Comparison of MRI and CT for Detection of Acute Intracerebral Hemorrhage

Chelsea S. Kidwell; Julio A. Chalela; Jeffrey L. Saver; et al.


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Comparison of MRI and CT for Detection of Acute Intracerebral Hemorrhage

In Reply:
Comparison of MRI and CT for Detection of Acute Intracerebral Hemorrhage

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Context Noncontrast computed tomography (CT) is the standard brain imaging study for the initial evaluation of patients with acute stroke symptoms. Multimodal magnetic resonance imaging (MRI) has been proposed as an alternative to CT in the emergency stroke setting. However, the accuracy of MRI relative to CT for the detection of hyperacute intracerebral hemorrhage has not been demonstrated.

Objective To compare the accuracy of MRI and CT for detection of acute intracerebral hemorrhage in patients presenting with acute focal stroke symptoms.

Design, Setting, and Patients A prospective, multicenter study was performed at 2 stroke centers (UCLA Medical Center and Suburban Hospital, Bethesda, Md), between October 2000 and February 2003. Patients presenting with focal stroke symptoms within 6 hours of onset underwent brain MRI followed by noncontrast CT.

Main Outcome Measures Acute intracerebral hemorrhage and any intracerebral hemorrhage diagnosed on gradient recalled echo (GRE) MRI and CT scans by a consensus of 4 blinded readers.

Results The study was stopped early, after 200 patients were enrolled, when it became apparent at the time of an unplanned interim analysis that MRI was detecting cases of hemorrhagic transformation not detected by CT. For the diagnosis of any hemorrhage, MRI was positive in 71 patients with CT positive in 29 (P < .001). For the diagnosis of acute hemorrhage, MRI and CT were equivalent (96% concordance). Acute hemorrhage was diagnosed in 25 patients on both MRI and CT. In 4 other patients, acute hemorrhage was present on MRI but not on the corresponding CT—each of these 4 cases was interpreted as hemorrhagic transformation of an ischemic infarct. In 3 patients, regions interpreted as acute hemorrhage on CT were interpreted as chronic hemorrhage on MRI. In 1 patient, subarachnoid hemorrhage was diagnosed on CT but not on MRI. In 49 patients, chronic hemorrhage, most often microbleeds, was visualized on MRI but not on CT.

Conclusion MRI may be as accurate as CT for the detection of acute hemorrhage in patients presenting with acute focal stroke symptoms and is more accurate than CT for the detection of chronic intracerebral hemorrhage.

JAMA. 2004;292:1823-1830 www.jama.com

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(Reprinted) JAMA, October 20, 2004—Vol 292, No. 15 1823

See also p 1883 and Patient Page.
the presence of hemorrhage. Accurate early detection of blood is crucial since a history of intracerebral hemorrhage is a contraindication to the use of thrombolytic agents. However, a major disadvantage of conventional CT within the first few hours of symptom onset is its limited sensitivity for identifying early evidence of cerebral ischemia.

Conversely, multimodal magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI), has excellent capacity to delineate the presence, size, location, and extent of hyperacute ischemia, but unproven reliability in identifying early parenchymal hemorrhage. The advent of thrombolytic therapy and other interventional therapies for acute ischemic stroke has led to increasing interest in using MRI to select and stratify candidates for treatments. Currently, many stroke centers obtain both CT and MRI in the initial evaluation of patients with stroke. The use of both modalities is time-consuming and expensive.

While conventional T1- and T2-weighted MRI pulse sequences are sensitive for the detection of subacute and chronic blood, they are less sensitive to parenchymal hemorrhage during the initial 6 hours after stroke symptom onset. A growing body of data have suggested that hyperacute parenchymal blood can be accurately detected using gradient recalled echo (GRE) pulse sequences that are sensitive to static magnetic field inhomogeneity (ie, T2*-sensitive). These sequences detect the paramagnetic effects of deoxyhemoglobin and methemoglobin. The hyperacute lesion on GRE/T2* typically consists of a core of heterogeneous signal intensity, reflecting the most recently extravasated blood that may still contain significant amounts of diamagnetic oxyhemoglobin, surrounded by a rim of hypointensity, signifying parenchymal blood that has had time to become more fully deoxygenated and paramagnetic (FIGURE 1).

