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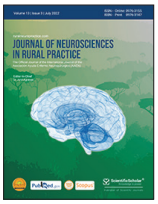

Original Article

Performance of serial CT ASPECTS for predicting stroke outcomes in patients with thrombolyzed acute ischemic stroke

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ABSTRACT

Objectives: The objective of this study was to compare the sensitivity and specificity of serial ASPECTS for predicting IHM and unfavorable outcome defined by a modified Rankin Scale score ≥3 at the time of discharge from the hospital in thrombolyzed AACIS patients.

Materials and Methods: This retrospective study examined thrombolyzed AACIS patients admitted at Saraburi Hospital, a regional health-care facility in Thailand. The study was conducted between January 2015 and July 2022. The comparative predictive performance of the baseline ASPECTS, 24-h ASPECTS, and change in ASPECTS for IHM and unfavorable outcome was examined using the receiver operating characteristic (ROC) curves. The optimal cutoff values were identified based on Youden's index and the nonparametric method to compare the area under the ROC curve (AuROC) among the three scales. The potential confounders adjusted by multivariable logistic regression were reported odds ratio (OR) and 95% confidence interval (CI).

Results: Three hundred and forty-five patients with thrombolyzed AACIS were analyzed; the median age was 61.8 ± 15.2 years. 53.0% were male, and the median National Institutes of Health Stroke Scale score was 11 points (interquartile range: 8–17). The AuROC for predicting IHM was 0.823 for the baseline ASPECTS, 0.955 for 24-h ASPECTS, and 0.920 for the change in ASPECTS. For predicting unfavorable outcome, the AuROC was 0.744 for the baseline ASPECTS, 0.853 for 24-h ASPECTS, and 0.800 for the change in ASPECTS. After adjusting for other factors, the OR for predicting IHM was 14.38 (95% CI: 1.69–122.57) for 24-h ASPECTS and 16.7 (95% CI: 4.36–64.01) for the change in ASPECTS. Regarding unfavorable outcome, the adjusted OR was 5.58 (95% CI: 1.83–17.01) for 24-h ASPECTS and 4.85 (95% CI: 2.45–9.60) for the change in ASPECTS.

Conclusion: The 24-h ASPECTS and change in ASPECTS could be more precise predictors for predicting IHM and unfavorable outcome in patients with thrombolyzed AACIS.

Keywords: Predictive accuracy, Alberta Stroke Program Early Computed Tomography Score, Thrombolyzed acute anterior circulation ischemic stroke, Mortality, Unfavorable outcome

INTRODUCTION

Stroke ranks the second-most widespread contributor to mortality and impairment globally, and its incidence continues to increase within the aging demographic.[1] In Thailand, the death rate from acute ischemic stroke (AIS) is 10%, and 50% of patients suffer from disabilities.[2] The availability of endovascular treatment remains restricted in many Thai hospitals. The predominant approach for treating AIS remains the intravenous recombinant tissue plasminogen activator (rt-PA).[3,4] Nevertheless, a comprehensive meta-analysis of observational studies and randomized trials identified a mortality rate of up to 17.5% among AIS patients treated with rt-PA.[5]

The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) is a commonly employed scoring system that utilizes CT or magnetic resonance imaging to assess early ischemic changes (EICs).[6] It demonstrates high sensitivity, specificity, and correlation with functional outcomes as symptomatic intracranial hemorrhage.[7] A study found a significant negative correlation coefficient of −0.680 ($P < 0.001$) between the ASPECTS and the National Institutes of Health Stroke Score (NIHSS).[8] Moreover, the 24- h NIHSS outperformed the baseline NIHSS in predicting long-term stroke outcomes. With substantial supporting data, this instrument has proven its reliability and validity as an early surrogate for clinical outcomes in AIS patients.[9] Therefore, analyzing EICs through a

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serial ASPECTS evaluation can help predict mortality in thrombolyzed AIS patients.

In resource-limited settings like Thailand, budget constraints hinder the routine use of advanced neuroimaging for diagnosing all AIS patients. The predictive ability of serial ASPECTS assessment using non-contrast CT (NCCT) for mortality following thrombolysis in Thailand is insufficient. Therefore, this retrospective study evaluated the predictive accuracy of serial ASPECTS evaluations for inhospital mortality (IHM) and unfavorable outcome in individuals with acute anterior circulation ischemic stroke (AACIS) who received thrombolytic treatment.

MATERIALS AND METHODS

Study population

The retrospective medical record review examined thrombolyzed AACIS patients admitted at Saraburi Hospital, a regional health-care facility in Thailand, between January 2015 and July 2022. The research was approved by the Institute's Ethics Committee (Certificate No. EC054/2565). Patients with thrombolyzed AACIS treated according to the 2019 AIS early treatment guidelines.[10]

Data collection

The patient demographic data, including age and sex, with comorbidities such as previous ischemic stroke, congestive heart failure, atrial fibrillation, ischemic heart disease, valvular heart disease, diabetes, hypertension, chronic renal disease, hyperlipidemia, history of malignancy, and renal replacement therapy, were extracted from the electronic medical records. The NIHSS scores, laboratory data, hospital duration, ASPECTS scores, stroke complications, and the diagnosis of AIS were confirmed by referencing the I63 International Classification of Diseases, Tenth Revision code.[11]

