Multiphasic Helical Computed Tomography Predicts Subsequent Development of Severe Brain Edema in Acute Ischemic Stroke

Soo Joo Lee, MD; Kwang Ho Lee, MD; Dong Gyu Na, MD; Hong Sik Byun, MD; Yong Boem Kim, MD; Young-Min Shon, MD; Soo-Jin Cho, MD; Jun Lee, MD; Chin-Sang Chung, MD; Seung-Chyul Hong, MD

Objective: To evaluate the use of multiphasic helical computed tomography (CT) in predicting subsequent development of severe brain edema in patients with acute middle cerebral artery (MCA) stroke.

Design: Case-control study.

Setting: Tertiary referral hospital.

Patients: We studied 31 patients with acute MCA stroke who had a baseline National Institutes of Health Stroke Scale score of 15 or higher within 6 hours of symptom onset. Sequential 4-phasic enhanced helical CT scans were performed after taking precontrast CT scans. The severity of perfusion deficit was graded as “severe” or “moderate” depending on collateral blood flow.

Main Outcome Measures: Patients were classified as having severe brain edema if they showed signs of uncal herniation or deterioration with mass effect leading to hemicraniectomy.

Results: Severe brain edema developed in 10 patients (32%). Severe perfusion deficit greater than 50% of the presumed MCA territory on multiphasic helical CT was more often found in patients with severe brain edema than in those without (8 of 10 vs 4 of 21, P = .002). In contrast, parenchymal hypodensity greater than 50% on postcontrast CT was observed only in 5 patients with severe brain edema (5 of 10 vs 4 of 21, P = .10). Additional involvement of the anterior or posterior cerebral artery territory was found in multiphasic CT (6 of 10 vs 0 of 21, P < .001) and on precontrast CT (4 of 10 vs 0 of 21, P = .007) only in patients with severe brain edema.

Conclusion: Multiphasic helical CT is more useful than postcontrast CT for predicting subsequent severe brain edema in acute MCA stroke based on the findings of severe perfusion deficit greater than 50% of the MCA territory and additional involvement of the anterior or posterior cerebral artery territory.

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Large hemispheric ischemic stroke may evolve with severe edema, resulting in transtentorial herniation. In most instances, this malignant infarction is caused by embolic occlusion of the internal carotid artery or the middle cerebral artery (MCA) trunk. In the first hours after stroke onset, symptoms may be severe but nonspecific with regard to a fatal outcome. Early identification of those who may develop fatal brain swelling is important for the following reasons: (1) specific treatments, such as decompressive hemicraniectomy and hypothermia, may be indicated and (2) patients with extended ischemic edema may not benefit from reperfusion therapy.

Patients with baseline National Institutes of Health Stroke Scale (NIHSS) scores of 20 or higher with left hemispheric infarction or 15 or higher with right hemispheric infarction within 6 hours of symptom onset who also had early nausea or vomiting within 24 hours are at high risk for developing fatal brain swelling. von Kummer et al observed in 53 patients with MCA trunk occlusion that a parenchymal hypodensity exceeding 50% of the MCA territory on noncontrast computed tomography (CT) within 6 hours of stroke onset had a positive predictive value of 85% for a fatal outcome. Cerebral blood flow evaluations within 6 hours of stroke using xenon-enhanced CT and single-photon emission CT were also used to predict subsequent development of edema and progression to life-threatening herniation.

Triphasic helical CT technique was useful in the detection of proximal arterial occlusion and assessment of collateral blood flow and perfusion deficits in ischemic areas. Perfusion deficits were graded as “severe” or “moderate” with angiographic correlation depending on colla...
were defined as the zone of severe perfusion deficit is the ischemic core and that of moderate perfusion deficit is the ischemic penumbra, similar to a diffusion-perfusion mismatch on magnetic resonance imaging. The aim of this study was to evaluate the use of multiphasic helical CT in predicting subsequent development of severe brain edema in patients with acute MCA stroke and to seek the potential radiological predictors.

### METHODS

**PATIENTS**

Between January 1, 1998, and May 31, 2000, 195 patients with acute ischemic stroke were admitted to Samsung Medical Center within 6 hours of symptom onset. Thirty-two patients who met the following inclusion criteria were enrolled into this study: (1) patients showed acute MCA territory stroke symptoms consisting of hemiparesis and sensory loss with or without aphasia or neglect, (2) their baseline NIHSS scores were 15 or higher, (3) precontrast CT excluded evidence of intracranial hemorrhage, and (4) multiphasic helical CT scans had been obtained within 6 hours of symptom onset.

