ASPECTS on CTA Source Images Versus Unenhanced CT Added Value in Predicting Final Infarct Extent and Clinical Outcome

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Background and Purpose—The Alberta Stroke Program Early CT Score (ASPECTS) is a grading system to assess ischemic changes on CT in acute ischemic stroke. CT angiography–source images (CTA-SI) predict final infarct volume. We examined whether the final infarct ASPECTS and clinical outcome were more related to acute CTA-SI ASPECTS than to the acute noncontrast CT (NCCT) ASPECTS.

Methods—ASPECTS was assigned by 2 raters on the acute NCCT, CTA-SI, and follow-up imaging. The mean baseline ASPECTS of acute NCCT and CTA-SI was compared with the follow-up ASPECTS. Rate ratios (RRs) were used to quantify the relationship between the dichotomized baseline ASPECTS (categorized as 0 to 7 versus 8 to 10) and favorable patient outcome.

Results—Thirty-nine patients were recruited. Proximal occlusion (internal carotid artery or middle cerebral artery) was seen in 62%, M2 occlusion in 18%, and no occlusion was seen in 20% of patients. The median time between symptom onset and imaging was 1.9 (1.2 to 2.5) hours. There was a significantly larger difference of 1.4 between the mean baseline NCCT and CTA-SI ASPECTS in patients who had more ischemic changes (follow-up ASPECTS 0 to 3) than a difference of 0.6 in patients who had near-to-normal CT scans (follow-up ASPECTS =8 to 10). The rate of favorable outcome for acute NCCT ASPECTS of 8 to 10 was 51.8% versus 25.0% for 0 to 7 (RR, 2.1, 95% CI: 0.7 to 5.9, P = 0.12). For acute CTA-SI ASPECTS of 8 to 10, the rate of favorable outcome was 58.8% versus 31.8% for 0 to 7 (RR, 1.8, 95% CI: 0.9 to 3.8, P = 0.09).

Conclusions—CTA-SI ASPECTS provides added information in the prediction of final infarct size. (Stroke. 2004;35:2472-2476.)

Key Words: computed tomography ■ stroke, acute ■ thrombolysis

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. Although noncontrast CT (NCCT) was initially used to exclude intracranial hemorrhage and other nonstroke pathologies, advanced CT techniques are increasingly recognized as a modality to characterize early signs of ischemia.

With the use of multislice CT scanners, the potential information available from a CT scan has increased. CT angiography and CT perfusion techniques can refine the current clinical criteria for patient selection for thrombolysis. Source images from CT angiography (CTA-SI) can be rapidly obtained with minimal delays after a NCCT in the emergency room. Although CTA has been shown to have value in identifying vessel occlusion, CTA-SI may also aid in the assessment of tissue status. Schramm et al found that the combination of CT, CTA, and CTA-SI was comparable to that of a magnetic resonance diffusion-weighted imaging. CTA-SI can also be useful in predicting final infarct volume. Brain tissue with a low cerebral blood volume appears as a region without enhancement on CTA-SI, effectively delineating the regions of ischemia. The Alberta Stroke Program Early CT Score (ASPECTS) was developed as a grading instrument to assess early ischemic changes on pretreatment CT scans in patients with acute ischemic stroke of the middle cerebral artery (MCA). The ASPECTS divides the MCA territory into 10 regions of interest. With training and experience, the early changes of acute ischemia

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can be reliably detected. One advantage of ASPECTS is that it combines a semiquantitative estimate of volume along with localization. It weights smaller volumes in the basal ganglia and internal capsule equally with larger volumes of brain designated M1 through M6. This approach is useful because lesion volume alone on NCCT is only weakly correlated with neurological outcome.

In this study, we sought to assess whether the final infarct ASPECTS and clinical outcome were associated with the acute CTA-SI ASPECTS.

Subjects and Methods

Patients
We assessed the clinical and imaging information of consecutive patients with acute ischemic stroke from 2 institutions, who had NCCT and CTA. Stroke onset was defined as the time the patient was last seen well. Exclusion criteria were CT scan evidence of hemorrhage or tumor; hypoglycemia (serum glucose <2.0 mmol/L); serious comorbid illness that would result in the patient being unlikely to survive 3 months, or contaminate evaluation scales, or a patient who did not complete any follow-up imaging due to severe neurological deterioration; <18 years old, premorbid status Rankin >3; or symptoms suggestive of a posterior circulation event. Exclusion criteria specific for CTA were a known history of contrast medium allergy or any degree of renal failure. Patient demographics and clinical characteristics were recorded at the time of admission to the emergency department. All patients received intravenous or intra-arterial thrombolysis if appropriate, as indicated by their clinical findings and if no contraindications existed. Informed consent was obtained from the patient or their next of kin and this project was approved by the local institutional ethics committees.

