Cranial Computed Tomographic Observations in Multi-Infarct Dementia
A Controlled Study

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Background and Purpose: We compared cranial computed tomography findings among 58 multi-infarct dementia index cases and 74 multi-infarct control subjects without cognitive impairment to identify potential determinants of multi-infarct dementia.

Methods: The cranial computed tomography records of acute ischemic stroke patients with a history of multiple cerebral infarcts were compared to determine the number, location, and size of cerebral infarcts; the pattern of infarction; brain volume loss; and the degree of white matter lucency, sulcal enlargement, and ventricular enlargement. Multi-infarct patients were divided into two groups: 1) index cases were defined as those with multi-infarct dementia as defined by the Diagnostic and Statistical Manual of Mental Disorders, edition 3 (DSM-III) criteria; and 2) control subjects were defined as those multi-infarct patients without dementia or multi-infarct dementia according to DSM-III criteria.

Results: Overall, multi-infarct index cases had more cerebral infarcts, more cortical and subcortical left hemisphere infarcts, higher mean ventricular volume to brain volume ratio, more extensive enlargement of the body of the lateral ventricles and cortical sulci, and a higher prevalence of white matter lucencies. Among multi-infarct cases and control subjects the most frequent site of infarction was the subcortical region, and the most frequent pattern of infarction was lacunar. Stepwise logistic regression analysis examined cranial computed tomography as well as other factors and showed that level of education, stroke severity, left cortical infarction, and diffuse enlargement of the left lateral ventricle were the best overall predictors of multi-infarct dementia.

Conclusions: Level of education, stroke severity, and left hemisphere infarction may be predictors of multi-infarct dementia. (Stroke 1992;23:804-811)

KEY WORDS • dementia • tomography, x-ray computed • cerebral infarction

Stroke is the second leading cause of progressive and irreversible dementia.1 2 Although much has been learned about the descriptive characteristics of cognitive impairment associated with cerebral infarction, epidemiological risk factors for vascular dementia need to be clarified. Since the seminal clinical-pathological correlations of Tomlinson and colleagues3 suggesting that the likelihood of developing vascular dementia may be related to the volume of cerebral hemisphere tissue infarcted or the location of infarcts, important clinical insights concerning possible markers or determinants of vascular dementia have been elucidated from neuroradiological study.4-34 In this study we analyzed cranial computed tomography (CT) findings among multi-infarct patients with and without dementia to determine the role of loss of brain volume and number, location, size, and mechanism of cerebral infarction as possible determinants of multi-infarct dementia (MID).

Subjects and Methods

Between November 1, 1987, and December 1, 1990, all patients admitted to the Michael Reese Hospital and Medical Center with a diagnosis of acute stroke were screened. Those with a history of multiple cerebral infarcts were selected for possible entry into the study. Acute stroke patients were identified by daily review of hospital admission records, surveillance of medical and neurological ward admission records, review of CT log books, and review of hospital discharge records. Each patient admitted with a diagnosis of acute stroke was screened by the investigators to determine if there was a history of multiple cerebral infarcts. Those patients with a history of multiple cerebral infarcts as defined by the Stroke Data Bank clinical and laboratory criteria of cerebral infarction35 were enrolled in a case–control
study designed to gather and compare descriptive epidemiological information about possible risk factors for vascular dementia among multi-infarct patients. Patients were enrolled in the study only after written informed consent was obtained.

As of December 1, 1990, 148 patients had completed the initial examination phase of the study. Cranial CT records were available in 132 of these patients. Sixteen patients were excluded from the analysis; in four patients CT films could not be obtained from outlying hospitals and only CT reports were available; in 10 patients only magnetic resonance imaging (MRI) of the head was performed; and in two patients CT records were incomplete. Overall, CT studies were analyzed in 58 MID index cases and 74 multi-infarct control subjects.