**MULTIPHASIC HELICAL CT TECHNIQUE AND IMAGE INTERPRETATION**

Multiphasic CT was performed with a helical scanner (High Speed Advantage; General Electric Medical Systems, Milwaukee, Wis). The number and timing of CT scans in the multiphasic helical protocol were modified from triphasic helical CT protocols.\(^9\)\(^,\)\(^10\) We considered the variable circulation time in each patient. Therefore, we added 1-phase CT scanning and changed the timing of scanning in multiphasic helical CT. After the acquisition of conventional precontrast CT images of the whole brain, contrast-enhanced multiphasic helical CT scans were obtained. The scan parameters are summarized in Table 1. The mean ± SD time to multiphasic helical CT was 2.6 ± 1.7 hours after stroke onset.

A neuroradiologist (D.G.N.) and a stroke neurologist (S.J.L.) read the precontrast CT and multiphasic helical CT scans with knowledge of the affected side, but without information on baseline NIHSS scores, follow-up images, or clinical outcome. All images were independently read in random order. The extent of hypodense areas on precontrast CT and nonenhancing segments on early- and middle-phase images was evaluated as the ischemic core and that of moderate perfusion deficit had higher attenuation than those of severe perfusion deficit on the late-phase images, and the mean Hounsfield unit difference was 7.6. The areas of moderate perfusion deficit had higher attenuation than those of severe perfusion deficit on the late-phase images, and the mean Hounsfield unit difference was 7.1.

**Table 1. Multiphasic Helical Computed Tomography Scan Variables**

<table>
<thead>
<tr>
<th>Range or level</th>
<th>From the level of 1 cm below the caudal proximal middle cerebral artery to the vertex; 8 sections at each phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scan timing or sequence</td>
<td>Baseline unenhanced scan; 20-, 34-, 48-, and 62-s delay after dye injection</td>
</tr>
<tr>
<td>Contrast dye</td>
<td>Total amount, 90 mL; infusion rate, 3 mL/s</td>
</tr>
<tr>
<td>Other scan variables</td>
<td>120 kV; 240 mA (conventional), 200 mA (helical); 512×512-image matrix; 23-cm field of view; 10-mm collimation; 10-mm/s table speed; 5-mm interval reconstruction</td>
</tr>
</tbody>
</table>

**OTHER VASCULAR TERRITORY INVOLVEMENT** was defined as hypodensity or perfusion deficits (moderate and severe perfusion deficit) in the anterior cerebral artery (ACA) or posterior cerebral artery (PCA) territory. We also determined the presence of proximal MCA (stem, bifurcation, and divisions) and internal carotid artery occlusion with hyperdense arterial signs on precontrast CT and nonenhancing segments on early- and middle-phase images of multiphasic helical CT.\(^9\)\(^,\)\(^10\)

We obtained agreement rates and \( \kappa \) values between the 2 readers. The readers agreed on the extent of parenchymal hypodensities in 27 of 32 patients (\( \kappa = 0.78 \)) and severe perfusion deficits in 29 (\( \kappa = 0.91 \)).

**FOLLOW-UP IMAGES**

Follow-up CT scanning or magnetic resonance imaging was performed when patients were first noticed to substantially worsen. The follow-up images were done between the second and seventh days after the initial events.

**END POINT**

Patients were classified as having severe brain edema if they showed clinical signs of uncal herniation or rapid deterioration of neurological and consciousness status, clinical symptoms of increased intracranial pressure (nausea or vomiting), and mass effect leading to hemicraniectomy. Decompressive hemicraniectomy was considered in the event of rapid neurological and consciousness deterioration, clinical symptoms and signs of increased intracranial pressure, or mass effect on the follow-up imaging.

**STATISTICAL ANALYSIS**

Categorical variables were compared with the 2-tailed Fisher exact test, and quantitative variables were compared with the Mann-Whitney test. Multivariate analysis was performed with logistic regression, \( P < .05 \) was regarded as significant. The analysis was performed using a statistical software package (SPSS-PC version 10.0; SPSS Inc, Chicago, Ill).

