Poststroke Dementia
Clinical Features and Risk Factors

Raquel Barba, MD; Susana Martínez-Espinosa, PhD; Elena Rodríguez-García, MD; Margarita Pondal, MD; José Vivancos, MD, PhD; Teodoro Del Ser, MD, PhD

Background and Purpose—The goal of the present study was to examine a series of putative risk factors of poststroke dementia (PSD), especially those factors usually associated with cerebrovascular disease and degenerative dementia, in a series of 251 consecutive unselected stroke patients.

Methods—A standard protocol was prospectively applied at admission and 3 months after stroke; this protocol included clinical, functional, and cognitive assessments, hematogram and serum biochemistry, ECG and CT exams, apolipoprotein E and angiotensin-converting enzyme genotype, and neuropsychological examination. After a neuropsychological examination and an interview with a relative, the following diagnostic criteria were used: the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV for dementia after stroke, DSM-III-R for previous dementia and dementia stage, and Association Internationale pour la Recherche et l’Enseignement en Neurologie (NINDS-AIREN) for vascular dementia.

Results—Seventy-five cases (30%) demonstrated dementia at 3-month follow up; 25 of them (10%) had demonstrated dementia before the stroke. Dementia was unrelated to type (ischemic/hemorrhagic) or location of stroke, vascular factors (hypertension, diabetes, ischemic heart disease, or hypercholesterolemia), apolipoprotein E or angiotensin-converting enzyme genotype, and serum homocysteine. Age (odds ratio [OR] 1.1, 95% CI 1.03 to 1.2), previous nephropathy (OR 6.1, 95% CI 1.5 to 24.3), atrial fibrillation (OR 4.4, 95% CI 1.4 to 13.9), low Canadian Neurological Scale score at discharge (OR 0.5, 95% CI 0.4 to 0.6), and previous mental decline assessed by the shortened Spanish version of the Informant Questionnaire on Cognitive Decline in the Elderly (SS-IQCODE; OR 1.2, 95% CI 1.1 to 1.4) were the correlates of dementia in logistic regression analyses. The same risk factors were found when cases with previous dementia and with hemorrhagic stroke were excluded.

Conclusions—Dementia is frequent after ischemic or hemorrhagic stroke. Age, nephropathy, atrial fibrillation, previous mental decline, and stroke severity independently contribute to the risk. (Stroke. 2000;31:1494-1501.)

Key Words: dementia ■ risk factors ■ stroke

Stroke was recognized as an important cause of dementia 1 century ago, but until the 1960s, most cases of dementia were attributed to atherosclerosis. Now cerebrovascular disease is considered to be the second most common cause of dementia and one of the rare preventable dementias. Poststroke dementia (PSD) has been an emerging field of research over the last decade. The frequency of PSD has been found to be higher than previously expected, and a stroke increases the risk of dementia 4 to 12 times. Reasons for a stroke patient to become demented are still insufficiently understood. Dementia is not always a direct consequence of cerebrovascular lesions, and in some cases, dementia occurring after stroke has a progressive onset and course, suggesting a degenerative rather than a vascular origin. Recent studies have demonstrated that many patients admitted for stroke seem to have had preexisting cognitive decline, and one sixth of them have had previous dementia.

All individuals with stroke do not develop dementia; therefore, it is important to determine the risk factors for PSD. Some studies have investigated these risk factors, but there has not been a consensus about them. Demographic, clinical, stroke-related, and lesion-related radiological factors have been reported to predict dementia in stroke patients. These conflicting results are probably due to differences in the rules of case selection and definition of dementia.

We studied the incidence of PSD and examined a series of putative risk factors for dementia, especially those usually associated with cerebrovascular disease and degenerative dementia, in a series of consecutive unselected stroke patients.

Subjects and Methods

Patients
From May 1, 1994, to September 30, 1995, 349 patients, aged ≥18 years, were admitted for acute stroke, either ischemic or hemor-

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rhagic, to the Hospital Severo Ochoa (Leganés, Madrid, Spain). The catchment area of our hospital included ≈350 000 habitants (6% were aged ≥65 years). Three hundred twenty-seven (93.6%) were entered in a prospective stroke registry. The diagnosis of stroke was established on clinical grounds, when there were focal signs of cerebral dysfunction of acute onset lasting for >24 hours. In 304 cases (93%), the diagnosis was also based on a brain CT scan. Patients with prior cerebrovascular events were included, but transient ischemic attack, subarachnoid hemorrhage, and stroke associated with other primary brain lesions (e.g., tumors and trauma) were excluded from the registry.