We undertook a prospective comparison study of MRI vs CT in a large cohort of patients with acute stroke to establish that GRE MRI sequences are sensitive to acute hemorrhage.

**METHODS**

**Patients and Settings**

The Hemorrhage and Early MRI Evaluation (HEME) study was performed at 2 academic stroke centers (UCLA Medical Center and National Institutes of Health [NIH] Stroke Center at Suburban Hospital, Bethesda, Md). Initially, 2 additional centers were involved but subsequently discontinued participation in the study because of inadequate patient enrollment. Patients presenting with focal stroke symptoms within 6 hours of onset were screened for enrollment. Only symptomatic patients with a definite last known well time when initial imaging took place were eligible. Patients were excluded if any of the following were present: coma; pace-maker or other contraindication to MRI; symptoms suggestive of subarachnoid hemorrhage (SAH); inability to obtain MRI within 6 hours from last known well time; initiation of thrombolytic therapy, intravenous antithrombotics or anticoagulants, or antithrombotic investigational drug prior to completion of both imaging studies; or cardiorespiratory instability precluding MRI.

Site participation in the study was contingent upon the site’s current routine clinical practice of obtaining MRI followed by CT for patients with potential acute stroke. The institutional review board (IRB) at each site gave approval to prospectively collect and analyze clinical and imaging data with identifying information removed. At UCLA, the IRB waived consent; at Suburban Hospital, the study was performed under an IRB approved natural history of stroke protocol in which waiver was permitted in individual cases if waiver of consent could not be obtained.

**Imaging Techniques**

All patients underwent MRI followed by CT. Imaging time goals were completion of both MRI and CT within 90 minutes of presentation to the emergency department, with no more than 30 minutes between the end of MRI and the start of CT. Each site was required to keep a monthly log of all patients presenting within 6 hours of stroke symptom onset to ensure that at least 50% of all fully eligible patients were being enrolled. To qualify for enrollment, both GRE and DWI had to be completed.
All MRIs were performed on 1.5-T scanners equipped with echo-planar imaging capability: UCLA, Siemens Vision (Siemens Medical System, Iselin, NJ); and Suburban Hospital, GE Signa scanner (General Electric Medical Systems, Milwaukee, Wis). Computed tomographic scans were performed on 1 of the following fourth-generation scanners: Somatom Plus scanner (Siemens), High Speed Advantage scanner (General Electric), or Lightspeed scanner (General Electric). Images were acquired following the orbito-meatal plane with 5 mm thickness for the entire examination. Both scanners used the following pulse sequence parameters: slice thickness, 7 mm (GRE and DWI); repetition time (TR), 800 ms (GRE); flip angle 30° (GRE); acquisition matrix, $256 \times 192$ (GRE) and $128 \times 128$ (DWI). Pulse parameters at UCLA and at Suburban Hospital, respectively, were: field of view, 24 cm and 22 cm (GRE and DWI); echo time (TE), 20 ms and 15 ms (GRE); TR, 6000 ms and 60000 ms (DWI) (20 contiguous slices, interleaved, and co-localized); and TE, 100 ms and 72 ms (DWI).

**Outcome Measures**

A panel of 4 readers (2 neuroradiologists and 2 stroke neurologists) independently evaluated each scan blinded to the clinical information and all patient identifiers. None of the 4 readers was involved in the clinical care or evaluation of the enrolled patients. Before performing study interpretations, the readers were given examples (compiled from an independent data set) of each hemorrhage type to ensure consistency of interpretation to a common standard. Inconsistencies in the interpretations of a complementary study analysis program.

If unanimous agreement regarding the presence and acuity of hemorrhage on an individual scan was not achieved by each of the 4 readers, the interpretation of the majority of readers was used as the final imaging diagnosis. In evenly distributed disagreements (2 vs 2), final interpretation was reached by group consensus discussion. Final hospital discharge diagnosis incorporating all available clinical, laboratory, and imaging data was made at the time of discharge by the attending physician.

