Measurements of Acute Cerebral Infarction: Lesion Size by Computed Tomography

Thomas Brott, MD, John R. Marler, MD, Charles P. Olinger, MD, Harold P. Adams Jr., MD, Thomas Tomsick, MD, William G. Barsan, MD, José Biller, MD, Robert Eberle, Vicki Hertzberg, PhD, and Michael Walker, MD

As part of a prospective therapy study of 65 patients with acute, nonhemorrhagic, cerebral infarction, computed tomographic scans of the head were obtained at admission, 7–10 days, and 3 months. The scans were analyzed for the presence, site, size, and volume measurement of the infarction. At 7–10 days, the mean infarction volume as measured by computed tomography was 55 cm³ or about 4 x 4 x 3.5 cm (range=0–507 cm³). At 3 months, the mean infarction volume decreased by 25% to 41 cm³. For the 26 scans showing infarction at the time of admission, the mean lesion volume was 33 cm³ at admission, 51 cm³ at 7–10 days, and 49 cm³ at 3 months. With lesion size at 7–10 days expressed as percentage of total brain volume, the mean infarction size was only 5%. Of the 49 patients with lesions revealed by computed tomography at 7–10 days, 20 had an infarction of 1% or less of total brain volume, while only six had an infarction of 20% or more of total brain volume. The lesion volumes as measured by the 7–10-day computed tomography correlated with the neurologic examination scores on admission (Spearman’s rank-order correlation=0.78) and with the scores at 1 week (Spearman’s rank-order correlation=0.79). (Stroke 1989;20:871–875)

Cerebral infarction size as reflected by computed tomography (CT) of the brain provides important clinical information. Patients with large lesions detected after stroke are at greater risk of developing life-threatening cerebral edema. They are also at greater risk for subsequent hemorrhagic conversion, with or without heparin. Lesion size measured by CT is used by clinicians to assist in prognosis, even though evidence linking lesion size to prognosis is limited.

Lesion volume has not yet been correlated to the clinical neurologic examination. We describe below a prospective analysis of CT scanning in the setting of acute cerebral infarction, carried out as part of a study of naloxone as therapy for acute ischemic stroke.

Subjects and Methods

Sixty-five patients with the clinical diagnosis of acute ischemic cerebral infarction were examined by CT scan without contrast at stroke onset, and without and with contrast at 7–10 days and at 3 months. The scans were performed on either a General Electric 9800 scanner or Picker scanner (600 or 1200) with a 512 × 512 matrix using 8–10-mm slices. The lesions’ anatomic location and vascular distribution were determined using the templates of Damasio. All patients had initial CT scans within 48 hours of stroke onset. The mean interval from time of latest progression of neurologic deficit to time of naloxone administration was 13 hours, 26 minutes (SD=10 hours, 11 minutes).

Lesion size was measured directly: the area of abnormal low attenuation was traced on each CT slice, and the area was summed for the slices showing the infarct (Figure 1). The volume was derived from the area and the slice thickness. For each CT slice, the total brain parenchyma area was also measured, and then the total brain parenchyma volume was calculated. Lesion size was also measured qualitatively as normal, lacunar, less than one-half lobe, up to one lobe, and several lobes (e.g., a lesion less than one-half lobe in size but involving two different anatomic lobes was scored as less than one-half lobe). The measurement sys-
tem was adapted from the methods of the Full-Phase Stroke Data Bank. Interpretations and measurements of the CT scans were performed by two coinvestigators without knowledge of the neurologic assessments.

The mean age of the patients was 64 years; 58% were white and 42% were black; 52% were men and 48% were women. Of the 65 cerebral infarctions, 57% involved the left hemisphere, 35% involved the right hemisphere, and 8% involved the brainstem-cerebellum. On admission, the infarction was thought to be large-artery atherothrombotic in 52%, small-artery atherothrombotic in 18%, cardiac embolic in 17%, and large-artery atheroembolic in 12%.

Each of the 65 patients was examined neurologically at admission and 24 hours after study entry. Sixty-three patients survived for examination at 7 days, and 58 patients survived for examination at 3 months. The examinations were performed in a uniform manner following a format (stroke scale) shown to be reliable and valid clinimetrically.

Patient outcome at 3 months was assessed by determining 1) the patient's performance class, 2) the patient's placement class, and 3) the patient's location in the community; these methods were modified from the suggestions of Spence and Donner.

Because neither CT measurements nor neurologic examination scores were anticipated to be normally distributed, Spearman's rank-order method was used for calculation of correlation coefficients.

Results

The CT scan was positive for a new cerebral infarction in 26 of 65 patients (40%) at admission and positive in 48 of 62 (77%) at 7–10 days, but sensitivity did not change significantly at 3 months (78%). The most frequent lesion category was “less than one-half lobe,” accounting for 37% of the patients scanned at 7–10 days and accounting for 48% of the positive scans at 7–10 days (Table 1). Lesions involving several lobes were more frequent than lacunar-sized lesions (19% vs. 10%).