**RESULTS**

Thirty-two patients were initially included. We excluded a patient who developed a large parenchymal he-

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matoma 1 day after symptom onset. Severe ischemic brain edema developed in 10 (32%) of 31 patients. Decompressive hemicraniectomy was performed in 6 patients.

The mean±SD age was younger in 10 patients with severe brain edema compared with the remaining 21 without severe edema, but did not reach statistical significance (58.9±15.5 vs 67.9±12.9 years; P=.17). The baseline NIHSS scores were not different between patients with severe brain edema and those without (median score [interquartile range], 19 [18-20] vs 18 [16-20]; P=.57).

The extent of hypodensity on precontrast CT did not differ from that of severe perfusion deficit on multiphasic helical CT in 28 patients. However, 3 patients showed a discrepancy (Figure 1). In all 3, precontrast CT showed hypodensity greater than 33% but less than or equal to 50% of the MCA territory. In 2 patients, multiphasic helical CT showed severe perfusion deficit greater than 50% but less than or equal to 66% of the MCA territory, with severe perfusion deficit greater than 66% in the third. Two of the 3 patients had additional perfusion deficit in the ACA and/or PCA territories on multiphasic helical CT, which was not evident on precontrast CT.

On univariate analysis (Table 2), significant differences were found between patients with severe brain edema and those without, with severe perfusion deficit greater than 50% of the MCA territory on multiphasic helical CT, parenchymal hypoattenuation greater than 66% on precontrast CT, and additional involvement of the ACA or PCA territory. There was no significant difference between the 2 groups in the presence of parenchymal hypodensity greater than 50% of the MCA territory on precontrast CT (P=.10). The site of arterial occlusion on multiphasic helical CT images was not significantly different between the 2 groups (P range, .25-.63). Using multivariate logistic regression analysis, we did not find any independent significant variable among these factors.

**COMMENT**

The major determinant of developing subsequent severe brain edema in acute MCA stroke is considered to be the extent of severe perfusion deficit on multiphasic helical CT and hypodensity on precontrast CT, ie, the extent of the initial ischemic core. Our results showed that all 5 patients who had severe perfusion deficit or hypodensity involving more than two thirds of the presumed MCA territory developed subsequent severe brain edema. However, only 3 of 7 patients with severe perfusion deficit greater than 50% but less than or equal to 66% of the MCA territory developed severe brain edema. The cutoff value of the extent of severe perfusion deficit that predicts the development of severe brain edema seems to be greater than 50% of the MCA territory.
An additional key factor for predicting severe edema may be involvement of the adjacent ACA or PCA territory in patients with high initial NIHSS scores (≥15). Severe brain edema developed in all 6 patients with additional perfusion deficit in the ACA or PCA territory. Four patients had severe perfusion deficit greater than 50% of the MCA territory, and the other 2 patients had severe perfusion deficit greater than 33% but less than or equal to 50%.

### Table 2. Radiological Predictive Factors of Subsequent Severe Brain Edema on CT

<table>
<thead>
<tr>
<th>Factor</th>
<th>Yes (n = 10)</th>
<th>No (n = 21)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time lapse from onset to CT, mean ± SD, h</td>
<td>2.8 ± 1.7</td>
<td>2.6 ± 1.8</td>
<td>.69</td>
</tr>
<tr>
<td>Side of infarction, left</td>
<td>6 (60)</td>
<td>8 (38)</td>
<td>.44</td>
</tr>
<tr>
<td>Precontrast CT hypodensity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;66% of the MCA territory</td>
<td>4 (40)</td>
<td>0</td>
<td>.007</td>
</tr>
<tr>
<td>&gt;50% of the MCA territory</td>
<td>5 (50)</td>
<td>4 (19)</td>
<td>.10</td>
</tr>
<tr>
<td>In the ACA or PCA territory</td>
<td>4 (40)</td>
<td>0</td>
<td>.007</td>
</tr>
<tr>
<td>Multiphasic helical CT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPD &gt;66% of the MCA territory</td>
<td>5 (50)</td>
<td>0</td>
<td>.001</td>
</tr>
<tr>
<td>SPD &gt;50% of the MCA territory</td>
<td>8 (80)</td>
<td>4 (19)</td>
<td>.002</td>
</tr>
<tr>
<td>Perfusion deficit in the ACA or PCA territory</td>
<td>6 (60)</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Occlusion sites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>6 (60)</td>
<td>7 (33)</td>
<td>.25</td>
</tr>
<tr>
<td>MCA stem</td>
<td>2 (20)</td>
<td>9 (43)</td>
<td>.26</td>
</tr>
<tr>
<td>MCA division</td>
<td>1 (10)</td>
<td>5 (24)</td>
<td>.63</td>
</tr>
</tbody>
</table>