Multiple cerebral infarct patients were excluded from study if there was evidence in the medical record, medical examination, or epidemiological interview of: 1) cognitive impairment caused by diseases other than multiple cerebral infarction; 2) concomitant illness such as cancer that was likely to cause death during longitudinal follow-up; 3) follow-up was judged to be unlikely because the patient did not have a permanent residence; 4) the patient was enrolled in an MID drug therapy trial; 5) there was moderate-to-severe aphasia, defined as a raw score of $\leq 10$ on the Boston Diagnostic Aphasia Examination (BDAE) "Commands" subtest or a score of $\leq 16$ on the BDAE “Responsive Naming" subtest; 6) moribund state; or 7) blood urea nitrogen $>40$ mg% or creatinine $>2.0$ mg%.

The operational definition of MID index cases included the following features: 1) history of multiple cerebral infarcts; 2) Stroke Data Bank clinical and laboratory criteria for cerebral infarction$^{15}$; 3) Diagnost ic and Statistical Manual of Mental Disorders, edition 3 (DSM-III) criteria for the diagnosis of dementia and MID$^{46}$; 4) Blessed Information-Memory-Concentration Test scores in the dementia range$^{37}$; and 5) Hachinski Ischemic scores $\geq 7.8$. Multi-infarct control subjects were operationally defined as those patients who met the study criteria for multi-infarcts but did not have evidence of dementia according to DSM-III criteria.

CT scans were obtained from the Radiology File Room at Michael Reese Hospital, and all identification markings were masked. Each scan was labeled with an identification number so that the study neuroradiologist would be blinded to the identity of the patient. The CT chosen for study was the last CT performed during the patient’s most recent acute hospitalization for cerebral infarction. This coincided temporally with the study subject’s enrollment into the main phase of the MID case–control study.

With the aid of a precoded scoring sheet the study neuroradiologist rated the CT scans for the number, location, and side of surface and deep infarcts and qualitatively estimated the degree of white matter lucencies (none, mild, moderate, severe) and sulcal enlargement (none, mild, moderate, severe) over the cerebral convexities. Reference templates were developed to illustrate the various degrees of white matter lucencies and sulcal enlargement (see below). The study neuroradiologist also referenced the location of infarcts with a wax pencil.

CT measurements were recorded according to the method of Damasio et al.$^{39,40}$ Using a light table, transparent paper, and a lead pencil, CT films from a scanner with standard incidence of cut were traced to identify the following cerebral structures: 1) the third ventricle at the level of the foramina of Monro; 2) the frontal horns at the level at which they were largest; 3) the bodies of the lateral ventricles at the first level in which they were fully seen; 4) the remainder of the ventricular system; 5) the interhemispheric fissure at the same level as the ventricular bodies; 6) the entire perimeter of the brain; and 7) the entire perimeter of any infarct. The surfaces circumscribed by those tracings were then retraced with a magnetic digitizer pen directly connected to a microcomputer graphics tablet.

Thirty-two percent of the CT scans were performed on the Elscint 2002, 3% on a Pfizer 200 FS, 50% on a Siemens Somatom DHR, 2% on a General Electric 9800 HQ, and 13% on other machines. Eighty-eight percent of cases and 88% of control subjects had CT scans without contrast; 9% of cases and 7% of control subjects had CT scans both with and without contrast; and the remainder of study subjects had CT scans with contrast only.

The following operational CT definitions were used to describe location and pattern of cerebral infarction, white matter lucencies, and enlargement of the body of the lateral ventricles and sulci:

**Location of Infarction**

1. **Cortical**: Superficial infarct of the frontal, temporal, parietal, or occipital lobe(s) that may extend into the underlying white matter but does not extend into the white matter at the level of the basal ganglia. The infarct is in the vascular territory of a large cerebral artery (e.g., carotid artery, middle cerebral artery, posterior cerebral artery).

2. **Subcortical (nonlacunar)**: Infarct of the underlying white matter, basal ganglia, or thalamus that measures $>15$ mm$^3$ and is in the vascular territory of a large cerebral artery.

3. **Subcortical (lacunar)**: Infarct of the underlying white matter, basal ganglia, or thalamus that measures $\leq 15$ mm$^3$ and is in the vascular territory of a deep penetrating artery (e.g., lenticulostriate arteries).

4. **Brain stem or cerebellum (nonlacunar)**: Infarct of the brain stem or cerebellum that measures $>15$ mm$^3$ and is in the vascular territory of a large cerebral artery.

