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

Philip B. Gorelick, MD, MPH; Anjan Chatterjee, MD; Dushyant Patel, MD; Gordon Flowerdew, DSc; Winnie Dollear, RN, MPH; Jesse Taber, MD; and Yvonne Harris, BA

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.

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

Stroke is the second leading cause of progressive and irreversible dementia. 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 clinico-pathological correlations of Tomlinson and colleagues 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. 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 infarction were enrolled in a case–control study.
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 ≤10 on the Boston Diagnostic Aphasia Examination (BDAE) “Commands” subtest or a score of ≤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; 3) Diagnostic and Statistical Manual of Mental Disorders, edition 3 (DSM-III) criteria for the diagnosis of dementia and MID; 4) Blessed Information-Memory-Concentration Test scores in the dementia range; and 5) Hachinski Ischemic scores ≥7.8.

The following operational CT definitions were used: 1) lacune: Infarct of the underlying white matter that measures ≤15 mm³ in the vascular territory of a deep penetrating artery (e.g., lenticulostriate arteries); 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) brain stem or cerebellum (nonlacunar): Infarct of the brain stem or cerebellum that measures ≤15 mm³ and is in the vascular territory of a deep penetrating artery (e.g., lenticulostriate arteries).}

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 mm³ 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 ≤15 mm³ 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 mm³ 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 ≤15 mm³ 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 ≤15 mm³ 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

Enlargement of Hemispheral Sulci

The test was also carried out with the number of infarcts grouped into four categories (0, 1, 2, >3). It 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 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 matter to brain volume (VV/BV) were analyzed using the two-sample t test. The test was identical to Fisher's exact test. Means and standard deviations were calculated as summary measures for each variable. Continuous variables such as the number of cerebral infarcts at a particular site were analyzed using the exact test for trend in a 2xK table.

### 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 2xK table. The number of infarcts grouped into four categories (0, 1, 2, >3). This was carried out using the exact test for trend in a 2xK table.

The test was also carried out with the number of infarcts grouped into four categories (0, 1, 2, >3). It 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 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 matter to brain volume (VV/BV) were analyzed using the two-sample t test. The test was identical to Fisher's exact test. Means and standard deviations were calculated as summary measures for each variable. Continuous variables such as the number of cerebral infarcts at a particular site were analyzed using the exact test for trend in a 2xK table.

The test was also carried out with the number of infarcts grouped into four categories (0, 1, 2, >3). It 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 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 matter to brain volume (VV/BV) were analyzed using the two-sample t test. The test was identical to Fisher's exact test. Means and standard deviations were calculated as summary measures for each variable. Continuous variables such as the number of cerebral infarcts at a particular site were analyzed using the exact test for trend in a 2xK table.
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>
<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>( \geq 1 ) (%)*</td>
</tr>
<tr>
<td>Lacunar</td>
<td></td>
<td></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 as determined from computed tomography. 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 summarizes 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), right (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 CT could influence our interpretation of the study results. Analyses showed that the different types of CT machine were used with about equal frequency among index cases and control subjects and that the ability of the various machines to detect an infarct did not differ significantly. Furthermore, there was no evidence that the type of CT study (e.g., plain, plain and contrast) affected the number of infarcts detected or that the 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 \((\beta(X_i-X_o))\), where \(\beta\) is the parameter estimate from the fitted model and \((X_i-X_o)\) denotes the difference be-
TABLE 5. Computed Tomographic Scan and Other Predictors of Multi-Infarct Dementia: Results of Stepwise Logistic Regression Analysis (Final Model)

