Role of Acute Lesion Topography in Initial Ischemic Stroke Severity and Long-Term Functional Outcomes

Ona Wu, PhD; Lisa Cloonan, BA; Steven J.T. Mocking, MS; Mark J.R.J. Bouts, PhD; William A. Copen, MD; Pedro T. Cougo-Pinto, MD; Kaitlin Fitzpatrick, BS; Allison Kanakis, MD; Pamela W. Schaefer, MD; Jonathan Rosand, MD, MSc; Karen L. Furie, MD, MPH; Natalia S. Rost, MD, MPH

Background and Purpose—Acute infarct volume, often proposed as a biomarker for evaluating novel interventions for acute ischemic stroke, correlates only moderately with traditional clinical end points, such as the modified Rankin Scale. We hypothesized that the topography of acute stroke lesions on diffusion-weighted magnetic resonance imaging may provide further information with regard to presenting stroke severity and long-term functional outcomes.

Methods—Data from a prospective stroke repository were limited to acute ischemic stroke subjects with magnetic resonance imaging completed within 48 hours from last known well, admission NIH Stroke Scale (NIHSS), and 3-to-6 months modified Rankin Scale scores. Using voxel-based lesion symptom mapping techniques, including age, sex, and diffusion-weighted magnetic resonance imaging lesion volume as covariates, statistical maps were calculated to determine the significance of lesion location for clinical outcome and admission stroke severity.

Results—Four hundred ninety subjects were analyzed. Acute stroke lesions in the left hemisphere were associated with more severe NIHSS at admission and poor modified Rankin Scale at 3 to 6 months. Specifically, injury to white matter (corona radiata, internal and external capsules, superior longitudinal fasciculus, and uncinate fasciculus), postcentral gyrus, putamen, and operculum were implicated in poor modified Rankin Scale. More severe NIHSS involved these regions, as well as the amygdala, caudate, pallidum, inferior frontal gyrus, insula, and precentral gyrus.

Conclusions—Acute lesion topography provides important insights into anatomic correlates of admission stroke severity and poststroke outcomes. Future models that account for infarct location in addition to diffusion-weighted magnetic resonance imaging volume may improve stroke outcome prediction and identify patients likely to benefit from aggressive acute intervention and personalized rehabilitation strategies. **(*Stroke*. 2015;46:2438-2444. DOI: 10.1161/STROKEAHA.115.009643.)**

Key Words: acute stroke ■ MRI ■ statistical model ■ topography ■ VLSM

Human stroke pathophysiology heterogeneity has been implicated in the limited success of therapeutic interventions for the treatment of acute ischemic stroke (AIS).[1] Neuroimaging biomarkers, such as infarct volume, have been proposed as potential surrogates for clinical outcome in the evaluation of novel AIS therapies. To date, studies[2] have found that lesion volumes are only moderately correlated with long-term clinical outcome measures. Small pilot studies have demonstrated that integration of lesion location and size can estimate stroke severity better than volume alone.[3] Here, we propose to build on these early studies by investigating the relationship between topography of acute diffusion-weighted magnetic resonance imaging (DWI) lesions and measures of AIS severity and long-term functional outcomes, using voxel-based lesion symptom mapping (VLSM) techniques.

VLSM compares neurobehavioral scores between patients with and without lesions on a voxel-wise basis.[4] VLSM methods have been used to examine motor recovery,[5] spatial neglect,[6] and aphasia[4,7] in chronic stroke patients, and 1-month modified Rankin Scale (mRS) score in subacute stroke (2–3 days)[8] patients. These studies have provided insight into clinical deficits linked to lesions in particular brain regions, but did not take into consideration important factors, such as age, sex, and lesion volume, that are known to be associated with long-term functional outcome after stroke. Furthermore, these studies used magnetic resonance imaging

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From the Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital (MGH), Charlestown, MA (O.W., S.J.T.M., M.J.R.J.B.); JP Kistler Stroke Research Center, Department of Neurology (L.C., P.T.C.-P., K.F., A.K., J.R., K.L.F., N.S.R.), Division of Neuroradiology, Department of Radiology (W.A.C., P.W.S.), Division of Neurocritical Care and Emergency Neurology (J.R.), and Center for Human Genetic Research (J.R.), MGH, Boston, MA; and Department of Neurology, Brown University, Providence, RI (K.L.F.).