5. **Brain stem or cerebellum (lacunar)**: Infarct of the brain stem or cerebellum that measures $\leq 15$ mm$^3$ and is in the vascular territory of a deep penetrating artery.

6. **Cortical/subcortical**: Superficial infarct that extends into the white matter at the level of the basal ganglia or beyond and is in the vascular territory of a large cerebral artery.

**Pattern of Infarction**

1. **Lacune**: Infarct that measures $\leq 15$ mm$^3$ in the vascular territory of a deep penetrating artery.

2. **Cortical wedge-shaped**: Cortical infarct that topographically resembles a wedge in its shape.

3. **Cortical non-wedge-shaped**: Cortical infarct that is non-wedge-shaped.

4. **Border zone**: Cortical or subcortical infarct that is located within the boundary zone of two major cerebral arteries (e.g., middle and anterior cerebral arteries).
Enlargement of the Body of the Lateral Ventricle

The test was also carried out with the number of infarcts grouped into four categories (0, 1, 2, ≥3).

Enlargement of Hemispheral Sulci

Categorization of White Matter Lucencies

Definition/Category
1. None/None
2. Punctate lucencies at the tips of the frontal or occipital horns or both/Mild
3. Lucencies more extensive but confined to the subependymal region/Mild
4. Lucencies more extensive and seen in the subcortical white matter outside the immediate periventricular area/Moderate
5. Coalescing subcortical white matter lucencies/Moderate
6. Extensive coalescing subcortical white matter lucencies/Extensive

Categorization of white matter lucencies was accomplished by using a reference template model.

Statistical Methods

The purpose of the analysis was to identify CT factors that might be markers or predictors of MID. Ordered categorical variables such as the number of cerebral infarcts at a particular site were analyzed using the exact test for trend in a 2×K table. The number of infarcts was grouped into four (K=4) categories (0, 1, 2, ≥3). The test was also carried out with the number of infarcts grouped into two (K=2) categories (0, ≥1), in which case the test is identical to Fisher's exact test. Means and standard deviations were calculated as summary measures for each variable. Continuous variables such as the stroke volume (SV) and the ratio of ventricular volume to brain volume (VV/BV) were analyzed using the two-sample t test. The ratios VV/BV, SV/BV, and SV/(BV-VV) were selected for comparison because they corrected for relative differences in the CT displays from different types of CT machines used during the study period. Stepwise logistic regression was used to determine the CT and other variables that were independently statistically significant predictors of dementia. The significance levels for variables to enter and remain in the model were set at α=0.2. Variables entered the model if p<0.2 by score test and remained in the model if p<0.2 by the Wald test.

Results

When comparing MID index cases with multi-infarct control subjects there were slightly more men (55% versus 45%), hypertensives (82% versus 81%), and diabetics (42% versus 37%) among control subjects, whereas there were slightly more blacks (93% versus 89%) and men (55% versus 45%) among index cases. The differences were not statistically significant. The mean age±SD among cases was 76.0±9.1 years and among control subjects was 69.6±9.1 years (p<0.0001).

Table 1 summarizes the number of CT-diagnosed cerebral infarcts grouped by site of infarction among MID index cases and multi-infarct control subjects. The exact 2×4 table of test for trend when considering the number of CT-diagnosed infarcts (0, 1, 2, and ≥3) showed that MID index cases had more infarcts at all sites combined (p=0.047), at all left hemisphere sites combined excluding the brain stem and cerebellum (p=0.013), at combined left and right cortical/subcortical sites (p=0.024), and at left cortical/subcortical sites (p=0.050) compared with multi-infarct control subjects. Furthermore, the result of the test for trend at left subcortical (nonlacunar) sites was borderline (p=0.056) and was indicative of more frequent infarcts among MID index cases. At most other sites there was a non-statistically significant trend for the frequency of CT-documented infarcts to be more common among MID index cases than among control subjects. In some instances the non-statistically significant trend was reversed in favor of the multi-infarct control group. However, the frequencies of infarction were relatively low, and the differences among MID index cases and control subjects at those sites were generally small.