### Table 1. Clinical Characteristics of HEME Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>75 (25-99)</td>
</tr>
<tr>
<td>Sex, No. (%) women</td>
<td>200 (58)</td>
</tr>
<tr>
<td>Time to MRI, median (range)*</td>
<td>2 h 13 min (23 min to 5 h 58 min)</td>
</tr>
<tr>
<td>Time to CT, median (range)</td>
<td>3 h 3 min (56 min to 6 h 20 min)</td>
</tr>
<tr>
<td>Baseline NIHSS† score, median (range)</td>
<td>6 (0-33)</td>
</tr>
<tr>
<td>Final discharge diagnosis, No. (%)</td>
<td></td>
</tr>
<tr>
<td>AICS</td>
<td>169 (84.5)</td>
</tr>
<tr>
<td>Acute intracerebral hemorrhage</td>
<td>27 (13.5)</td>
</tr>
<tr>
<td>Both</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

**Statistical Analysis**

The primary objective of the study was to compare the accuracy of MRI vs CT for the detection of acute hemorrhage. Secondary objectives were to compare the accuracy of MRI vs CT for any hemorrhage (acute or chronic) and for chronic hemorrhage alone.

Initial sample size calculations assumed that CT was 100% accurate for hemorrhage and sought to demonstrate that MRI was also 100% accurate. In this noninferiority design, the sample size required to narrow the difference in the 95% confidence interval (CI) between MRI and CT to less than 3% was exact concordance between MRI and CT on 55 hemorrhages. The selected software was Microsoft Excel, using binomial theory. The a priori confidence level is 95%; however, an a priori significance level is unavailable since we are making a confidence bound, not significance testing.

In early 2003, an unplanned interim analysis was performed when preliminary results of a complementary study became available. During the interim analysis, it became apparent that MRI was detecting acute hemorrhages not visualized on CT and, therefore, the initial
sample size, based on the assumption of using CT as the criterion standard, was not valid. Accordingly, the primary analysis plan was changed to bidirectional comparison of CT vs MRI without assuming that one technique was inherently a criterion standard. In addition, at this juncture, the study was stopped early after 200 patients were enrolled, as the investigators believed it would be important to expedite, complete, and report the analysis of these patients because of the potential major impact the findings could have on current acute stroke management.

Inter-rater reliability was calculated for paired observers of both CT and MRI interpretations using the kappa (κ) statistic. The McNemar test for paired proportions was used to determine if one imaging modality diagnosed hemorrhage more frequently than the other.

RESULTS

Between October 2000 and February 2003, 391 consecutive patients presenting with focal stroke symptoms within 6 hours of onset were screened for enrollment in the study and a total of 200 patients were enrolled. Reasons for exclusion of the 191 patients who were not enrolled include: pacemaker or other contraindication to MRI (43); medical instability for MRI such as vomiting, coma, or cardiorespiratory instability (10); non-availability of both imaging techniques within the time window (99); initiation of thrombolytic or anticoagulant therapy before or between scans (9); and other reasons (30).

Characteristics of enrolled patients are summarized in Table 1. The comparisons between CT and MRI performance for any hemorrhage, acute hemorrhage, and chronic hemorrhage are shown in Table 2 and Table 3. Ranges for inter-rater reliability based on the κ statistic for paired observers were: 0.75 to 0.82 for acute hemorrhage on MRI and 0.87 to 0.94 for acute hemorrhage on CT; 0.42 to 0.66 for chronic hemorrhage on MRI (not applicable for CT); 0.58 to 0.80 for any hemorrhage on MRI and 0.85 to 0.92 for any hemorrhage on CT.

The panel read acute hemorrhage in 25 patients on both CT and MRI. In 4 additional patients, acute hemorrhage was interpreted as being present on MRI but not on the corresponding CT (Figure 2). In all 4 of these patients, regions of hypointensity were seen on the GRE images within an ischemic field (identified by DWI). Each of these cases was interpreted as hemorrhagic transformation of an ischemic infarct by the treating physicians based on all clinical and radiologic data.

In 4 patients, acute hemorrhage was read by the panel on CT but not the corresponding MRI (Figure 3). In 3 of these patients, the region of acute hemorrhage apparent on CT was also apparent on MRI but was interpreted as “chronic hemorrhage” rather than acute. In the fourth patient, a region of hyperdensity on CT in the left frontal lobe was interpreted as subarachnoid blood by 2 of 4 readers on CT; on MRI this abnormality was clearly apparent as a serpiginous, hypointense lesion in a sulcus on GRE images. Although 1 of the readers did initially interpret this lesion as acute SAH on MRI, 3 did not. The final discharge diagnosis for this patient was acute ischemic stroke with SAH.