Imaging

Standard NCCT was performed with a multislice CT scanner (GE Medical Systems) using 120 kV, 170 mA, 2-second scan time, and 5-mm slice thickness. Coverage was from skull base to vertex with contiguous axial slices parallel to the inferior orbitomeatal line.

NCCT scanning was followed immediately on the same scanner by CTA imaging with a helical scan technique. Previous work has shown that this adds ~10 minutes to the scanning time. Acquisitions were obtained after a single bolus intravenous contrast injection of 90 to 120 mL of nonionic contrast into an antecubital vein at 3 to 4 mL/s with a 20 to 25 s delay from the start of the contrast injection to the onset of imaging. The image sequence covered the foramen magnum to centrum semiovale or vertex with a scan field of view (25.0 cm; 140 kV, 170 mA; table speed 3.75 mm/s; 2.5-mm slice thickness with 2.5-mm interval; 1.0 s per rotation). Source images (CTA-SI) were reconstructed to 1.25-mm thickness at 0.625-mm intervals.

Follow-up imaging was performed on all patients. T2-weighted MRI was substituted among patients for whom follow-up NCCT was unavailable. All follow-up imaging was performed at a minimum of 24 hours after symptom onset. Clinical outcome was assessed using the modified Rankin Scale during an in-clinic visit. Favorable patient outcome at 90 days was defined as a Rankin score of 0 or 1.

Image Analysis

The assignment of an ASPECTS to each patient’s image was performed independently by a neuroradiologist and a stroke neurologist. Both readers were experienced in the interpretation of CT scans in acute stroke. Two other individuals, a neuroradiologist and a stroke neurologist, interpreted a subset of images for calculation of interrater agreement. Raters were blinded to all clinical information except for symptom side. The scoring of NCCT, CTA-SI, and follow-up imaging (NCCT or MRI–fluid-attenuated inversion recovery [FLAIR]) was in a random order. Baseline and follow-up imaging interpretation was spaced over several weeks.

All images were reviewed digitally at a 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. NCCT images were evaluated for evidence of focal parenchymal low attenuation, loss of gray-white differentiation, and sulcal effacement using ASPECTS as previously described. On the CTA-SI, regions of relatively diminished contrast enhancement were scored as abnormal (Figure 1). The CTA-SI was viewed at the window and level that allowed the maximum contrast between normal and ischemic tissue. The CTA-SI and circle of Willis maximum intensity projection reconstructions of the CT angiogram were evaluated for the presence of occlusion. ASPECTS on MRI was assigned in a similar manner to NCCT as previously described.

Statistical Analyses

The unit of analysis was the mean of the 2 readers’ ASPECTS. Two-factor repeated measures ANOVA was used to compare the mean baseline ASPECTS of acute NCCT and CTA-SI. In the analysis of variance, the between-subject factor was the follow-up ASPECTS, categorized as 0 to 3, 4 to 7, and 8 to 10. The within-subject factor was the baseline ASPECTS. Two-factor repeated measures ANOVA was used to quantify the relationship between the dichotomized baseline ASPECTS (categorized as 0 to 3 versus 4 to 10) and favorable patient outcome. The chosen cut point has been previously used for acute ischemic stroke patients. Interrater agreement in assigning ASPECTS was estimated using an intraclass correlation coefficient, computed from 1-way ANOVA.

Results

A total of 39 patients were recruited. There were no adverse events related to the use of the contrast medium. Demographic results are described in this section as median, and the interquartile range is shown. The median age of the patients was 74 (62 to 81) years, and 54% were female. The median baseline National Institutes Of Health Stroke Scale was 16 (9 to 22), and 90% of the patients were treated with tissue plasminogen activator (tPA). Four patients were treated with
IV/intra-arterial (IA) therapy, 13 were treated with IV alone, and 18 were treated with IA tPA alone. The median time between symptom onset and imaging was 1.9 (1.2 to 2.5) hours, with 41% of the scans performed within 90 minutes of symptoms. Proximal occlusion (internal carotid artery or MCA) was identified in 62% of the patients, M2 occlusion in 18%, and no large vessel occlusion in 20%. The follow-up scan was performed at a median time of 10 (4 to 34) days. T2-weighted MRI was substituted for follow-up NCCT in 14 patients.