At discharge, a clinical follow-up was proposed, and all patients who accepted were reassessed 3 months after the stroke.

**Clinical Assessment During Admission**

During admission, every patient underwent a structured medical history, neurological, functional, and cognitive examinations, and ancillary examinations, according to a previously stated protocol. The following data were obtained: demographic data, previous diseases and habits, previous cardiovascular diseases, previous cerebrovascular diseases, previous functional and cognitive status, present clinical, functional, and cognitive status, complementary data, type of stroke, and neuroimaging.

**Demographic Data**

These data included age, sex, and education (illiterate or able to read and education below high school level, at high school level, and above high school level).

**Previous Diseases and Habits**

These data included moderate-to-severe renal disease (creatinine >106.7 μmol/L [1.4 mg/dL] and diagnosis validated by an internist or nephrologist), lung disease (clinical criteria of chronic obstructive lung disease), or liver disease (serum transaminases >2.5 times normal); seizures; depression (diagnosed by a psychiatrist according to Diagnostic and Statistical Manual of Mental Disorders [DSM]-IV criteria); obesity (body mass index >30); number of surgical procedures according to previous medical diagnoses; smoking (smoker, exsmoker, or nonsmoker; number of cigarettes per day); and alcohol intake (drinker, exdrinker, or nondrinker; grams of alcohol per day; number of years as usual drinker).

**Previous Cardiovascular Diseases**

These data included hypertension (previously diagnosed and treated or systolic pressure >160 mm Hg and/or diastolic pressure >90 mm Hg persistently observed during admission after the acute phase), diabetes (previously diagnosed and treated or fasting glucose 7 mmol/L [126 mg/dL] in 2 blood samples after the acute phase), hypercholesterolemia (previously diagnosed and treated or serum cholesterol 6 mmol/L [230 mg/dL] in 2 blood samples), myocardial infarction, congestive heart failure, atrial fibrillation and/or other arrhythmias according to clinical diagnosis and ECG after the acute phase, or peripheral arterial disease (intermittent claudication or loss of pulse in feet).

**Previous Cerebrovascular Diseases**

These data included previous transient ischemic attack or stroke according to previous medical diagnoses.

**Previous Functional and Cognitive Status**

Functional status before the stroke was assessed by the Barthel Index. A shortened Spanish version of the Informant Questionnaire on Cognitive Decline in the Elderly (SS-IQCODE), previously validated in the Spanish population and clinical settings, was used to assess cognitive decline during the 5 years before the stroke; information was provided by a proxy relative. A cutoff point of 57 was used. In 20 cases, there was not a good informant; thus, the SS-IQCODE was not applied.

**Present Clinical, Functional, and Cognitive Status**

These data included systolic and diastolic blood pressure and axillary temperature. Stroke severity was assessed by the Canadian Neurological Scale (CNS), and present cognitive status was assessed by the Short Portable Mental Status Questionnaire (SPMSQ) on the first day of admission and at discharge. A modified scoring of the SPMSQ ranging from 0 to 20 was used. The Barthel Index was also obtained at discharge.

**Type of Stroke**

The stroke was categorized according to its mechanism as probably embolic (when atrial fibrillation, mitral valve, or another cardiac embolic source was present) or probably thrombotic (when no embolic source was detected) and according to the CT findings as ischemic (lacunar, <2 cm²; nonlacunar, ≥2 cm²), hemorrhagic (hemorrhagic infarct, hematoma), or indefinite (if the CT was not performed); the stroke was also categorized as single or multiple lesion.

The stroke was located on clinicoradiological grounds to the carotid (left or right, anterior or middle cerebral artery) or vertebrobasilar artery.

**Quality Status**

Routine cranial CT was performed without contrast in most cases between the first and 30th day after the stroke.

**Clinical Assessment at Follow-Up**

A follow-up was proposed to all patients who survived 3 months after the stroke. Two hundred thirteen patients were assessed at the Neurology Clinic, and 38 were assessed by phone. The following protocol was applied when possible after informed consent: determination of clinical and functional status, cognitive status, and complementary data.

