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The Association between Diffusion MRI-Defined Infarct Volume and NIHSS Score in Patients with Minor Acute Stroke

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Abstract

BACKGROUND—Prior studies have shown a correlation between the National Institutes of Health Stroke Scale (NIHSS) and stroke volume on diffusion weighted imaging (DWI); data are more limited in patients with minor stroke. We sought to determine the association between DWI lesion(s) volume and the (1) total NIHSS score and (2) NIHSS component scores in patients with minor stroke.

METHODS—We included all patients with minor stroke (NIHSS 0–5) enrolled in the Stroke Warning Information and Faster Treatment study. We calculated lesion(s) volume (cm^3) on the DWI sequence using Medical Image Processing, Analysis, and Visualization (MIPAV, NIH, Version 7.1.1). We used nonparametric tests to study the association between the primary outcome, DWI lesion(s) volume, and the predictors (NIHSS score and its components).

RESULTS—We identified 894 patients with a discharge diagnosis of minor stroke; 709 underwent magnetic resonance imaging and 510 were DWI positive. There was a graded relationship between the NIHSS score and median DWI lesion volume in cm^3: (NIHSS 0: 7.1, NIHSS 1: 8.0, NIHSS 2: 17.1, NIHSS 3: 11.6, NIHSS 4: 19.0, and NIHSS 5: 23.6, $P < .01$). The median lesion volume was significantly higher in patients with neglect (105.6 vs. 12.5, $P = .025$),

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language disorder (34.6 vs. 11.9, $P < .001$), and visual field impairment (185.6 vs. 11.6, $P < .001$). Other components of the NIHSS were not associated with lesion volume.

CONCLUSION—In patients with minor stroke, the nature of deficit when used with the NIHSS score can improve prediction of infarct volume. This may have clinical and therapeutic implications.

Keywords

Minor stroke; ischemic stroke; neuroimaging; infarct volume; outcome; NIHSS

Introduction

Minor ischemic stroke constitutes approximately two thirds of ischemic stroke;[1] however, treatment and functional outcome predictors of these patients remain controversial.[2] Traditionally, the bedside neurological examination has been used to predict the degree of long-term disability with reasonable success in patients with moderate-to-severe deficits at stroke onset. Standardized neurological assessments, such as the National Institutes of Health Stroke Scale (NIHSS) score, however, appear to have less predictive value in milder stroke.[3] Imaging parameters may potentially improve outcome prediction in patients with ischemic stroke. While some studies show that infarct volume does not add to the NIHSS score obtained on day 5 in predicting 3-month outcome,[4] other studies suggested that infarct volume adds to the baseline NIHSS score in predicting outcome.[5–7] In addition, in case series with a significant proportion of mild strokes, there is a strong association between infarct growth and 3-month functional outcome,[8,9] and final infarct volume has been used as a surrogate end-point in the most recently published endovascular acute stroke trials.[10] Diffusion weighted imaging (DWI) is the gold standard imaging modality in the diagnosis of acute ischemic stroke, although it is not widely available and can be time-consuming in the acute therapeutic window.[11–13] Computerized tomography (CT) therefore remains the primary imaging modality used during the acute stroke evaluation in most centers.[14] While CT imaging is more readily available and less expensive than magnetic resonance imaging (MRI), it is of limited use in predicting infarct volume in the acute setting.[11] Previous studies have shown a correlation between the NIHSS and infarct volume in patients with acute ischemic stroke.[15,16] There have been fewer reports, however, on the ability of the NIHSS to predict infarct volume in patients with mild deficits. The mild stroke patient presents a unique clinical challenge given a wide variability in outcomes, and controversies surrounding treatment.[2] Better understanding of clinical predictors of large infarct volume in patients with mild deficits may potentially have clinical and therapeutic implications. Our aim was to determine the association between infarct volume on DWI and (1) NIHSS score and (2) the NIHSS score components.