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Correspondence to Ona Wu, PhD, Athinoula A. Martinos Center for Biomedical Imaging, 149 13th St, CNY 2301, Charlestown, MA 02129. E-mail ona@nmr.mgh.harvard.edu

(MRI) scans acquired relatively late (>48 hours) in the clinical course of stroke, that is, completed outside of the time window when clinical decision-making occurs. To improve clinical relevance, we investigated the role of stroke lesion topography of acute DWI acquired in AIS patients within 48 hours from last known well on initial stroke severity (admission National Institute of Health Stroke Scale [NIHSS]) and long-term disability (3–6 month mRS), accounting for age, sex, and lesion volumes.

Methods

Participants

Ischemic stroke patients prospectively enrolled in our Institutional Review Board–approved Genes Associated With Stroke Risk and Outcomes Study (GASROS) between 2007 and 2011 with an MRI performed within 48 hours of last known well were retrospectively analyzed. GASROS is a cross-sectional, hospital-based cohort of consecutive adults admitted to our neurology service with diagnosis of ischemic stroke confirmed by neuroimaging (computed tomography or MRI). Exclusion criteria include inability to obtain informed consent from the subject or proxy or a verified diagnosis of secondary cerebral ischemia (eg, vasculitis, subacute bacterial endocarditis, vasospasm, or tumor). All patients were evaluated emergently by a neurologist at the time of admission, and clinical and laboratory data from this encounter (eg, admission NIHSS score) were abstracted from corresponding medical records. The long-term functional outcomes were assessed using the mRS score collected either in person or via a telephone interview at 3 to 6 months poststroke. If the subject could not be reached, the mRS was reconstructed from the subject's medical record. Only the subset of stroke patients with evidence of infarction on acute DWI and available admission NIHSS and follow-up mRS was included in this analysis.

MRI

DWI was performed for the majority of studies on 1.5 T General Electric Signa scanners with a few cases performed on 1.5 T or 3 T Siemens scanners (N=5) with the following acquisition parameters: repetition time of 5000 ms, minimum echo time of 62 to 117 ms, 220 mm field-of-view, 128×128 acquisition matrix upsampled to 256×256, 5-mm slice thickness with a 1-mm gap, and 0 s/mm^2 (b-zero) and 1000 s/mm^2 b-values. DWI data sets were corrected for motion and eddy current distortions.[9] Apparent diffusion coefficient maps were calculated from the slope of the linear regression fit of the log of the DWI and b-zero images. Lesion volumes were outlined on the acute DWI using a semiautomated algorithm[10] by a reader blinded to the admission NIHSS and follow-up mRS scores. All DWI data sets were coregistered to one another using nonlinear coregistration techniques (MNI Autoreg[11,12]) and to the MNI 152 1 mm atlas.[13]

VLSM was performed on the coregistered data sets using VLSM version 2.55 (http://neuroling.arizona.edu/resources.html) with age and sex as covariates against admission NIHSS or follow-up mRS.[4] Analyses were repeated with DWI lesion volume as a covariate. Subset analyses were performed in survivors (ie, follow-up mRS<6) to remove potential confounds from death being unrelated to the stroke. For all analyses, a voxel was only tested if at least 10 subjects exhibited a lesion at its location. Resulting T-scores maps were thresholded voxelwise (P<0.001), then corrected for multiple comparisons based on cluster size permutation method (1000 permutations; P<0.05) in which mRS or NIHSS were randomly reassigned.[14] The Harvard-Oxford Cortical and Sub-cortical Structural Atlases[15] and the JHU ICBM-DTI-81 white matter atlas[16] distributed as part of FSL (FMRIB's Software Library)[17] were combined for region of interest analysis. Results were displayed using MRIcroGL (http://www.mricro.com) in radiological convention, with MNI coordinates provided in mm.