The evaluation of individuals suffering from a middle cerebral artery (MCA) stroke commonly includes using a quantitative ASPECTS score. This scoring system assesses the MCA vascular area in segments and deducts one point from the total score for each affected region.[12] The baseline ASPECTS score establishes an initial measurement, and the brain NCCT is determined before administering rt-PA treatment. The 24-h ASPECTS score was obtained from the NCCT scan after 24 h of rt-PA therapy. The changes in the ASPECTS were determined by calculating the difference between the initial score at 24 h. The baseline and 24-h ASPECTS scores followed the same grading methodology evaluated by certified neurologists and neuroradiologists. The imaging readers were unaware of the patient's medical history to ensure a blinded evaluation. In instances of inconsistencies in the ASPECTS values, collaborative discussions were conducted among the experts to ensure precise findings. The ASPECTS method was applied to evaluate the brain images pre- and post-treatment. NCCT scan in this study was done by the TOSHIBA 160-slice (Aquilion Prime; Canon Medical Systems, Otawara, Japan), capturing continuous cross-sections from the base to the top of the head, aligned with the inferior orbitomeatal line.

The inclusion criteria were AACIS patients aged 18 years or older, who had AACIS and were treated with rt-PA. Exclusion criteria comprised pregnancy, posterior circulation ischemic stroke, patients referred to other hospitals whose treatment information could not follow up, and those with incomplete NIHSS, NCCT images, or laboratory findings.

Outcomes

The primary outcome was predictive accuracy for IHM referred to patients who died during hospitalization; the survivor group referred to patients who were discharged alive. The secondary outcome was predictive accuracy for unfavorable outcome defined by a modified Rankin Scale score (mRS) ≥3 at hospital discharge,[13-15] determined by a neurologist or a specialized stroke nurse.

Statistical analysis

Stata Statistical Software 17 was applied for data analysis and statistical calculations. Quantitative data were analyzed using means, standard deviations, medians, and interquartile ranges (IQR), while categorical data were assessed by counting and calculating percentages. Three distributions of the ASPECTS were created to examine consistency among the measures in patients with IHM and unfavorable outcome. The comparative predictive performance of the baseline ASPECTS, 24-h ASPECTS, and change in ASPECTS for IHM and unfavorable outcome was examined using the receiver operating characteristic (ROC) curves. The optimal cutoff values were identified based on Youden's index and the nonparametric method to compare the area under the ROC curve (AuROC) among the three scales.[16] Multivariate logistic regression analysis examined the independent association of each cutoff value on IHM and unfavorable outcome while adjusting for potential confounders. The strength of the association was assessed and presented with adjusted odds ratios (AOR) with corresponding 95% confidence intervals (CIs).

RESULTS

Data from 345 individuals with thrombolyzed AACIS were included in this retrospective study; 42 patients were excluded, as detailed in [Figure 1]. The median NIHSS score was 11 (IQR: 8–17), the mean age was 61.8 ± 15.2 years, 53.4% were male, and the average follow-up duration was 8.8 ± 10.7 days. [Table 1] compares serial ASPECTS assessment findings between non-survivors and survivors and between

those with unfavorable and favorable outcome. The rate of IHM was 18.4% (64/345), and the unfavorable outcome was 61.5% (213/345). The non-survivors, compared to the survivors, were more likely to have been aged 70 years or older and had a higher prevalence of comorbidities such as atrial fibrillation, congestive heart failure, chronic kidney disease, a history of malignancy, swallowing dysfunction, alteration of consciousness, aphasia, neglect, cranial nerve disorder, gaze paresis, pre-stroke functional status (mRS of ≥2), higher systolic and diastolic blood pressure, NIHSS ≥16, large artery atherosclerosis, cardioembolic stroke, and prior antihypertensive treatment before rt-PA administration. Patients who experienced an unfavorable outcome demonstrated a greater incidence of predisposing factors and medical conditions, including a history of atrial fibrillation, dysarthria, swallowing dysfunction, altered consciousness, aphasia, neglect, gaze paresis, elevated blood pressure on admission, NIHSS score ≥16, large artery atherosclerosis, cardioembolic stroke, and antihypertensive treatment before rt-PA administration, in comparison to patients with a favorable outcome. The IHM and unfavorable outcome predictability between the laboratory findings and serial ASPECTS assessment of thrombolyzed AIS patients who survived and those who experienced IHM were evaluated. Non-survivors had higher neutrophil-to-lymphocyte count ratio, lower hemoglobin and hematocrit levels, higher blood glucose levels at admission, lower baseline ASPECTS, lower 24-h ASPECTS, and greater change in ASPECTS compared to survivors. Similarly, patients with an unfavorable outcome exhibited lower hematocrit levels, higher blood glucose levels at admission, lower baseline ASPECTS, lower 24-h ASPECTS, and greater change in ASPECTS than those with a favorable outcome. [Figures 2 and 3] present the distributions of the baseline ASPECTS, 24-h ASPECTS, and change in ASPECTS for patients classified by IHM or survival and unfavorable or favorable outcome. A significant difference in the distribution of serial ASPECTS assessment was observed between patients with IHM and unfavorable outcome [$P < 0.001$, Supplemental Table 1]. No deaths occurred among patients with 24-h ASPECTS scores of 7–10, while the mortality rates were 18.75% and 81.25% for scores of 5–6 and 0–4, respectively. Patients with baseline ASPECTS ≤7, 24-h ASPECTS ≤4, and change in ASPECTS ≥3 had mortality rates of 62.5% (40/64), 81.25% (52/64), and 86.15% (56/64), respectively.

