Validation of Computed Tomographic Middle Cerebral Artery “Dot” Sign
An Angiographic Correlation Study

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Background and Purpose—The middle cerebral artery (MCA) “dot” sign consists of hyperdensity of an arterial structure, seen as a dot in the sylvian fissure. The MCA dot sign has been proposed to indicate thrombosis of M2 or M3 MCA branches, analogous to the hyperdense middle cerebral artery (HMCA) sign indicating M1 thrombosis. The MCA dot sign has not been validated previously against the gold standard of conventional cerebral angiography.

Methods—Noncontrast CT scans and immediately subsequent cerebral angiograms from 54 acute stroke patients within 8 hours of symptom onset were analyzed. CT films were inspected for the MCA dot sign and HMCA sign. Vascular findings on CT were compared with findings at angiography.

Results—Mean patient age was 71 years; median National Institutes of Health Stroke Scale score was 16.5. Mean time from symptom onset to CT was 125 minutes, and that from CT to angiography was 117 minutes. All patients had arterial occlusion at angiography. Of the anterior circulation occlusions, M1 occlusions were noted in 28 patients, isolated M2 in 15, and isolated M3 in 4. One definite MCA dot sign was observed in 16.7% of patients, and an HMCA sign was observed in 13.9%. MCA dot sign performance in predicting the presence of M2 or M3 clot at angiography was as follows: sensitivity 38%, specificity 100%, positive predictive value 100%, negative predictive value 68%, and overall accuracy 73%.

Conclusions—The MCA dot sign is a highly specific and moderately sensitive indicator of acute thrombus in the M2/M3 MCA branches, as validated by catheter angiography. The MCA dot sign is a useful additional acute stroke CT marker.

Key Words: cerebral angiography • infarction, middle cerebral artery • middle cerebral artery • radiography, interventional • stroke, acute

The primary role of noncontrast CT scanning in acute stroke patients has been to rule out intracranial hemorrhage. With the advent of thrombolytic therapy for acute stroke, however, it has become increasingly important for neurologists and other stroke team physicians to also recognize changes on CT that may more definitively rule in early brain ischemia.

During the first hours after the onset of cerebral ischemia, brain CT scans can often appear normal. However, subtle CT signs indicating acute ischemia or infarction frequently may be detected, including obscuration of the lentiform nucleus, hypodensity of the insular ribbon, cortical hypodensity, sulcal effacement, and the hyperdense middle cerebral artery (HMCA) sign. Observation of these subtle clues to ischemia and infarction on CT is important because these signs have diagnostic as well as prognostic value in the acute stroke setting. Increased density of a cerebral artery on noncontrast CT indicating the presence of intraluminal thrombus was one of the first early CT signs described in ischemic stroke patients. Initial descriptions of the HMCA sign focused on M1 segment occlusions, which appear as linear streaks of hyper-

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density running along the imaging plane of axial CT slices, following the course of the M1 from its origin to the sylvian fissure.5,9–12 Later observers additionally delineated M2 occlusions on CT appearing as hyperdensities in the region of the M2 divisions.13–16 Barber et al noted the HMCA sign presence in 5% of their patient population, while other studies report a much higher prevalence.5,10,13,14,16 The specificity of the HMCA sign for middle cerebral artery (MCA) occlusion approaches 100%, although its sensitivity is low.4,5,14,17–19

More recently, the term MCA dot sign was introduced to particularly label unilateral hyperdense circles in the sylvian fissure, suggested to represent intraluminal thrombus visualized en face in distal M2 or M3 MCA branches.16 In the study of Barber and colleagues,16 of 100 consecutive acute stroke patients imaged within 3 hours of anterior circulation symptom onset before intravenous tissue plasminogen activator, a CT MCA dot sign was noted in 16%. However, angiographic correlation studies to demonstrate the validity of the MCA dot sign were not performed.

The primary purpose of this study was to validate the CT MCA dot sign against the gold standard of conventional cerebral catheter angiography.

Subjects and Methods

Case Identification

Consecutive cases were chosen for analysis from the University of California at Los Angeles (UCLA) intra-arterial thrombolysis patient registry; the following inclusion criteria were used: (1) retrievable noncontrast CT scan performed on patient arrival at hospital and (2) diagnostic catheter angiogram performed directly after CT. All patients subsequently received intra-arterial tissue plasminogen activator.

CT Interpretation

A neuroradiologist (J.P.V.) and a stroke neurologist (M.C.L.), blinded to all clinical information, inspected initial noncontrast CT films for the presence of the MCA dot sign and the HMCA sign. The HMCA sign was defined as “an MCA denser than its contralateral counterpart.”16 The MCA dot sign was defined as “hyperdensity of an arterial structure (seen as a dot) in the Sylvian fissure relative to the contralateral side or to other vessels within the Sylvian fissure.”16

Both the CT MCA dot sign and the HMCA sign were rated as absent, borderline, or present. All rating disagreements were settled by a third rater (J.L.S.). For dichotomized analyses, the categories of absent and borderline were collapsed into an “any definite sign absent” category.