The mean lesion volume at 7–10 days was 55 cm$^3$. Nineteen patients (29%) had a lesion volume of 10 cm$^3$ or less (Figure 2). With lesion size expressed as percentage of brain volume, the largest infarction was 47%, but the mean infarction size was only 5% of brain volume, and one third of lesions were 1% or less of total brain volume.

<table>
<thead>
<tr>
<th>Table 1. Computed Tomography and Cerebral Infarction: Sensitivity and Lesion Size by Qualitative Categorization</th>
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<tbody>
<tr>
<td><strong>Time of CT</strong></td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>&lt;48 hours from stroke onset</td>
</tr>
<tr>
<td>7–10 days from stroke onset</td>
</tr>
<tr>
<td>3 months from stroke onset</td>
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</table>

CT, computed tomography.
After excluding patients with normal CTs at baseline, the mean increase in lesion volume during the 1st week was 18 cm³ (54%) (Table 3). Lesion volume decreased by 25% between the 1st week and 3 months when considering all patients, but it did not decrease significantly for patients with an initially positive CT (Table 3).

The infarction was shown by CT at 7–10 days to involve the middle cerebral artery distribution in 40 of the 49 positive scans (82%) (Table 4). The CT scans did not demonstrate a lesion in four of the seven patients diagnosed clinically as having brainstem infarctions. At 7–10 days, contrast enhancement was identified in 22 of the 49 positive scans (45%) (Table 5). Mass effect was seen in 37% of all scans at 7–10 days and in 47% of the positive CTs (Table 5).

The Spearman’s rank-order correlation between the stroke scale score at 7 days and the CT scan lesion volume at 7–10 days was 0.74 (Table 6). After converting the lesion volume to a ratio of total brain volume, the lesion size–scale score correlation was 0.76 ($p<0.0001$). The admission neurologic deficit as measured by the stroke scale also correlated strongly with the 7–10 day CT lesion volume ($r=0.74$, $p<0.0001$). Correlations between infarction volume and neurologic deficit were the same regardless of the cerebral hemisphere involved ($r=0.72$ for left hemisphere, $r=0.74$ for right hemisphere).

**Discussion**

The quantitative assessment of CT lesion volume for acute stroke patients provides an objective measure of ischemic cerebral infarction. At 7–10 days the mean lesion volume was 55 cm³ or about 4×4×3.5 cm. Fourteen patients had no detectable lesion at 7–10 days (22%), and 19 patients had a volume of 10 cm³ or less (29%). Mean infarction size was only 4.4% of total brain volume (Table 2), and 20 of the 65 patients had a lesion size of 1% or less of total brain volume.

For future stroke therapy trials, comparison of the infarction volumes for the treated patients with those of the control patients could provide objective means of assessment. If a treatment is found effective, the CT measurements in the study could also allow comparisons among treated patients to determine any selectivity for that treatment. For example, analysis may reveal the therapy to be primarily effective for patients with lesions below a particular volume.

The validity of the volumetric method is suggested by the relation of the infarction volumes to the other methods of patient assessment. The neurologic deficit at 7 days correlated highly with the volume of infarction measured by CT at 7–10 days (Spearman’s rank-order correlation coefficient=0.74). Patient outcome at 3 months also correlated with the CT lesion volume at 7–10 days ($r=0.54$). Of further interest, the neurologic deficit present on admission also correlated strongly to the 7–10 day CT lesion volume ($r=0.74$). This implies that for many stroke patients the first neurologic examination could be a predictor of subsequent tissue loss as later shown by CT measurement. The clinical deficit–infarction volume correlations also provide incentive for further analysis and improvement of neurologic examination scales. For example, examination items that have no correlation to CT lesion size could be deleted.

We recognize that infarction location may be more important for some patients than infarction volume in determining the eventual clinical handicap. Certain brain regions have classically been thought more important or "eloquent" than others. We might agree, for example, that a given volume...
TABLE 3. Lesion Volume Serially in Patients With Positive Baseline Computed Tomography

<table>
<thead>
<tr>
<th>Time of CT</th>
<th>Volume range</th>
<th>Mean volume</th>
<th>Mean size of infarction (% of brain volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;48 hours from stroke onset</td>
<td>0.3–238 cm³</td>
<td>33 cm³ (SD 61.4)</td>
<td>2.7</td>
</tr>
<tr>
<td>7–10 days from stroke onset</td>
<td>0–327 cm³</td>
<td>51 cm³ (SD 76.1)</td>
<td>4.0</td>
</tr>
<tr>
<td>3 months from stroke onset</td>
<td>0–291 cm³</td>
<td>49 cm³ (SD 67.0)</td>
<td>3.5</td>
</tr>
</tbody>
</table>

n=26.
CT, computed tomography.

of cerebellum is less important than the same volume of left perisylvian cortex. However, comparisons today among most brain regions would be difficult if not arbitrary. We would rather proceed from the assumption that all brain regions are nearly equal in importance regardless of location but that some regions are more difficult to test than others. Volume measurements do not require value judgments. More important, perhaps, effective therapies for acute cerebral infarction are not likely to change lesion location. Effective therapies will be effective by their ability to decrease infarction size.