[Table 2] shows the performance and cutoff scores of the baseline ASPECTS, 24-h ASPECTS, and changes in ASPECTS in predicting IHM and unfavorable outcome. Change in ASPECTS showed the highest sensitivity but the lowest specificity, whereas the baseline ASPECTS exhibited the lowest sensitivity. The optimal cutoff values for predicting IHM were ≤7 for baseline ASPECTS, ≤4 for 24-h ASPECTS, and ≥3 for change in ASPECTS, with corresponding Youden's indices of 0.571, 0.832, and 0.726, respectively. In predicting unfavorable outcome, the optimal cutoff values were ≤8 for baseline ASPECTS, ≤6 for 24-h ASPECTS, and ≥1 for change in ASPECTS, yielding Youden's indices of 0.440, 0.535, and 0.459, respectively – [Figure 4] presents the ROC curves for the serial ASPECTS assessment. The AuROC of the baseline ASPECTS, 24-h ASPECTS, and change in ASPECTS for predicting IHM was 0.823, 0.955, and 0.920, respectively. The AuROC of the baseline ASPECTS, 24-h ASPECTS, and change in ASPECTS for predicting unfavorable outcome was 0.744, 0.853, and 0.800, respectively. The 24-h ASPECTS and change in ASPECTS outperformed the baseline ASPECTS in predicting IHM

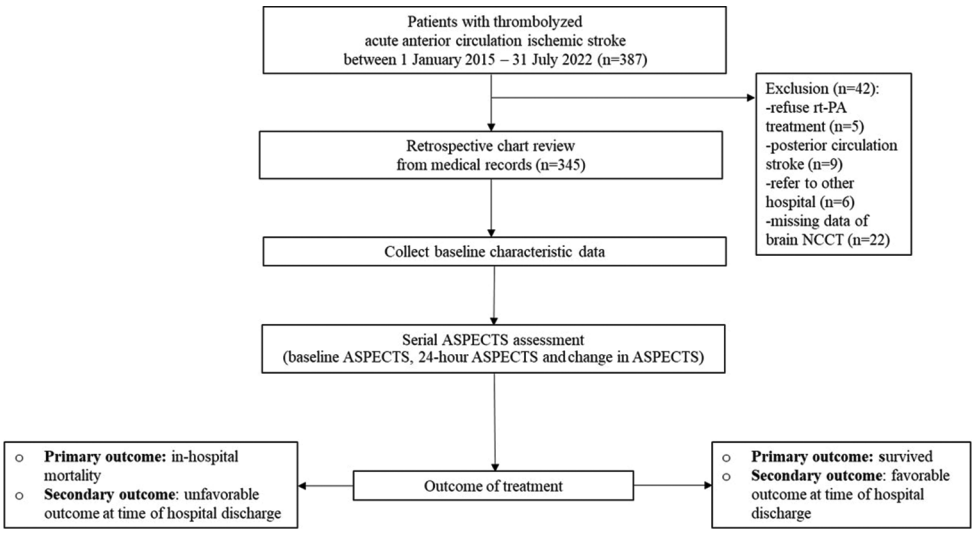

Figure 1: The patient flow chart. ASPECTS: Alberta Stroke Program Early CT Score, NCCT: Non-contrast computed tomography, rt-PA: Recombinant tissue plasminogen activator.

Table 1: Comparison of the demographic, clinical, and laboratory findings among patients grouped according to IHM and unfavorable outcome.

