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Post-stroke ASPECTS predicts outcome after thrombectomy

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Abstract

Purpose Infarct growth and final infarct volume are established outcome modifiers following endovascular thrombectomy (EVT) for patients with large vessel occlusion stroke (LVO). Simple techniques for final infarct volume measurement are lacking, and therefore, we tested whether post-EVT ASPECTS can be used for prognostic evaluation after EVT.

Methods Infarct size at baseline was measured in a prospective cohort of patients with LVO that underwent EVT with the ASPECTS score on admission non-contrast CT. Final infarct size was assessed with a post-EVT ASPECTS (ASPECTS-POST) obtained from a follow-up CT 24–72 h post-EVT. The best performing ASPECTS-POST was chosen based on comparisons of different thresholds. Outcome measures included survival rates and modified Rankin Score at 90 days.

Results A total of 272 patients were included and 166 of them had an ASPECTS-POST ≥ 7. ASPECTS-POST ≥ 7 was associated with increased likelihood of favorable outcome at 90 days (67% vs. 21%, $p < 0.001$) with sensitivity, specificity, and positive and negative predictive values of 86%, 58%, 61%, and 85%, respectively. On multivariate analysis, ASPECTS-POST ≥ 7 was found to be a significant modifier of favorable outcome (Odds Ratio [OR] 6.2, 95% confidence intervals [CI] 3.1–12.4) and survival (OR 5.8 95% CI 2.4–14.3).

Conclusion ASPECTS can be rapidly and easily obtained from the post-EVT NCCT and ASPECTS-POST ≥ 7 correlates with good outcome.

Keywords Cerebrovascular disease · Endovascular · Stroke · Thrombectomy · ASPECTS

Introduction

Large vessel occlusion (LVO) in the anterior circulation causes large hemispheric infarctions that are amenable to treatment with endovascular thrombectomy (EVT) [1]. Early infarct growth [2–4] and final infarct volume [2, 5–9] have been associated with outcome in these patients. However, methods for evaluation of these parameters usually involved employing sophisticated software that is both time and resource consuming [2, 5–12]. A simpler, less expensive method of assessing infarct volumes may be advantageous under these circumstances. The Alberta Stroke Project Early CT Changes Score (ASPECTS) is a well-established simple-to-use tool for assessing infarct volumes on the pre-EVT non-contrast CT scans (NCCT) [13–18]. As such, it can be used for patient selection for EVT and is associated with outcome after EVT [13–18]. We therefore reasoned that assessment of ASPECTS on the post-EVT NCCT (ASPECTS-POST) can be used to prognosticate and may assist in making therapeutic decisions after EVT including rehabilitation status, nursing care placement, and withdrawal of care. Therefore, we aimed to identify cutoffs optimally correlated with outcome and examine the predictive value of these ASPECTS-POST cutoffs after EVT.

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Patients and methods

All consecutive patients undergoing EVT for LVO were recruited into a prospective ongoing single-center database, and the data was retrospectively analyzed as previously described. The study was approved by the institutional review board that waived the need for obtaining informed consent due to the retrospective nature of the study.

The current study included patients who experienced an acute ischemic stroke with occlusion of the distal internal carotid artery (ICA) or M1 or M2 segments of the middle cerebral artery (MCA) proven on vascular imaging. Tandem occlusions were included. Distal occlusions to M3 segments of the MCA were not included. All patients underwent stentriever-assisted thrombectomy as the primary EVT modality but aspiration techniques were allowed as rescue. Patients that underwent systemic thrombolysis prior to EVT were included. Before 2018, only patients that presented within 7.5 h from symptom onset were included, but since 7/2018, patients treated up to 24 h from symptom onset were also included.

Overall, 282 consecutive patients with LVO that underwent EVT (mean age 70.2 ± 14.6, 53% females) were included in the database. The baseline characteristics of the study population are presented in Table 1. Of these, 272 patients (96%) had follow-up NCCT obtained 24–72 h after EVT that allowed scoring ASPECTS-POST and were included in the current study. Unenhanced brain CT images were obtained using standardized images on IQon-Spectral CT (Philips, Eindhoven, Holland) using the following parameters: kVp 120, mA 312, and ST 3 mm.