Statistical Analysis

Pearson's Chi-squared test was used to evaluate differences between categorical variables. Continuous variables were compared using 2-tailed Wilcoxon rank-sum tests. Differences in patient demographics with respect to lesion laterality were compared using 1-way analysis of variance with post hoc Tukey–Kramer Honest Significant Different testing. Correlation between acute DWI volumes and NIHSS and mRS scores were performed using Spearman's test. Backward step-wise regression was performed to investigate the relationship between age, sex, lesion volume, admission NIHSS and IV thrombolysis (tissue-type plasminogen activator), time-to-MRI, and endovascular therapy on follow-up mRS. Multicollinearity was assessed by calculating variance inflation factors for the final model parameters for which variance inflation factors >10 was considered an indication of multicollinearity.[18] Statistical analyses were performed using JMP Pro 11.0 (SAS Institute Inc) with significance at P<0.05 unless otherwise noted.

Results

Four hundred ninety subjects met inclusion and exclusion criteria. Patient demographics are shown in Table 1. Nineteen percent of the subjects were treated with tissue-type plasminogen activator or endovascular therapy, or both, and had significantly worse mRS than those not receiving revascularization treatment (2 [1–4] versus 1 [0–2]; P=0.006), most likely because of more severe admission NIHSS in these patients (11 [5–16] versus 3 [1–5]; P<0.0001) and larger acute DWI lesion volumes (12.1 [3.6–44.2] versus 2.2 [0.8–14.8]; P<0.0001). MRI was performed before the revascularization therapy in 9 patients (−1 [−0.5 to 3.5] h) and postintervention in 77 (3.2 [1.5–9.6] h) with the precise time of treatment not documented for 7. Acute DWI lesion volume significantly correlated with both admission NIHSS score (ρ=0.51, P<0.0001) and follow-up mRS (ρ=0.32, P<0.0001). Subjects who died before follow-up (mRS=6) presented with significantly more severe stroke symptoms and larger lesion volumes.

Multivariable regression analysis found that age (P<0.0001), sex (P=0.0002), acute DWI lesion volume (P=0.004), and admission NIHSS (P<0.0001) were significant factors for follow-up mRS. This relationship between mRS and age (P<0.0001), sex (P=0.001), acute DWI lesion volume (P<0.0001), and NIHSS (P<0.0001) held for the survivors subset. Age, sex, and DWI volume variance inflation factors were 1.04, 1.05, and 1.01, respectively, indicating no multicollinearity issues. Age and sex were, therefore, used as covariates in subsequent VLSM analysis. In a separate analysis, lesion size was also included. Because admission NIHSS was likely a reflection of extent and location of brain injury, NIHSS was not included as a covariate in the mRS analysis.

Figure 1 shows the incidence map of lesions for all 490 subjects, along with the statistical power for alpha=0.001. The distribution of stroke lesions was comparable for both left and right hemispheres, with slightly greater incidence/higher power in the right hemisphere (maximum incidence of 64, 99.8%) than the left hemisphere (maximum incidence 39, 94.8%). Table 2 shows the differences between patients with left, right, or bilateral (including brain stem) strokes. Patients with bilateral/brain stem strokes had more severe acute stroke symptoms and worse follow-up outcome.

Figure 2 shows the VLSM results for admission NIHSS overlayed on the MNI 152 1 mm atlas using a voxel-wise threshold of P<0.001, corrected for multiple comparison.

Table 1. Demographic Characteristics

	All (N=490)	mRS<6 (N=439)	mRS=6 (N=51)
Age, y*	65.0±14.9	63.8±14.8	75.2±12.1
Male, %*	303 (62%)	284 (65%)	19 (37%)
Admission NIHSS*	3 [1–8]	3 [1–6]	12 [5–20]
Time-to-MRI, h†	15.9 [6.7–26.5]	16.2 [6.9–27.1]	11.5 [4.8–20.0]
DWI lesion volume, cm^3*	3.7 [1–21.2]	3.0 [0.9–17.3]	12.9 [2.8–52.3]
3–6 month mRS*	1 [0–3]	1 [0–2]	6
Treated with tPA/EVT, %*	93 (19%)	73 (17%)	20 (39%)
Stroke location*			
Left	232 (47%)	209 (48%)	23 (45%)
Right	212 (43%)	197 (45%)	15 (29%)
Bilateral	46 (9.4%)	33 (7.5%)	13 (25%)

Values are mean±SD or median [IQR]. DWI indicates diffusion-weighted MRI; EVT, endovascular therapy; IQR, interquartile range; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; and tPA, tissue-type plasminogen activator.