Characteristic	All patients (*n*=345)	IHM		*P*-value	Unfavorable outcome		*P*-value
		IHM (*n*=64)	Survived (*n*=281)		Unfavorable (*n*=213)	Favorable (*n*=132)	
Age, years, *n* (%)							
18–59	151 (43.8)	20 (31.3)	131 (46.6)	0.001	76 (35.7)	75 (56.8)	<0.001
60–69	81 (23.5)	11 (17.2)	70 (24.9)		48 (22.5)	33 (25)	
70–79	62 (18)	14 (21.9)	48 (17.1)		47 (22.1)	15 (11.4)	
≥80	51 (14.8)	19 (29.7)	32 (11.4)		42 (19.7)	9 (6.8)	
Gender, *n* (%)							
Male	183 (53)	33 (51.6)	150 (53.4)	0.793	112 (52.6)	71 (53.8)	0.827
Female	162 (47)	31 (48.4)	131 (46.6)		101 (47.4)	61 (46.2)	
Vascular risk factor and comorbidities, *n* (%)							
Smoking	123 (35.7)	19 (29.7)	104 (37)	0.27	69 (32.4)	54 (40.9)	0.109
Alcohol	142 (41.2)	27 (42.2)	115 (40.9)	0.853	84 (39.4)	58 (43.9)	0.409
Prior stroke	41 (11.9)	9 (14.1)	32 (11.4)	0.551	23 (10.8)	18 (13.6)	0.428
Atrial fibrillation	102 (29.6)	36 (56.3)	66 (23.5)	<0.001	72 (33.8)	30 (22.7)	0.028
MI	29 (8.4)	9 (14.1)	20 (7.1)	0.071	18 (8.5)	11 (8.3)	0.97
CHF	37 (10.7)	12 (18.8)	25 (8.9)	0.022	26 (12.2)	11 (8.3)	0.258
Valvular heart disease	22 (6.4)	4 (6.3)	18 (6.4)	0.963	13 (6.1)	9 (6.8)	0.792
Diabetes mellitus	93 (27)	16 (25)	77 (27.4)	0.696	63 (29.6)	30 (22.7)	0.163
Hypertension	243 (70.4)	48 (75)	195 (69.4)	0.375	156 (73.2)	87 (65.9)	0.147
Chronic kidney disease	44 (12.8)	13 (20.3)	31 (11)	0.045	30 (14.1)	14 (10.6)	0.347
Dyslipidemia	141 (40.9)	25 (39.1)	116 (41.3)	0.745	95 (44.6)	46 (34.8)	0.073
History of malignancy	8 (2.3)	4 (6.3)	4 (1.4)	0.021	6 (2.8)	2 (1.5)	0.435
History of renal replacement therapy	5 (1.4)	2 (3.1)	3 (1.1)	0.214	3 (1.4)	2 (1.5)	0.936
Clinical presentation, *n* (%)							
Hemiparesis	341 (98.8)	63 (98.4)	278 (98.9)	0.739	211 (99.1)	130 (98.5)	0.627
Dysarthria	275 (79.7)	53 (82.8)	222 (79)	0.494	179 (84)	96 (72.7)	0.011
Swallowing dysfunction	129 (37.4)	51 (79.7)	78 (27.8)	<0.001	118 (55.4)	11 (8.3)	<0.001
Ataxia	37 (10.7)	7 (10.9)	30 (10.7)	0.951	24 (11.3)	13 (9.8)	0.679
Alteration of consciousness	109 (31.6)	54 (84.4)	55 (19.6)	<0.001	93 (43.7)	16 (12.1)	<0.001
Hemianopia	23 (6.7)	6 (9.4)	17 (6)	0.336	18 (8.5)	5 (3.8)	0.092
Aphasia	132 (38.3)	46 (71.9)	86 (30.6)	<0.001	105 (49.3)	27 (20.5)	<0.001
Neglect	62 (18)	19 (29.7)	43 (15.3)	0.007	53 (24.9)	9 (6.8)	<0.001
Cranial nerve disorder	12 (3.5)	5 (7.8)	7 (2.5)	0.036	7 (3.3)	5 (3.8)	0.805
Gaze paresis	112 (32.5)	49 (76.6)	63 (22.4)	<0.001	100 (46.9)	12 (9.1)	<0.001
Prestroke functional status (mRS), *n* (%)							
0	320 (92.8)	49 (76.6)	271 (96.4)	<0.001	191 (89.7)	129 (97.7)	0.002
1	6 (1.7)	1 (1.6)	5 (1.8)		3 (1.4)	3 (2.3)	
2–3	19 (5.5)	14 (21.9)	5 (1.8)		19 (8.9)	0 (0)	
Time to rt-PA, hours, *n* (%)							
<3 h	233 (67.5)	39 (60.9)	194 (69)	0.212	140 (65.7)	93 (70.5)	0.362
3–4.5 h	112 (32.5)	25 (39.1)	87 (31)		73 (34.3)	39 (29.5)	

(Contd...)