Methods

This study is a post-hoc analysis of the Stroke Warning Information and Faster Treatment (SWIFT) trial that enrolled 1,635 patients with stroke or transient ischemic attack between February 2006 and February 2010.[17] Patients were evaluated by a vascular neurologist and the NIHSS score was recorded by a certified vascular neurology fellow at our institution. In

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general, our primary neuroimaging modality was CT in the acute setting, and MRI was usually performed within the first 24 hours after admission unless there was a contraindication to MRI and after the NIHSS was obtained. The diagnosis of stroke was based on clinical criteria, with MRI aiding in the diagnosis. For the purpose of this analysis, we included patients with: (1) clinical diagnosis of ischemic stroke, (2) baseline NIHSS 0–5, (3) and brain imaging evidence of infarction on DWI. We excluded patients who received intravenous thrombolytic therapy due to a possible effect of thrombolytic therapy on infarct volume. Each itemized NIHSS component on admission was dichotomized into two groups (0 for no score and 1 for a score of 1 or more). For simplicity and due to the expected low number of patients with minor stroke with deficits in level of consciousness,[18] items 1a, 1b, and 1c were combined into one category. Brain MRI sequences were reviewed by the research team (S.Y. and C.H.) (blinded to clinical data) for the presence of acute infarction on DWI. We used Medical Image Processing, Analysis, and Visualization (MIPAV, NIH) (Version 7.1.1) to calculate lesion volume (cm^3). DWI b 1000 images were imported into MIPAV from the GE database. Apparent diffusion coefficient less than 620×10-6 mm^2/second was used to identify the infarct(s). Contouring for each slice was manually performed with the Polygon VOI (Voxel of Interest) tool, and the VOI statistic then was calculated. Using the pixel spacing (PS) and slice thickness (ST) variables from the Digital Imaging and Communications in Medicine (DICOM) settings, we calculated the lesion volume with the formula: Volume (cm^3) = $((PS/10)^2) \times (\# \text{ of voxels}) \times (ST/10)$. Our primary predictors were total NIHSS score and the individual components of the NIHSS: level of consciousness, best gaze, visual field, face, motor, ataxia, sensory, language, dysarthria, and neglect.[19] The primary outcome was DWI lesion volume in cm^3. We used nonparametric tests to study the association between the primary outcome, DWI lesion(s) volume, and the predictors (NIHSS score and its components). Statistical analysis was performed using SPSS version 18.0 (IBM, Chicago, IL, USA), and $P < .05$ was considered significant. The study was approved by the institutional board review.

Results

There were 894 patients with an NIHSS of 0–5 enrolled in SWIFT who had a discharge diagnosis of ischemic stroke. There were a total of 709 (79%) participants who underwent MRI, with those not completing it due to claustrophobia, weight, or ferromagnetic implants. Among those undergoing MRI, 510 (72%) were DWI positive. Patients with and without MRI did not differ in baseline characteristics. Figure 1 shows the study flow chart. In our cohort, the mean age in years was 63.5 ± 15.1, and 49% were men. The median DWI lesion volume in cm^3 was 13.1 interquartile range (IQR) (5.0–59.5).

There was a graded relationship between the NIHSS score and median DWI lesion volume in cm^3 and IQR: (NIHSS 0: 7.1 [2.5–45.2], NIHSS 1: 8.0 [3.4–44.7], NIHSS 2: 17.1 [7.6–51.4], NIHSS 3: 11.6 [5.1–61.2], NIHSS 4: 19.0 [6.4–69.6], and NIHSS 5: 23.6 [8–149.2]; $P < .01$) (Fig 2).

Among the components of the NIHSS score, the median DWI lesion volume was significantly higher in patients with deficits in: neglect (105.6 vs. 12.5, $P = .025$), language

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(34.6 vs. 11.9, $P < .001$), and visual field (185.6 vs. 11.6, $P < .001$). Other components of the NIHSS were not associated with a DWI lesion volume (Table 1).

Discussion

Our study demonstrated that patients with mild stroke symptoms usually have relatively small infarcts on neuroimaging. However, certain components of the NIHSS score when present were significantly associated with larger infarct volumes on DWI. The NIHSS components that were associated with larger infarct volumes in our study were neglect, language, and visual deficits. The finding of neglect in our study was not surprising given prior reports highlighting that patients with right hemispheric deficits can have relatively large infarcts with relatively low NIHSS scores.[20] Indeed, symptomatic intracerebral hemorrhage after thrombolysis, which correlates with infarct size, may be more common in nondominant hemisphere infarcts.[21] There are, however, fewer reports on the association between infarct size and language or visual field deficits. Therefore, when added to the NIHSS score, the nature of deficits may improve prediction of larger infarcts and add value when evaluating and treating patients with minor ischemic stroke. This is particularly useful since acute care decision such as timing of initiation of anticoagulation therapy and risk of post intravenous thrombolysis and mechanical thrombectomy intracerebral hemorrhage can be influenced by infarct size.[22] In addition, certain patients in our series who had considerably large infarcts had a relatively low NIHSS scale on presentation. Clinical deterioration may have occurred if their infarct is complicated by significant cytotoxic edema.