The overall mean baseline ASPECTS differed by 1.1 (P < 0.001). Figure 2 summarizes the mean differences at each follow-up ASPECTS category. There was a significantly larger difference of 1.4 between the mean baseline NCCT and CTA-SI ASPECTS in patients who had more ischemic changes (follow-up ASPECTS = 0 to 3) than a difference of 0.6 in patients who had near-to-normal CT scans (follow-up ASPECTS = 8 to 10). There were no cases of CTA-SI overestimating the final infarct size. There were 10 cases in which the NCCT was rated as having an ASPECTS of 10 by at least 1 rater. In 3 cases, the NCCT, the CTA-SI, and the follow-up CT were rated by both observers as having an ASPECTS of 10. In 7 of the cases that ultimately had a stroke, (follow-up ASPECTS < 10) 1 reader interpreted the NCCT as normal (ASPECTS < 10), but interpreted the CTA-SI as showing at least some ischemic change (ASPECTS < 10). There was no evidence of reversibility of CTA-SI seen in this study. Figure 3 shows a scatter plot of mean ASPECTS scores for CTA-SI and NCCT as compared with final ASPECTS scores on follow-up imaging.

The rate of favorable outcome for NCCT ASPECTS of 8 to 10 was 51.8% versus 25.0% for 0 to 7 (RR, 2.1; 95% CI, 0.7 to 5.9; P = 0.12). For CTA-SI ASPECTS of 8 to 10, the rate of favorable outcome was 58.8% versus 31.8% for 0 to 7 (RR, 1.8; 95% CI, 0.9 to 3.8; P = 0.09). The interrater agreement for baseline ASPECTS using NCCT was 0.71 versus 0.73 for CTA-SI.

**Discussion**

Acute ischemic stroke requires urgent assessment of the clinical and radiological features of the brain insult. The ability to identify an acute infarct on CT is helpful in confirming the diagnosis of acute stroke. A completely normal NCCT scan seems ideal in terms of potential benefit (because no damage is currently seen) from any possible therapies but may introduce diagnostic uncertainty for the stroke neurologist. Normal CT scans are relatively common if the scans are performed very early into the stroke symptoms. The European Cooperative Acute Stroke Study (ECASS II) experienced reviewers did not detect early ischemic changes in ~1/3 of infarcts that later appeared on follow-up CT, and the National Institute of Neurological Disorders and Stroke...
(NINDS) investigators reported that only 31% of patients in the NINDS tPA trial had evidence of early ischemic changes. Our results suggest that CTA-SI ASPECTS has a greater sensitivity to ischemic changes and more accurately identifies the volume of tissue that will ultimately infarct compared with NCCT alone. The cases where 1 rater scored the scan as 10 show the potential advantage of using CTA-SI. In 7 of these cases, the ischemia would have been totally missed by 1 of the expert raters. It is in this setting (ASPECTS=10 of the NCCT) where CTA-SI is most likely to be helpful.

CTA is 1 method of quickly and accurately identifying vessel occlusion and ischemia. Using a follow-up ASPECTS as the final infarct size, CTA-SI gives a more accurate estimate of tissue that is at risk of infarcting than does a NCCT alone. The value of a combined CTA, CTA-SI over NCCT in predicting clinical outcome has also been demonstrated using a scale that differs from ASPECTS.

It is important to recognize that hypoattenuation on NCCT and CTA-SI hypoattenuation probably imply different pathophysiological abnormalities. These may not always represent core of infarction. A CTA-SI region showing a lack of enhancement provides an estimate of cerebral blood volume, whereas NCCT measures shifts in brain tissue water content. It is the net uptake of water in brain regions with <12 mL/100 g×minutes that causes hypoattenuation. Large shifts of water are needed for the human eye to visualize hypoattenuation. Animal studies have shown that a 1% increase in brain water content results in an x-ray attenuation decrease of 2 to 3 Hounsfield units. Optimal window width and leveling can help with reliably identifying such changes in water content. Recent work confirms that the volume of abnormality on CTA at baseline is a very close match to the volume of final infarct on follow-up scanning if there is prompt recanalization. Further work is needed on this subject.

Both NCCT and CTA-SI showed a trend toward a better clinical outcome for baseline ASPECTS of 8 to 10. This is consistent with observations from the Prolyse in Acute Cerebral Thromboembolism Trial (PROACT II) where an ASPECTS of 8 to 10 was found to differentially predict response to thrombolytic treatment. Larger numbers of patients will be needed to assess and confirm the relationship of ASPECTS on CTA-SI with clinical outcome.

The possibility of CT fogging effect is a relative limitation of our study. The timing and degree of fogging is variable, and has mostly been studied in small series, on older generation CT scanners. More recent studies suggest that fogging can start as early as 5 to 10 days post ictus, but that it may also occur months after stroke onset, coincident with the time period of poststroke hyperemia (a potential mechanism of fogging). The timing and degree of fogging likely varies with factors such as infarct size as well as the severity of the initial deficit. Importantly for our results, previous work suggests that fogging of large infarcts is typically not complete.

The reliability of assessing ASPECTS on the CTA-SI was very good and similar to that on NCCT. Larger studies are needed very early from stroke onset to compare both techniques. NCCT changes are particularly difficult to appreciate in such patients and may be greatly aided by CTA-SI information.

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