Table 1: *(Continued)*

Characteristic	All patients (*n*=345)	IHM		*P*-value	Unfavorable outcome		*P*-value
		IHM (*n*=64)	Survived (*n*=281)		Unfavorable (*n*=213)	Favorable (*n*=132)	
Blood pressure at admission, mmHg							
SBP, mmHg	159.2±28.88	168.61±30.17	157.06±28.2	0.004	162.49±29.04	153.9±27.93	0.007
DBP, mmHg	92.34±19.16	98.56±17.63	90.93±19.24	0.004	94.12±19.97	89.47±17.47	0.028
NIHSS at admission, *n* (%)							
5–15	232 (67.2)	10 (15.6)	222 (79)	<0.001	110 (51.6)	122 (92.4)	<0.001
16–20	76 (22)	33 (51.6)	43 (15.3)		69 (32.4)	7 (5.3)	
>20	37 (10.7)	21 (32.8)	16 (5.7)		34 (16)	3 (2.3)	
TOAST classification, *n* (%)							
Large artery atherosclerosis	76 (22)	17 (26.6)	59 (21)	<0.001	65 (30.5)	11 (8.3)	<0.001
Cardioembolic stroke	119 (34.5)	45 (70.3)	74 (26.3)		87 (40.8)	32 (24.2)	
Small-vessel occlusion	134 (38.8)	1 (1.6)	133 (47.3)		57 (26.8)	77 (58.3)	
Stroke of other determined etiology	9 (2.6)	1 (1.6)	8 (2.8)		4 (1.9)	5 (3.8)	
Stroke of undetermined etiology	7 (2)	0 (0)	7 (2.5)		0 (0)	7 (5.3)	
Hospital stay, days	5 (3, 9)	8 (3, 22)	5 (4, 8)	0.008	6 (4, 11)	4 (3, 6.5)	<0.001
Antihypertensive before rt-PA	97 (28.1)	36 (56.3)	61 (21.7)	<0.001	77 (36.2)	20 (15.2)	<0.001
Laboratory							
WBC (cells/mm^3) – median (IQR)	8500 (7100, 10400)	8750 (7300, 11200)	8500 (7000, 10300)	0.312	8500 (7200, 10400)	8500 (6900, 9950)	0.215
NLR – median (IQR)	2.21 (1.53, 3.67)	2.78 (1.76, 5.23)	2.17 (1.5, 3.5)	0.020	2.3 (1.59, 3.75)	2.12 (1.46, 3.57)	0.204
Hb (g/dL) – mean (SD)	12.55±2.13	11.91±2.31	12.7±2.07	0.013	12.4±2.19	12.8±2.01	0.093
Hct (%)– mean (SD)	38.19±6.29	36.35±7.12	38.6±6.02	0.021	37.65±6.48	39.05±5.9	0.044
Platelet (×10^{3}cells/mm^3) – mean (SD)	251.51±81.36	237.11±81.34	254.79±81.15	0.117	251.67±89.31	251.26±66.87	0.964
INR – mean (SD)	0.97±0.14	0.98±0.17	0.97±0.13	0.356	0.97±0.13	0.97±0.14	0.672
Creatinine (mg/dL) – median (IQR)	0.95 (0.78, 1.15)	1 (0.81, 1.24)	0.94 (0.78, 1.14)	0.198	0.97 (0.78, 1.16)	0.93 (0.79, 1.11)	0.314
Blood glucose at first admission (mg/dL) – median (IQR)	119 (102, 150)	134 (109.5, 176)	116 (101, 145)	0.004	124 (106, 160)	106.5 (94.5, 135.5)	<0.001
Workflow time							
Onset to door, min – median (IQR)	90 (60, 120)	90 (60, 130)	90 (60, 120)	0.181	90 (60, 120)	90 (60, 120)	0.871
Onset to treatment time, min – median (IQR)	140 (96, 182)	151.5 (97, 189.5)	135 (96, 180)	0.370	136 (91, 179)	140.5 (100, 186)	0.307
ASPECTS							
Baseline ASPECTS	10 (8, 10)	7 (6, 8)	10 (9, 10)	<0.001	9 (7, 10)	10 (10, 10)	<0.001
24-h ASPECTS	8 (5, 9)	2 (1, 4)	9 (7, 10)	<0.001	6 (3, 8)	9 (9, 10)	<0.001
Change in ASPECTS	1 (0, 3)	4.5 (3, 6)	1 (0, 2)	<0.001	2 (1, 4)	0 (0, 1)	<0.001
Hospital stay, days	5 (3, 9)	8 (3, 22)	5 (4, 8)	0.008	6 (4, 11)	4 (3, 6.5)	<0.001

ASPECTS: Alberta Stroke Program Early CT Score, CHF: Congestive heart failure, CI: Confidence interval, DBP: Diastolic blood pressure, Hb: Hemoglobin, Hct: Hematocrit, MI: Myocardial infarction, IHM: Inhospital mortality; mRS: modified Rankin Scale, NIHSS: National institutes of health stroke scale, NLR: Neutrophil-lymphocyte count ratio, rt-PA: Recombinant tissue plasminogen activator, SBP: Systolic blood pressure, TOAST classification: Trial of ORG 10172 in acute stroke treatment classification, WBC: White blood cell count, IQR: Interquartile range, SD: Standard deviation

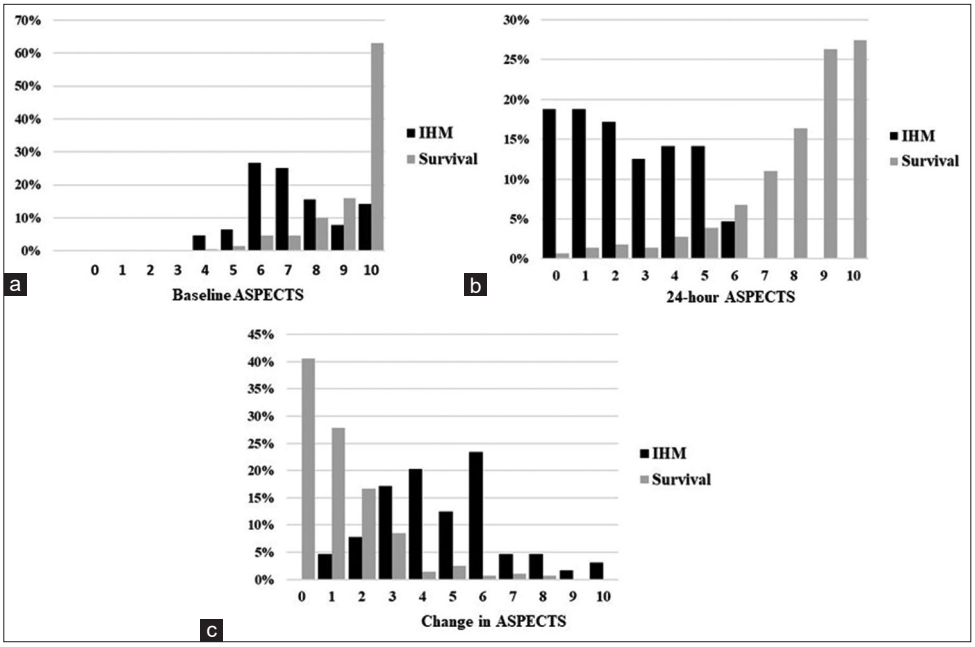

Figure 2: Bar graph depicting the proportion of patients with varying serial ASPECTS from baseline to 24-h imaging, grouped by IHM or survival status. (a) Bar graph of the baseline ASPECTS. (b) Bar graph of the 24-h ASPECTS. (c) Bar graph of the change in ASPECTS. ASPECTS: Alberta Stroke Program Early CT Score, IHM: Inhospital mortality.