While some studies have found a correlation between infarct volume and stroke severity,[15,16] severity does not always correlate with infarct volume. For example, small subcortical infarcts can produce a significant clinical deficit.[23] Therefore, analyses of outcomes in ischemic stroke trials included both stroke severity and infarct volume.[10] In a recent study, for example, investigators improved prediction of functional outcomes when stroke severity scores and infarct volumes were combined rather than used separately.[24] The three NIHSS elements identified as correlating with the lesion volume represent important functional syndromes, indicating that aphasia, neglect, and visual field cuts are underrepresented by the NIHSS. Therefore, “mild” strokes that have these elements on presentation may not be mild in terms of functional outcomes. Prior studies have shown that elements such as neglect[18] and aphasia[25] in patients with minor stroke were predictors of poor functional outcome at 3 months; this may be partially due to the fact that the presence of such deficits indicates a larger infarct volume. Therefore, in the hyperacute evaluation of patients with a mild stroke, the type of deficits may help predict infarct size and therefore factor into the decision of thrombolytic therapy which remains controversial in this patient population.

Our study has several limitations including its retrospective nature, lack of data on infarct location, and nonstandardized MRI magnet used for every patient (3.0 T vs. 1.5 T). The results of our study may also not be generalizable to the entire population of minor ischemic strokes due to excluding patients unable to undergo an MRI and being DWI negative. On the other hand, the proportion of patients who received an MRI during the diagnostic evaluation in our study is similar to that reported in other studies,[26] minimizing the likelihood of

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selection bias. In addition, our study lacks vascular imaging data which would have been useful especially as studies show an increased odds of large vessel occlusion in patients with aphasia or neglect.[27] A major limitation of this study, however, was that the time from symptom onset to MRI was not collected in the SWIFT trial. Since the DWI lesion volume changes with time, not adjusting for time from ictus to MRI may affect the lesion volumes calculated and therefore our findings need to be interpreted with caution. In addition, since the time from onset to MRI is not available, neurologic deterioration from initial severity may have contributed to the very large infarct volumes that were measured in patients with initial visual field deficit and neglect.

Improving DWI volume prediction tools in patients with mild deficits can potentially have therapeutic implications. This is useful especially since certain treatment decisions may rely on infarct size, which can be particularly large in patients with mild stroke but presence of deficits in neglect, language function, or visual fields as shown in our study. Future prospective studies that adjust for time from symptom onset to MRI are needed to confirm the findings of our study.