Abbreviations: ACA, anterior cerebral artery; CT, computed tomography; MCA, middle cerebral artery; PCA, posterior cerebral artery; SPD, severe perfusion deficit.

*Data are given as number (percentage) of patients unless otherwise indicated.

Figure 2. Infarction extending to the areas of moderate perfusion deficit (presumed penumbral zone). A, Precontrast computed tomography (CT) scans show small hypodensity less than or equal to 33% of the left middle cerebral artery (MCA) territory involving the insula and basal ganglia. B, Early-phase images of multiphasic helical CT show a large perfusion deficit in the left MCA territory. Middle-phase (C) and late-phase (D) images show small persistent hypodense areas (severe perfusion deficit) and a change of hypoattenuating areas to isodense in the frontal and temporal cortex (moderate perfusion deficit). E, Follow-up CT scans 2 days later reveal that the infarct extends to the left frontotemporal cortex but do not show significant mass effect.
to 50% of the MCA territory. Of these 2 patients, one had an enlarging infarct involving the whole hemisphere with fatal brain swelling (mass effect), and the other showed rapid clinical deterioration with the subsequent infarct involving MCA andACA territories with subfalcial herniation leading to hemicraniectomy. Reduction of leptomeningal collateral blood flow from these adjacent arteries may drastically reduce blood flow and promote further ischemia and edema.

In contrast, severe brain edema did not develop in 3 patients who had severe perfusion deficit less than 50% of the MCA territory and no perfusion deficit in the ACA and PCA territories, although the enlarging infarcts extended to the penumbra zone and finally involved almost the entire MCA territory (Figure 2). It is possible that the enlarging MCA infarctions may not develop malignant brain swelling if additional perfusion deficit is not present in the ACA or PCA territory. However, this hypothesis should be further studied, as the number of patients studied was small.

Multiphasic helical CT showed higher interobserver agreement than precontrast CT in determining the extent of lesions. This can be explained by the accentuation of the contrast between normal and abnormal tissue on enhanced CT images. Therefore, we did not use an Alberta Stroke Programme Early CT Score to apply consistent methods in estimating the lesion extents on precontrast CT and multiphasic helical CT scans, although the score was proven to be more accurate than the one-third MCA rule or percentage estimations on precontrast CT.11

In conclusion, the major determinants of developing subsequent severe brain edema in acute ischemic MCA stroke are considered to be the extent of severe perfusion deficit of the MCA territory and the presence of additional perfusion deficit in the ACA or PCA territory on multiphasic helical CT. Multiphasic helical CT can be performed easily and rapidly in conjunction with precontrast CT and is a useful method for predicting subsequent severe brain edema in hyperacute stroke and for warranting aggressive medical or neurosurgical intervention.

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Author contributions: Study concept and design (Drs S. J. Lee, K. H. Lee, Byun, Cho, Chung, and Hong); acquisition of data (Drs S. J. Lee, Kim, Shon, Cho, and J. Lee); analysis and interpretation of data (Drs S. J. Lee, H. Lee, Na, Kim, Shon, and J. Lee); drafting of the manuscript (Drs S. J. Lee, K. H. Lee, and Chung); critical revision of the manuscript for important intellectual content (Drs S. J. Lee, K. H. Lee, Na, Byun, Kim, Shon, Cho, J. Lee, Chung, and Hong); statistical expertise (Drs S. J. Lee, Na, Kim, Shon, and Cho); obtained funding (Dr K. H. Lee); administrative, technical, and material support (Drs Na, Byun, Cho, J. Lee, Chung, and Hong); study supervision (Dr K. H. Lee).

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Corresponding author and reprints: Kwang Ho Lee, MD, Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul, 133-710, South Korea (e-mail: kha@smc.samsung.co.kr).

REFERENCES