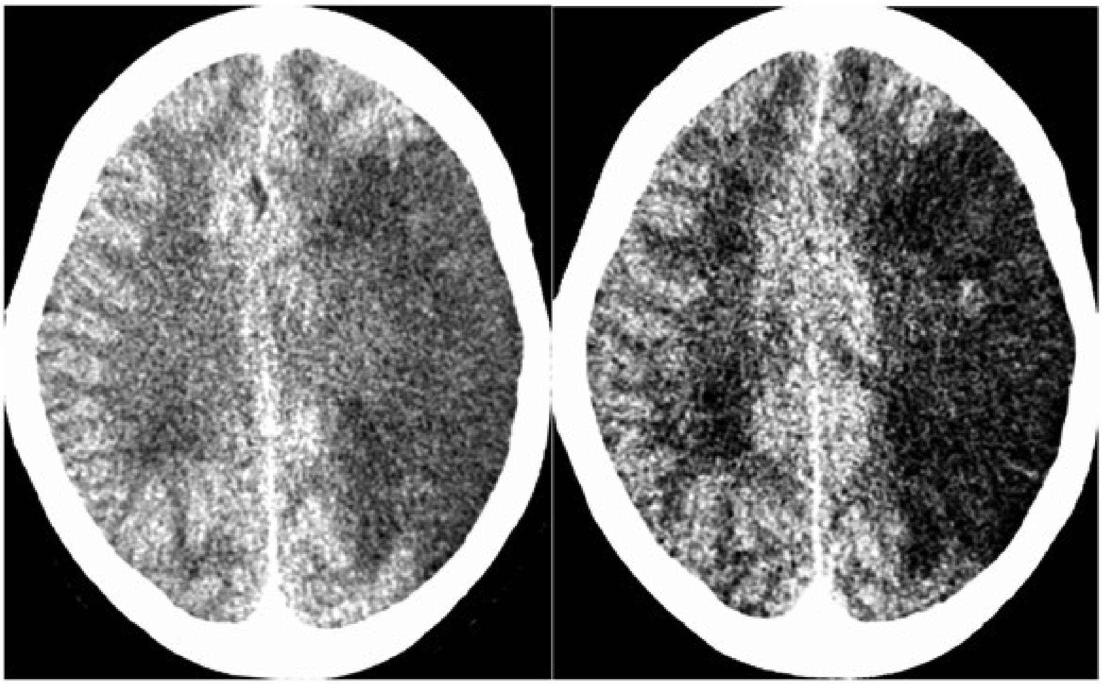

Figure 1: Unenhanced CT scan, both same images at same axial level. Note the difference in density is evident between films on either side (hypodensity on left hemisphere on right film is better appreciated). This is done by changing in window setting to better evaluate area of hypodensity.

at different levels with better clinician agreement than 1/3 MCA rule.[7] ASPECTS is a valid, robust and reliable method to judge degree of IEC on CT scan in patients with acute ischemic stroke.

GCS and NIHSS are widely used parameters in stroke trials for assessing severity at admission and also to judge early morbidity.[8,9] The mRS and BI are commonly used scales that measure

