ORIGINAL ARTICLE

ASPECT Scoring to Estimate >1/3 Middle Cerebral Artery Territory Infarction

Bart M. Demaerschalk, Brian Silver, Edward Wong, Jose G. Merino, Arturo Tamayo, Vladimir Hachinski

ABSTRACT: ***Purpose:*** To compare the inter-observer reliability of Alberta Stroke Programme Early CT Scoring (ASPECTS) with the ICE (Idealize-Close-Estimate) method of estimating > 1/3 middle cerebral artery territory (MCAT) infarction amongst stroke neurologists and to determine how well ASPECT Scoring predicts > 1/3 MCAT infarctions in acute ischemic stroke (AIS). ***Background:*** The European Cooperative Acute Stroke Study suggested that > 1/3 involvement of the MCAT on early CT scan was a risk factor for symptomatic intracerebral hemorrhage (SICH) following treatment with tissue plasminogen activator (tPA) for AIS but, in the absence of a systematic method of estimation had poor interobserver reliability (Kappa 0.49). The ICE method was developed to standardize the approach to estimating early MCAT infarct size and has very good interobserver reliability (Kappa 0.72). ASPECTS has comparable interobserver reliability and is reported to predict both neurological outcome and SICH. ***Methods:*** Five stroke neurologists were tested with 40 AIS CT scans. Each performed blinded independent assessments of early ischemic changes with both ASPECTS and ICE. The reference standard was majority opinion of 1/3 MCAT determination of five neuroradiologists. A receiver operator curve (ROC) was constructed and likelihood ratios (LR) were calculated. Chance corrected agreement (kappa) and chance independent agreement (phi) were calculated for both methods, and analysis of variance was used to calculate reliability by intraclass correlation coefficient (ICC) for ASPECTS. ***Results:*** The LR for a positive test (> 1/3 MCAT) were extremely large and conclusive (approaching infinity) for ASPECTS of 0-3; were large and conclusive (30, 20, and 10) for ASPECTS of 4, 5, and 6 respectively; was an unhelpful 1 for ASPECTS of 7, and were again extremely large and conclusive (approaching zero) for ASPECTS of 8-10. A ROC plot supported an ASPECTS cutoff of < 7 as best for 1/3 MCAT estimation (94% sensitivity and 98% specificity). Kappa and Phi statistics were moderately good for both ASPECTS and ICE (0.7). ICC for ASPECTS was 0.8. ***Conclusions:*** When experienced stroke neurologists utilize a formalized method of quantifying early ischemic changes on CT, either ASPECTS or ICE, the interobserver agreement and reliability are satisfactory. ASPECTS allows for a strong and conclusive estimation of the presence of 1/3 MCAT involvement and a cutoff point of < 7 results in best test performance.

