Demographic and Clinical Predictors of Leptomeningeal Collaterals in Stroke Patients

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Background: Leptomeningeal collaterals improve outcome after stroke, including reduction of hemorrhagic complications after thrombolytic or endovascular therapy, smaller infarct size, and reduction in symptoms at follow-up evaluation. The purpose of this study was to determine the demographic and clinical variables that are associated with a greater degree of cerebral collaterals. *Methods:* Clinical data of patients presenting with M1 occlusions of the middle cerebral artery (MCA) and associated computed tomography angiography studies after admission from 3 separate institutions were retrospectively compiled (n = 82). Occluded hemispheres were evaluated against the intact hemisphere for degree of collateralization in the MCA territory. Regression analysis of variance was conducted between clinical variables and collateral score to determine which variables associate with greater collateral development. *Results:* Smaller infarct size corresponded to greater collateral scores, whereas older age and statin use corresponded to lower collateral scores ($P < .001$). *Conclusions:* Cerebral collateralization is influenced by age and statin use and influences infarct size. **Key Words:** Predictors of collaterals in stroke—stroke—collaterals—computed tomography angiography—prediction.

Greater degree of collaterals in affected brain regions after occlusive stroke has been shown to correlate with reduced hemorrhagic complications after systemic thrombolysis or endovascular therapy,[1,2] improved recanalization rate after endovascular therapy,[3] smaller infarct size,[4] smaller infarct growth,[5] and improved clinical outcome.[6,7] Collaterals may contribute to recanalization effects by improving thrombolytic delivery downstream of the clot.[8-11]

The clinical and demographic variables that influence the degree of collateral circulation, however, are poorly understood. Previous studies provide evidence supporting the association of a stronger cerebral collateral network in patients with age,[12,13] atherosclerosis,[14,15] acute hyperglycemia,[16,17] statin use,[18] sex,[2,15] history of hypertension,[6,19] systolic blood pressure (BP) at admission,[6,19] admission National Institutes of Health Stroke Scale (NIHSS) score,[4] time to imaging after stroke symptom onset,[7,13] and Alberta Stroke Program Early CT Score (ASPECTS).[6] Other studies, however, indicate no independent association of age,[20] history of diabetes,[21] presymptomatic NIHSS or modified Rankin Scale score,[7] sex,[20] history of hypertension,[15] systolic BP,[14,15] or time to imaging after stroke symptom onset[15] to the degree of the cerebral collaterals.

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Based on the inconsistencies between these studies, the goal of our study was to determine which demographic and clinical variables are predictors of the degree of cerebral collaterals in patients with acute ischemic stroke.

Materials and Methods

Study Population

A repository of clinical and imaging data of patients with acute ischemic stroke compiled from 3 institutions (University of Virginia, University Hospital of Lausanne, and University of Pittsburgh Medical Center) was retrospectively searched for patients who underwent their baseline imaging workup within 12 hours of stroke onset, including noncontrast head computed tomography (NCT) and a computed tomography angiogram (CTA) that demonstrated an M1 occlusion. The data in the repository followed all the Health Insurance Portability and Accountability Act of 1996 guidelines, and all the data were deidentified and anonymized. Respective institutional review boards for each institution approved collection and analysis of data from the repository.

Clinical Variables

Demographic variables included age, gender, and time to baseline imaging from symptom onset. Variables from medical history included history of diabetes, history of hypertension, history of atrial fibrillation, and concurrent statin use at the time of admission. Variables from physical examination and laboratory data included blood glucose level at admission, systolic BP at admission, and the NIHSS score at admission.

Imaging Variables

All patients underwent baseline NCT followed by CTA. The image acquisition protocols have been previously described by Zhu et al.[22]

ASPECTS was determined for each patient by assessing NCT images for infarction in 10 standardized regions. Starting with a score of 10, 1 point was subtracted for each region that showed evidence of infarction, producing a final score of 0-10.[23]

Because there is no standardized scoring system for measuring collateralization in CTA, 5 different collateral grading systems were used. From CTA data sets, 20-mm-thick maximal intensity projections were reconstructed. Each CTA study was reviewed and graded according to the following systems:

1. Menon et al[24]: The brain was divided into 9 ASPECTS-like regions, and each region was graded in comparison with the contralateral hemisphere according to the following scale: 0 = poor collaterals, 1 = moderate collaterals, and 2 = good collaterals, except at the Sylvian sulcus, which was scored as 0 = poor collaterals, 2 = moderate collaterals, and 4 = good collaterals. All 9 scores were summed, and a score from 0 to 20 was generated for each brain.
2. Miteff et al[25]: Collateral score was determined according to whether the entire middle cerebral artery (MCA) distal to occlusion was reconstituted with contrast (good), some branches of the MCA were reconstituted in the Sylvian fissure (moderate), or distal superficial branches of the MCA were reconstituted (poor).
3. Lima et al[6]: Leptomeningeal vascularity in the occluded hemisphere was compared with the contralateral hemisphere according to the following scale: 1 = absent, 2 = less than contralateral side, 3 = equal to contralateral side, 4 = greater than contralateral side, and 5 = exuberant.
4. Tan et al[26]: A score from 0 to 3 was assigned where 0 = minimal or none of the ischemic region filled by pial vessels, 1 = greater than 0 and less than or equal to 50% of ischemic region filled, 2 = greater than 50 and less than 100% of ischemic region filled, and 3 = 100% of ischemic region filled. This system was derived from Kim et al.[27]
5. Modified Tan et al[26]: In a modified methodology, this grading system was dichotomized such that scores of 0-1 in the unmodified system by Tan et al were designated as "poor" and scores of 2-3 were designated as "good". This system was similarly reported in Schramm et al.[28]

Statistical Analysis

The statistical analyses were conducted in 3 steps. In step 1, we used principal component analyses[29] in conjunction with Spearman correlation analyses to determine which of the 5 collateral grading systems best captured the overall information about cerebral collaterals and to use that system as a reference standard in subsequent analyses.

In step 2, we conducted an ordinary least squares multivariate regression analysis that used the collateral grading system scores of the reference system identified in step 1 as outcome data. The intent of the multivariate regression analysis was to determine if the collateral grading system scores of the reference system were uniquely associated with clinical and imaging information collected at the time of hospital admission of the stroke patients.

Regarding the predictor variables, the multivariate regression model included several continuous, ordinal, and categorical scaled predictor variables. The set of continuous and ordinal predictor variables included patient age, time to baseline imaging after symptom onset, admission NIHSS score, blood glucose at admission, systolic BP at admission, and NCT ASPECTS. The set of