*$P \leq 0.0001$, †$P=0.03$ mRS<6 versus mRS=6.

The differences between T-score maps, including no covariates and those including age and sex, was minimal for both the left (187 cm^3 versus 185 cm^3) and right (184 cm^3 versus 192 cm^3) hemispheres. Poor admission NIHSS scores were associated with injury in both left and right hemispheres, principally in middle cerebral artery vascular territories. Table 3 shows the percentage of each region of interest that overlap with the T-map clusters. Only regions that were found to be significant for all T-maps for either NIHSS or mRS are shown. Tables I and II in the online-only Data Supplement provide a detailed breakdown by region of interest for both left and right hemispheres. The T-scores were higher in the left hemisphere than right, despite lower power in the left hemisphere, for VLSM results without covariates (5.9 [4.7–7.0] versus 4.4 [3.8 – 4.9]) as well as with age and sex (5.8 [4.6–6.8]) versus 4.5 [3.9–5.1]) included. Furthermore, with acute DWI lesion size included as a covariate, the volume of tissue locations associated with more severe NIHSS was reduced to 24.8 cm^3 and limited to the left hemisphere—in particular to white matter (56% of total cluster), pre- and postcentral gyri (10%), putamen (11%), insula (10%), operculum (5%), inferior frontal gyrus (IFG, 2%), pallidum (2%), caudate (1%), and amygdala (1%). The thalamus, frontal orbital cortex, hippocampus, and unclassified cerebral cortex each made up <1% of the cluster. Subset analysis in survivors produced similar distributions in a slighter larger cluster (36.6 cm^3) involving more of the IFG, insula, operculum, and white matter (Table 3).

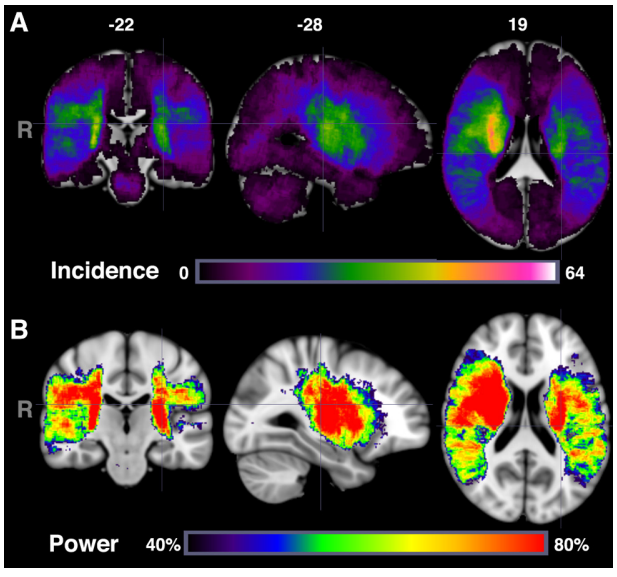

Figure 1. Number of patients with lesions within each voxel (**A**) using range 0 to 64 (maximum incidence) and (**B**) power map between 40% and 80% for alpha=0.001 for voxel-based lesion symptom mapping (VLSM) analysis for follow-up modified Rankin Scale (mRS).