RÉSUMÉ: Le score ASPECT dans l'évaluation de l'infarctus >1/3 du territoire de l'artère cérébrale moyenne. ***Objectif:*** Comparer la fiabilité interobservateur, chez des neurologues spécialisés dans l'accident vasculaire cérébral (AVC), pour le score ASPECT et la méthode ICE (idealize-close-estimate) d'estimation de l'infarctus >1/3 du territoire de l'artère cérébrale moyenne (TACM) et déterminer si le score ASPECT prédit bien l'infarctus >1/3 du TACM dans l'AVC ischémique aigu. ***Contexte:*** Selon les données du European Cooperative Acute Stroke Study, l'atteinte >1/3 du TACM à la tomodensitométrie réalisée tôt après l'événement serait un facteur de risque de l'hémorragie intracérébrale symptomatique (HICS) suite au traitement par l'activateur du plasminogène tissulaire (t-PA) dans l'AVC ischémique aigu, mais sa fiabilité interobservateur serait médiocre (kappa 0,49) en l'absence d'une méthode systématique d'estimation. La méthode ICE a été développée pour standardiser la démarche d'estimation de la taille de l'infarctus du TACM en phase précoce et elle a une très bonne fiabilité interobservateur (kappa 0,72). ASPECTS possède une fiabilité interobservateur comparable et on considère qu'il peut prédire tant l'issue neurologique que l'HICS. ***Méthodes:*** Cinq neurologues spécialistes de l'AVC ont participé à l'étude de 40 tomodensitométries d'AVC ischémique aigu. Chaque neurologue a fait une évaluation indépendante des changements ischémiques précoces, à l'aveugle, au moyen du score ASPECT et de la méthode ICE. Le standard de référence était l'opinion majoritaire de 1/3 TACM déterminé par cinq neuroradiologistes. Une courbe ROC a été établie et des rapports de vraisemblances ont été calculés. La concordance aléatoire corrigée (kappa) et la concordance aléatoire indépendante (phi) ont été calculées pour les deux méthodes et une analyse de variance a été utilisée pour estimer la fiabilité au moyen du coefficient de corrélation intraclasse pour ASPECTS. ***Résultats:*** Les rapports de vraisemblances pour un test positif (>1/3 TACM) étaient extrêmement élevés et concluants (près de l'infini) pour des scores ASPECT de 0 à 3; ils étaient élevés et concluants (30, 20 et 10) pour des scores ASPECT de 4, 5 et 6 respectivement; ils étaient de 1 et inutiles pour un score ASPECT de 7 et de nouveau extrêmement élevés et concluants (près de zéro) pour des scores ASPECT de 8 à 10. La courbe ROC suggérait qu'un point de coupe ASPECTS de moins de sept était optimal pour estimer 1/3 TACM (sensibilité de 94% et spécificité de 98%). Les statistiques kappa et phi étaient assez bonnes pour ASPECTS et ICE (0,7). Le coefficient de corrélation intraclasse était de 0,8. ***Conclusions:*** Quand des neurologues possédant une vaste expérience de l'AVC utilisent une méthode standard reconnue, soit ASPECTS ou ICE, pour l'évaluation quantitative des changements précoces observés à la tomodensitométrie de l'AVC ischémique aigu, la concordance interobservateur et la fiabilité en sont améliorées et sont satisfaisantes. ASPECTS permet un estimé robuste et concluant de la présence de l'atteinte de 1/3 TACM et un point de coupe < 7 donne la meilleure performance.

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The 1995 NINDS recombinant tissue plasminogen activator (tPA) study showed the three month efficacy of tPA when given within three hours of onset of acute ischemic stroke.[1] The European Cooperative Acute Stroke Study (ECASS) first suggested that involvement of greater than one-third of the MCAT on early computed tomography (CT) scan was a significant risk factor for hemorrhage and that patients with these findings did not appear to benefit from treatment.[2] Despite this latter report, there was no description of the technique to perform such an estimation. In the absence of a standardized method of estimation, the 1/3 rule has poor inter-observer reliability amongst stroke neurologists without knowledge of affected hemisphere (Kappa 0.49).[3] The ICE method was developed to standardize the approach to estimating early MCAT infarct size and has a better inter-observer reliability amongst stroke neurologists blinded to clinical information (Kappa 0.72).[4] ASPECTS Study Group reported that ASPECT Scoring has comparable inter-observer reliability (Kappa 0.69), but the methods have never been subjected to head-to-head testing.

Our purpose was to compare the inter-observer reliability of ASPECT Scoring with the ICE (Idealize-Close-Estimate) method of estimating > 1/3 middle cerebral artery territory (MCAT) infarction amongst stroke neurologists and to determine how well ASPECT Scoring predicts > 1/3 MCAT infarctions in acute ischemic stroke (AIS).

The ICE method was developed by the Southwestern Ontario Stroke Team at University of Western Ontario, London, Ontario, Canada.[5] The technique bears the acronym ICE, corresponding to the three steps in the process. In step one, the observer idealizes (I) in their mind the area represented by the MCAT. The shape of the area is trapezoidal. In step two, the observer looks for areas of asymmetry between the hemispheres which are typically represented in acute stroke by loss of normal gray-white interface, sulcal effacement, and subtle lucency. The observer then closes (C) a geometric figure around the area or areas judged to be abnormal. In step three, the observer estimates (E) the ratio of the geometric figure in step two (C) to the trapezoid in step one (I) or C/I. See Figure 1.

The Alberta Stroke Programme Early CT Scoring (ASPECTS) is a quantitative scoring system to assess the amount of early ischemic change in the MCAT. The observer, using ASPECTS, assesses the MCAT on the basis of two standardized axial cuts, one at the level of the thalamus and basal ganglia, and one superior to this level at corona radiata. The MCA distribution is allotted 10 points, encompassing 3 subcortical (caudate (C), lentiform (L), and internal capsule (IC)) and 7 cortical structures (insular ribbon (I), M1, 2, 3 representing the anterior, middle, and posterior branches of the MCAT and M4, 5, 6 representing anterior, lateral, and posterior branches of MCAT superior to those previously listed). One point is removed if an ischemia related abnormality is detected in each of the defined regions. A normal scan would receive an ASPECT score of 10 points. See Figure 2.