All EVT procedures were performed by two experienced interventionists (JEC and JMG), and the imaging data were analyzed retrospectively by 4 experienced stroke neurologists and fellows (RRL, AH, AF, and NS) that were blinded to outcomes. We collected demographics and vascular risk factor profile. Neurological deficits were measured with the National Institutes of Health Stroke Scale (NIHSS) at admission and discharge [19]. Stroke etiology was classified with the TOAST classification [20]. We also assessed time metrics, imaging variables including ASPECTS before and after treatment, and collateral status on the admission CTA when available [13]. In patients with previous strokes, the ASPECTS was calculated for the new stroke only.

Data on procedural variables including the modified thrombolysis in cerebral infarction (mTICI) score at the end of the procedure and the number of passes needed to achieve the best possible recanalization were also studied [21]. mTICI2b-3 was considered as successful target vessel recanalization.

Functional outcome was assessed with the modified Rankin scale (mRS) [22] at 90 days from stroke, and an mRS ≤ 2 was considered as favorable outcome. Survival and symptomatic intracranial hemorrhage (sICH) rates determined according to the ECASS III criteria [23] were used as other outcome parameters.

Statistical analysis was performed using the SPSS 25 (IBM USA). $p < 0.05$ was considered significant. The χ^2 test was used to explore the link between categorical variables. The Student's t test was used to compare continuous variables. We determined sensitivity, specificity, and positive and negative predictive values for different ASPECTS-POST using crosstabs in order to determine the best values for clinical use. We next performed multivariate logistic regression modeling to test whether ASPECTS-POST had an impact on favorable outcome and survival. In the regression, we included variables that were shown to affect outcome in previous

Table 1 Baseline characteristics of the study population

Variable	*N* = 272
Age (± sd)	70.2 ± 14.6
Gender (male %)	47
Hypertension (%)	69
Ischemic heart disease (%)	32
Atrial fibrillation (%)	45
Diabetes mellitus (%)	32
Hyperlipidemia (%)	46
Smoking (%)	26
Prior stroke (%)	16
TOAST classification (%)	
Cardioembolic	59
Large vessel	23
Other known	3
Unknown	15
Admission NIHSS (± sd)	16.8 ± 6.8
Onset to reperfusion (min ± sd)	302 ± 201
Admission ASPECTS > 7 (%)	62
Favorable collaterals (%)	42
Number of passes (%)	
0*	3
1	43
2	14
> 3	40
mTICI (%)	
0–2a	15
2b–3	85
Permanent stent placed (%)	14
Any ICH (%)	17
Symptomatic ICH (%)	5
ASPECTS-POST (%)	
0–4	21
5	10
6	8
≥ 7	61
mRS 90 0–2 (%)	43
Survival 90 days (%)	84

Data are presented as mean ± SD or percentages of the entire group

ASPECTS, Alberta Stroke Project Early CT Score; *ASPECTS-POST*, ASPECTS obtained on follow-up CT; *NIHSS*, National Institutes of Health Stroke Scale; *mRS*, modified Rankin score; *mTICI*, modified thrombolysis in cerebral infarction; *ICH*, intracerebral hemorrhage

*0 number of passes = clot aspiration only studies including age, successful reperfusion, collateral state, and stroke severity [5, 24] in addition to ASPECTS-POST.

Data availability Individual de-identified participant data including vascular risk factor profiles, demographics, and procedural data as well as imaging findings will be shared in accordance with the Ministry of Health policies and regulations. Data sharing is limited for academic purposes only pending approval by the local IRB.