For the 26 primary intraparenchymal hematomas visualized on CT, median hematoma volume was 20.8 mL (range, 0.2-157.2 mL). Subarachnoid blood was visualized in 2 cases, including 1 isolated SAH associated with acute ischemic stroke (case above) and 1 SAH with an intracerebral and intraventricular hemorrhage. In the latter, the subarachnoid blood component was noted on CT only, although both CT and MRI detected the intraparenchymal and intraventricular components. Intraventricular blood was interpreted as being present in 16 patients, all with intraparenchymal hematomas. The intraventricular blood was apparent on both CT and MRI in 11 cases, on MRI only in 1, and on CT only in 4. Subdural hemorrhage was seen in only 1 patient and was identified on both MRI and CT. No epidural hematomas were identified.

Chronic hemorrhage was seen in 52 patients on MRI and in no patients on CT. Of these 52 MRI patients, 4 were interpreted as regions of chronic hemorrhagic transformation, 9 as chronic hematomas, 34 as 1 or more microbleeds (Figure 4), and 7 as both one or more microbleeds and one or more hematomas. Three of the cases interpreted as chronic hematomas on MRI were visualized as acute blood on CT. Of the 41 patients with MRI-evident microbleeds, 10 had single lesions and 31 multiple lesions—with none visualized on CT.

Compared with final discharge diagnosis, which incorporated informa-

<table>
<thead>
<tr>
<th>Table 2. MRI vs CT Panel Results (n=200)</th>
<th>CT+</th>
<th>CT−</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any hemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI+</td>
<td>28</td>
<td>43</td>
<td>.001</td>
</tr>
<tr>
<td>MRI−</td>
<td>1</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Acute hemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI+</td>
<td>25</td>
<td>4</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>MRI−</td>
<td>1</td>
<td>167</td>
<td></td>
</tr>
<tr>
<td>Chronic hemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI+</td>
<td>0</td>
<td>52</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MRI−</td>
<td>0</td>
<td>146</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

<table>
<thead>
<tr>
<th>Table 3. Comparison of Individual and Consensus Interpretations for Acute Hemorrhage for MRI vs CT</th>
<th>CT</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Readers Diagnosing Acute Hemorrhage</td>
<td>CT</td>
<td>MRI</td>
</tr>
<tr>
<td>No. (%)</td>
<td>Consensus Read, % Positive</td>
<td>Consensus Read, % Positive</td>
</tr>
<tr>
<td>All 4 Yes</td>
<td>26 (13)</td>
<td>100</td>
</tr>
<tr>
<td>3 Yes</td>
<td>4 (2)</td>
<td>100</td>
</tr>
<tr>
<td>2 Yes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 Yes</td>
<td>5 (2.5)</td>
<td>0</td>
</tr>
<tr>
<td>None Yes</td>
<td>165 (82.5)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>200 (100)</td>
<td>200 (100)</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.
tion from both imaging studies as well as additional laboratory, pathologic, and clinical data, CT and MRI performed equally well with no significant difference in the accuracy of the scans obtained from UCLA Medical Center vs Suburban Hospital (TABLE 4).

A first imaging study was performed within 3 hours of onset for 129 patients. Nineteen of the cases with a final discharge diagnosis of hemorrhage and 6 of the 8 discordant hemorrhage cases (3 each for CT negative, and MRI negative) were within this cohort. Thirty-four patients were treated with intravenous tissue plasminogen activator (tPA) within 3 hours of onset. The remaining patients were not treated due to rapidly resolving or nondisabling deficits, or other contraindication to thrombolytic therapy.

**COMMENT**

Neuroimaging plays a crucial role in the evaluation of patients presenting with acute stroke symptoms. While patient symptoms and clinical examinations may suggest the diagnosis, only brain imaging studies can confirm the diagnosis and differentiate hemorrhage from ischemia with high accuracy. This differentiation is critical in making acute treatment decisions, including patient...
eligibility for thrombolytic therapy. Although noncontrast CT has been considered the criterion standard for assessing intracerebral hemorrhage, formal studies have never been performed to validate the accuracy of this technique compared to the true criterion standard, pathology. In our study, hemorrhage was accurately identified on MRI in all cases of CT positive acute intraparenchymal hematomas; in 25 cases, the blood was interpreted as acute and in 3 cases as chronic.