Table 1 also summarizes the frequencies of one or more CT-documented infarcts by site of infarction among multi-infarct cases and control subjects. A significantly higher percentage of MID index cases than control subjects had one or more CT-diagnosed infarcts at the left cortical/subcortical site (16% versus 4%, p=0.05). For MID index cases the sites at which the frequency of one or more CT-documented infarcts was highest were the left subcortical (lacunar) site (47%), the right subcortical (lacunar) site (41%), and the left cortical and left cortical/subcortical sites (both 16%). Striking differences indicating a higher mean number of infarcts among MID index cases than controls were noted at the following sites: left subcortical (nonlacunar) (0.14 versus 0.03), left cortical/subcortical sites (0.17 versus 0.05), combined left and right cortical/subcortical sites (0.35 versus 0.12), all sites combined (2.29 versus 1.78), and all left sites combined excluding the brain stem and cerebellum (1.10 versus 0.74). Although not as striking, the mean number of infarcts at most other sites was higher among MID index cases than among control subjects. For MID index cases the three sites in which the mean number of infarcts was greatest were the right subcortical (lacunar) site (0.60), the left subcortical (lacunar) site (0.59), and the left cortical site (0.21). There was no statistically significant difference in the mean number of left, right, or total thalamic infarcts for index cases and control subjects.

Table 2 summarizes the number of CT-diagnosed infarcts grouped by pattern of infarction among MID index cases and multi-infarct control subjects. Computed tomography pattern of infarction was chosen as a study variable for analysis because it provides potentially useful information about underlying stroke mechanism. The exact test for trend when considering number of infarcts (0, 1, 2, and ≥3) showed that MID index cases had more cortical wedge-shaped infarcts than did controls (p=0.025). In addition, the percentage with one or more CT-diagnosed subcortical white
Table 1. Frequency of Computed Tomography–Documented Infarctions and Mean No. of Infarctions by Site

<table>
<thead>
<tr>
<th>Site</th>
<th>Multi-infarct dementia cases (n=58)</th>
<th>Multi-infarct control subjects (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of infarcts</td>
<td>Mean±SD</td>
</tr>
<tr>
<td></td>
<td>0 1 2  ≥3</td>
<td>≥1 (%)*</td>
</tr>
<tr>
<td>L cortical‡</td>
<td>49 6 3 0 9 (16)</td>
<td>0.21±0.52</td>
</tr>
<tr>
<td>R cortical</td>
<td>51 7 0 0 7 (12)</td>
<td>0.12±0.33</td>
</tr>
<tr>
<td>Brain stem (nonlacunar)</td>
<td>57 1 0 0 1 (2)</td>
<td>0.02±0.13</td>
</tr>
<tr>
<td>Cerebellum (nonlacunar)</td>
<td>51 7 0 0 7 (12)</td>
<td>0.12±0.33</td>
</tr>
<tr>
<td>L subcortical (nonlacunar)</td>
<td>52 5 0 1 6 (10)</td>
<td>0.14±0.48</td>
</tr>
<tr>
<td>R subcortical (nonlacunar)</td>
<td>56 2 0 0 2 (4)</td>
<td>0.03±0.18</td>
</tr>
<tr>
<td>L subcortical (lacunar)</td>
<td>31 22 3 2 27 (47)</td>
<td>0.59±0.75</td>
</tr>
<tr>
<td>R subcortical (lacunar)</td>
<td>34 16 5 3 24 (41)</td>
<td>0.60±0.86</td>
</tr>
<tr>
<td>Brain stem (lacunar)</td>
<td>51 7 0 0 7 (12)</td>
<td>0.12±0.33</td>
</tr>
<tr>
<td>Cerebellum (lacunar)</td>
<td>58 0 0 0 0 (0)</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>L cortical/subcortical§</td>
<td>49 8 1 0 9 (16)</td>
<td>0.17±0.43</td>
</tr>
<tr>
<td>R cortical/subcortical§</td>
<td>50 6 2 0 8 (14)</td>
<td>0.17±0.46</td>
</tr>
<tr>
<td>Combined L and R cortical</td>
<td>44 9 5 0 14 (24)</td>
<td>0.33±0.63</td>
</tr>
<tr>
<td>Combined L and R brain stem and cerebellum (nonlacunar)</td>
<td>50 8 0 0 8 (14)</td>
<td>0.14±0.35</td>
</tr>
<tr>
<td>Combined L and R brain stem and cerebellum (lacunar)</td>
<td>50 7 0 1 8 (14)</td>
<td>0.17±0.50</td>
</tr>
<tr>
<td>Combined L and R subcortical (lacunar)</td>
<td>21 20 7 10 37 (64)</td>
<td>1.19±1.30</td>
</tr>
<tr>
<td>Combined L and R brain stem and cerebellum (lacunar)</td>
<td>51 7 0 0 7 (12)</td>
<td>0.12±0.33</td>
</tr>
<tr>
<td>Combined L and R cortical/subcortical</td>
<td>46 7 2 3 12 (21)</td>
<td>0.35±0.79</td>
</tr>
<tr>
<td>Combined L and R subcortical, brain stem, and cerebellum (lacunar)</td>
<td>19 20 9 10 39 (68)</td>
<td>1.31±1.42</td>
</tr>
<tr>
<td>All sites combined</td>
<td>6 17 12 23 52 (90)</td>
<td>2.29±1.70</td>
</tr>
<tr>
<td>All L sites (excluding brain stem and cerebellum) combined</td>
<td>16 28 8 6 42 (72)</td>
<td>1.10±1.02</td>
</tr>
<tr>
<td>All R sites (excluding brain stem and cerebellum) combined</td>
<td>24 20 9 5 34 (59)</td>
<td>0.93±1.01</td>
</tr>
</tbody>
</table>