Methods

Five stroke neurologists (BD, BS, EW, JGM, and AT) acted as the observers. Each served as an active member of the Southwestern Ontario acute stroke team at University of Western Ontario, London, Canada during a two year term of cerebrovascular neurology fellowship training. Computed tomography scans from 40 patients presenting within six hours of acute onset of focal neurological symptoms and signs were used. Time from symptom onset to CT was 30-60 minutes in 3%, 61-90 minutes in 12%, 91-120 minutes in 12%, 121-150 minutes in 24%, 151-180 minutes in 18%, 181-210 minutes in 12%, 211-240 minutes in 9%, 241-270 minutes in 5%, and 271-300 minutes in 5%. All patients were confirmed radiologically, by a subsequent CT scan at 24 hours, to have sustained a new cerebral infarction. Fifty-nine percent were female. Mean (median) age

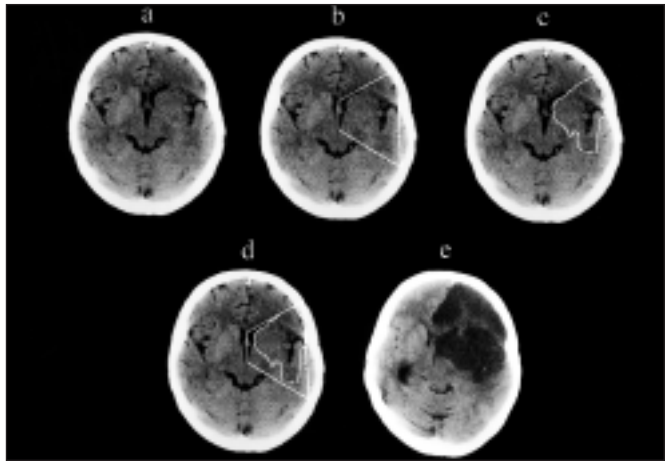

Figure 1: *"ICE" method of estimation of greater than one-third middle cerebral artery territory infarction on initial CT scan: a. Baseline scan; b. Idealized MCA territory (trapezoid) onto baseline scan; c. Closure around area of abnormality; d. Estimate of ratio; e. 24-hour scan.*

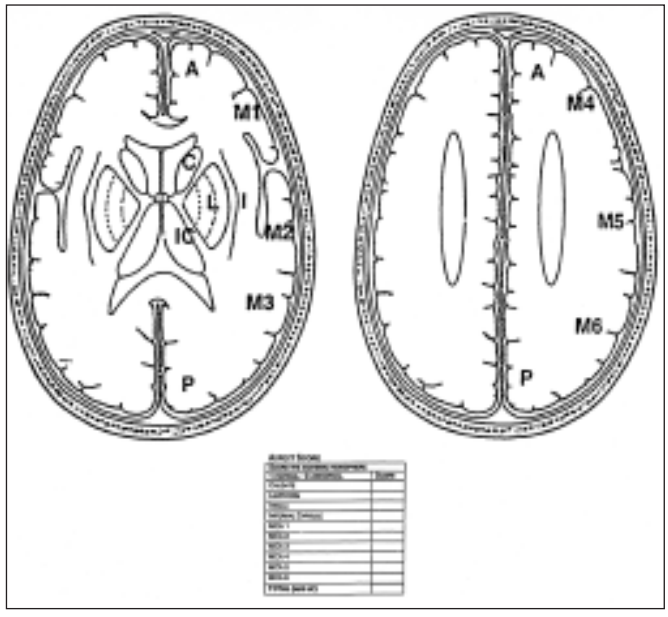

Figure 2: *ASPECT Scoring*

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Table 1: Receiver Operator Curve Data Table

ASPECT Score Cut-Off	Sensitivity	95% Confidence Interval	Specificity	95% Confidence Interval
< 5	73.6	63.4 – 83.8	99.6	98.8 - 100
< 6	81.9	73.1 – 90.8	99.2	98.0 - 100
< 7	94.4	89.2 – 99.7	97.9	96.1 – 99.7
< 8	100	98.3 - 100	93.0	89.8 – 96.2

was 68.4 (69.5) years. The hard copies of the 40 films were used for testing. All CT studies were performed on a third generation General Electric Hi-Speed Advantage scanner with average windowing of 80 and average leveling of 40. Films were displayed on conventional radiology viewing boxes. Consecutively numbered viewing stations were set up. No clinical information, including the side of affected hemisphere, was provided to the observer stroke neurologists. Three minutes was allotted for the viewing, grading, and scoring of each scan. On a standardized form, the stroke neurologist indicated whether or not any detected early ischemic changes exceeded 1/3 MCAT by the ICE method (yes or no) and the ASPECT score (0 to 10). The reference standard was majority opinion designation of five neuroradiologists of each scan as < or > 1/3 MCAT.

