Incidence of Vascular Dementia in Rochester, Minn, 1985-1989

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Objective: To examine the contribution of cerebrovascular disease to dementia.

Methods: We used the records-linkage system of the Rochester Epidemiology Project to ascertain incident cases of dementia in Rochester, Minn, for 1985 through 1989. We defined dementia using the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. To define dementia types, we reviewed neuroimaging reports, which were available for two thirds of dementia cases, in addition to medical histories and neurologic examination results. Vascular dementia (VaD) was defined by 1 of the following criteria: dementia onset or worsening within 3 months of a clinical stroke or bilateral gray matter infarctlike lesions shown by imaging that fulfilled specified location criteria (critical imaging lesions).

Results: We found 482 incident cases of dementia. Overall, 10% of patients had onset or worsening of their dementia within 3 months of a stroke. Eleven percent of the incident dementia cases had bilateral gray matter lesions on imaging that were considered critical. Eighteen percent of patients had one or the other of these features (VaD by our criteria), but only 4% of patients had both. The incidence rate of VaD increased steeply with advancing age and was similar in men and women. Our incidence rates were similar to those from a recent European meta-analysis.

Conclusion: The presence of either a stroke temporally related to dementia onset or worsening or of critical imaging lesions was common among dementia patients, whereas the occurrence of both features together was rare.

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THE CONTRIBUTION OF CEREBROVASCULAR DISEASE (CVD) TO DEMENTIA HAS BEEN DIFFICULT TO DEFINE, AND EPIDEMIOLOGIC STUDIES SHOW CONSIDERABLE VARIABILITY IN THE PROPORTION OF DEMENTIA ATTRIBUTED TO CVD. THESE STUDIES USED CLINICAL DIAGNOSTIC CRITERIA FOR VASCULAR DEMENTIA (VaD)¹⁻² THAT LACK SENSITIVITY AND SPECIFICITY³ AND MEASURE DIFFERENT ASPECTS OF CVD.⁴⁻⁵ THE DIVERGENCE IN ESTIMATES OF PREVALENCE¹¹⁻¹⁸ AND INCIDENCE¹⁰⁻²⁴ OF VaD SUGGESTS THAT THE CONCEPT OF VaD ITSELF NEEDS FURTHER INVESTIGATION.

We investigated the incidence of VaD in Rochester, Minn, from 1985 through 1989. Although diagnoses of dementia in retrospective series may undercount mild cases, the diagnosis of stroke through record review is accurate.⁵⁻²⁵ Therefore, the records-linkage system of the Rochester Epidemiology Project allows a population-based view of the relationship between stroke and dementia. In contrast to most other studies of the incidence of dementia, we report rates for specific features of CVD, including imaging studies, in addition to rates based on several particular diagnostic criteria for VaD. Incidence rates for Alzheimer disease (AD) have been reported separately.²⁶

METHODS

CASE ASCERTAINMENT

We ascertained cases of dementia through the records-linkage system of the Rochester Epidemiology Project as described previously.²⁷⁻²⁸ Medical care for the population of Rochester and Olmsted County, Minnesota, is provided largely by the Mayo Clinic at the primary, secondary, and tertiary levels. Additional health care providers in the community participate in the Rochester Epidemiology Project, which provides the infrastructure for indexing essentially all the medical information of the local population. Each provider in the community uses a dossier system whereby all medical information for each individual is accumulated in a single file. Medical diagnoses, surgical interventions, and other key information from the dossier are routinely abstracted. The abstracted information is coded using the International Classification of Diseases adapted code for hospitals (H-ICDA) and entered into computerized indices.²⁹ Therefore, each individual in the system can be searched for a given...
condition through extensive indices of clinical or histologic diagnoses and surgical procedures.