L, left; R, right.

*Statistically significant probability values for this category are denoted in text.
†Exact 2×4 table test for trend; one-sided p. Values >0.05 are nonsignificant (NS). Those >0.1 are marked "NS."
‡Cortical designation refers to infarcts in any of the following sites: frontal, temporal, parietal, or occipital lobes.
§Refers to a superficial (cortical) infarction that extends into the white matter at the level of the basal ganglia or beyond.

Matter nonlacunar infarcts was greater in MID index cases than in control subjects (14% versus 4%, p=0.045), although the difference was not statistically significant by the exact 2×4 table test for trend. The most common pattern of infarction among both MID index cases and control subjects was lacunar infarc-

Table 2. Frequency of Computed Tomography–Documented Infarctions and Mean No. of Infarctions by Pattern of Infarction

<table>
<thead>
<tr>
<th>Pattern of infarct</th>
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<td></td>
<td>0 1 2  ≥3</td>
<td>≥1 (%)*</td>
</tr>
<tr>
<td>Lacunar</td>
<td>19 20 9 10 39 (67)</td>
<td>1.31±1.42</td>
</tr>
<tr>
<td>Cortical wedge-shaped‡</td>
<td>31 16 5 6 27 (47)</td>
<td>0.78±1.04</td>
</tr>
<tr>
<td>Cortical non-wedge-shaped‡</td>
<td>54 4 0 0 4 (7)</td>
<td>0.07±0.26</td>
</tr>
<tr>
<td>Border zone</td>
<td>58 0 0 0 0 (0)</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Subcortical white matter (nonlacunar)</td>
<td>50 8 0 0 8 (14)§</td>
<td>0.14±0.35</td>
</tr>
</tbody>
</table>

*Statistically significant probability values for this category are denoted in text.
†Exact 2×4 table test for trend; one-sided p. Values >0.05 are nonsignificant (NS). Those >0.1 are marked "NS."
‡These categories include superficial cortical infarcts as well as cortical infarcts with significant extension into subcortical areas.
§p=0.045 different from control group by Fisher's exact test.
tion, with 67% of cases and 58% of control subjects having this pattern.

Review of the mean number of infarcts by pattern of infarction showed a striking difference in the mean number of cortical wedge-shaped infarcts between the two groups (cases, 0.78 versus control subjects, 0.45). For lacunar infarctions the means were 1.31 and 1.15, respectively, different from control group by two-sample, one-tailed t test.