**Clinical and Functional Status**

These data included systolic and diastolic blood pressure, neurological examination, and the Barthel Index.

**Cognitive Status**

The SPMSQ (as a screening test) and the SS-IQCODE (as an assessment of cognitive decline during the last 5 years, including the poststroke period) were applied by a neuropsychologist (T.D.S.). The following neuropsychological battery was administered by a neuropsychologist (S.M.-E.): Mini Mental State Examination, visual and hearing reaction time, bell test (visual attention), verbal fluency, picture recognition (visual memory), word learning (free and cued recall, immediate and delayed recall), logic memory (immediate and delayed), block test (Wechsler Adult Intelligence Scale), naming (verbal and picture from the Boston Aphasia Battery), Token test, similarities (Wechsler Adult Intelligence Scale), and Lawton-Brody scale (activities of daily living). These tests were selected because they have very few motor or reading requirements. Normative data for theses tests had been previously established in a control group of healthy elderly volunteers living in the same urban area and with the same age, sex distribution, and cultural background.

**Complementary Data**

Hemogram and serum biochemistry were repeated at this time, but data were not introduced in the analyses. Serum ferritin, vitamins A and E, and homocysteine levels were obtained 3 months after stroke to avoid the acute effects of the illness. The apolipoprotein E (apoE) and angiotensin-converting enzyme (ACE) genotype was determined in this blood sample in 149 and 134 cases, respectively.
Diagnosis of Dementia

During the admission, the information gathered from the medical history, from a clinical interview with a close informant, and from the assessment of functional (Barthel Index) and cognitive (SS-IQCODE) status before the stroke was used to establish a retrospective diagnosis of previous dementia according to DSM-III-R criteria.

Three months after the stroke, all patients were diagnosed as demented or nondemented by one experienced neurologist (T.D.S.) on the basis of clinical interview with the patient and with a close informant (in the majority of cases), the present score on the SPMSQ, the SS-IQCODE, and the results of the neuropsychological battery. This diagnosis was stated according to the DSM-IV criteria when scores in recent and late memory and in other cognitive domains were below 1 SD of the control group, when instrumental activities of daily living were impaired independently of motor or sensory defects, and when relatives provided information about relevant cognitive decay (SS-IQCODE >57).

The neuropsychological battery could not be applied in 51 cases (20%) because they did not report to the Neurology Clinic (38 cases) or because they were too ill (13 cases) to perform the tests, and the DSM-III-R criteria were used on the basis of the information provided by the relatives, the SS-IQCODE (>57 for dementia), and the SPMSQ when available.

Twenty-four cases were severely aphasic or motor-impaired, and diagnosis of PSD was delayed several months until the language or motor functions improved.

Vascular dementia was established according to the Association Internationale pour la Recherche et l’Enseignement en Neurologie (NINDS-AIREN) criteria as possible or probable. The dementia stage was defined according to the DSM-III-R criteria.

Statistical Analysis

Patients were divided into 2 groups according to the diagnosis of dementia. All demographic, clinical, and complementary data at baseline and 3 months after stroke were compared between these 2 groups. The 2-tailed Student t test for quantitative variables and the χ² test for dichotomous variables were used. All the univariate analyses were performed after adjusting for age. The odds ratios (ORs) and 95% CIs were estimated from the regression coefficients.

Several multiple-logistic models were calculated to identify independent correlates of PSD in 5 different subgroups of patients: model I, 231 patients (20 cases with previous dementia or possible vascular dementia and 19 with missing data were excluded); model II, 206 patients (25 cases who were demented before the stroke and 20 with missing data were excluded); model III, 204 patients (29 cases with hemorrhagic stroke and 18 with missing data were excluded); model IV, 183 patients (52 cases with previous dementia or hemorrhagic stroke and 16 with missing data were excluded); and model V, 201 patients (31 cases with previous dementia or possible vascular dementia and 19 with missing data were excluded).

The most clinically relevant variables and those with statistical significance (P<0.1) in the univariate analyses of every subgroup were introduced in the logistic regression analyses. The final sets of independent variables selected was very similar for all the subgroups. A logistic regression analysis with a backward stepwise procedure and with P>0.10 as the criterion for exclusion was used to find the best predictive models of PSD in every group. Stratified analyses were performed to examine confounders and interactions where appropriate. All these analyses were performed with SPSS for Windows, version 7.5 (SPSS Inc.).