We searched these indices for 112 specific H-ICDA codes that might indicate dementia. Any patient with at least 1 of the study codes was considered as a potential case. Cases of dementia in the general population may remain undetected for a number of years, but may be eventually diagnosed as having dementia at some point during their natural history. To increase the likelihood of capturing these individuals, the indices were searched for the study interval and for 6 additional years following the last year of the study interval. Cases of dementia identified in the 6 subsequent years were then reviewed for evidence of dementia onset in 1985 through 1989. All medical records of each potential case were screened by a specifically trained nurse abstractor and a diagnosis obtained, as previously described. The primary study neurologist (E.K.) confirmed the presence of dementia, classified the dementia by type, and determined the year of onset. To standardize and operationalize the diagnoses, each cardinal feature required for a diagnosis of dementia (see “Diagnostic Criteria” subsection that follows) was considered and scored separately. All medical records, including physician and nurse notes, were reviewed and all available data pertinent to the criteria were abstracted.

To be included in the study, patients with dementia were required to reside in Rochester in the year of onset of dementia and for at least 1 preceding year. Dementia cases who moved to Rochester for the management of a preexisting dementing illness were excluded. All study procedures were reviewed and approved by the Mayo Institutional Review Board. Persons obtaining medical care at the Mayo Clinic and other medical services affiliated with the Rochester Epidemiology Project are given the opportunity to deny access to their medical records for research purposes. Ten individuals were excluded from our study for this reason, and their dementia status remained unknown.

**DIAGNOSTIC CRITERIA**

The principal sources of diagnostic information were the medical history, neurologic examinations, and neuroimaging studies as recorded historically in the patient dossier of the records-linkage system. Diagnostic criteria for dementia were those of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). The criteria for dementia in DSM-IV include the following features: memory impairment as a prominent early feature; at least 1 of the following: aphasia, apraxia, agnosia, or disturbance of executive function; and loss of function sufficient to interfere with social or occupational activities. The criteria were scored separately, and the diagnosis of dementia was made only if all of the requirements for the diagnosis were fulfilled. However, we were unable to estimate the severity of dementia through our retrospective chart review.

Clinical stroke was defined as a medical record documentation of a focal neurologic deficit of acute onset that persisted for more than 24 hours and occurred at any time before the onset of dementia. All types of stroke were included. For a stroke to be considered temporally related to dementia, it had to precede the onset of the dementia by no more than 3 months or to cause an abrupt worsening of cognitive function in patients with prior cognitive deficits. We also reviewed the neurologic examinations at the time of the diagnosis of dementia to document the presence of the following focal neurologic signs: hemiparesis, lower facial palsy, extensor toe signs, sensory deficits, hemianopia, dysarthria, or other signs traditionally observed in CVD.

It was not possible to review the actual computed tomography (CT) or magnetic resonance (MR) scans of our patients; however, the primary study neurologist (E.K.) reviewed the radiologists’ written reports of these studies. Most imaging studies were CT; only 8% of cases with imaging (28 of 354) had at least 1 MR scan. We classified infarctlike lesions as likely to undermine cognition (which we will refer to as critical lesions) when they fulfilled 1 of the following 2 criteria: (1) bilateral frontal, temporal, or parietal lobe cortical infarctions or (2) bilateral thalamic or basal ganglia infarctions. We further required that the imaging occurred in the time window from 1 year before through 3 years after the onset of dementia to avoid considering imaging lesions that clearly postdated the onset of dementia. We also noted the presence of bilateral diffuse subcortical or periventricular white matter lesions; however, because of the uncertain relationship of white matter lesions to infarction, we excluded purely white matter lesions from our definition of critical lesions.

For the diagnosis of VaD, we required 1 of the following 2 criteria: (1) clear evidence for the onset or worsening of dementia within 3 months of a clinical stroke or (2) bilateral gray matter infarctlike lesions shown by imaging and judged to be critical. In addition, we independently applied 3 sets of published diagnostic criteria for VaD to our incident series: the DSM-IV criteria, the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l’Enseignement en Neurosciences (NINDS-AIREN) criteria, and the *International Classification of Diseases, 10th Revision (ICD-10)* criteria.