Table 2: Likelihood Ratios for ASPECT Scores

ASPECT Score	Likelihood Ratio for Positive Test (> 1/3 MCAT)	95% Confidence Interval
0	217.4	4.2 – 11 193.8
1	139.1	2.6 – 7 185.5
2	97.0	1.8 – 5 182.7
3	150.5	2.9 – 7 853.4
4	30.3	3.9 – 234.8
5	20.2	2.5 – 164.8
6	10.1	2.8 – 36.3
7	1.1	0.4 – 3.4
8	0.0	0.0 – 1.7
9	0.0	0.0 – 0.9
10	0.0	0.0 – 0.3

A receiver operator curve (ROC) was constructed. Likelihood ratios (LR) for ASPECT scores were calculated. Chance corrected interobserver agreement (unweighted Kappa) was calculated for both methods, ASPECT and ICE. Interobserver reliability by intraclass correlation coefficient (ICC) was calculated for ASPECTS. Whenever possible, 95% confidence intervals were calculated and presented.

Results

Likelihood ratios for a positive test (> 1/3 MCAT) were extremely large and conclusive (approaching infinity) for ASPECTS of 0-3, were large and conclusive (30, 20, and 10) for ASPECTS of 4, 5, and 6 respectively, was an unhelpful 1 for ASPECTS of 7, and were again extremely large and conclusive

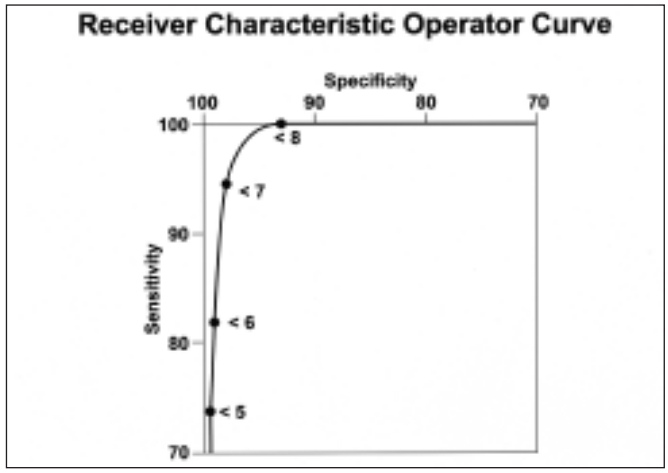

Figure 3: *For ASPECTS, the ROC curve suggests that the most favorable cut point is < 7, which is the one nearest the upper left corner.*

(approaching zero) for ASPECTS of 8-10. See Table 2. Receiver operator curve plot supported an ASPECTS cutoff of < 7 as best for 1/3 MCAT estimation (94% sensitivity and 98% specificity). See Table 1 and Figure 3. Unweighted Kappa and Phi statistics were moderately good for both ASPECTS and ICE (0.7). Intraclass correlation coefficient for ASPECTS was 0.8. See Table 3.

Discussion

Early ischemic changes on CT in the first few hours after AIS represent early cytotoxic edema and probably the development of irreversible injury. It has been postulated that the larger the volume of early ischemic changes visible prior to IV tPA the higher the risk of intracerebral hemorrhage and the lower the probability of favorable functional outcome post stroke. The 1/3 MCAT rule was established after ECASS, through a post-hoc analysis, and has not been sufficiently validated in a prospective fashion as being predictive of patient outcomes. This issue has

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Table 3: Interobserver Agreement and Inter-Rater Reliability