References

1. Reeves M, Khoury J, Alwell K, et al. Distribution of National Institutes of Health Stroke Scale in the Cincinnati/Northern Kentucky stroke study. Stroke. 2013; 44:3211–3. [PubMed: 24003048]
2. Yu AY, Hill MD, Coutts SB. Should minor stroke patients be thrombolyzed? A focused review and future directions. Int J Stroke. 2015; 10:292–7. [PubMed: 25546628]
3. Coutts SB, Modi J, Patel SK, et al. What causes disability after transient ischemic attack and minor stroke?: results from the CT and MRI in the triage of TIA and minor cerebrovascular events to identify high risk patients (CATCH) study. Stroke. 2012; 43:3018–22. [PubMed: 22984013]
4. Johnston KC, Barrett KM, Ding YH, et al. Clinical and imaging data at 5 days as a surrogate for 90-day outcome in ischemic stroke. Stroke. 2009; 40:1332–3. [PubMed: 19228853]
5. Campbell BC, Tu HT, Christensen S, et al. Assessing response to stroke thrombolysis: validation of 24-hour multimodal magnetic resonance imaging. Arch Neurol. 2012; 69:46–50. [PubMed: 21911654]
6. Vogt G, Laage R, Shuaib A, et al. Initial lesion volume is an independent predictor of clinical stroke outcome at day 90: an analysis of the Virtual International Stroke Trials Archive (VISTA) database. Stroke. 2012; 43:1266–72. [PubMed: 22403046]
7. Vagal AS, Sucharew H, Prabhakaran S, et al. Final infarct volume discriminates outcome in mild strokes. Neuroradiol J. 2015; 28:404–8. [PubMed: 26427891]
8. Barrett KM, Ding YH, Wagner DP, et al. Change in diffusion-weighted imaging infarct volume predicts neurologic outcome at 90 days: results of the Acute Stroke Accurate Prediction (ASAP) trial serial imaging substudy. Stroke. 2009; 40:2422–7. [PubMed: 19443798]
9. Khatri P, Conaway MR, Johnston KC. Ninety-day outcome rates of a prospective cohort of consecutive patients with mild ischemic stroke. Stroke. 2012; 43:560–2. [PubMed: 22052513]
10. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015; 372:1009–18. [PubMed: 25671797]
11. Merino JG, Warach S. Imaging of acute stroke. Nat Rev Neurol. 2010; 6:560–71. [PubMed: 20842186]
12. Albers GW. Diffusion-weighted MRI for evaluation of acute stroke. Neurology. 1998; 51:S47–9. [PubMed: 9744834]
13. Wintermark M, Sanelli PC, Albers GW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients: a joint statement by the American Society of Neuroradiology, the American College of Radiology, and the Society of Neurointerventional Surgery. AJNR Am J Neuroradiol. 2013; 34:E117–27. [PubMed: 23907247]

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14. Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013; 44:870–947. [PubMed: 23370205]
15. Tong DC, Yenari MA, Albers GW, et al. Correlation of perfusion-and diffusion-weighted MRI with NIHSS score in acute (<6.5 hour) ischemic stroke. Neurology. 1998; 50:864–70. [PubMed: 9566364]
16. Lovblad KO, Baird AE, Schlaug G, et al. Ischemic lesion volumes in acute stroke by diffusion-weighted magnetic resonance imaging correlate with clinical outcome. Ann Neurol. 1997; 42:164–70. [PubMed: 9266725]
17. Boden-Albala B, Stillman J, Perez T, et al. A stroke preparedness RCT in a multi-ethnic cohort: design and methods. Contemp Clin Trials. 2010; 31:235–41. [PubMed: 20193777]
18. Sato S, Uehara T, Ohara T, et al. Factors associated with unfavorable outcome in minor ischemic stroke. Neurology. 2014; 83:174–81. [PubMed: 24907232]
19. Lyden P, Brott T, Tilley B, et al. Improved reliability of the NIH Stroke Scale using video training. NINDS TPA stroke study group. Stroke. 1994; 25:2220–6. [PubMed: 7974549]
20. Fink JN, Selim MH, Kumar S, et al. Is the association of National Institutes of Health Stroke Scale Scores and acute magnetic resonance imaging stroke volume equal for patients with right- and left-hemisphere ischemic stroke? Stroke. 2002; 33:954–8. [PubMed: 11935043]
21. Audebert HJ, Singer OC, Gotzler B, et al. Postthrombolysis hemorrhage risk is affected by stroke assessment bias between hemispheres. Neurology. 2011; 76:629–36. [PubMed: 21248275]
22. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014; 45:2160–236. [PubMed: 24788967]
23. Duan Z, Fu C, Chen B, et al. Lesion patterns of single small subcortical infarct and its association with early neurological deterioration. Neurol Sci. 2015; 36:1851–7. [PubMed: 26032577]
24. Nowinski WL, Gupta V, Qian G, et al. Population-based stroke atlas for outcome prediction: method and preliminary results for ischemic stroke from CT. PLoS One. 2014; 9:e102048. [PubMed: 25121979]
25. Wendt M, Tutuncu S, Fiebach JB, et al. Preclusion of ischemic stroke patients from intravenous tissue plasminogen activator treatment for mild symptoms should not be based on low National Institutes of Health Stroke Scale Scores. J Stroke Cerebrovasc Dis. 2013; 22:550–3. [PubMed: 23433783]
26. Schellinger PD, Bryan RN, Caplan LR, et al. Evidence-based guideline: the role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2010; 75:177–85. [PubMed: 20625171]
27. Heldner MR, Hsieh K, Broeg-Morvay A, et al. Clinical prediction of large vessel occlusion in anterior circulation stroke: mission impossible? J Neurol. 2016; 263:1633–40. [PubMed: 27272907]