Results

Sensitivity, specificity, and positive and negative predictive values (PPV, NPV) for the correlation of different APSECTS-POST on favorite functional outcome (mRS ≤ 2) showed that the best predictive values are obtained with a cutoff of ASPECTS-POST ≥ 7 (Table 2). The sensitivity of ASPECTS-POST ≥ 7 was high (86%) but the specificity was relatively low (58%) with a high negative predictive value of 85% but a medium positive predictive value of 61%. For ASPECTS-POST ≥ 6, the sensitivity and NPV were slightly higher but the specificity and PPV were slightly lower which led us to use a cutoff of ASPECTS-POST ≥ 7 for the multivariate analyses.

In comparison with patients that had an ASPECTS-POST of < 7, those that had a score of ≥ 7 were significantly younger (68 ± 15 vs. 72 ± 18, $p = 0.017$), and less frequently had diabetes (23% vs. 40%; $p = 0.003$; Table 3). Patients in the ASPECTS-POST group ≥ 7 also had significantly lower admission and discharge NIHSS scores (15.3 ± 7 and 3.3 ± 4 vs. 18.1 ± 6 and 11.8 ± 7, respectively; $p < 0.001$ for both), and more often had favorable collateral profiles (62% vs. 25%; $p < 0.001$). These patients also had higher likelihood of favorable target recanalization (92% vs. 80%; $p = 0.003$) and lower likelihood of symptomatic ICH (1% vs. 9%; $p = 0.002$). Survival and favorable functional outcome rates were also significantly higher in patients that had an ASPECTS-POST ≥ 7 (95% vs. 76% and 67% vs. 21%; $p < 0.001$ for both, Table 3).

Table 2 Sensitivity, specificity, and predictive values of different ASPECTS-POST on favorable outcome (mRS ≤ 2)

ASPECTS-POST	Sensitivity	Specificity	PPV	NPV
≥ 5	98%	35%	46%	96%
≥ 6	92%	49%	58%	89%
≥ 7	86%	58%	61%	84%
≥ 8	74%	73%	67%	79%

ASPECTS, Alberta Stroke Project Early CT Score; *ASPECTS-POST*, ASPECTS obtained on follow-up CT; *PPV*, positive predictive value; *NPV*, negative predictive value

On the multivariate analysis for favorable outcome at 90 days post-stroke (Table 4), ASPECTS-POST ≥ 7 and successful recanalization remained significant positive modifiers for achieving functional independence while age and admission NIHSS remained negative modifiers of favorable outcome.

On multivariate analysis for survival at 90 days post-EVT (Table 5), ASPECTS-POST ≥ 7 remained the sole positive modifier of survival whereas age and admission NIHSS were found to negatively affect survival.

Discussion

The current study identifies ASPECTS-POST ≥ 7 as a positive marker of survival and favorable functional outcome at 90 days post-EVT. We hypothesized that the effect of ASPECTS-POST should be similar to the effect of lesion growth and final infarct volume that were previously shown to affect long-term outcome after EVT [3, 5, 6, 8–12]. Our results corroborate this association although ASPECTS-POST estimation of lesion volume may possibly be less accurate compared with more precise measurement of lesion volume with dedicated volumetric software [10, 11]. Furthermore, magnetic resonance imaging parameters such as diffusion- and perfusion-weighted sequences may better correlate with outcome [25, 26], and an MRI-based ASPECTS-like imaging may be easily obtained. However, MRI may be problematic in that it is not as widely available as CT and that there are patients with absolute (e.g., shrapnel) or relative (e.g., claustrophobia, pacemakers) contraindications for imaging. Therefore, we suggest that using ASPECTS-POST ≥ 7 as a prognostic marker is advantageous given the simplicity and reproducibility of ASPECTS acquisition compared with the use of designated specialized software or naked eye estimations of the lesion volume. Furthermore, recent studies have shown that automated software determination of ASPECTS is feasible and more accurate than ascertainment of ASPECTS even by experienced radiologists [27]. Use of such strategies will simplify data acquisition even further making it very accurate and simple to use. Furthermore, while sophisticated multimodal neurovascular imaging is usually used before EVT for optimal patient selection, this type of imaging studies is usually not used after EVT. The sole use of clinical parameters such as the degree of neurological disability obtained on the NIHSS [28] or similar scales post-procedure may have its values but may be inaccurate in itself because other conditions such as infections, pulmonary embolism, and cardiac decompensation may influence the degree of neurological deficits. Thus, a prognostic imaging marker after completion of EVT is needed. As