Angiogram Interpretation

Angiographic sites of arterial occlusion were abstracted from interventional neuroradiological reports in all patients. The accuracy of data abstracted from angiography reports was confirmed by direct reinspection of angiographic films in one half of all cases (100% agreement between data abstraction and direct read in all analyzed cases).

Statistical Analyses

Interrater reliability in identifying the MCA dot sign and HMCA sign was characterized with the $\kappa$ statistic. The presence of an MCA dot sign was compared with the gold standard of an ipsilateral M2 or M3 arterial occlusion at angiography, and sensitivity, specificity, positive predictive value, negative predictive value, overall accuracy, positive likelihood ratio, and negative likelihood ratio were calculated. The presence of an HMCA sign was correlated similarly with the presence of M1 occlusion at angiography. Group differences in clinical outcome by presence or absence of CT signs were analyzed with $t$ tests. Demographic and clinical predictors of the presence or absence of the MCA dot and HMCA signs were analyzed with $t$ tests for continuous variables and $\chi^2$ tests for binary variables.

Results

Subjects were 54 acute stroke patients presenting to UCLA Medical Center within 8 hours of symptom onset for interventional treatment between 1996 and 2001. In the cohort, 43% of subjects were male and 57% female. The mean patient age was 71 years (range, 27 to 96 years). The median entry National Institutes of Health Stroke Scale (NIHSS) score was 16.5, with scores ranging from 2 to 38.

Mean time from stroke symptom onset (defined as time last known well) to pretreatment noncontrast CT brain scan was 125 minutes (range, 35 to 537 minutes). Mean time from CT scan to catheter angiography was 117 minutes (range, 20 to 296 minutes). All patients had vessel occlusions at angiography. Among occlusions, 93% were located in the anterior circulation and 7% (n=4) in the posterior circulation. Of the anterior circulation occlusions (n=50), 1 occurred within the internal carotid artery in isolation, 1 within the anterior cerebral artery in isolation, 28 within the MCA M1 division, 15 within the MCA M2 division, and 4 within the MCA M3 division. Regarding the posterior circulation occlusions (n=4), 2 occurred within the vertebral artery, 1 within the posterior cerebral artery, and 1 within the basilar and posterior cerebral artery.

Presence of MCA Dot Sign and HMCA Sign

Interrater reliability for the 2 CT raters showed a $\kappa$ score of 0.76 for the presence of the MCA dot sign and a $\kappa$ score of 0.91 for the presence of the HMCA sign.

Figure 1 shows the frequency of the MCA dot sign and the HMCA sign ratings of absent, borderline, and present. A present dot sign was noted in 16.7% of cases. If the categories of absent and borderline MCA dot sign are collapsed, this “any definite sign absent” category was noted in 83.3% of cases.

The relationship between the presence of the HMCA sign and MCA dot sign was analyzed in anterior circulation cases (n=50). Nine percent of all patients had a solitary positive MCA dot sign, 6% had an isolated HMCA sign, 9% had the combination of both a dot sign and an HMCA sign, and 76% of patients had neither.

Performance of MCA Dot Sign and HMCA Sign

The diagnostic performance of a present MCA dot sign in predicting M2 or M3 occlusion at angiography is shown in
Table 1. Performance of a present HMCA sign in predicting M1 occlusion is also shown in Table 1. In our cohort, performance of the HMCA sign in predicting M1 occlusion was similar to that of the MCA dot sign. Both MCA dot signs and HMCA signs correlated with ipsilateral arterial occlusions; no contralateral arterial occlusions were noted at angiography.

Table 1. Diagnostic Performance of the MCA Dot Sign and HMCA Sign Compared With Catheter Angiography (n=54)

<table>
<thead>
<tr>
<th></th>
<th>MCA Dot Sign</th>
<th>HMCA Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>NPV, %</td>
<td>68</td>
<td>82</td>
</tr>
<tr>
<td>PPV, %</td>
<td>100</td>
<td>73</td>
</tr>
<tr>
<td>Accuracy, %</td>
<td>73</td>
<td>81</td>
</tr>
<tr>
<td>Positive LR</td>
<td>Infinite</td>
<td>7.9</td>
</tr>
<tr>
<td>Negative LR</td>
<td>0.62</td>
<td>0.64</td>
</tr>
</tbody>
</table>

NPV indicates negative predictive value; PPV, positive predictive value; LR, likelihood ratio.

An illustrative example of the MCA dot sign is shown in Figure 2.

Correlation With Outcome and Clinical Variables
Table 2 examines the correlation of the MCA dot sign and the HMCA sign with clinical outcome. As shown, there is a trend for solitary “dot-positive” patients to have less severe median pretreatment and day 7 NIHSS scores than patients with the HMCA sign. Similarly, patients with isolated positive MCA dot signs had better day 7 modified Rankin Scale outcomes than patients with HMCA signs.