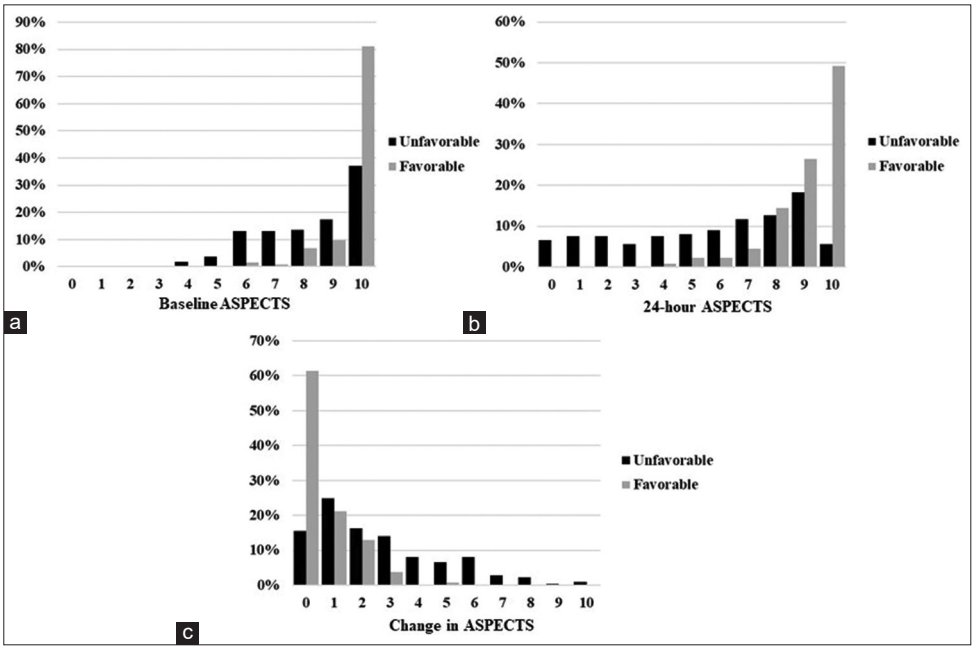

Figure 3: Bar graph depicting the proportion of patients with varying serial ASPECTS from baseline to 24-h imaging, grouped by favorable or unfavorable outcome. (a) Bar graph of the baseline ASPECTS. (b) Bar graph of the 24-h ASPECTS. (c) Bar graph of the change in ASPECTS. ASPECTS: Alberta Stroke Program Early CT Score.

and unfavorable outcome. These three scales exhibited a significant association with IHM and unfavorable outcome in univariate and multivariate analyses. Furthermore, the 24-h ASPECTS and change in ASPECTS emerged as robust predictors for IHM (AOR: 14.38, 95% CI: 1.69–122.57, P = 0.015 and AOR: 16.70, 95% CI: 4.36–64.01, $P < 0.001$), as well as unfavorable outcome (AOR: 5.58, 95% CI: 1.83–17.01, P = 0.002 and AOR: 4.85, 95% CI: 2.45–9.60, $P < 0.001$), according to the findings presented in [Supplemental Table 2].

Table 2: The optimal cutoff score of the ASPECTS and prognostic value of the ASPECTS for predicting IHM and unfavorable outcome.

Variable	AuROC (95% CI)	Optimal cut-off	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
IHM						
Baseline ASPECTS	0.823 (0.762, 0.884)	≤7	62.5 (49.5–74.3)	89.0 (84.7–92.4)	56.3 (44.0–68.1)	91.2 (87.2–94.3)
24-h ASPECTS	0.955 (0.935, 0.975)	≤4	81.3 (69.5–89.9)	91.8 (88.0–94.7)	69.3 (57.6–79.5)	95.6 (92.4–97.7)
Change in ASPECTS	0.920 (0.888, 0.953)	≥3	87.5 (76.8–94.4)	85.1 (80.3–89.0)	57.1 (46.7–67.1)	96.8 (93.7–98.6)
Unfavorable outcome at the time of hospital discharge						
Baseline ASPECTS	0.744 (0.693, 0.795)	≤8	45.5 (38.7–52.5)	90.9 (84.7–95.2)	89 (81.6–94.2)	50.8 (44.3–57.4)
24-h ASPECTS	0.853 (0.814, 0.892)	≤6	51.6 (44.7–58.5)	94.7 (89.4–97.8)	94 (88.1–97.6)	54.8 (48.1–61.4)
Change in ASPECTS	0.800 (0.754, 0.846)	≥1	84.5 (78.9–89.1)	61.4 (52.5–69.7)	77.9 (72–83.1)	71.1 (61.8–79.2)

ASPECTS: Alberta Stroke Program Early CT Score, AuROC: Area under the receiver operating characteristic curve, CI: Confidence interval, IHM: Inhospital mortality, NPV: Negative predictive value, PPV: Positive predictive value