**DATA ANALYSIS**

We described the distribution of clinical strokes, imaging lesions, focal signs, and their combination in all incident cases of dementia. In addition, we calculated age- and sex-specific incidence rates using different diagnostic criteria. The number of person-years at risk was estimated from census data with an adjustment for prevalent cases of dementia. Demographic data for the city of Rochester by sex and single year of age were available for the census years 1980 and 1990. Counts for the intercensal years were estimated by linear interpolation. These numbers were corrected by removing patients already affected by dementia and therefore not at risk, as described elsewhere. Average annual incidence rates were reported by sex and 5-year age classes between 50 and 99 years. The objectives of this study were descriptive. Because the study covered the target population completely, no sampling was involved, and we did not use statistical tests to interpret our findings.

There were 482 incident cases of dementia who were residents of Rochester in the 5 years from 1985 through 1989; 479 of them were between the ages of 50 and 99 years and 3 were older than 99 years. Figure 1 shows the principal subsets of cases. Of these 482 cases, 59 had other medical or neurologic diseases, such as brain tumor, head injury, and a number of miscellaneous conditions that either antedated the dementia or occurred simultaneously with the dementia, and were thought to cause their dementia. Two (3%) of these 59 patients also had critical imaging findings, suggesting that CVD may have contributed to their dementia. Eight (14%) of these 59 patients also had a stroke; however, none had a stroke with a clear temporal relationship to the dementia.

Fifty (12%) of the 423 patients with no other cause of dementia had a history of a clear temporal relationship (within 3 months) between a stroke and onset or worsening of their dementia (Figure 1), of whom only 16 also had a critical imaging lesion. Of the 50 patients who exhibited the temporal relationship between a clini-
cal stroke and their dementia, onset of dementia occurred with the stroke in 26 and exacerbation of existing dementia occurred in the remainder.

Imaging studies were available in 354 (73%) of the entire group of 482 patients. There were 51 cases with critical imaging lesions (Figure 1). The location of critical infarctlike lesions on imaging was bilateral frontal, parietal, or temporal cortex in 51%, bilateral basal ganglia or thalamus in 33%, and both cortical and subcortical in 16%. Patients with cortical lesions outnumbered patients with subcortical locations.

Of the 423 patients with no other cause of dementia, 70 (17%) had at least 1 infarctlike lesion on imaging regardless of its critical status. Of these 70 patients, 31 also had a clinical stroke, whereas 39 did not (Figure 1). An additional 94 cases (22%) had white matter lesions, of which 45 (11%) met NINDS-AIREN imaging criteria. Six of these 45 patients also had a stroke with temporal relationship and were included in our definition of VaD.

Among the 482 patients, 132 (27%) had at least 1 focal neurologic sign. Among the 423 patients with no other cause of dementia, 109 (26%) had 1 or more focal signs on examination, 73 (17%) had 2 or more, and 47 (11%) had 3 signs or more. Twenty-three (39%) of the 59 patients with dementia due to other medical or neurologic diseases also had focal neurologic signs.

The overlap of clinical strokes and critical imaging lesions was small; only 16 (32%) of the 50 patients with dementia temporally related to a stroke also had critical imaging lesions. On the other hand, of the 51 cases with critical imaging lesions and no other cause of dementia, 35 (69%) lacked a history of clinical stroke temporally related to the onset or worsening of dementia, and 27 (53%) had no history of clinical stroke ever.

Focal neurologic signs and clinical strokes were related. Of the 50 patients with dementia temporally related to a stroke, 42 (84%) had at least 1 focal sign at the time of onset of dementia. In contrast, of the 109 patients with at least 1 focal finding at the time of onset of dementia, 79% had a history of stroke but only 39% had strokes within the 3-month time frame. There was a variable association between focal signs and critical lesions on imaging. Among the 51 patients with critical imaging lesions and no other cause of dementia, only 27 (53%) had at least 1 focal neurologic sign. However, if the enumeration was limited to cases who had both critical imaging lesions and at least 1 clinical stroke regardless of its temporal relationship to dementia, 22 (92%) of the 24 had at least 1 focal sign.