CT Scoring Method	Median Kappa Interobserver Agreement	Intraclass Correlation Coefficient Inter-Rater Reliability
ASPECT	0.72	0.79
ICE	0.72	NA

not yet been fully settled in the literature. The ASPECTS Study Group reported that an individual with an ASPECTS score of 7 or less had a risk of symptomatic intracerebral hemorrhage 14 times that of patients with a score of greater than 7.[3] In the Canadian Alteplase for Stroke Effectiveness Study the baseline ASPECTS score was not a predictor of symptomatic intracranial hemorrhage, but was a strong predictor of outcome.[6] Lower ASPECTS scores were associated with a lower probability of an independent functional outcome following thrombolysis. In contrast, the NINDS rt-PA Stroke Study Group reported that early ischemic changes on CT are prevalent and correlate with stroke severity, however they are not independently associated with increased risk of adverse outcome after thrombolysis.[7] Given the continued uncertainty, neurologists and neuroradiologists at stroke centers are still in the habit of carefully evaluating the CT brain of acute ischemic stroke patients for the presence of early ischemic changes. They largely rely on one or both of these tools, ASPECTS and ICE.

Most neurologists treating acute stroke still depend most heavily on CT because it is more readily available than MRI. Computed tomography methods for estimating the MCAT involved have been developed. The 1/3 MCAT rule applied in the absence of a formal technique has an unacceptably low interobserver agreement for stroke neurologists of 0.49. In contrast, systematic approaches to the quantification of early ischemic changes, like ASPECTS and ICE, have a more substantial interobserver agreement amongst stroke neurologists. The ASPECTS Study Group reported a kappa statistic for ASPECTS of 0.69 for blinded stroke neurologists. We report a comparable median kappa statistic for ASPECTS and ICE of 0.72. The inter-observer agreement amongst stroke neurologists aware of the affected hemisphere and the intra-observer agreement would predictably be even higher.

Although continuous measures are preferable to categorical ones, there are times when it is necessary to use a continuous scale to predict a dichotomous outcome. The ASPECT Scoring system is a good example of an ordinal scale which must eventually be used to decide whether or not the early ischemic changes exceed some threshold for acceptable administration of IV tPA. A technique for establishing the optimal cut point is the Receiver Operating Characteristic curve. The cut point nearest the upper left corner results in the smallest overall error rate. For ASPECTS, the ROC curve suggests that the most favorable cut point is < 7. This cut point is very similar to that already suggested by the ASPECTS Study Group, ≤ 7.[3,8]

The likelihood ratios indicate by how much a given ASPECT score will raise or lower the probability that the early ischemic changes are > 1/3 MCAT. ASPECT scores of 0 - 6 have likelihood ratios of > 10, generating conclusive evidence to support early ischemic changes in excess of 1/3 MCAT. An ASPECT score of 7 is accompanied by an unhelpful likelihood ratio of 1. ASPECT scores of 8 – 10 have likelihood ratios of < 0.1, generating conclusive evidence to support early ischemic changes which are less than 1/3 MCAT.

It appears, from head-to-head comparison, that the ICE judgement of > 1/3 MCAT is comparable to the ASPECT score of < 7. Although both of these scoring systems are relatively simple to learn and quick to apply, the important and unanswered question is: What is the most appropriate threshold for early ischemic change volume on CT, below which patients should be considered for IV TPA and above which they should be denied? A reference standard of five experienced neuroradiologists' judgement of 1/3 MCAT presumes that the 1/3 rule is the correct threshold. Validation of these scoring systems in randomized controlled trials of thrombolytics may allow for a more accurate estimate of the best threshold, if a clinically meaningful threshold should actually exist.

Barber et al[8] reported that CT and diffusion weighted imaging (DWI) are comparable for detecting and quantifying signs of cerebral ischemia in acute stroke when assessed systematically using ASPECTS. ASPECTS, it appears, provides a reliable method of assessing the DWI stroke lesion. Therefore, the results of our ICE determination of > 1/3 MCAT and ASPECT score of < 7 may be generalizable to DWI as well as CT.

A potential limitation of the study is that hard copies of CT scans were employed exclusively. This is not properly representative of the current state in stroke centers, many of which use digitized images. Inter-rater reliability for assessment of early ischemic changes and tPA eligibility on CT brain via teleradiology versus viewing boxes has been assessed elsewhere and reported as 0.65 and 1.0 respectively.[9] These are likely to be underestimates given that the teleradiology images were scanned rather than digitally imaged in that study.

In conclusion, when stroke neurologists utilize a formalized method, either ASPECTS or ICE, of evaluating early CT changes in AIS, interobserver agreement and reliability are improved. ASPECTS allows for a strong and conclusive estimation of the presence of 1/3 MCAT involvement and a cutoff point of < 7 results in best test performance.

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