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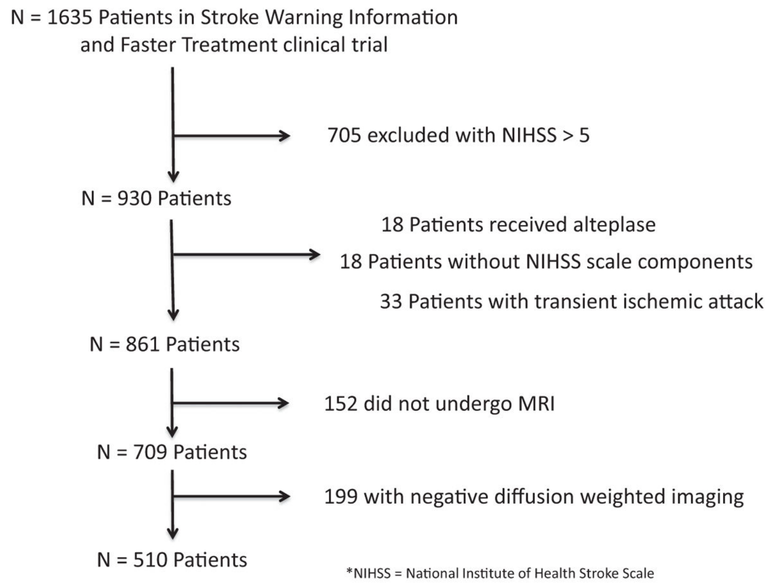

Fig. 1.
Flow chart of study sample.

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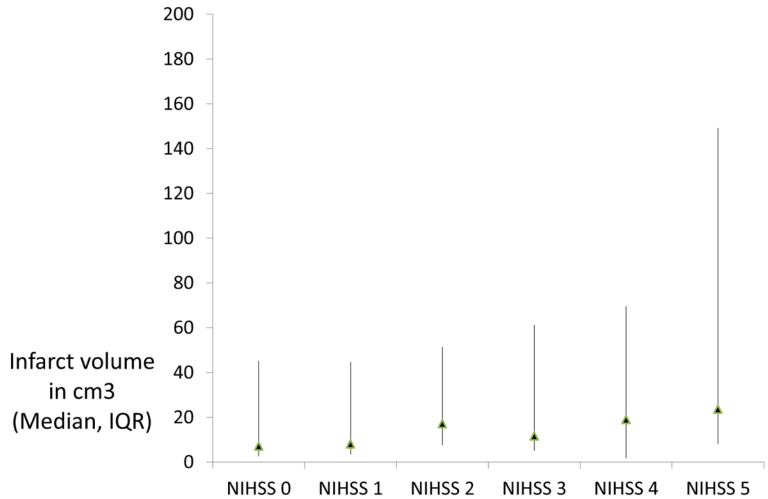

Fig. 2.

Association between National Institute of Health Stroke Scale (NIHSS) score and diffusion weight imaging lesion volume. IQR = interquartile range.

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Table 1

Association between Diffusion Weighted Imaging Lesion Volume and Type of Deficit

Deficit Type	Median DWI Lesion Volume with and without Deficit in cm^3	*P*-value
Level of consciousness (*n* = 7)	119.5 versus 12.9	.1
Gaze (*n* = 18)	8.8 versus 13.5	.09
Visual (*n* = 39)	185.6 versus 11.6	<.001
Facial (*n* = 189)	13.1 versus 13.2	.9
Motor (*n* = 205)	14.5 versus 11.9	.3
Sensory (*n* = 97)	11.2 versus 13.5	.4
Ataxia (*n* = 79)	13.5 versus 10.8	.3
Language (*n* = 49)	34.6 versus 11.9	<.001
Dysarthria (*n* = 85)	13.0 versus 13.1	.9
Neglect (*n* = 31)	105.6 versus 12.5	.03

DWI = diffusion weighted imaging.