Reliability and Utility of the Alberta Stroke Program Early Computed Tomography Score in Hyperacute Stroke

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Goal: The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on non-contrast computed tomography (NCCT) is dependent on the visibility of early ischemic change. The goal of our study was to evaluate whether time from ischemic stroke onset to initial NCCT influences the inter-rater variability and prognostic accuracy of ASPECTS for a 3-month functional outcome. *Materials and Methods:* Ischemic stroke patients treated with intravenous tissue plasminogen activator (IV-tPA) from 2007 to 2014 at the Royal Melbourne Hospital were included. ASPECTS were blindly assessed by 2 independent raters with inter-rater agreement determined by weighted kappa. Onset time to computed tomography time was dichotomized at the median (≤100 and >100 minutes). Outcome was assessed using the modified Rankin Scale. Logistic regression and receiver operating characteristic analysis were used to assess the prognostic utility of ASPECTS in the early and later time periods. *Results:* There were 379 patients included. Inter-rater agreement was significantly lower in the early time period: kappa = .75 (95% confidence interval (CI), .59-.84) ≤ 100 minutes versus .92 (95% CI, .91-.93) > 100 minutes, $P < .001$. The distributions of absolute inter-rater differences in ASPECTS differed significantly between time epochs ($P = .03$). The prognostic accuracies of ASPECTS across time epochs were area under the receiver operating characteristic curve ≤ 100 minutes = .57 (95% CI, .50-.64) and >100 minutes = .66 (95% CI, .59-.73), $P = .055$. *Conclusions:* This study demonstrated a significantly lower inter-rater agreement and a trend toward reduced prognostic accuracy of ASPECTS in earlier time periods. The use of ASPECTS to select patients for revascularization in early time windows may be unreliable. **Key Words:** Ischemic—stroke—CT—ASPECTS—time.

Introduction

Stroke interventions are time critical, and patients who present to the hospital within the first 60 minutes of onset have the greatest chance of benefitting from revascularization therapies.[1] Thus, it has been clinically crucial to develop systems, tools, and technologies to optimize the number of patients receiving treatment earlier.[2] For example, education in recognizing stroke symptoms, efficient code stroke methods, and the introduction of telemedicine have led to an increase in the proportion of stroke patients arriving at the hospital earlier.[3] The preliminary implementation of mobile stroke units has allowed the use of pre-hospital treatment to reduce the median time from stroke onset to therapy decision to as little as 35 minutes.[4] Currently, the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on non-contrast computed tomography (NCCT) represents a commonly used imaging tool for detecting early ischemic change

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(EIC). However, the use of ASPECTS is highly time dependent, with optimal detection on NCCT hours to days from stroke onset.[5-7] As such, and with a shift to earlier stroke treatment times, it is currently unknown whether the utility of ASPECTS will persist as a simple and reliable method for assessing ischemic change.

Five randomized controlled trials demonstrated the superiority of intra-arterial and intravenous tissue plasminogen activator (IV-tPA) treatment over standard treatment for acute ischemic stroke patients with large artery occlusion.[8-12] For most of these trials, the ASPECTS was used to grade the degree of EIC, allowing the prediction of irreversible ischemic injury.[13] Similarly, for patients only eligible for IV-tPA, the ASPECTS on NCCT has proven a simple and reliable method to identify stroke patients unlikely to make an independent recovery despite this treatment.[14,15] Important advantages of ASPECTS on NCCT are its geographical and temporal ubiquity and its high sensitivity for the detection of intracerebral hemorrhage.[14] EIC on NCCT is measured by a reduction in Hounsfield units (HU), which are time dependent. Parenchymal hypoattenuation is due to an increase in brain tissue water content as a result of ischemic injury, leading to ionic or vasogenic edema.[16,17] Thus, the visibility of ischemic change on NCCT varies from hours to days later depending on the magnitude of water uptake in ischemic tissues.[5-7] As it is established that time affects the visibility of ischemic change, we hypothesized that the ASPECTS in hyperacute times is not a reliable measure for selecting patients for reperfusion therapies. Consequently, the objective of our study was to evaluate whether hyperacute time from ischemic stroke onset to initial NCCT influences the inter-rater variability and prognostic accuracy of ASPECTS for a 3-month functional outcome.

Methods

Study Population

This was a retrospective, single-center, cohort study of acute anterior circulation ischemic stroke patients admitted to the Royal Melbourne Hospital between December 26, 2007, and April 20, 2014, who received thrombolysis. Patients were excluded if baseline demographic or follow-up clinical data were unavailable during the patients' time in the ward or if a 3-month follow-up modified Rankin Scale (mRS) was unavailable. Patients were also excluded if the NCCT was severely movement degraded. The study was approved by the Royal Melbourne Hospital Human Research Ethics Committee.

ASPECTS Assessment on NCCT

The initial NCCT (Somatom 16 slice and Definition FLASH 128 slice scanners, Siemens, Erlangen, Germany) was reviewed using the Picture Archiving and Communicating System on radiology workstations. NCCT ASPECTS were assessed using 5-mm axial slices as per standard recommendations (aspectsinstroke.com). The regions included M1, M2, M3, M4, M5, M6, Caudate Nucleus, Lentiform Nucleus, Insula, and the posterior limb of the Internal Capsule. The ASPECTS provides a semiquantitative score out of 10 with a score of 10 indicating a normal computed tomography (CT) scan. A score of >7 has been validated as being associated with a favorable prognosis for patients receiving thrombolytic therapy, and a score of ≤7 is generally associated with poor prognosis in thrombolysis patients.[18] A point was deducted for each region of the brain with loss of gray–white differentiation or hypointensity visible on at least 2 adjacent slices. Established, chronic infarction was ignored and not included in the analysis. The assessors (a neuroradiology fellow and a stroke research fellow) were aware of the affected hemisphere and rated ASPECTS independently with subsequent consensus for disagreements.

Statistical Analyses

Statistical analyses were performed using STATA (v13.1; StataCorp, College Station, TX). The time from stroke onset (time the patient was last known to be well) to initial NCCT was dichotomized at the median into 2 time epochs to achieve the most efficient estimates by balancing the groups when assessing the effect of time. The ultra-early phase of stroke was defined as the median or earlier time from stroke onset to initial NCCT. Fisher's exact tests were used to assess the differences in patients' baseline characteristics between 2 time epochs. The inter-rater agreement was estimated using a kappa with quadratic weights and cross-validated using Lin's concordance coefficient within each epoch. The distributions of absolute inter-rater differences in ASPECTS were compared over time epochs using a Fisher's exact test. The comparison across the time epochs of the utility of ASPECTS as a diagnostic tool for good functional outcome (scores of 0-2 on mRS at 3 months) was made using a Chi-squared test for respective areas under the receiver operating characteristic curve (AUCs). We also used multivariable logistic regression models with an appropriate interaction term to assess the effect of time epoch on the strength of association between ASPECTS and mRS 0-2 adjusted for age and the National Institutes of Health Stroke Scale (NIHSS).

Results

Subject Characteristics

There were a total of 379 participants who met the inclusion criteria and were included in this single-center, retrospective, observational study. The median (interquartile range (IQR)) time of acute stroke onset to CT scan (OCT) was 100 (73-142) minutes. Thus, 100 minutes was used as the time point to define the earlier (≤100 minutes) and later time periods (>100 minutes) of OCT. Baseline