For the mRS results (Figure 3), despite comparable incidence of acute left and right lesions, lesions primarily in the left middle cerebral artery territory were associated with poor mRS. When age and sex were included as covariates, larger regions of tissue in the right hemisphere were implicated with worse mRS (46.9 cm^3 versus 81.8 cm^3), whereas the opposite was true for the left hemisphere (138.9 cm^3 versus 116.9 cm^3). When including lesion volume as a covariate, only injury to the left hemisphere (4.1 cm^3) was associated with poor mRS. The distribution of the total cluster by region of interest were predominantly white matter (84%), with some involvement of the postcentral gyrus (9%), putamen (4%), and operculum (2%). The anterior division of the supramarginal gyrus, amygdala, caudate, insula and unclassified cerebral cortex made up the remainder of the cluster (<1% each). Subset analysis in survivors resulted in a slightly larger cluster (6.0 cm^3) that encompassed more of the internal and external capsules and involved more of the pallidum and putamen, but not the postcentral gyrus, likely because of reduced power in this region (see Figure I in the online-only Data Supplement for power maps among survivors).

Discussion

VLSM techniques have been developed to understand which regions of the brain are critical for brain functions.[4] We used these methods to investigate how ischemic injury to particular brain regions is associated with acute stroke severity and long-term functional outcome. We found that despite greater

Table 2. Demographic Differences Between Patients With Left Versus Right Hemispheric Versus Bilateral (Including Brain Stem) Strokes

	Left (N=232)	Right (N=212)	Bilateral (N=46)	*P* Value
Age, y	65.9±14.2	64.2±15.8	64.3±14.5	0.45
Male, %	146 (63%)	126 (59%)	31 (67%)	0.54
Admission NIHSS	3 [1–7]	4 [1–9]	3 [1–14]*	0.01
Time-to-MRI, h	15.8 [6.5–26.0]	15.9 [6.7–27.8]	16.8 [7–29.8]	0.88
DWI volume, cm^3	2.7 [0.8–17.8]	5.4 [1.0–28.9]	2.8 [1.1–10.5]	0.59
3–6 month mRS	1 [0–3]	1 [0–2]	2 [1–6]†	0.0002
Treated with tPA/EVT, %	44 (19%)	39 (18%)	10 (22%)	0.87

DWI indicates diffusion-weighted MRI; EVT, endovascular therapy; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; and tPA, tissue-type plasminogen activator.

*P=0.01, †P<0.001 bilateral versus left or right hemisphere.

incidence of right-hemispheric lesions in this cohort, injury to the left hemisphere—and, in particular, to the motor pathway (ie, posterior limb of the internal capsule, corona radiata) and white matter tracts, were associated with greater severity of acute stroke symptoms and poor long-term outcome. The association between poor mRS and injury to the motor pathway may partly be explained by the mRS score being heavily weighted by the degree of motor disability from the dominant hemisphere. In contrast, the NIHSS score reflects various symptomatology, including aphasia, dysarthria, ataxia, and neglect that are captured in a limited way by the mRS score; hence, more severe NIHSS scores were associated with greater expanses of tissue injury in both hemispheres. However, even for NIHSS, asymmetry between the left and right hemisphere T-scores was observed, with more severe NIHSS associated with the left-sided infarcts. This suggests that study designs, which flip right-sided lesions into left-sided ones to increase statistical power, may lead to inaccurate conclusions and should be avoided, if possible.