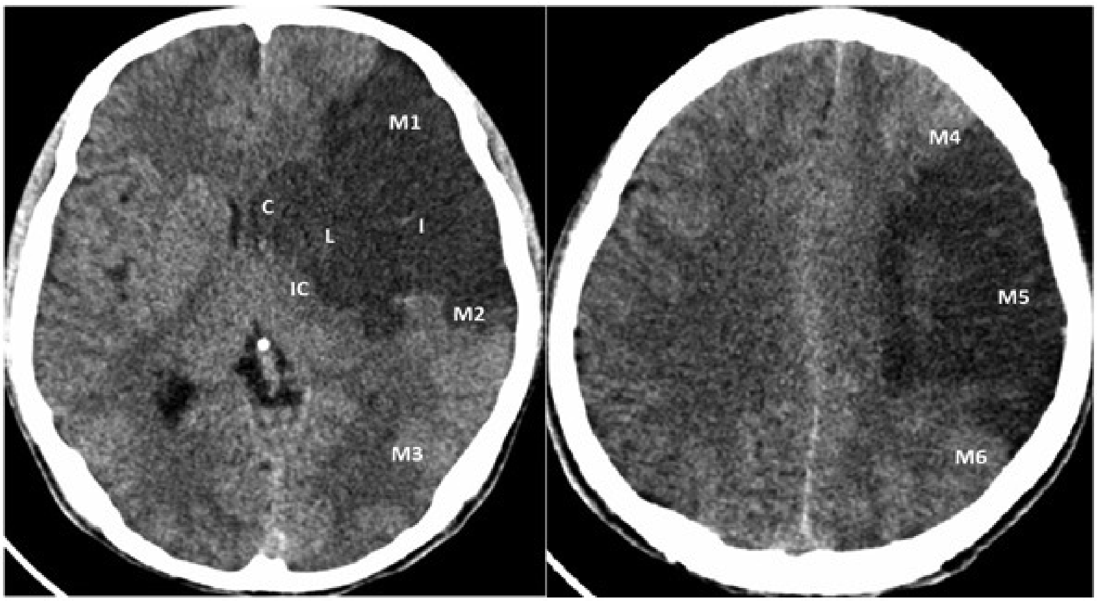

Figure 2: Unenhanced CT brain (Patient no. 18), axial section at level of basal ganglia on left image and at supraganglionic level on right image. There is hypodensity in caudate nucleus, lentiform nucleus, insular cortex, M1, M2, M4, M5 and M6 regions on left side, resulting ASPECTS of 2.

disability or dependence in activities of daily living in stroke patients. Previous stroke trials suggests the evidence overall is quite strong, supporting the use of BI and mRS as prognostic tools.[10]

Statistical analysis

The data was entered into Microsoft excel format and was analysed using SPSS version 15. The data was represented as mean ± SD (standard deviation) as well as median (with range). The comparison between the two groups in case of continuous variables was made by applying One way ANOVA or Kruskal-Wallis test followed by post hoc analysis by Bonferroni post hoc test, wherever applicable. The categorical data was compared by applying Chi-Square test or Chi-square trend. 'p' value less than 0.05 was considered as significant. Inter-rater agreement was calculated according to Intraclass correlation coefficient.

RESULTS

In this study, we examined 180 patients with acute ischemic stroke presenting within 48 hours to either emergency ward or outpatient department of our institute during the index period. After considering eligibility criteria and consent, 100 patients were recruited in the study. The median age of the patients was 55 yrs, ranging from 21 to 90 years and study population consisted of 62 males and 38 females. 90% of the patient had at least 1 known risk factor. Most common risk factor was hypertension (49%), followed by in decreasing order, diabetes mellitus (27%), coronary artery disease (20%), valvular heart disease (16%), excessive use of alcohol (14%), atrial fibrillations (8%), previous transient ischaemic attack (TIA) (7%), dyslipidemia (6%) and positive family history of stroke (1%). 56 patients had right side and 44% had left side limb and/or facial weakness.

ASPECTS varied from 0 to 10 in different CT scan of all the patients, reported independently by both the observer. The median ASPECTS was 8 (0-10) in observer 1 (AG) and 7 (0-10) in observer 2 (PZ). There was good inter-observer reliability of 0.82.

Based on the ASPECTS at admission, we divided the patients into two groups: Better ASPECTS, Group 1 with ASPECTS 8-10 (n=52) and Worse ASPECTS 0-7 (n=48) which further divided into two subgroups, Group 2 with ASPECTS 5-7 (n=20) and Group 3 with ASPECTS 0-4 (n=28). At the baseline, there is no statistically significant difference in age, gender, risk factors (except smoking, with p=0.02) and time of CT scan after stroke onset (Table 1).

In primary outcome measures (Table 2), there is statistically significant difference in mortality between Better and Worse ASPECTS group. However, this difference was not statistically significant between group 2 and 3 (p=0.06). Likewise, GCS at discharge, mRS at 3 months and BI at 3 months was statistically significantly better in group with Better ASPECTS compared to Worse ASPECTS group; but no statistically significant difference was noticed between group 2 and 3. Only NIHSS at discharge was significantly different among all 3 groups (p=0.02).