Univariate analysis of clinical and demographic variables associated with the presence or absence of any CT-visible intraluminal thrombus (MCA dot and/or HMCA signs) was performed. Significant predictors of the presence of CT-visible intraluminal thrombus were younger patient age (66 versus 75 years; \( P=0.003 \)) and higher platelet count (270 versus 202; \( P=0.03 \)). There was a trend toward a longer interval from symptom onset to CT in patients exhibiting an MCA dot sign than in patients not exhibiting an MCA dot sign (Figure 3).

Discussion
The goal of this study was to validate the CT MCA dot sign, including direct comparison with the gold standard of conventional cerebral catheter angiography. Angiographic comparison demonstrated that the MCA dot sign clearly has diagnostic value as a highly specific and moderately sensitive indicator of acute thrombus or slow flow within the M2 or M3 branches of the MCA. In addition, in our analysis, both the MCA dot sign and the HMCA sign demonstrated good interrater reliability. We detected the presence of an MCA dot sign on CT in 16.7%, similar to the 16% incidence observed by Barber and colleagues\(^{16} \) in their acute stroke patient population.

The MCA dot sign also demonstrated good prognostic value. The presence of an isolated MCA dot sign, an MCA dot sign in conjunction with an HMCA sign, or an isolated HMCA sign were all associated with more severe neurological deficits at the time of patient presentation than the absence of any CT-visible intraluminal thrombus. There was a trend for patients with a solitary MCA dot sign to have milder neurological deficits at presentation than those with the HMCA sign. Compared with the presence of an HMCA sign, the presence of a solitary positive MCA dot sign tended to be associated with less severe stroke neurological deficits.

Table 2. Median Outcome Scores for MCA Dot–Positive and HMCA Positive Patients

<table>
<thead>
<tr>
<th></th>
<th>Pretreatment NIHSS</th>
<th>Day 7 NIHSS</th>
<th>Day 7 Modified Rankin Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated MCA dot patients (n=9)</td>
<td>14.0</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Isolated HMCA patients (n=6)</td>
<td>18.5</td>
<td>13.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Dot and HMCA positive patients (n=9)</td>
<td>20.0</td>
<td>7.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>
and better functional outcome 1 week after stroke. There are likely several reasons for this observation. A solitary MCA dot sign, reflecting isolated M2/M3 occlusions, indicates a lesser volume of territory at risk than an HMCA sign reflecting M1 occlusion. Additionally, in our series in which all patients underwent intra-arterial thrombolytic therapy, patients with solitary MCA dot signs and M2/M3 occlusions had less clot burden than patients with HMCA signs and M1 occlusions and were more likely to recanalize in response to endovascular treatment.

Our analysis identified younger age and higher platelet count as predictors of the presence of CT visibility of intraluminal thrombus. Factors that may account for association of CT-visible clots with younger age include vessel calcification in older individuals obscuring the presence of intraluminal thrombus and formation of less densely packed clots at older age. Factors favoring the association of CT-visible clots with higher platelet count may include greater red blood cell packing density in thrombi formed when serum platelet count is higher and x-ray opacity of platelets themselves. No prior study has attempted to link patient clinical factors with the presence of a CT MCA dot sign or HMCA sign in the setting of angiographically documented anterior circulation occlusions. In a non-angiographically confirmed study, the presence of a hyperattenuating HMCA sign was associated with lower age point estimate, but the difference did not reach statistical significance, and an association with platelet counts was not explored.15 Giroud and colleagues17 found a relationship between the HMCA sign and hypertension, vomiting, headache, and hyperglycemia, as would be expected if the HMCA sign is associated with larger infarctions due to M1 occlusions.19 False-positive HMCA signs have been reported in association with atherosclerosis as well as with an elevation in hematocrit. However, in both settings the HMCA signs were typically bilateral.5,14,18,19 Unilateral false-positive HMCA signs have been reported with herpes simplex encephalitis, subacute stroke, and polycythemia.20

Our study has several important limitations. The population studied (patients undergoing intra-arterial thrombolysis) may not be fully representative of the entire acute stroke population. Additionally, because this patient population with known vessel occlusion was studied retrospectively, a degree of bias in the CT readers could have been introduced. However, while CT readers would be aware that all patients would have some occlusion, readers would also be aware that the occlusion would not necessarily occur within the MCA. A final limitation was the factor that the number of patients exhibiting an MCA dot sign was modest, limiting study precision.

The MCA dot sign occurs in roughly 1 of every 6 acute stroke patients. It is an important radiological finding for clinicians to recognize since the MCA dot sign has high specificity in indicating the presence of M2 or M3 branch occlusion and provides prognostic as well as diagnostic value. However, since the sensitivity of the sign is modest, its absence does not exclude distal MCA occlusion. In making the diagnosis of acute MCA territory infarction, it will be important for clinicians to inspect CT scans for the presence of the MCA dot sign as well as other subtle acute ischemic stroke findings, such as obscuration of the lentiform nucleus, hypodensity of the insular ribbon, cortical hypodensity, sulcal effacement, and the hyperdense MCA sign. The MCA dot sign, however, represents a useful addition to the catalog of signs of acute cerebral ischemia evident on early CT studies.

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References


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