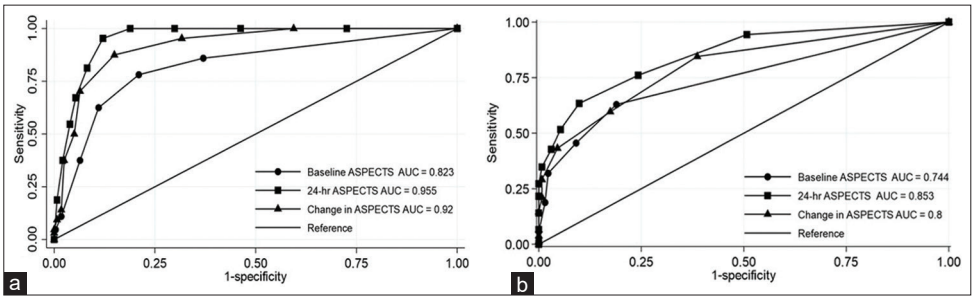

Figure 4: (a) ROC curve and AuROC for IHM of the three scales among thrombolyzed stroke patients. (b) ROC curve and AuROC for unfavorable outcome of the three scales at the time of hospital discharge among thrombolyzed stroke patients. ASPECTS: Alberta Stroke Program Early CT Score, AuROC: Area under the receiver operating characteristic curve, IHM: Inhospital mortality, ROC: Receiver operating characteristic.

DISCUSSION

Our study found that the 24-h ASPECTS and change in ASPECTS had a greater predictive accuracy for IHM and unfavorable outcome than the baseline ASPECTS. In line with recent research, 24-h ASPECTS on NCCT demonstrated superior predictive accuracy in predicting unfavorable outcome at 3 months compared to the baseline ASPECTS and change in ASPECTS (AuROC = 0.78).[17,18]

Our findings were consistent with those of the SWIFT study, which examined the efficacy of 24-h ASPECTS in predicting the therapeutic benefits of reperfusion. Participants in the study were randomly assigned to receive either the Merci device or the Solitaire stent retriever for arterial recanalization. In endovascular therapy, the 24-h ASPECTS emerged as the most robust predictor for predicting clinical outcomes at the 3-month follow-up. However, our study differed from the SWIFT trial regarding demographics and treatment approach, as we specifically administered rt-PA. Second, our study differed from the SWIFT trial regarding the patient population, as we included multiple stroke etiologies rather than focusing solely on large vessel occlusion. The SWIFT study reported a higher median NIHSS score (18 [IQR 8–28] vs. 11 [IQR 8–17]), indicating more severe stroke severity.[19]

Our research revealed that the change in ASPECTS and the 24-h ASPECTS had relatively similar predictive abilities for IHM and unfavorable outcome. The change in ASPECTS might be correlated with the occurrence of reperfusion syndrome. Complications of reperfusion injury, including penumbral damage, ischemic expansion, hemorrhagic transformation, seizures, malignant cerebral edema, and herniation, were all found to be associated with poorer outcomes in AIS patients. Accurately assessing severity and criticality is crucial to determining enhanced monitoring or treatment requirements. Serial changes in tissue damage on routine NCCT can offer valuable insights into how brain tissues respond to varying degrees of reperfusion.[20] The findings indicated that the 24-h ASPECTS and change in ASPECTS outperformed the baseline ASPECTS in predicting IHM after intravenous rt-PA administration. Furthermore, the change in ASPECTS exhibited the most incredible sensitivity in predicting unfavorable outcome. These measures demonstrated higher AuROC and sensitivity, suggesting their potential to identify individuals at risk of IHM.

The baseline ASPECTS had a lower sensitivity than the 24-h ASPECTS and change in ASPECTS for predicting IHM and unfavorable outcome; this suggested a higher likelihood of incorrectly identifying non-high-risk patients as having a risk of mortality or unfavorable outcome. However, considering the critical importance of predicting IHM, caution should be exercised when using the baseline ASPECTS. Our study contrasted with the report of Esmael *et al.*[21] regarding the predictive value of the baseline ASPECTS for unfavorable outcome. Specifically, we observed a sensitivity of 73% and a specificity of 81% when using a baseline ASPECTS cutoff score of ≤7. Our study revealed different cutoff scores; however, a baseline ASPECTS of ≤8 was consistently associated with an unfavorable outcome, showing a lower sensitivity (45.5%) than previous studies. The duration of the follow-up period employed to assess adverse events across various studies contributes to variation in study results. Our research examined outcomes at the point of hospital discharge, whereas other studies measured outcomes during a 3-month follow-up period.