Results

From the 327 consecutive patients included in the Stroke Registry, 251 were examined 3 months after the stroke. The remaining 76 patients were lost to follow-up: 63 (19%) died before 3 months, 7 (2%) did not report to the scheduled follow-up (5 moved away and 2 refused to participate), and 6 (2%) were excluded because they had severe aphasia (3), persistent loss of consciousness (2), or previous long-lasting mental retardation (1) interfering with the assessment of cognitive status. Therefore, 251 cases (76.7% of the registry sample and 95% of survivors) were included in the present study.

The 13 lost patients did not differ from the examined cases (Table 1); the 63 cases who died were older, had lower cognitive function previous to the stroke, and had poorer scores on neurological and functional scales during admission (Table 1).

The sample of 251 stroke patients had a mean age of 69±13 years (47% were female, and 78% were aged >60 years). Their demographic data are shown in Table 1. The vascular territory of the stroke was left carotid in 119 cases (47.4%), right carotid in 87 (34.6%), vertebrobasilar in 43 (17.1%), and indefinite in 1. The stroke was ischemic in 222 cases (88.4%) and hemorrhagic in 29 (11.6%); it was considered embolic in 34 cases (13.5%).

Among the 251 stroke patients of the cohort, 25 cases (10%) were demented before the stroke, and 75 (30%) were...
demented 3 months after the stroke. The severity of PSD was mild in 22 cases (29.3%), moderate in 22 (29.3%), and severe in 31 (41.3%). The vascular lesions producing or contributing to PSD were territorial infarcts or gross hemmoraghes in 34 cases (49.3%), small vessel lacunar lesions in 26 (37.7%), and strategic lesions in 6 (8%; left caudate [2], left lenticular [3], and left thalamus [1]). PSD was considered probable vascular dementia (due to vascular lesions alone) in 53 cases (33 versus 2.3, \( P = 0.001 \)) (Table 3). Demented patients had more concomitant diseases (3 versus 2.3, \( P = 0.004 \)), psychiatric diseases (OR 4.4 and 95% CI 1.7 to 10.9), and nephropathy (OR 3.6 and 95% CI 1.4 to 9.5) even after adjusting for age (Table 3).

The majority of vascular risk factors, such as high blood pressure, diabetes, ischemic heart disease, congestive heart failure, aortic valve disease, transient ischemic attacks, intermittent claudication, hypercholesterolemia, alcohol intake, and current smoking, were not associated with the presence of PSD (Table 4). Compared with nondemented patients, demented patients had more frequent atrial fibrillation (OR 2.9 and 95% CI 1.2 to 6.7), mitral valve disease (OR 3.8 and 95% CI 1.2 to 12.5), and aortic arch calcification (OR 1.9 and 95% CI 1.03 to 3.7) (Table 4); the frequency of previous stroke almost reached statistical significance (OR 2.2 and 95% CI 0.9 to 5.2).

### Univariate Analysis

The location and type (ischemic versus hemorrhagic) of stroke did not differ between demented and nondemented patients (Table 2). Demented patients had significantly more multiple vascular lesions (33 cases [44%]) and embolic strokes (16 cases [21.3%]) than did nondemented patients (49 [28.5%] and 18 [10.3%] cases, respectively) (Table 2).

Mean age was significantly older in demented patients (76.9 years) than in nondemented patients (65.4 years, \( P < 0.0001 \)) (Table 3). There were more women and illiterate individuals in the group of demented patients, but after adjusting for age, the differences were not significant (sex, OR 1.6 and 95% CI 0.8 to 3.0; education, OR 1.2 and 95% CI 0.9 to 5.2) (Table 3). Demented patients had more concomitant diseases (3 versus 2.3, \( P = 0.004 \)), psychiatric diseases (OR 4.4 and 95% CI 1.7 to 10.9), and nephropathy (OR 3.6 and 95% CI 1.4 to 9.5) even after adjusting for age (Table 3).