The HEME study provides complementary data to that of a recently published study performed by the German Stroke Competence Network (B5 Hemorrhage Study).14 This group evaluated the accuracy of CT vs MRI in distinguishing acute intracerebral hemorrhage (50 patients) from acute ischemic stroke (50 patients) using a design in which patients were randomized to either CT or MRI first. The HEME study enrolled all eligible patients, rather than simply an equal number of patients with hemorrhagic and ischemic stroke.

Figure 3. Hemorrhage Visualized on Computed Tomography but Not Interpreted as Acute Blood on Magnetic Resonance Imaging

Computed tomography (CT) and magnetic resonance (MR) images from representative axial slices from 2 patients (A,B) in whom hemorrhage was visualized on CT, but not interpreted as acute blood on MRI, by our consensus panel. For each patient, the left panel shows the CT image, the middle panel shows the corresponding gradient recalled echo (GRE) image, and the right panel shows the diffusion-weighted image (DWI). In patient 3, the hemorrhage is apparent on CT as a hyperdense lesion (white arrowhead). A corresponding hypointensity is marked on the GRE (black arrowhead) and on the DWI image (yellow arrowhead). In this patient, the MRI lesion was recognized as blood but was interpreted as chronic, not acute, hemorrhage. In patient 4, a left frontal lesion is interpreted as subarachnoid blood on CT (white arrowhead). This lesion is apparent on the GRE sequence (black arrowhead) but was interpreted as blood by only 1 of 4 members of our panel. The corresponding DWI image shows hyperintensity indicative of acute ischemia within the left anterior cerebral artery territory (yellow arrowheads).
Our panel of readers identified acute hemorrhage on MRI in 4 cases in which hemorrhage was not apparent on CT. Each of these was interpreted as a region of hemorrhagic transformation (petechial blood) within an acute ischemic infarct field. These results are supported by recent case reports of “CT-negative intracerebral hemorrhages.”

It is possible that hyperacute hemorrhagic transformation of ischemic infarcts is an underrecognized phenomenon. The implication of this finding for the neuroimaging evaluation of acute stroke patients who are candidates for thrombolytic therapy is unclear. In the National Institute of Neurological Disorders and Stroke (NINDS) trial, intravenous tPA was shown to be effective based on CT enrollment criteria. While it may be hypothesized that patients with MRI evidence of hemorrhagic transformation are at higher risk of developing symptomatic hemorrhage if treated with thrombolytics, it is also possible that overall this group of patients may receive net benefit from therapy. A prospective study will be needed to answer this question.

All 3 acute hemorrhages that the panel misclassified as chronic on MRI were relatively small, but none were classified as chronic microbleeds. In these cases, the typical pattern of acute hemorrhage on GRE was more difficult for reviewers to appreciate (2 patients) or not present (1 patient). Physicians should be aware that in cases of small hemorrhages (non-microbleeds), it may be difficult to make an exact distinction between acute and chronic hemorrhage based on GRE images alone. A noncontrast CT may be necessary in these cases to determine hemorrhage age. With acute medium-large hemorrhages, the characteristic appearance of mixed signal intensity and the surrounding hyperintensity due to edema is very specific and will make the age of the hemorrhage apparent. However, small hemorrhages may have similar characteristics to calcifications and intravascular thrombus and have minimal edema making the determination of hemorrhage age as well as the distinction of hemorrhage vs non-hemorrhage more difficult.

The HEME study confirms the superiority of GRE MRI sequences for the identification of chronic hemorrhage. In 49 patients, GRE demonstrated chronic blood not apparent on CT. The majority of these chronic hemorrhages were categorized as microbleeds—clinically silent, small, punctate hemosiderin lesions appearing hypointense on GRE sequences. The role of microbleeds in determining patient eligibility for thrombolytic therapy remains unknown. However, prior studies suggest that the presence of microbleeds may be an independent risk factor for hemorrhage in patients treated with antithrombotic or thrombolytic therapy.