Table 1 provides the operational criteria used to define VaD in our study and by others and gives the proportion of all cases of dementia assigned to VaD using different criteria. By our criteria (a history of stroke within 3 months of the onset or worsening of dementia or critical imaging lesions on imaging), VaD was present in 18% of incident cases of dementia in Rochester in 1985 through 1989. Age- and sex-specific incidence rates using our definition are shown in Table 2 and Figure 2. For comparison, Table 2 and Figure 2 also show the incidence rates obtained when only patients who underwent a clinical stroke temporally related to dementia were included in the analysis. The incidence of VaD continued to increase with age. However, VaD represented 21% of all dementia cases with onset before the age of 80 years but only 16% of dementia cases with onset at 80 years and older.

We studied the incidence rates of specific features of CVD that may play a role in causing dementia in a well-defined population. Eighteen percent of our incident dementia cases had onset or worsening of dementia within 3 months of a clinical stroke or had bilateral gray matter infarctlike critical lesions shown by imaging (critical lesions). We suggest that the presence of either feature is sufficient to assume that CVD is contributing to the origin and course of the dementia. Requiring the presence of both features for a diagnosis of VaD (which is the core of the NINDS-AIREN criteria) may lead to an underrecognition of relevant CVD in patients with dementia. We observed both features in only 4% of our incident cases. Neuropathologic correlation studies in our series of incident cases of dementia have shown moderate sensitivity and specificity of our criteria and poor sensitivity of the NINDS-AIREN criteria for “pure” VaD (D.S.K., Joseph E. Parisi, MD, W.A.R., Bradley F. Boeve, MD, R.H.C., Hulya Apaydin, MD, Alessandro Salvati, MD, S.D.E., unpublished data, 2002).

Application of different diagnostic criteria in our incidence study of dementia resulted in significantly different estimates of VaD frequency, a result observed by others. The estimated incidence rates of VaD were much higher using our criteria than using the NINDS-AIREN criteria, but lower than using the DSM-IV or ICD-10 criteria. Perhaps because of the averaging of results from studies using various criteria and diverse interpretations of the same criteria by different groups, the estimated incidence of VaD from the pooled European studies of 17.6% was similar to our estimate of 18%. Age-specific incidence rates were also similar in Rochester and the pooled European studies (Figure 3).

We did not attempt to distinguish between “pure” VaD and combined VaD and AD. Given the low sensitivity of the diagnostic criteria for VaD, we chose to report only the rates for cases that we thought had relevant CVD. To avoid confusion by adding new terms, we have used the
Table 1. Number of Incident Cases of Vascular Dementia According to Different Criteria, Rochester, Minn, 1985-1989

<table>
<thead>
<tr>
<th>Diagnostic Criteria</th>
<th>Operational Features†</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal link between stroke and dementia</td>
<td>Clinical stroke temporally related to dementia (within 3 months)‡</td>
<td>50 (10)</td>
</tr>
<tr>
<td>Imaging findings strictly defined</td>
<td>Critical imaging lesions on imaging§</td>
<td>51 (11)</td>
</tr>
<tr>
<td>VaD, our criteria</td>
<td>Dementia temporally related to stroke or critical imaging lesions (exclusive of white matter lesions)</td>
<td>85 (18)</td>
</tr>
<tr>
<td>VaD, our criteria including white matter lesions</td>
<td>Dementia temporally related to stroke or critical imaging lesions or bilateral extensive subcortical white matter lesions on imaging</td>
<td>124 (26)</td>
</tr>
<tr>
<td>Criteria from the literature</td>
<td>Dementia temporally related to a stroke and critical imaging lesions (including white matter lesions) and at least 1 focal sign</td>
<td>20 (4)</td>
</tr>
<tr>
<td>NINDS-AIREN probable VaD</td>
<td>Dementia temporally related to a stroke and critical imaging lesions (including white matter lesions) or ≥1 focal neurologic signs</td>
<td>141 (29)</td>
</tr>
<tr>
<td>DSM-IV</td>
<td>Critical imaging lesions (including white matter lesions) or ≥1 focal neurologic signs or critical imaging lesions (including white matter lesions)</td>
<td>118 (24)</td>
</tr>
<tr>
<td>ICD-10</td>
<td>Dementia temporally related to a stroke or critical imaging lesions or critical imaging lesions (including white matter lesions)</td>
<td></td>
</tr>
</tbody>
</table>