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### Table 2. Stroke Features in Demented and Nondemented Patients

<table>
<thead>
<tr>
<th>Location, n (%)</th>
<th>Demented (N=75)</th>
<th>Nondemented (N=176)</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left carotid</td>
<td>39 (52)</td>
<td>80 (45)</td>
<td></td>
</tr>
<tr>
<td>Right carotid</td>
<td>27 (36)</td>
<td>60 (34)</td>
<td></td>
</tr>
<tr>
<td>Vertebobasilar</td>
<td>8 (10.7)</td>
<td>35 (20)</td>
<td></td>
</tr>
<tr>
<td>Undeinite</td>
<td>1 (1.3)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Type of stroke, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>67 (85.8)</td>
<td>155 (89.3)</td>
<td>0.9 (0.3–2)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>8 (11)</td>
<td>21 (12.3)</td>
<td></td>
</tr>
<tr>
<td>Type of lesion,† n (%)</td>
<td>2.2 (1.2–4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>33 (44)</td>
<td>109 (62)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>33 (44)</td>
<td>50 (28)</td>
<td></td>
</tr>
<tr>
<td>Mechanism of ischemic stroke, n (%)</td>
<td>2.2 (1.1–4.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombotic</td>
<td>48 (69)</td>
<td>132 (78)</td>
<td></td>
</tr>
<tr>
<td>Embolic</td>
<td>13 (21)</td>
<td>26 (14)</td>
<td></td>
</tr>
</tbody>
</table>

*Left vs right (there were not significant differences between anterior, middle, and posterior territories or between left and right carotid vs vertebobasilar territories; data not presented).†P<0.001; values given as mean (range).

### Table 3. Demographic and Clinical Data of Demented and Nondemented Patients

<table>
<thead>
<tr>
<th>Location, n (%)</th>
<th>Demented (N=75)</th>
<th>Nondemented (N=176)</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD age, y†</td>
<td>76.9±13.6</td>
<td>65.4±9.3</td>
<td>...</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>49 (65.3)</td>
<td>68 (38.8)</td>
<td>1.6 (0.8–3.0)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td>...</td>
<td>...</td>
<td>1.2 (0.4–1.7)‡</td>
</tr>
<tr>
<td>Illiterate</td>
<td>28 (37.3)</td>
<td>40 (22.8)</td>
<td>...</td>
</tr>
<tr>
<td>Able to read and write</td>
<td>44 (56.8)</td>
<td>87 (49.7)</td>
<td>...</td>
</tr>
<tr>
<td>Below high school</td>
<td>3 (4)</td>
<td>31 (17.7)</td>
<td>...</td>
</tr>
<tr>
<td>High school</td>
<td>0</td>
<td>10 (5.7)</td>
<td>...</td>
</tr>
<tr>
<td>University</td>
<td>0</td>
<td>3 (1.7)</td>
<td>...</td>
</tr>
<tr>
<td>Concomitant illnesses†</td>
<td>3 (0–7)</td>
<td>2.3 (0–6)</td>
<td>...</td>
</tr>
<tr>
<td>Nephropathy, n (%)</td>
<td>13 (17.3)</td>
<td>11 (6.3)</td>
<td>3.6 (1.4–9.5)</td>
</tr>
<tr>
<td>Psychiatric disease, n (%)</td>
<td>16 (21)</td>
<td>13 (7)</td>
<td>4.4 (1.7–10.9)</td>
</tr>
</tbody>
</table>

*After adjusting for age. †P<0.001; values given as mean (range). ‡Illiterate vs the others.