Our study has several limitations. We initiated the study using CT as the criterion standard for diagnosis of hemorrhage. However, following the unplanned interim analysis indicating that GRE sequences were detecting hemorrhage not seen on CT, we switched to a 2-sided analysis based on the assumption that these MRI findings represented...
sented genuine acute hemorrhage. We also specifically excluded any patient with symptoms suggestive of SAH. Although prior studies have suggested that both GRE MRI and fluid-attenuated inversion recovery images may be accurate in identifying subarachnoid blood, this will need to be prospectively confirmed in a future study. Because neither CT nor MRI can exclude SAH with 100% reliability, the clinician should pursue an extensive evaluation in any patient with whom SAH is contemplated, including CT as well as lumbar puncture if CT is negative.

Interreader reliability (κ statistic) for detection of hemorrhage was better for CT than for MRI. This is likely due to several factors, including less experience of the readers in interpreting acute MRI for hemorrhage and differences in the intrinsic conspicuity of hemorrhage appearance on CT and MRI. Therefore, a comprehensive educational program should be undertaken at any institution choosing to perform only MRI and not CT for the evaluation of acute stroke patients.

Recent reports have indicated widespread availability of advanced MRI techniques in the United States for the evaluation of patients with acute stroke. However, concerns have been raised regarding the logistical aspects of acquiring multimodal MRI in the acute stroke setting, particularly with regard to image acquisition times (and potential delays in initiating thrombolytic therapy).

Based on our overall experience, the comprehensive MRI stroke protocol we used generally takes 10 to 15 minutes. An abbreviated protocol, including DWI, GRE, and perfusion-weighted imaging (PWI), takes less than 5 minutes and still provides substantially more information than a noncontrast CT.

Our study may have implications for the imaging evaluation of patients with acute stroke symptoms. Our findings support prior studies suggesting that MRI is as accurate as CT for the detection of hyperacute hemorrhage. One important caveat is that with small hemorrhages, blood that appears as acute on CT may appear as chronic on GRE MRI and a noncontrast CT may be required to confirm the diagnosis in these cases. Our study suggests that GRE MRI may be able to detect regions of hemorrhagic transformation of an acute ischemic stroke not evident on CT. Our study confirms the superiority of MRI for detection of chronic hemorrhage, particularly microbleeds. The role of these findings in the decision-making process for treatment of patients who are candidates for thrombolytic therapy is currently unknown. Due to its advantages in delineating ischemic pathophysiology, in combination with the findings suggesting equivalency to CT for detecting acute hemorrhage, MRI may be acceptable as the sole imaging technique for acute stroke at centers with expertise in interpreting these findings.

Author Contributions: Dr Kidwell had full access to all of the data in the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Kidwell, Chalela, Saver, Starkman, Warach.


Drafting of the manuscript: Kidwell, Chalela, Fredieu, Davis Warach, Saver.

Critical revision of the manuscript for important intellectual content: Kidwell, Chalela, Saver, Starkman, Hill, Demchuk, Butman, Patronas, Alger, Laby, Baird, Leary, Trellewd, Ovbiaghe, Suzuki, Villablanca, Davis, Dunn, Todd, Ezzedine, Mayenh, Lynch, Dav. Warach.

Statistical analysis: Kidwell, Chalela, Saver, Warach.

Obtained funding: Kidwell, Saver, Warach.

Administrative, technical, or material support: Kidwell, Saver, Starkman, Hill, Alger, Latour, Leary, Fredieu, Davis, Todd, Mayenh, Warach.

Study supervision: Kidwell, Chalela, Starkman, Baird, Ezzedine, Warach.

Funding/Support: This study was supported in part by the Division of Intramural Research, National Institute of Neurological Disorders and Stroke (NINDS) and grants from the American Heart Association (0170033N, Dr Kidwell; AHA Western States Affiliate Fellowship Award, Dr Leary) and NINDS (N23 NS 02888, Dr Kidwell; NS 39498/EB 00238/EB, Dr Alger; K24 NS 002992, Dr Saver). Dr Hill was supported in part by the Heart & Stroke Foundation of Alberta/NWT/NU and the Canadian Institutes for Health Research.

Role of the Sponsor: The study was wholly designed, conducted, analyzed, and reported by the authors without any input from industrial sponsors.

Acknowledgments: We would like to acknowledge the invaluable assistance provided by Patricia Lyall, BA, Vickie Hyeneman, Elisa Landis, BA, and Sarah Hilton, BS, for the completion of this project.

REFERENCES


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