*VaD indicates vascular dementia; NINDS-AIREN, National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l’Enseignement en Neurosciences; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; and ICD-10, International Classification of Diseases, 10th Revision.

†In all definitions, patients with dementia due to other cause were excluded.

‡Clinical stroke temporarily related was defined as a stroke occurring within 3 months of onset or worsening of dementia.

§Critical imaging lesions were (1) bilateral frontal, temporal, or parietal lobe infarctions and (2) bilateral thalamic or basal ganglia infarctions. Imaging lesions had to be documented in the period from 1 year before through 3 years after the presumed onset of dementia.

Table 2. Age- and Sex-Specific Incidence Rates (per 100 000 Person-years) of Vascular Dementia in Rochester, Minn, 1985-1989

<table>
<thead>
<tr>
<th>Age Class, y</th>
<th>Sex</th>
<th>50-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75-79</th>
<th>80-84</th>
<th>85-89</th>
<th>90-99</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia With Temporal Relationship to a Stroke†</td>
<td>M‡</td>
<td>16.9 (3)</td>
<td>72.6 (3)</td>
<td>159.0 (5)</td>
<td>90.3 (2)</td>
<td>240.8 (3)</td>
<td>424.3 (3)</td>
<td>434.8 (1)</td>
<td>68.0 (20)</td>
</tr>
<tr>
<td></td>
<td>F‡</td>
<td>16.9 (3)</td>
<td>96.9 (4)</td>
<td>131.7 (6)</td>
<td>159.0 (5)</td>
<td>213.6 (10)</td>
<td>410.8 (11)</td>
<td>460.5 (6)</td>
<td>70.7 (50)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>33.8 (6)</td>
<td>169.5 (7)</td>
<td>310.7 (11)</td>
<td>249.3 (7)</td>
<td>655.6 (13)</td>
<td>835.1 (14)</td>
<td>842.3 (7)</td>
<td>138.7 (70)</td>
</tr>
<tr>
<td>Vascular Dementia (Our Criteria)¶</td>
<td>M§</td>
<td>16.9 (3)</td>
<td>78.3 (4)</td>
<td>159.0 (5)</td>
<td>108.6 (4)</td>
<td>240.8 (3)</td>
<td>990.1 (7)</td>
<td>869.6 (2)</td>
<td>95.2 (30)</td>
</tr>
<tr>
<td></td>
<td>F§</td>
<td>16.9 (3)</td>
<td>98.3 (4)</td>
<td>159.0 (5)</td>
<td>108.6 (4)</td>
<td>240.8 (3)</td>
<td>990.1 (7)</td>
<td>869.6 (2)</td>
<td>95.2 (30)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>33.8 (6)</td>
<td>176.6 (8)</td>
<td>318.0 (9)</td>
<td>217.2 (8)</td>
<td>481.6 (10)</td>
<td>1,859.2 (14)</td>
<td>1,739.2 (4)</td>
<td>190.4 (60)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses indicate the actual number of cases observed.

†Dementia onset or worsening within 3 months of a stroke.

‡Denominators (in person-years) for women were as follows: 50 to 54 years, 6821; 55 to 59 years, 6043; 60 to 64 years, 5965; 65 to 69 years, 5566; 70 to 74 years, 5106; 75 to 79 years, 4557; 80 to 84 years, 3436; 85 to 89 years, 378.3 (13); 90 to 94 years, 240.8 (3); and 95 to 99 years, 46.0 (6).