The results from the categoric method of infarction size measurement did not accurately describe our population. The infarction volume distribution showed a preponderance of very small lesions with a gradual transition to larger ones. The breakdown of lesion size by categories resulted in few very small lesions, with a preponderance of lesions larger than lacunar size but smaller than one-half lobe in size (Table 1). We suspect a reluctance to label an infarction "lacunar"; if the lacunar category had been designated as "small, deep infarct," then smaller infarcts may have been more appropriately categorized.

In the setting of acute stroke, analysis of lesion size as measured by CT has been limited. Correlation of aphasia severity and lesion volume as well as correlation between nonverbal performance and lesion volume have been demonstrated. Correlation between upper limb weakness and lesion volume (r=0.59) and between presence of a lesion in the corticospinal system and lesion volume (r=0.75) have also been reported.16 Yamaguchi et al estimated infarction size by comparing the area of CT hypodensity with the area measured by CT of the affected cerebral hemisphere, deriving what they called an infarct index.17 Infarctions thought to be embolic were more than twice as large as infarctions thought to be thrombotic (n=209). The infarct index was not compared to a detailed neurologic examination.

As has been reported in previous studies, we found CT sensitivity at 7–10 days to be considerably higher for infarction (77%) than CT sensitivity at admission (40%). Not previously reported, this CT sensitivity did not decline at 3 months (78%) as might have been expected (Table 2). The increase in infarction size (mean 54%) over the 1st week in those patients with initially positive scans was not a surprise, but the modest change in size thereafter (25% decrease at 3 months for all patients) was encouraging. We conclude that the timing for CTs performed in future therapy studies to detect and measure cerebral infarction may involve a generous window from 1 week or earlier to 1–3 months. Prospective therapy studies may require only two CT scans, one at admission to rule out hemorrhage and one at a later date (e.g., 1–2 weeks) for optimal infarction detection and measurement.

Our study has several limitations. Interrater reliability of the CT scan volume measurements was not assessed, and the 65 stroke patients may have had somewhat smaller infarctions and less severe neurologic deficits than the general acute stroke population (e.g., our patient mortality at 3 months was 8%). All patients received a 24-hour infusion of naloxone, which could have affected lesion imaging (we were unable to detect any positive or negative clinical effects that may have had a bearing on lesion size). Finally, the correlations reported should be interpreted cautiously, given the wide range of the CT infarction volumes and the clustering of patients with normal CT scans.

Measurements of cerebral infarction will become increasingly important as effective early treatment options are developed. Clinical assessment techniques will continue to miss silent cerebral infarctions. Likewise, high-resolution CT scanners will continue to miss clinically significant cerebral infarctions. With magnetic resonance imaging, greater sensitivity is possible, but imaging may be less specific. We suggest that clinical and anatomic measures of cerebral infarction are fundamentally complementary and that neither measurement approach can be adequately evaluated independent of the other.

Acknowledgments

The authors wish to thank Drs. Carlos Kase, Oscar Reinmuth, and Percy Karanjia for their assis-
tion in design of the CT assessment methods and the stroke scale (neurologic examination and scale).

References

Table 5. Edema, Mass Effect, and Contrast Enhancement Measured by Computed Tomography

<table>
<thead>
<tr>
<th>Time of CT</th>
<th>No. with infarct</th>
<th>Edema No. (%)</th>
<th>Mass effect No. (%)</th>
<th>Contrast enhancement No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;48 hours from stroke onset</td>
<td>26</td>
<td>16 (62)</td>
<td>10 (38)</td>
<td>CTs noncontrast</td>
</tr>
<tr>
<td>7-10 days from stroke onset</td>
<td>49</td>
<td>29 (59)</td>
<td>23 (47)</td>
<td>22 (45)</td>
</tr>
<tr>
<td>3 months from stroke onset</td>
<td>45</td>
<td>1 (2)</td>
<td>0</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

n=65.
CT, computed tomography.

Table 6. Spearman's Rank-Order Correlation of Infarction Volume (cm³) to Neurologic Deficit

<table>
<thead>
<tr>
<th>Time of CT</th>
<th>Neurologic exam on admission (ρ)</th>
<th>Neurologic exam at 1 week (r)</th>
<th>Neurologic exam at 3 months (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;48 hours from stroke onset</td>
<td>0.35</td>
<td>0.28*</td>
<td>0.38*</td>
</tr>
<tr>
<td>7-10 days from stroke onset</td>
<td>0.78*</td>
<td>0.79*</td>
<td>0.68*</td>
</tr>
<tr>
<td>3 months from stroke onset</td>
<td>0.76*</td>
<td>0.70*</td>
<td>0.62*</td>
</tr>
</tbody>
</table>

CT, computed tomography.

*p<0.0001.
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