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of MID index cases</th>
<th>No. of multi-infarct control subjects</th>
<th>Odds ratio</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of education‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ Grade 8</td>
<td>29</td>
<td>14</td>
<td>1.00</td>
<td>0.0025</td>
</tr>
<tr>
<td>Grade 9–12</td>
<td>19</td>
<td>40</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>6</td>
<td>17</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>Postgraduate</td>
<td>1</td>
<td>3</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Stroke Data Bank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke Severity Score‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>4</td>
<td>7</td>
<td>1.26</td>
<td>0.0007</td>
</tr>
<tr>
<td>3–4</td>
<td>14</td>
<td>36</td>
<td>1.62</td>
<td></td>
</tr>
<tr>
<td>5–6</td>
<td>0</td>
<td>0</td>
<td>2.63</td>
<td></td>
</tr>
<tr>
<td>7–8</td>
<td>12</td>
<td>16</td>
<td>4.27</td>
<td></td>
</tr>
<tr>
<td>9–10</td>
<td>21</td>
<td>7</td>
<td>6.93</td>
<td></td>
</tr>
<tr>
<td>11–13</td>
<td>6</td>
<td>0</td>
<td>12.69</td>
<td></td>
</tr>
<tr>
<td>Diffuse enlargement of body of left lateral ventricle§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>15</td>
<td>1.00</td>
<td>0.0018</td>
</tr>
<tr>
<td>Mild</td>
<td>11</td>
<td>31</td>
<td>2.61</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>37</td>
<td>22</td>
<td>6.79</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>8</td>
<td>6</td>
<td>17.71</td>
<td></td>
</tr>
<tr>
<td>Left cortical infarctions (No.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>36</td>
<td>59</td>
<td>1.00</td>
<td>0.0481</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>14</td>
<td>1.98</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>1</td>
<td>3.90</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>0</td>
<td>7.71</td>
<td></td>
</tr>
</tbody>
</table>

MID, multi-infarct dementia.
*By two-sided Wald test.
†Three patients had unknown levels of education.
‡Nine patients had unknown stroke severity scores.
§Status of enlargement of body of left lateral ventricle was unknown in one patient.

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 V/V/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. 32–34 Ladurner and colleagues 32 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 ofBinswanger's subcortical encephalopathy.

Loeb and colleagues 33 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. Loss
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, temporopolar, 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. White matter disease appears on CT as periventricular zones of lucency termed "leukoaraisis" (rarefaction or thinning of the white matter) or on T2-weighted MRI as hyperintense thick rims surrounding the lateral ventricles, caps around the poles of the lateral ventricles, or unifocal or multifocal subcortical patches that at times are confluent. 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 hemispheric 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.

Acknowledgments

The principal investigator, Philip B. Gorelick, MD, MPH, wishes to thank Dr. Jacob Brody, Dean, and Dr. Donna Cohen, Professor of Gerontology, School of Public Health, University of Illinois at Chicago, who served as sponsor and cosponsor, respectively, for the main phase of the National Institute on Aging-sponsored Clinical Investigator Award to P.B.G.

References

4. DeCarli C, Kaye JA, Horwitz B, Rapoport SI: Critical analysis of the use of computer assisted transverse axial tomography to study...


17. Awan IA, Spetzler RF, Hodak JA, Awan CA, Carey R: Incidental subcortical lesions identified on magnetic resonance imaging in the elderly. I. Correlation with age and cerebrovascular risk factors. Stroke 1986;17:1084–1089

18. Awan IA, Johnson PC, Spetzler RF, Hodak JA: Incidental subcortical lesions identified on magnetic resonance imaging in the elderly. II. Postmortem pathological correlations. Stroke 1986;17:1090–1097


44. Moody DM, Bell MA, Challa VR: Regional cerebral vulnerability to perfusion deficits in the elderly. Presented at the NINDS/AIREN International Workshop on Vascular Dementia, Bethesda, Md, April 19–21, 1991


Cranial computed tomographic observations in multi-infarct dementia. A controlled study.
P B Gorelick, A Chatterjee, D Patel, G Flowerdew, W Dollear, J Taber and Y Harris

Stroke. 1992;23:804-811
doi: 10.1161/01.STR.23.6.804

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/23/6/804