In secondary outcome measures (Table 3), Admission NIHSS was significantly different among all 3 groups (p=0.01), while GCS was statistically significantly different in Better and Worse ASPECTS group but not between Group 2 and Group 3. There was no statistically significant difference in development of Inpatient complications between Better and Worse ASPECTS group. Although significantly shorter hospital stay was noted in Group 1 compared to Group 3, this difference was not significant statistically between Better ASPECTS and Worse ASPECTS group.

DISCUSSION

In this study, we predicted stroke outcome by topographic quantitative scoring of EIC on CT scan after acute ischemic stroke who had presented within 48 hours of stroke onset. The inter-rater reliability of ASPECTS was 0.82 in our study. This is comparable to good inter-rater agreement of 0.71 and 0.85 in ASPECTS between stroke neurologist and neuroradiologist in other studies.[11,3] This translates the fact that inter-rater agreement in ASPECTS is better than one third MCA rule.[7] Moreover, ASPECTS seems easy to calculate with little experience and practice, and gives quantitative measurement of the lesion volume on CT scan.

We found that ASPECTS of 8-10 was associated with lower NIHSS and higher GCS at admission, suggestive of minor stroke, which showed good early (lower NIHSS and higher GCS than at admission) and delayed (≤ 3 mRS) outcome. ASPECTS is good predictor of mortality and early (at discharge) and delayed (at 3 months) morbidity following stroke onset. These results agree with previous studies.[3,12-14] In the original ASPECTS

Table 1: Baseline characteristics of the patients

Variables	Better ASPECTS	Worse ASPECTS		p value
	8-10 (n=52)	5-7 (n=20)	0-4 (n=28)	
Personal details				
1. Age	58.77±16.85	54.02±16.11	49.68±13.56	0.06
2. Sex (male)	30 (57.7%)	12 (60%)	20 (71.4%)	0.47
Risk factors				
1. Hypertension	26 (50%)	9 (45%)	14 (50%)	0.92
2. Diabetes mellitus	19 (36.5%)	3 (15%)	5 (17.9%)	0.08
3. Coronary artery disease	9 (17.3%)	6 (30%)	5 (17.9%)	0.46
4. Dyslipidemia	5 (9.6%)	1 (5.0%)	0 (0%)	0.22
5. Transient ischaemic attack	4 (7.7%)	0 (0%)	3 (10.7%)	0.34
6. Valvular heart disease	8 (15.4%)	5 (25%)	5 (10.7%)	0.41
7. Atrial fibrillation	4 (7.7%)	2 (10%)	2 (7.1%)	0.93
8. positive family history	1 (1.9%)	0	0	0.62
9. Smoking	18 (34.6%)	10 (50%)	18 (64.3%)	**0.01**[a]
10. Alcohol	5 (9.6%)	3 (15%)	6 (21.4%)	0.34
Time of CT scan after stroke onset				
1. Time to reach to hospital (hrs)	6.25 (0.25-48)	6.5 (2-35)	7.5 (1-47)	0.49
2. Time to do CT scan in hospital (hrs)	1 (0.25-5.25)	0.88 (0.25-5.25)	1 (0.25-48)	0.81
3. Time of CT scan from stroke onset (hrs)	7.63 (1-49)	7.13 (2.5-37.75)	9 (1.5-89)	0.30

[a] linear by linear association

Table 2: Primary outcome measures based on ASPECTS

Variables	Better ASPECTS	Worse ASPECTS		p value
	8-10 (n=52)	5-7 (n=20)	0-4 (n=28)	
Mortality				
1. Death	0	2 (10%)	3 (10.71%)	0.06
Morbidity				
1. GCS at discharge	14.69±0.70	13.30±2.08	13.23±1.42	0.01[a]
2. NIHSS at discharge	5.62±2.93	12.0±5.79	15.19±3.93	0.02
3. mRS at 3 months	1.46±0.91	3.10±1.41	3.96±1.07	0.02[a]
4. BI at 3 months	84.33±13.90	50.25±29.40	28.04±21.14	0.01[a]

