Multivariate Prognostic Model of Acute Stroke Combining Admission Infarct Location and Symptom Severity: A Proof-of-Concept Study

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Background: The information on topographic distribution of acute ischemic infarct can contribute to prediction of functional outcome. We aimed to develop a multivariate model for stroke prognostication, combining admission clinical and imaging variables, including the infarct topology. *Methods:* Acute ischemic stroke patients without baseline functional disability who had magnetic resonance imaging within 24 hours of onset or last-seen-well were included. The admission stroke severity was determined using the National Institutes of Health Stroke Scale (NIHSS) score. The relation between infarct location and outcome was assessed using both voxel-based and visual atlas-based analyses. The disability/death was defined by a modified Rankin Scale score greater than 2 at 3-month follow-up. *Results:* Among 198 patients included in this study, higher admission NIHSS score ($P < .001$), larger infarct volume ($P < .001$), and major arterial occlusions ($P < .001$) were associated with disability/death in univariate analyses. On voxel-based analysis, infarcts in the middle centrum semiovale, insula, and midbrain/pons were associated with higher rates of disability/death. In multivariate analysis, admission NIHSS score ($P < .001$), infarction of insula ($P = .005$), and midbrain/pons ($P = .006$) were independent predictors of disability/death. In receiver operating characteristics analysis, a simple 0-to-3 scoring system using these 3 variables had an area under the curve of .812 for prediction of disability/death ($P < .001$). *Conclusions:* Admission symptom severity, infarction of insula, and midbrain/pons were independent predictors of clinical outcome in acute ischemic stroke patients. The methodology of this hypothesis-generating study can help conceive quantitative population-based probabilistic models for prognostication or treatment triage in stroke patients, combining admission clinical and imaging findings—including infarct topography. **Key Words:** Ischemic stroke—topography—prognosis—brainstem—insula.

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Introduction

The ability to predict the expected level of functional recovery and outcome after stroke is crucial for targeting appropriate treatment and timing of rehabilitation.[1] Prognostic models in acute ischemic stroke can determine in which patients efficacious but potentially risky therapies, namely, endovascular intervention, are warranted. Moreover, early and reliable prediction of functional recovery can help provide focused, cost-effective rehabilitation for those stroke patients who benefit the most from these therapies. Inclusion of prognostic information in controlled clinical trials can also help with patient selection and reduce required sample sizes.[2,3]

Prior studies have shown the prognostic value of different imaging and clinical biomarkers in stroke patients, including the National Institutes of Health Stroke Scale (NIHSS) score,[3] age, infarct volume,[4] malignant computed tomography angiography collateral profile,[5] and presence of arterial occlusion.[6,7] Prior studies have also shown the value of multivariate prognostic models combining the imaging and clinical predictors of outcome.[8-10] For example, the 10-point DRAGON scoring method combining the glucose level, age, severity of stroke, abnormal computed tomography (CT) finding, and onset-to-treatment time have shown strong prognostic performance in patients with anterior and posterior circulation stroke.[8,11] Although both ischemic infarct volume and location affect the stroke presentation and outcome, the infarct topography is far less commonly evaluated in predictive models compared to the lesion volume, which is perhaps due to the lack of a standardized analysis method for the assessment of infarct topographic distribution.

The present study was designed to combine imaging and clinical findings of acute ischemic stroke patients at the time of admission to build a multivariate prognostic model. The imaging characteristics of acute infarct lesion including the volume, infarct topography, and arterial occlusion were assessed on admission magnetic resonance imaging (MRI) obtained within 24 hours of stroke onset (or last-seen-well). The association of infarct location with clinical outcome was evaluated using both voxel-based analysis with no a priori assessment and atlas-based visual assessment of admission MRI scans.

Methods

Patients

This is a retrospective analysis of a prospectively maintained database of consecutive ischemic stroke admitted to 2 university-affiliated hospitals over a 4-year period, from January 2011 to December 2014. Criteria for inclusion in this study were (1) unilateral acute ischemic stroke with no evidence of intracranial hemorrhage on admission CT/MRI scans, (2) brain MRI scan within 24 hours of witnessed symptom onset or last time seen well, (3) magnetic resonance angiography or computed tomography angiography done within 3 hours of admission MRI, (4) no functional disability at presentation with baseline modified Rankin Scale (mRS) score of 0 or 1, and (5) reliable clinical outcome assessment based on 3 months (±14 days) follow-up exam from the stroke onset. This study was reviewed and approved by the Institutional Review Boards at corresponding hospitals.

Clinical Data

The patients' clinical data were extracted from the stroke registry and electronic medical records, including the demographics, time gap between the symptom onset or last-seen-well and MRI scan, admission NIHSS score, reperfusion treatments, stroke risk factors, and 3 months' mRS scores. The clinical outcome was dichotomized with functional independence defined by 3 months' mRS score of 2 or less and disability/death by mRS score greater than 2.

Voxel-Based Image Analysis

The infarct lesions were manually segmented on admission MRI diffusion-weighted imaging (DWI) scan of each patient with help of the intensity filter in the MRIcron software (McCausland Center for Brain Imaging, University of South Carolina, Columbia, SC).[12-14] The segmented infarct lesions, along with corresponding DWI scan, were coregistered onto the MNI-152 standardized brain map using the FLIRT tool in FSL software (Oxford Centre for Functional MRI of the Brain, University of Oxford, Oxford, UK).[13,14] A summation map was developed to show the distribution of infarct lesions in the patients' cohort (Fig 1), where each voxel value reflects the total

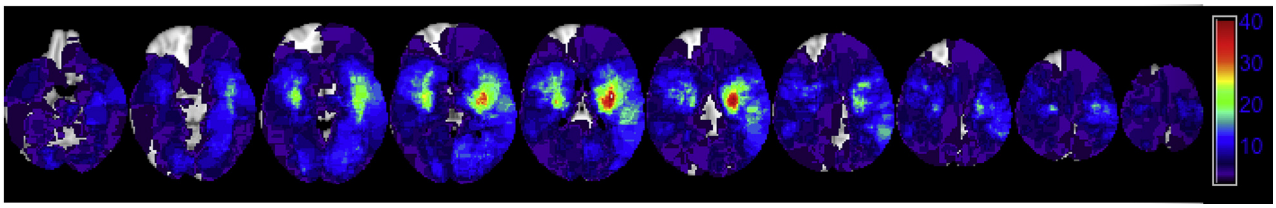

Figure 1. *The summation map showing the distribution of infarct lesions in our patient population (n = 198), overlaid on the MNI-152 brain map. Each voxel value reflects the total number of patients with infarct lesion in that particular coordinate.*