Interhemispheric Asymmetry in Distribution of Infarct Lesions among Acute Ischemic Stroke Patients Presenting to Hospital

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Backgrounds: This study aimed to investigate the possible asymmetric distribution of acute ischemic infarct lesions between patients with right-sided stroke versus left-sided stroke. *Methods:* Acute ischemic stroke patients with unilateral infarct who underwent magnetic resonance imaging scan within 24 hours of onset were included. Infarct lesions were segmented on diffusion-weighted-imaging series and coregistered on the MNI-152 brain map. After flipping all lesions to the left side, voxel-based analysis was performed to evaluate for asymmetric distribution of infarct lesions using the stroke side as an independent variable. Symptom severity at admission was evaluated using the National Institutes of Health Stroke Scale score, and early clinical outcome with the modified Rankin Scale score at discharge. *Results:* Of the 218 patients included in this study, 110 had right-sided ischemic infarcts whereas 108 had left-sided ischemic infarcts. There was no significant difference between patients with right-sided stroke versus left-sided stroke in terms of admission symptom severity, rate of treatment, stroke risk factors, and early clinical outcome. However, voxel-based analysis showed that ischemic infarcts of insular ribbon and lentiform nucleus were asymmetrically more common on the left-sided stroke compared to the right-sided stroke. The admission symptoms were more severe among patients with left insular ribbon and lentiform nucleus infarct compared to those with infarction of mirrored right anatomical regions ($P = .019$). *Conclusions:* Acute ischemic infarcts of the left insular ribbon and lentiform nucleus are asymmetrically more common compared to mirrored counterpart regions, presumably due to more severe symptoms at presentation. Otherwise, distribution of symptomatic infarcts to the rest of the brain is roughly symmetric. **Key Words:** Ischemic infarct—stroke—laterality—hemisphere.

Introduction

Patients with cerebrovascular accidents frequently present with characteristic unilateral neurological deficits, depending on the side of the infarction—e.g., aphasia in left hemisphere stroke and neglect in right-sided infarct.[1-3] This difference in presentation could affect the awareness and recognition of symptoms by patients, relatives, and even physicians. Prior studies have suggested that patients with left hemisphere stroke may be recognized more quickly and receive earlier disease management, whereas patients with right hemisphere stroke tend to present later to hospital, do not receive thrombolytic therapy as frequently as patients with left hemisphere

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Conflict of interest: Dr. Alexander McKinney currently serves on the Medical Advisory Board of Vital Images (a division of Toshiba Medical, Minnetonka, MN) and receives less than $5000 per year for consultation from Vital Images.

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stroke, and are under-represented in cerebrovascular disease trials.[1-3]

Although prior studies have evaluated the interhemispheric differences of ischemic infarcts with regard to the severity symptoms at presentation, clinical outcome, and rate of treatment, possible asymmetric anatomical distribution of ischemic infarct lesions has not yet been examined. In this study, a voxel-based analysis was applied to evaluate whether ischemic infarcts are symmetrically distributed between hemispheres throughout different anatomical regions, focusing on patients presenting with symptoms of an acute ischemic stroke. We also investigated whether such asymmetries affect clinical severity, early clinical outcome, or the rate of treatment.

Methods

Patients

This is a retrospective analysis of prospectively collected database of consecutive ischemic stroke patients admitted to 2 university-affiliated hospitals between January 2011 and December 2014. Patients were included in our analysis if (1) they had unilateral ischemic infarct confirmed by (2) magnetic resonance imaging (MRI) scan within 24 hours of witnessed symptom onset or last time seen well. Patients with bilateral stroke lesions were excluded from this study. This study was reviewed and approved by the institutional review boards at corresponding centers.

Clinical Data

Baseline data extracted for the analysis included patients' demographics, time gap between presentation or last seen well and the MRI scan, treatments received, and admission stroke severity based on the National Institutes of Health Stroke Scale (NIHSS) score. Intravenous (IV) and intra-arterial (IA) thrombolytic therapy, and thrombectomy were performed according to current stroke treatment guidelines at both institutions. The modified Rankin Scale (mRS) score at discharge was used as a measure of early clinical outcome. A positive history of coronary artery disease, atrial fibrillation, transient ischemic attack, stroke, hypertension, diabetes mellitus, hyperlipidemia, or tobacco consumption was extracted from each patient's electronic medical record.

Voxel-Based Image Analysis

Infarct lesions were manually segmented on diffusion-weighted-imaging (DWI) series with help from intensity filtering. Each DWI scan along with corresponding segmented lesion volume was coregistered onto the MNI-152 standardized brain map using the FLIRT tool included in FSL software (Oxford Centre for Functional MRI of the Brain, University of Oxford, Oxford, United Kingdom).[4] A summation map of ischemic infarct lesions among all patients was created to depict the topographic distribution of ischemic stroke in the present cohort. In the summation map, each voxel value represented the number of patients with ischemic infarct lesion involving that particular voxel coordinate; this is illustrated in Figure 1. Regarding the voxel-based lesion-symptom mapping (VLSM) analysis, we utilized the nonparametric mapping tool included in the MRIcron software package (McCausland Center for Brain Imaging, University of South Carolina, Columbia, SC).[5] All right-sided lesions were flipped onto the left hemisphere for comparison of asymmetric distribution of infarct between the right and left hemispheres. Thereafter, a binary group and binary image comparison was performed for each voxel (infarcted versus noninfarcted) using the lesion side as the dependent variable. The Brunner and Munzel rank order test was used to develop a Z-score map, in which higher score values indicate more frequent infarct occurrence on 1 side compared to the contralateral hemisphere for each particular voxel. To correct for multiple comparisons, the family-wise error rates corresponding to the Bonferroni-corrected values were used. We also applied 2000 permutations, which allow the test to be applied to small sample size. A color-coded map of Z scores with a narrowed window to Z-score ranges corresponding to .05-to-.01 thresholds, after Bonferroni correction, is depicted in Figure 2.

Statistics

The data are presented as mean ± standard deviation for continuous variables, median (interquartile) for ordinal variables, and number (frequency) for nominal variables. The Student's *t*-test, Mann–Whitney *U*-test, and Fisher exact test were used for comparison of data wherever appropriate. Two-sided significance tests were implemented throughout, and a threshold of $P < .05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics 23 (IBM, Armonk, NY).

Results

Patients' Characteristics

A total of 218 patients were included in this study. The patients' average age at the time of presentation was 64.4 ± 16.9 years, and 134 (61.5%) were male. The median admission NIHSS score was 4 (interquartile: 2-7). The MRI scans were performed 13.6 ± 7.2 hours after symptom onset or last seen well. Fifty patients had major intracranial arterial occlusion including 7 (3.2%) with internal carotid, 30 (13.8%) middle cerebral, 1 (.5%) anterior cerebral, 1 (.5%) basilar, and 11 (5.0%) posterior cerebral artery occlusions.