Table 3 summarizes mean stroke, brain, and ventricular volumes and ratios among MID index cases and control subjects. The ratios are a more valid measure than the crude volume measurements because they adjust for relative differences among the CT display techniques. The mean ratio VV/BV was significantly higher among MID index cases than control subjects (0.07 versus 0.05, p=0.006). There was no statistically significant difference among index cases and control subjects for the ratios SV/BV or SV/(BV-VV).

Table 4 shows data on white matter lucencies and ventricular and sulcal CT measures in MID index cases and control subjects. Multi-infarct control subjects more frequently had no evidence of white matter lucencies (55% versus 34%, p=0.016); no evidence of enlargement of the body of the left (19% versus 2%, p=0.001), right (20% versus 5%, p=0.010), or either (16% versus 2%, p=0.004) lateral ventricle; and no evidence of enlargement of cortical sulci on the left side (14% versus 3%, p=0.042) compared with MID index cases. However, MID index cases more frequently had moderate or severe enlargement of the body of the left (79% versus 38%, p<0.0005), right (71% versus 35%, p<0.0005), or either (79% versus 39%, p<0.0005) lateral ventricle, or moderate or severe enlargement of the left (66% versus 31%, p<0.0005), or either (62% versus 35%, p=0.002), or either (66% versus 35%, p<0.0005) cortical sulci.

Additional analyses were performed to determine if such factors as type of CT machine, type of CT study (e.g., plain, plain and contrast), and timing of the CT had any significant effect on detection of cerebral infarction among cases and control subjects in our study.

Stepwise logistic regression analysis was used to determine the best CT scan, demographic, and medical predictors of MID. To accomplish this analysis the CT study data base was merged with the main phase study data base, which included demographic (e.g., age, race, sex, educational level, income) and medical factors (e.g., history of hypertension and diabetes mellitus, and systolic and diastolic blood pressure recordings). The stepwise logistic regression procedure was first used to select the best predictors from within a variable category (e.g., CT factors, medical factors) and was then used to select the best combination of predictors from all of the variable categories combined. Since the likelihood of dementia increased with severity of stroke, the Stroke Data Bank Stroke Severity Score was included as a covariate in all of the above analyses. Odds ratios associated with different levels of each predictor variable in the final model, controlling for other predictors, were derived from the formula odds ratio=exp (β(Xi−Xo)), where β is the parameter estimate from the fitted model and (Xi−Xo) denotes the difference be-
The results of the stepwise logistic regression analysis for the best combination of CT scan and other predictors of MID are summarized in Table 5. Stroke severity, level of education, diffuse enlargement of the body of the left lateral ventricle, and number of left cortical infarctions were the best overall predictors of MID. The table shows the independent effects of these four predictors. For a patient with an education level of grade 8 or less, the dementia odds were approximately nine times the dementia odds for a patient with at least some college education, other factors being equal. Similarly, the dementia odds for a patient with moderate enlargement of the body of the left lateral ventricle were almost seven times those for a patient with no enlargement, other factors being equal. Furthermore, each additional left cortical infarction diagnosed on CT scan nearly doubled the dementia odds, other factors again being equal. No significant interaction effects were observed in the analysis. Thus, each predictor was assumed to contribute multiplicatively to the overall dementia odds.

A significant correlation existed between the Stroke Data Bank Stroke Severity Score and enlargement of the body of the left lateral ventricle (Pearson's $r=0.237$, $p=0.009$). A slight negative correlation was observed between the level of education and the number of left cortical infarcts; those with higher levels of education had fewer left cortical infarcts (Pearson's $r=-0.150$, $p=0.089$). No other noteworthy correlations were found among the four predictor variables.