### Table 4. Vascular Risk Factors in Demented and Nondemented Patients

<table>
<thead>
<tr>
<th>Vascular Risk Factors</th>
<th>Demented (N=75)</th>
<th>Nondemented (N=176)</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure, n (%)</td>
<td>49 (65.3)</td>
<td>101 (57.1)</td>
<td>1.3 (0.6–2.4)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>23 (30.6)</td>
<td>41 (23.4)</td>
<td>1.2 (0.6–2.5)</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>8 (10.6)</td>
<td>22 (12.5)</td>
<td>0.7 (0.3–1.8)</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>6 (8)</td>
<td>8 (4)</td>
<td>1.4 (0.4–6.4)</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>19 (25.3)</td>
<td>14 (8)</td>
<td>2.9 (1.2–6.7)</td>
</tr>
<tr>
<td>Mitral valve disease, n (%)</td>
<td>10 (13.3)</td>
<td>8 (4.6)</td>
<td>3.8 (1.2–12.5)</td>
</tr>
<tr>
<td>Aortic valve disease, n (%)</td>
<td>3 (4.3)</td>
<td>6 (4)</td>
<td>1.3 (0.2–6.2)</td>
</tr>
<tr>
<td>Transient ischemic attacks, n (%)</td>
<td>11 (14.6)</td>
<td>23 (13)</td>
<td>1.1 (0.4–2.6)</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>13 (17.3)</td>
<td>18 (10.2)</td>
<td>2.2 (0.9–5.2)</td>
</tr>
<tr>
<td>Aortic arch calcification, n (%)</td>
<td>34 (45.3)</td>
<td>34 (19.3)</td>
<td>1.9 (1.02–9.5)</td>
</tr>
<tr>
<td>Intermittent claudication, n (%)</td>
<td>5 (6.7)</td>
<td>15 (8.6)</td>
<td>0.8 (0.2–2.8)</td>
</tr>
<tr>
<td>Alcohol intake, n (%)</td>
<td>21 (28)</td>
<td>84 (48)</td>
<td>0.7 (0.3–1.4)</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>22 (29.3)</td>
<td>97 (55.1)</td>
<td>0.6 (0.3–1.1)</td>
</tr>
</tbody>
</table>

*Values are numbers (percentages) of patients with specific risk factors. †After adjusting for age.
TABLE 5. Functional, Cognitive, and Neurological Status of Demented and Nondemented Patients

<table>
<thead>
<tr>
<th></th>
<th>Demented (N=75)</th>
<th>Nondemented (N=176)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS-IQCODE †</td>
<td>62±12.4</td>
<td>53±3.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>87±20.7</td>
<td>98±5.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urinary incontinence, n (%)</td>
<td>23 (30.6)</td>
<td>17 (9.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>At admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian neurological scale</td>
<td>5.6±2.5</td>
<td>7.6±1.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SPMSQ ‡</td>
<td>10±3.5</td>
<td>16±3.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urinary incontinence, n (%)</td>
<td>56 (74.7)</td>
<td>27 (15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>At discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barthel Index</td>
<td>42±34.2</td>
<td>80±26.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Canadian neurological scale</td>
<td>6.5±2.4</td>
<td>8.5±1.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3 mo after stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPMSQ ‡</td>
<td>9.7±4.3</td>
<td>17.6±3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>47±33.8</td>
<td>88.7±21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SS-IQCODE †</td>
<td>77.8±8.4</td>
<td>60±5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are mean±SD, except for urinary incontinence.
*Student t test for contrast of means or χ² test for comparison of proportions.
†A modified scoring ranging from 0 to 20 was used.

Functional and cognitive status as measured by the IQCODE, the Barthel Index, and the SPMSQ was significantly worse in demented than in nondemented patients during admission, 3 months after the stroke, and also before the stroke (Table 5). The same trend was found in the neurological status assessed by the CNS during admission (Table 5).

In the hematologic and biochemical complementary studies, demented patients were found to have significantly lower hematocrit, serum cholesterol, triglyceride, protein, and albumin levels at admission as well as 3 months after the stroke, and serum glucose was significantly higher at admission (Table 6). There were no differences between groups in the remaining complementary data. The apoE and ACE genotypes did not differ between demented patients (apoE genotype 4/4, 0 cases; 3/4, 5 cases; 2/4, 0 cases; 3/3, 25 cases; 2/2, 2 cases; and 2/0, 0 cases; ACE genotype DD, 10 cases; DI, 16 cases; and II, 2 cases) and nondemented patients (apoE genotype 4/4, 1 case; 3/4, 19 cases; 2/4, 3 cases; 3/3, 82 cases; 3/2, 11 cases; and 2/2, 1 case [P=0.86]; ACE genotype DD, 29 cases; DI, 57 cases; and II, 17 cases [P=0.41]). This information was only available in 8 cases with dementia previous to stroke (apoE genotype 3/4, 1 case; 3/3, 7 cases).

The study of the CT scans did not show differences between groups in the frequency of hemorrhagic or ischemic lesions in their location in any vascular territory. All the remaining data listed in Methods did not show statistical differences between demented and nondemented patients in the univariate analyses.