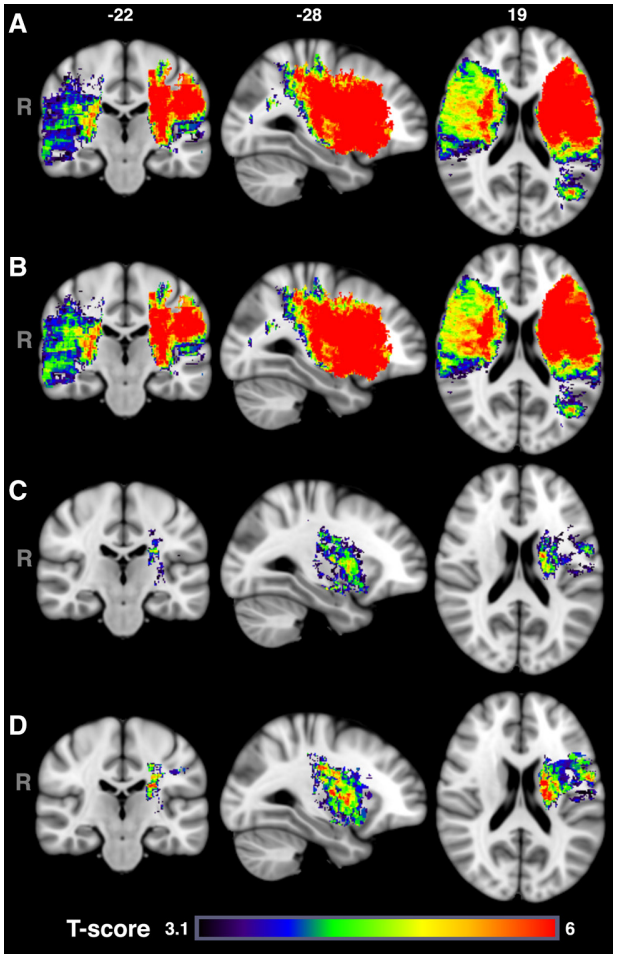

Figure 2. T-maps with voxel-wise threshold of P<0.001, thresholded based on cluster size (P<0.05), and permutation method for admission National Institute of Health Stroke Scale (NIHSS) scores using (**A**) no covariates, (**B**) sex and age covariates, or (**C**) sex, age, and lesion volume as covariates. The differences between (**B**) and (**C**) demonstrate the importance of lesion volume for severity of stroke symptoms at admission. However, even after taking into account lesion size, injury to the left hemisphere, in particular motor pathways and white matter tracts, insula, and putamen was associated with more severe symptoms. **D**, Subset analysis for patients, who were alive at 6 months, demonstrates similar findings, but with more involvement of the insula and operculum.

Our findings suggest that if one does not take into consideration age, sex, or lesion volume, locations of the lesion are associated with degree of stroke severity and long-term disability—and more so with lesions in the left hemisphere. Interestingly, including age and sex into our model for mRS increased the number of voxels in the right hemisphere. This suggests that for a given age and sex, the risk that a patient will have greater admission stroke severity and long-term disability is increased by where the stroke is located. Patients with strokes in certain regions of the right hemisphere—in particular, the insula, operculum, or putamen—are more likely to have more severe long-term disability. This effect is less pronounced on the admission NIHSS, for which lesion location seems to be an important factor independent of age and sex.

Once volume is included in the models, lesion location in the right hemisphere is no longer significant for either NIHSS or mRS. That is, for a given acute DWI lesion volume for a patient with specific age and sex, if the lesion is located in certain regions (in particular, left-hemispheric white matter and subcortical gray matter), the likelihood of greater severity on admission and long-term disability is increased. We speculate that the reason individual voxels in the right hemisphere are no longer significant once volume is taken into consideration is that the size of the lesion in right hemispheric strokes determines the degree of admission stroke severity and outcome, independent of where the large lesion is located in the right hemisphere. A major determinant of poor outcome in right hemispheric stroke is unilateral neglect,[19] which is typically associated with large strokes.

Table 3. Distribution of the Cluster in the Left Hemisphere as a Percentage of the Region of Interest

	NIHSS (N=490)	NIHSS Age+Sex (N=490)	NIHSS Age+Sex+Volume (N=490)*	NIHSS Age+Sex+Volume (Alive N=439)*	mRS (N=490)	mRS Age+Sex (N=490)	mRS Age+Sex+Volume (N=490)*	mRS Age+Sex+Volume (Alive N=439)*
Amygdala	30	30	10	4	28	28	1	0
Caudate	34	35	10	11	20	30	0	1
Corona radiata	65	65	17	24	63	58	5	9
External capsule	98	98	70	70	98	96	8	16
Fornix	31	32	3	0	15	21	0	0
Frontal orbital cortex	30	30	1	0	27	17	0	0
Inferior frontal Gyrus pars opercularis	80	80	8	31	47	25	0	0
Insula	76	76	23	34	65	67	0	1
Internal capsule	81	81	33	35	68	68	5	12
Operculum	93	93	8	18	72	68	1	0
Pallidum	71	71	29	31	64	68	0	19
Postcentral gyrus	33	33	2	3	32	32	1	0
Precentral gyrus	29	29	5	9	19	14	0	0
Putamen	91	91	52	61	86	88	3	17
Superior longitudinal fasciculus	92	91	6	21	80	78	12	4
Thalamus	1	1	1	0	1	1	0	0
Uncinate fasciculus	87	87	18	5	86	87	7	6

mRS indicates modified Rankin Scale; and NIHSS, National Institute of Health Stroke Scale.