### Discussion

Results from this case–control study of CT observations in multi-infarct patients can be summarized as follows: 1) Overall, there were more CT-diagnosed cerebral infarcts, especially left cortical and subcortical infarcts, among MID index cases compared with multi-infarct control subjects; 2) The predominant site of infarction among index cases and control subjects was subcortical; 3) The predominant pattern of infarction was lacunar; 4) The mean VV/BV ratio was significantly higher among MID index cases than control subjects; 5) MID index cases more frequently had moderate or severe enlargement of the body of the lateral ventricle and cortical sulci and were more likely to have evidence of white matter lucencies than control subjects; and 6) Stepwise logistic regression analysis showed that level of education, stroke severity, left cortical infarction, and diffuse enlargement of the body of the left lateral ventricle were the best overall predictors of MID.

Prior CT studies have shown that vascular dementia patients have more cerebral atrophy and infarcts than control subjects. Ladurner and colleagues studied 71 patients with ischemic stroke; 40 patients showed early dementia and 31 were without mental impairment. The mean age, mean duration of cerebrovascular disease, frequency of strokes, and history of neurological symptoms and neurological deficits were comparable in the two groups. However, hypertension, dominant hemisphere disease, bilateral symptoms, generalized atrophy in combination with an infarct on CT, and bilateral infarcts on CT were more common in the dementia group. Furthermore, infarcts in both groups were mainly small in size and located in the basal ganglia or nearby structures. In addition to the higher number of infarcts in the dementia patients, this group also had a higher proportion of thalamic infarcts. In five patients with dementia the CT characteristics were considered to be typical of Binswanger's subcortical encephalopathy.

Loeb and colleagues studied CT features in 40 patients with MID, 44 multi-infarct patients without dementia, and 30 control subjects matched for age and sex. Patients with MID had a slightly greater loss of cerebral substance when volume of ischemic lesions was assessed, particularly in patients with unilateral focal lesions or bilateral multiple cortical and subcortical lesions. An association with multiple lesions in the thalamic and cortical areas supplied by the middle cerebral arteries and a higher degree of cerebral atrophy as evaluated by measurements of ventricular size, area of ventricular space, and area of subarachnoid space were also noted among patients with MID.

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Results from this case–control study of CT observations in multi-infarct patients can be summarized as follows: 1) Overall, there were more CT-diagnosed cerebral infarcts, especially left cortical and subcortical infarcts, among MID index cases compared with multi-infarct control subjects; 2) The predominant site of infarction among index cases and control subjects was subcortical; 3) The predominant pattern of infarction was lacunar; 4) The mean VV/BV ratio was significantly higher among MID index cases than control subjects; 5) MID index cases more frequently had moderate or severe enlargement of the body of the lateral ventricle and cortical sulci and were more likely to have evidence of white matter lucencies than control subjects; and 6) Stepwise logistic regression analysis showed that level of education, stroke severity, left cortical infarction, and diffuse enlargement of the body of the left lateral ventricle were the best overall predictors of MID.

Prior CT studies have shown that vascular dementia patients have more cerebral atrophy and infarcts than control subjects. Ladurner and colleagues studied 71 patients with ischemic stroke; 40 patients showed early dementia and 31 were without mental impairment. The mean age, mean duration of cerebrovascular disease, frequency of strokes, and history of neurological symptoms and neurological deficits were comparable in the two groups. However, hypertension, dominant hemisphere disease, bilateral symptoms, generalized atrophy in combination with an infarct on CT, and bilateral infarcts on CT were more common in the dementia group. Furthermore, infarcts in both groups were mainly small in size and located in the basal ganglia or nearby structures. In addition to the higher number of infarcts in the dementia patients, this group also had a higher proportion of thalamic infarcts. In five patients with dementia the CT characteristics were considered to be typical of Binswanger's subcortical encephalopathy.

Loeb and colleagues studied CT features in 40 patients with MID, 44 multi-infarct patients without dementia, and 30 control subjects matched for age and sex. Patients with MID had a slightly greater loss of cerebral substance when volume of ischemic lesions was assessed, particularly in patients with unilateral focal lesions or bilateral multiple cortical and subcortical lesions. An association with multiple lesions in the thalamic and cortical areas supplied by the middle cerebral arteries and a higher degree of cerebral atrophy as evaluated by measurements of ventricular size, area of ventricular space, and area of subarachnoid space were also noted among patients with MID.
of cerebral substance in multi-infarct patients ranged from 1.17 to 45.21 ml. The investigators found that when lesion volume was <50 ml, the dementia syndrome was significantly related to brain atrophy except in persons with one-sided multiple lesions or bilateral multiple cortical and subcortical lesions. Meyer and colleagues concluded that cognitive impairment was more strongly related to the location of cerebral infarcts than to the total volume of infarcted tissue. The most important correlate of MID in Meyer's series was subcortical lacunar infarcts.