Multivariate Analysis

The following independent variables were introduced in the logistic regression analyses: age, sex, antecedents of nephropathy, atrial fibrillation, mitral valve disease, stroke, seizures, psychiatric disease, urinary incontinence, previous mental decline recorded in the IQCODE, functional defects assessed by the Barthel Index, hematocrit, fasting blood glucose, serum cholesterol, triglyceride, and albumin levels and aortic arch calcification at admission, and the scores in the CNS and Barthel Index at discharge. The univariate analyses disclosed the same set of variables for the 5 models.

A logistic regression model identified the following independent prognostic factors of PSD in the whole sample (model I, n=231): age (OR 1.1 and 95% CI 1.03 to 1.2), nephropathy (OR 6.1 and 95% CI 1.5 to 24.3), atrial fibrillation (OR 4.4 and 95% CI 1.4 to 13.9), psychiatric disease (OR 3.7 and 95% CI 1.2 to 11.6), IQCODE score previous to the stroke (OR 1.2 and CI 1.1 to 1.4), and CNS score at discharge (OR 0.5 and CI 0.4 to 0.6) (Table 7).

When patients with previous dementia (model II, n=206), hemorrhagic stroke (model III, n=204), or both (model IV, n=183) were excluded and when only probable vascular dementia cases (model V, n=201) were introduced in the analyses, the same predicting factors were obtained (Table 7), except for psychiatric disease in the last model.

All these analyses were performed with and without cases who did not report to the Neurology Clinic and were followed up by phone. The results were the same in both cases.

Discussion

Previous reports from several research groups indicate that PSD is a frequent finding, ranging from 25%12 to 41%30 of cases. The proportion of stroke patients with PSD depends mainly on the age range, length of follow-up, and diagnostic criteria.9,31,32 Some studies involving PSD have been performed on nonprospective16,33 or nonconsecutive samples16,33–35; some others have excluded hemorrhagic6–8,10,13,16,33,36,37 or recurrent6,8,16,16 strokes; usually, the cognitive status before the stroke has not been considered.16,34,38

We recruited a series of consecutive, unselected, incident stroke cases who reported to a general secondary hospital in an urban area without other alternative specialized health care
TABLE 7. Predictors of Poststroke Dementia in Several Multiple Logistic Regression Models

<table>
<thead>
<tr>
<th></th>
<th>Model I (Total Group)</th>
<th>Model II (Excluding Previously Demented Cases)</th>
<th>Model III (Excluding Hemorrhagic Cases)</th>
<th>Model IV (Excluding Previously Demented and Hemorrhagic Cases)</th>
<th>Model V (Excluding Previously Demented and Possible Vascular Demented Cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases*</td>
<td>231/251</td>
<td>206/226</td>
<td>204/222</td>
<td>183/199</td>
<td>201/220</td>
</tr>
<tr>
<td>Age</td>
<td>1.1 (1.03–1.2)</td>
<td>1.1 (1.03–1.1)</td>
<td>1.1 (1.03–1.1)</td>
<td>1.1 (1.03–1.1)</td>
<td>1.1 (1.03–1.1)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4.4 (1.4–13.9)</td>
<td>4.4 (1.4–14.3)</td>
<td>4.9 (1.3–18)</td>
<td>6.1 (1.7–21.5)</td>
<td>3.5 (1.1–11.9)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>6.1 (1.5–24.3)</td>
<td>5.8 (1.4–23.1)</td>
<td>6.1 (1.7–20.1)</td>
<td>6.2 (1.3–28.8)</td>
<td>4.8 (1.1–23.1)</td>
</tr>
<tr>
<td>Psychiatric disease</td>
<td>3.7 (1.2–11.6)</td>
<td>3.6 (1.1–12.2)</td>
<td>3.5 (0.9–12.6)</td>
<td>3.9 (1.1–14.7)</td>
<td></td>
</tr>
<tr>
<td>SS-IQCODE†</td>
<td>1.2 (1.1–1.4)</td>
<td>1.1 (1.03–1.3)</td>
<td>1.2 (1.1–1.3)</td>
<td>1.1 (1.03–1.3)</td>
<td>1.2 (1.05–1.3)</td>
</tr>
<tr>
<td>CNS‡</td>
<td>0.5 (0.4–0.6)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.5 (0.4–0.6)</td>
</tr>
</tbody>
</table>

Values are ORs (with 95% CIs in parentheses).
*Cases without missing data introduced in the model/total number of cases in the group.
†Questionnaire on cognitive decline in the elderly assessing mental decline before stroke.
‡CNS at discharge.