The superior predictive ability of 24-h ASPECTS and change in ASPECTS, compared to the baseline ASPECTS, can be attributed to the following reasons. First, there was a significant error rate when using the brain NCCT to identify EICs. The challenge lies in precisely interpreting the indistinct appearance of EICs on the baseline brain NCCT, which demands considerable expertise for accurate interpretation. Early brain NCCT might not have reliably detected ASPECTS changes, which could have indicated ischemic changes or associated vasogenic and cytotoxic edema due to inherent technical limitations.[22] Second, NCCT ASPECTS has a lower sensitivity for detecting EICs than DWI ASPECTS.[23] Third, it is crucial to consider the methodological limitations associated with the ASPECTS cutoff scores, which stem from the unequal weighting given to regions affected by EICs. Ischemic lesions with identical ASPECTS ratings can differ in size depending on their location.[8]

This study has several limitations. First, the study was carried out at a single center using a retrospective cohort design, encompassing a relatively small sample size. Further validation through larger, multicenter studies was necessary. Second, it is important to acknowledge that the absence of endovascular treatment at our center could impact the generalizability of the findings. While a meta-analysis has demonstrated the significant advantages of endovascular thrombectomy compared to standard medical care, our study included only patients who received rt-PA without endovascular treatment. This limitation poses challenges in evaluating the overall treatment effect.[24] Further research should explore the impact of serial ASPECTS on mortality in various stroke treatment approaches, including endovascular thrombectomy. In addition, investigating the influence of 24-h ASPECTS and change in ASPECTS on other complications, such as malignant cerebral edema or stroke-associated pneumonia following thrombolytic treatment, warrants further investigation. Finally, it is essential to mention that our study did not include patients with posterior circulation ischemic stroke, as the ASPECTS score cannot reliably predict their prognosis.

CONCLUSION

Our study demonstrated that 24-h ASPECTS and change in ASPECTS on NCCT were more effective in predicting IHM and unfavorable outcome in patients with thrombolyzed AACIS treated with rt-PA. These findings will highlight the importance of incorporating 24-h ASPECTS and change in ASPECTS to assist physicians in risk stratification, make early decisions in stroke care, prioritize immediate care, and provide intensive neurological monitoring. However, further external validation research will be necessary to corroborate these findings.

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Declaration of patient consent

The Institutional Review Board (IRB) permission was obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY TABLES

Supplemental Table 1: Distribution of the ASPECTS in patients stratified by IHM and unfavorable outcome.

ASPECTS	Primary outcome		*P*-value	ASPECTS	Secondary outcome		*P*-value
	IHM (*n*=64) (%)	Survived (*n*=281) (%)			Unfavorable (*n*=213) (%)	Favorable (*n*=132) (%)	
Baseline ASPECTS				Baseline ASPECTS			
0–5	7 (10.94)	5 (1.78)	<0.001	0–5	12 (5.63)	0 (0)	<0.001
6–7	33 (51.56)	26 (9.25)		6–7	56 (26.29)	3 (2.27)	
8–10	24 (37.50)	250 (89.97)		8–10	145 (68.08)	129 (97.73)	
24-h ASPECTS				24-h ASPECTS			
0–4	52 (81.25)	23 (8.19)	<0.001	0–3	58 (27.23)	0 (0)	<0.001
5–6	12 (18.75)	30 (10.68)		4–6	52 (24.41)	7 (5.30)	
7–10	0 (0)	228 (81.13)		7–10	103 (48.36)	125 (94.70)	
Change in ASPECTS				Change in ASPECTS			
0	0 (0)	114 (40.57)	<0.001	0	33 (15.49)	81 (61.36)	<0.001
1–2	8 (12.50)	125 (44.48)		1–5	149 (69.95)	51 (38.64)	
3–10	56 (87.50)	42 (14.95)		6–10	31 (14.55)	0 (0)	

ASPECTS: Alberta Stroke Program Early CT Score; IHM: Inhospital mortality

Supplemental Table 2: Multivariable logistic regression analysis of the cutoff score of the ASPECTS for predicting IHM and unfavorable outcome.

Scales	Optimal cut-off	Univariable analysis		Multivariable analysis	
		OR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
Inhospital mortality[a]					
Baseline ASPECTS	≤7	13.44 (7.17, 25.21)	<0.001	7.83 (1.73, 35.41)	0.007
24-h ASPECTS	≤4	48.61 (22.76, 103.82)	<0.001	14.38 (1.69, 122.57)	0.015
Change in ASPECTS	≥3	39.83 (17.72, 89.55)	<0.001	16.70 (4.36, 64.01)	<0.001
Unfavorable outcome at the time of hospital discharge[b]					
Baseline ASPECTS	≤8	8.36 (4.36, 16.05)	<0.001	2.63 (1.05, 6.58)	0.039
24-h ASPECTS	≤6	19.07 (8.51, 42.75)	<0.001	5.58 (1.83, 17.01)	0.002
Change in ASPECTS	≥1	8.66 (5.2, 14.43)	<0.001	4.85 (2.45, 9.60)	<0.001

ASPECTS: Alberta Stroke Program Early CT Score, OR: odds ratio, AOR: Adjusted odds ratio; CI: confidence interval. [a]The model was adjusted for age, systolic blood pressure, diastolic blood pressure, atrial fibrillation, congestive heart failure, chronic kidney disease, history of malignancy, swallowing dysfunction, alteration of consciousness, aphasia, neglect, cranial nerve disorder, gaze paresis, prestroke functional status, the National Institutes of Health Stroke Scale, TOAST classification, neutrophil-to-lymphocyte ratio, hemoglobin, and blood glucose at first admission. [b]The model was adjusted for age, systolic blood pressure, diastolic blood pressure, atrial fibrillation, dysarthria, swallowing dysfunction, alteration of consciousness, aphasia, neglect, gaze paresis, prestroke functional status, the National Institutes of Health Stroke Scale, TOAST classification, antihypertensive treatment before rt-PA, hematocrit, and blood glucose at first admission