Table 3 Comparison of patients according to APSECTS-POST

Characteristics	ASPECTS-POST ≥ 7 *n* = 129	ASPECTS-POST < 7 *n* = 143	*p*
Age (SD)	68.1 (15.1)	72.3 (18.4)	0.017
Gender male (%)	56 (43)	72 (50)	0.252
Hypertension (%)	82 (64)	103 (72)	0.135
Diabetes (%)	30 (23)	57 (40)	0.003
Atrial fibrillation (%)	55 (43)	67 (47)	0.485
Hyperlipidemia (%)	60 (47)	62 (43)	0.601
Ischemic heart disease (%)	39 (30)	48 (34)	0.556
Current smoking (%)	31 (24)	37 (26)	0.726
Previous stroke (%)	20 (16)	25 (18)	0.661
TOAST (%)			0.631
Cardioembolic	75 (58)	87 (61)	
Atherosclerotic large vessel	30 (23)	30 (21)	
Other known	6 (5)	4 (2)	
Unknown	18 (14)	22 (16)	
Involved side (left; %)	70 (55)	75 (54)	0.905
Site of occlusion (%)			0.371
ICA	29 (23)	18 (13)	
M1-MCA	64 (50)	81 (57)	
M2-MCA	12 (9)	16 (11)	
Tandem occlusion	24 (18)	28 (19)	
Admission NIHSS (SD)	15.3 (7.0)	18.1 (6.4)	< 0.001
Discharge NIHSS (SD)	3.3 (4)	11.8 (7.4)	< 0.001
Favorable collaterals (%)	77 (62)	34 (25)	< 0.001
Bridging with tPA (%)	27 (21)	44 (31)	0.065
OTD (SD)	138 (172)	138 (148)	0.984
OTR (SD)	296 (228)	305 (174)	0.652
Passes (SD)	2.1 (1.9)	3.8 (5.8)	0.002
Eptifibatide (%)	29 (23)	27 (19)	0.463
Stent (%)	30 (23)	29 (20)	0.552
mTICI 2b-3 (%)	119 (92)	114 (80)	0.003
Any ICH (%)	8 (6)	41 (29)	< 0.001
Symptomatic ICH (%)	1 (1)	13 (9)	0.002
Survival (%)	123 (95)	108 (76)	< 0.001
mRS 0–2 (%)	87 (67)	30 (21)	< 0.001

Data are presented as mean ± SD or percentages of the entire group

ASPECTS, Alberta Stroke Project Early CT Score; *ASPECTS-POST*, ASPECTS obtained on follow-up CT; *NIHSS*, National Institutes of Health Stroke Scale; *mRS*, modified Rankin score; *mTICI*, modified thrombolysis in cerebral infarction; *ICH*, intracerebral hemorrhage

such, ASPECTS-POST can theoretically be used to prognosticate outcomes and guide therapeutic decisions after EVT such as suitability for rehabilitation on the one hand and withdrawal of care on the other. Other known markers for favorable outcome such as younger age, lower stroke severity, favorable collateral profile, lower number of stentriever passes needed to recanalize the occluded vessel, and higher likelihoods of favorable recanalization were all correlated with ASPECTS-POST ≥ 7.