*Volume=acute diffusion-weighted magnetic resonance imaging lesion volume.

Our findings are consistent with previously published results in a subacute stroke patient population reporting that injury to the corticospinal tract in the left hemisphere was associated with poor outcomes.[20] Furthermore, the right angular, left middle, and superior temporal gyri were also implicated in that analysis that did not account for a lesion volume and was also seen in our intermediate models. However, after including lesion volume as a covariate in our study, only injury to the left hemisphere further explained high NIHSS or poor mRS. These findings highlight the importance of accounting for the acute infarct volume in prediction models of poststroke outcomes. Significant correlation between the acute DWI lesion volume and long-term mRS score observed in our data and in the large Virtual International Stroke Trials Archive collaborative show that initial lesion volumes were an independent predictor of mRS scores at day 90.[21] Thus, studies of brain topology and outcomes that do not account for lesion size may mistakenly attribute disproportionate significance of injury to regions that tend to be associated with large lesion volumes (eg, the insular cortex[20]); however, these regions may not be independently associated with poor outcome. On the other hand, despite being highly significant, the correlation of acute DWI lesion volume with mRS was only moderate, suggesting that other factors, such as lesion location, are necessary for building better stroke outcome prediction models, which our results support.

Our findings show the promise and importance of incorporating lesion location and lesion volume into models that predict stroke outcome. In addition, we can use a similar framework to combine multimodal imaging information with clinical information to predict disability and stroke severity. The output of these models will be a voxel-based map of predicted disability scores, by which one weighs actual DWI lesion location. These models will need to be validated in an independent cohort of patients and compared against actual outcome to assess for accuracy.

There are a few limitations to our study. Our findings are primarily limited to middle cerebral artery territory strokes as reflected in our power map. It is likely that with greater number of patients, the brain stem would also be highlighted. Indeed, we found a cluster in the brain stem with T-scores >3.1 for both NIHSS and mRS (see Figure II in the online-only Data Supplement); however, after correction for multiple comparisons, that cluster did not meet statistical significance. In addition, the importance of the asymmetry between left compared with the right hemisphere may not generalize to investigations that involve thousands of patients for which a difference of 4% between incidences of left versus right hemispheric strokes may become significant. Another limitation is our study's retrospective nature in that MRI was not performed at prespecified time points. The acute DWI lesion may not fully encompass dysfunctional tissue at presentation, which perhaps would be better captured using MR perfusion-weighted imaging. One hundred ten of our subjects were imaged before 6 hours, a time frame in which lesion evolution is highly dynamic.[22] Furthermore, for the IV tissue-type plasminogen activator/endovascular therapy subset, MRI was not uniformly acquired before intervention. Subject enrollment into GASROS required informed consent, potentially skewing out patient population toward milder strokes. Another potential