GCS: Glasgow coma scale, NIHSS: National Institute of Health Stroke Scale, mRS: modified Rankin Scale, BI: Barthel Index

[a]significant between Group 1 & 2, 1 & 3 but not between 2 & 3

Table 3: Secondary outcome measures based on ASPECTS

Variables	Better ASPECTS	Worse ASPECTS		p value
	8-10 (n=52)	5-7 (n=20)	0-4 (n=28)	
Stroke Severity				
1. GCS at admisison	14.02±1.36	11.40±3.37	9.89±2.61	0.01*
2. NIHSS at admission	10.67±4.34	18.0±6.91	22.29±4.56	0.01
Others				
1. Inpatient complication	8 (15.4%)	8 (40%)	7 (25%)	0.10
2. Hospital Stay	9.04±6.32	12.05±6.67	14.79±7.36	0.01[b]

GCS: Glasgow coma scale, NIHSS: National Institute of Health Stroke Scale
[a]significant between group 1 & 2, 1 & 3 but not between 2 & 3; [b]significant for group 1 & 3 only.

study on patients who were thrombolysed within 3 hours from symptom onset, a baseline ASPECTS value of 7 or below sharply discriminated the patients who were highly unlikely to achieve an independent functional outcome.[3] Since then, several studies have confirmed the prognostic value of ASPECTS in a 0–3 hr[12,13] and 0–6-hr[14] time window. Patients with low ASPECTS are unlikely to achieve an independent functional outcome, as evident by our study with ASPECTS <5.

In our study, only 27 patients presented within window period of less than 4.5 hours, and 14 patients received i.v. tPA. Rest of them had presented after 4.5 hours due to various reasons, which included 20 patients with wake up stroke. Two prior retrospective studies found that early ischemic changes on CT from wake-up strokes were similar to acute ischemic stroke patients with known symptoms onset.[15,16] In a subgroup analysis from the Abciximab in Emergency Stroke Treatment Trial-II (AbESTT-II), more new strokes were detected in head CTs from the wake-up stroke group compared with the group presented from 0 to 6 hours from the onset of the symptoms; but the difference did not reach statistical significance.[17] The sensitivity of CT detecting EIC in acute ischemic stroke depends on the severity and duration of the focal cerebral ischemia.[3] EIC on CT do not have clinical correlation unless follow up CT changes are available, therefore EIC on CT have never been shown to correlate with acute ischaemic stroke outcomes and it do not guide medical treatment in acute stroke patients.[18] Conversely, ASPECTS performed in real time, is a reliable method for quantification of EIC.[3] We chose two groups of Better ASPECTS 8-10 and Worse ASPECTS (0-7), because EIC on CT measured by ASPECTS of **>7** correlate well with clinical outcomes, and although not proved, it has been suggested as predictor of thrombolytic treatment response. In 0 to 3 hour time window, there is a suggestive evidence of a greater magnitude of treatment benefit among patients with favourable ASPECTS > 7[13] and in patients from 3 to 6 hours from stroke onset, ASPECTS of **≤7** has predicted a poor response to intra-arterial tPA treatment.[19] We further highlight the fact that these correlations of APSECTS remain same even after 6 hours of stroke onset, which is evident in our results, in which many patients are recruited after 6 hours and up to 48 hours of stroke onset.

Minor stroke patients usually recover sooner and do not develop many inpatients complications. However, we noticed that development of inpatient complications do not correlate with better or worse ASPECTS. Various reasons for development of inpatient complications could be patient's immunity level, tendency to acquire infection, development of iatrogenic infections, worsening of co-morbid illness and development dyselectrolytemia. Nevertheless, patients with Better ASPECTS >7 tend to recover faster despite of inpatient complication, and have shorter stay at hospital, mainly due to better mRS and BI at discharge, as evident in our study.

We conclude that in the setting of acute ischemic stroke, ASPECTS at less than 48 hours of stroke onset has good correlation with severity of stroke, and is strong predictor of early and delayed outcome in acute ischemic stroke.

DISCLOSURE

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