Despite the high sensitivity and NPV observed, our data suggests that ASPECTS-POST ≥ 7 is still not a perfect surrogate predictor of outcome given the relatively low specificity and PPV observed in the current study. Interestingly, it was argued that since infarcts continue

Table 4 Multivariate analysis on chances for having a favorable outcome (mRS ≤ 2) at 90 days

	OR	95% C.I		p
Age	0.96	0.94	0.98	0.001
mTICI 2b-3	10.39	2.96	36.54	0.000
Admission NIHSS	0.95	0.90	0.99	0.035
ASPECTS-POST ≥ 7	6.18	3.09	12.37	0.000
Favorable collaterals	1.40	0.72	2.70	0.318

ASPECTS, Alberta Stroke Project Early CT Score; *ASPECTS-POST*, ASPECTS obtained on follow-up CT; *NIHSS*, National Institutes of Health Stroke Scale; *mTICI*, modified thrombolysis in cerebral infarction

to grow over time in some patients, possibly due to progressive collateral failure, measurement of final infarct volume should be delayed for one week [11]. Thus, the relatively early determination of ASPECTS-POST in the current study which utilized the first post-EVT NCCT scan may have contributed to the relatively low specificity and PPV values observed in the current study. Therefore, and for reasons of simplicity, we suggest to further study the correlation of ASPECTS-POST obtained at 4–7 days post-EVT compared with outcome measures in future studies and examine whether PPV and specificity will improve. Another limitation for using the ASPECTS as a predictor of outcome is that the ASPECTS only accounts for lesions involving the MCA territory, and in cases with ICA occlusion affecting also the anterior cerebral, it may underestimate the actual damage, thus lowering its ability to predict outcome in such patients with a known poor prognostic marker such as ACA involvement [29]. Furthermore, ASPECTS is not calibrated to account for lesion eloquence. Thus, it is likely that patients with an ASPECTS of 7 with points taken off because of three separate eloquent cortical lesions (e.g., including the language area and motor cortex) will fare differently than those with an APSECTS of 7 in whom the points were deducted due to lesions involving less eloquent areas (e.g., right frontal area). Lesion side which is not accounted for in the ASPECTS may also influence outcomes such that a small infarct in the left temporal cortex could be more disabling than a large right frontal infarct. These drawbacks which are shared by all methods of infarct volume measurement may be responsible for the imperfect prediction of outcome by such methods. Ongoing research combining total lesion volume assessment with lesion side and relative eloquence of the affected brain lesions should help to determine if such a combinatory approaches may better predict outcome.

Table 5 Multivariate analysis on chances for survival at 90 days

	OR	95% C.I.		p
Age	0.95	0.92	0.98	0.002
mTICI 2b-3	1.28	0.49	3.34	0.614
Admission NIHSS	0.93	0.88	0.99	0.035
ASPECTS-POST ≥ 7	5.87	2.42	14.26	0.0001
Favorable collaterals	0.80	0.33	1.92	0.611

ASPECTS, Alberta Stroke Project Early CT Score; *ASPECTS-POST*, ASPECTS obtained on follow-up CT; *NIHSS*, National Institutes of Health Stroke Scale; *mTICI*, modified thrombolysis in cerebral infarction

The current study has several advantages including the facts that the patients represent a typical non-selected population of LVO patients which depicts real-life status and that it did not use strict inclusion criteria.

Our study also has several limitations including the fact that it was based on single-center data and that the data was retrospectively analyzed. Furthermore, ASPECTS-POST was not determined by investigators that were blinded to the EVT result; although given the retrospective nature of the study, it is unlikely that the evaluators were biased in their scoring. Third, by assessing properties at multiple thresholds and then choosing the best performing cutoff for further analyses within the same dataset, a bias that favors the prognostic tool may have been created, and external validation will be needed to test whether these cutoffs are the best. Fourth, the multivariable model for assessment of the impact of ASPECTS-POST on survival model could be under-powered. Therefore, the results should be interpreted cautiously and need corroboration in a larger data set.

In conclusion, ASPECTS-POST ≥ 7 is an easily obtained marker that is correlated to survival and favorable functional outcome. ASPECTS-POST ≥ 7 may add significant prognostic information following EVT in patients with LVO, and future studies could use this marker as part of a prognostic scale after EVT.

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Compliance with ethical standards

Conflict of interest The authors declare they have no conflicts of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was not obtained from all individual participants included in the study because the IRB approved a retrospective analysis of anonymized data without the need to obtain informed consent.

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