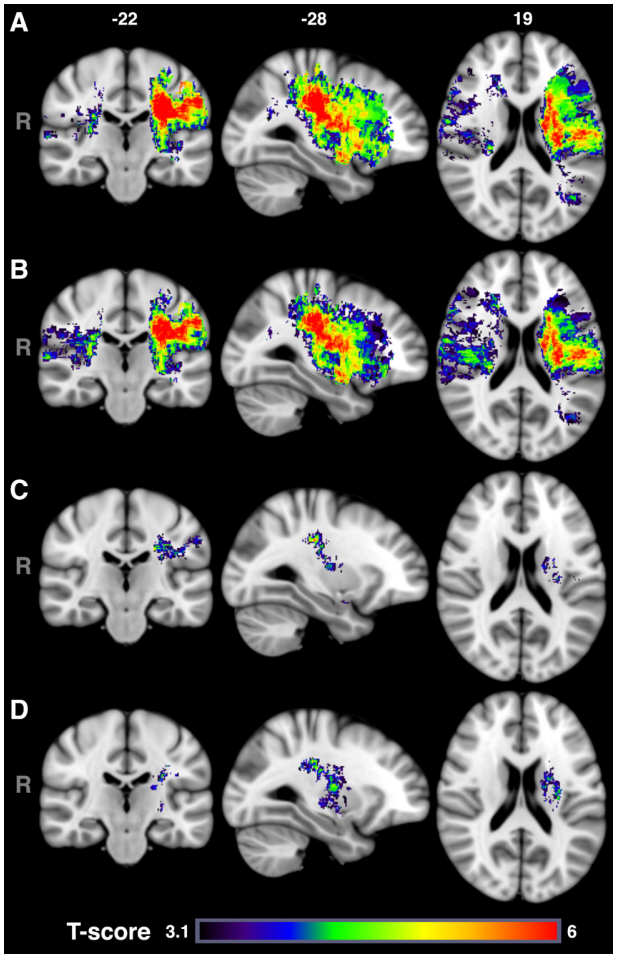

Figure 3. T-maps with voxel-wise threshold of $P<0.001$, thresholded based on cluster size ($P<0.05$), and permutation method for follow-up modified Rankin Scale (mRS) scores (**A**) without covariates and using (**B**) sex and age or (**C**) sex, age, and lesion volume as covariates. The differences between (**B**) and (**C**) demonstrate the association between lesion volume and severity of stroke symptoms at admission. In comparison with admission National Institute of Health Stroke Scale (NIHSS), injury to the right hemisphere seems less important for long-term outcome than acute stroke symptoms. Injury to primarily white matter tracts in the left hemisphere was associated with worse long-term outcome with lesion volume included as a covariate. **D**, Subset analysis for patients who were alive at 6 months demonstrates similar findings, but more involvement of the putamen.

limitation is the use of the MNI 152 1 mm atlas, which was derived from young healthy adults, as a reference template. Co-registration errors when transforming the clinical low-resolution DWI scans to the high-resolution atlas may have led to inaccuracies when assessing regional involvement of small structures; therefore, caution is needed in the interpretation of their results. An alternate approach is to perform manual segmentation and to coregister all images to one another; however, manual segmentation is also subject to measurement errors. We also did not record the cause of death for patients. It may be that patients either had care withdrawn as a result of large DWI lesion volumes, thereby leading to a self-fulfilling prophecy, or died because of a cause unrelated to the stroke. We attempted to control for this by performing subset analysis in only survivors and found similar results, albeit at the cost of power. Furthermore, both NIHSS and mRS do not measure unilateral neglect,[23] which is a major predictor of poor outcome in right hemispheric strokes. In addition, mRS[24] is a measure of global disability that is relatively insensitive to cognitive dysfunction. We chose the mRS score as our outcome measurement because it is the most widely used validated disability scale and is the traditional end point for many clinical trials. Future prospective studies should use outcome instruments that are sensitive to deficits across a variety of cognitive domains. There is increased realization that, for stroke trials targeting specific brain regions, outcome scales sensitive to recovery of brain function rather than only physical disability will be needed.[25] With such instruments, VLSM may be useful for identifying potential responders to novel treatments as has been recently done in a study of brain stimulation treatment for aphasia.[26]

Conclusions

Our results confirm the hypothesis that the location of AIS lesions is an important determinant of presenting stroke severity and long-term functional outcomes. Outcome prediction models that account both for acute infarct topography and volume, as well as clinical characteristics, highlight the complex mechanisms that contribute to the severity of the neurological syndrome and its long-term recovery. Therefore, integration of VLSM into clinical assessment of AIS patients may facilitate early identification of patients at risk for poor long-term functional outcomes and enhance significantly our current strategies for selection of patients for aggressive acute intervention and focused poststroke rehabilitation programs.

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Disclosures

None.

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