¶Dementia onset or worsening within 3 months of a stroke.

§Denominators (in person-years) for men were as follows: 50 to 54 years, 6821; 55 to 59 years, 6043; 60 to 64 years, 4869; 65 to 69 years, 4130; 70 to 74 years, 3145; 75 to 79 years, 2215; 80 to 84 years, 1246; 85 to 89 years, 707; 90 to 94 years, 184; and 95 to 99 years, 46.

The drawbacks of a retrospective analysis such as ours are important and include the difficulties in the assignment of diagnoses based on record review alone. The lack of consistently available data on all patients can make assignment of a diagnosis of dementia difficult. The fact that neurologists did not examine all patients might have led to an undercounting of focal neurologic signs. In our methods, we were conservative in diagnosing dementia, and we may have failed to identify individuals with milder illnesses. We were also unable to characterize the severity of the dementia at onset. Individuals with mild dementia can only be detected using direct neuropsychological testing. However, in our studies of mortality in this cohort, the median survival of our patients with AD was comparable to that reported from prospectively recruited patients.

The use of CT images in our study instead of MR images may have underestimated the burden of infarcts. Although CT may have failed to detect some chronic infarctions, those missed were likely too small and well below our threshold to be critical. Some CT scans may have been performed in the acute stroke period when a new infarct could have been missed. Another source of underestimation of cerebral infarctions was the unavailability of imaging for 27% of our cases.
unlikely that the patients who did not undergo imaging had the same frequency of critical infarcts as those who underwent imaging, we have no basis for imputing the burden of infarcts in those without imaging studies.

Cerebral cortical infarctlike lesions predominated, but subcortical gray matter infarctlike lesions were also common among critical imaging lesions, which is consistent with other studies in our series. A prior study in Rochester found an association between multiple infarctions and dementia; however, that study did not investigate infarct location. In selected series of patients, infarction in the territory of the middle cerebral artery and the left hemisphere region of the thalamocortical radiations were more closely associated with dementia after stroke than were infarctions in other regions. We are not aware of any other population-based studies that have detailed the locations of infarctions in patients with dementia. We adopted most of the NINDS-AIREN perspective on critical infarctions in dementia. We did not accept the broader view that any infarctlike lesion on imaging is critical. More quantitative work is needed to define better the locations of infarctions that are invariably associated with dementia.

We excluded extensive white matter lesions from our definition of critical lesions. We did not accept them as imaging evidence for stroke. In contrast, DSM-IV and ICD-10 criteria include white matter lesions (Table 1). Although white matter lesions are seen with considerable frequency in patients thought to have VaD, the preponderance of evidence is that white matter lesions do not usually represent infarction per se. In addition, white matter lesions lack specificity for VaD because they are seen also in AD. If we accepted bilateral and extensive subcortical white matter lesions as critical lesions, 39 additional patients would have been classified as VaD by our criteria, increasing the VaD representation from 18% to 26% of all cases of dementia (Table 1).

Only about half of the patients with critical imaging lesions had a clinical history of stroke or focal neurologic signs. Clinically silent critical imaging lesions were a major contributor to the increasing incidence of VaD in our oldest population. Other studies have found that silent cerebral infarctions are common and increase with advancing age.

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Author contributions: Study concept and design (Drs Knopman, Rocca, Edland, and Kokmen); acquisition of data (Ms Cha and Dr Kokmen); analysis and interpretation of data (Drs Knopman, Rocca, and Edland and Ms Cha); drafting of the manuscript (Drs Knopman, Rocca, Edland, and Kokmen and Ms Cha); critical revision of the manuscript for important intellectual content (Drs Knopman, Rocca, and Edland); statistical expertise (Dr Rocca and Ms Cha); obtained funding (Dr Kokmen); and administrative, technical, and material support (Drs Knopman, Rocca, Edland, and Kokmen).

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