Tatemichi and colleagues determined CT findings related to prevalence of dementia in 927 patients with acute ischemic stroke aged ≥60 years in the Stroke Data Bank cohort. Computed tomography findings that related to prevalence of dementia included infarct number (new related lesions and old unrelated lesions), infarct site (occipital, tempo-occipital, and temporoparietal lobe infarctions), and presence of cortical atrophy or hydrocephalus. Infarct volume showed no significant relation to dementia. Periventricular lucencies were rated in only 77 patients, limiting the interpretation of this information. The most important CT predictors of incidence of dementia among 610 patients who were followed longitudinally but who were not demented at stroke onset were the occurrence of previous stroke and presence of cortical atrophy at stroke onset.

There is uncertainty about the relation between radiologically diagnosed brain white matter disease and the occurrence of dementia. Although some studies have shown a relation between these lesions and dementia, others have shown no such association. The underlying pathophysiology of this white matter disease is thought to be vascular in origin. In select patients with motor and cognitive deficits, pathological study may show diffuse demyelination of the deep white matter, gliosis, necrosis, small subcortical infarcts, arteriolar sclerosis, and dilation of the ventricular system. In patients dying of nonneurological causes, the spectrum of white matter pathology may include dilated perivascular spaces (état criblé), arteriosclerosis, vascular ectasia, periventricular demyelination, and an occasional small subcortical infarction. Even in Alzheimer's disease white matter changes may be seen that are characterized pathologically by partial loss of myelin, axons, and oligodendroglial cells, reactive astrocytic gliosis, macrophage infiltration, and fibrohyalinized arterioles. Clinical histories in these Alzheimer patients suggest that the white matter disease may be associated with hypotensive episodes and incomplete infarction confined to the white matter. It has been hypothesized that damage to the deep white matter may be in an arrestable phase if it appears only on MRI and not on CT.

Our data suggest that two key CT factors, left cortical infarction and diffuse enlargement of the body of the left lateral ventricle, and two key non-CT factors, level of education and stroke severity, may be determinants of MID. It is plausible that left cortical infarction is a predictor of MID because the left hemisphere is dominant for language function in most individuals. While this finding may be interpreted by some as a left hemisphere bias for dementia because of dominance for language, we excluded from study a number of more severe aphasias based on the BDAE “Commands” and “Responsive Naming” screening criteria. Furthermore, although we do not have neuropathological validation of the diagnosis of MID and we cannot be absolutely certain that some of the patients did not have Alzheimer changes, our examination findings are consistent with the DSM-III clinical criteria for a diagnosis of MID. The role of diffuse enlargement of the body of the left lateral ventricle as a predictor of MID more likely represents the preponderance of left hemispheral infarcts in our study patients. Both left cortical and left subcortical infarcts were common in our MID cases and could lead to compensatory enlargement of the left ventricular system.

Among the non-CT factors one must interpret cautiously the MID predictor variable stroke severity. It is plausible that more severe stroke deficits would be causally related to MID. However, when measured by the Stroke Data Bank Stroke Severity Score, stroke severity could also be interpreted as being highly correlated with our study definition of MID. Thus, this predictor variable might be explained away based on this reasoning.

The other non-CT factor, level of education, has only more recently been recognized as a possible risk factor for dementia. Although higher educational attainment may be interpreted as being a protective factor, the results of studies using clinical diagnosis are weakened by the possibility of educational bias in assigning diagnosis and the possibility that tests of neuropsychological performance that are used in diagnosing dementia show bias in measuring cognition among persons with low education. Furthermore, educational attainment could be a surrogate for another associated environmental or genetic factor that plays a substantial role in the risk equation for susceptibility to or development of dementia. Prospective study of this factor may help to clarify the issue.

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