PSD seems to be unrelated to stroke features, such as size (gross or small), location, and number of vascular lesions, in our cohort. The limited influence of well-established vascular risk factors on PSD is also remarkable. High blood pressure, diabetes, myocardial infarction, heart failure, aortic valve disease, transient ischemic attacks, current smoking, and intermittent claudication are not associated with PSD in our sample. Hypertension, diabetes, smoking, and myocardial infarction were found to predict PSD in some studies but not in others. Previous stroke has been more consistently found in PSD but in our cohort, it did not reach statistical significance.

Higher educational attainment has been found to be a protective factor for PSD; however, we cannot ascertain this effect in our series because the majority of patients were illiterate. In some series of ischemic strokes, left lesions were associated with PSD; although we found the same proportion of left lesions (47%), this finding is not confirmed in the present study, possibly because we included both ischemic and hemorrhagic cases and excluded few aphasic patients. The association between PSD and diabetes was described by Tatemichi et al and Censori et al. but it has not been confirmed in other studies or in the present study.

The correlates of dementia in logistic regression analyses were age, psychiatric disease, nephropathy, atrial fibrillation, cognitive function previous to the stroke (SS-IQCODE), and stroke severity (CNS). When those cases with hemorrhagic stroke, previous dementia, or mixed dementia were excluded, the correlates remained the same.

As in other studies, we found a relationship between age and dementia. Atrial fibrillation as a risk factor for PSD was reported by other authors. Speculatively, regularization of cardiac rhythm and the use of oral anticoagulants in patients with atrial fibrillation might reduce the risk of PSD, but this hypothesis is a subject for a randomized trial.

Depressive disorders, including both major depression and other less severe but nonetheless clinically significant depressions, are common comorbidities, components, or complications of dementia. Depression has been considered a risk factor for the expression of Alzheimer's disease in later life.

facilities. The short distance to this single hospital in all the catchment area and the absence of financial restrictions for health care in Spain preclude referral bias in this sample, which can be considered rather representative of our population of stroke cases. To avoid further bias, all strokes listed in our registry were included in the cohort, without excluding hemorrhagic or recurrent stroke; we excluded only transient ischemic attacks, subarachnoid hemorrhage, and nonspontaneous causes of stroke. We also carefully examined the existence of previous dementia, and we used the DSM-IV criteria of dementia as the more conservative. Moreover, the main cause of attrition in our cohort was death, and the small group of patients lost to follow-up did not differ from the followed up cohort (251 cases, 95% of survivors).

Our data confirm that almost a third (30%) of unselected patients become demented 3 months after stroke; most of them demonstrate a severe stage. The frequency of dementia in ischemic (30.1%) and hemorrhagic (27.5%) cases is very similar and very close to the frequency reported by Tatemichi et al (26.3%) and Pohjasvaara et al (31.8%), who also followed up their samples of ischemic stroke patients for 3 months.

Previous and present studies agree on the evidence that PSD is not solely due to cerebrovascular lesions. We found that almost 30% of PSD cases (22 of 75) were considered “possible vascular dementia” because they had other coexistent illnesses affecting the brain. Moreover, before the stroke, a sizable proportion of patients with PSD may in fact have dementia that is due to degenerative as well as vascular conditions. In our series, preexisting dementia was found in 10% of the stroke patients (25 of 251) who were followed up for 3 months after stroke and in 15% (49 of 327) of the total sample. Our results are similar to those previously reported and our figures of prestroke dementia are very close to those of Tatemichi et al (9.6%), the Helsinki Stroke Aging Memory Study Cohort (9.2%), Inzitari et al (11.5%), and Hénon et al (16.3%). In the last study, the retrospective diagnosis of dementia was based on the same standardized questionnaire that we used, and we agree with these authors that preexisting dementia contributes (to an important extent) to the high risk of PSD.

The correlates of dementia in logistic regression analyses were age, psychiatric disease, nephropathy, atrial fibrillation, cognitive function previous to the stroke (SS-IQCODE), and stroke severity (CNS). When those cases with hemorrhagic stroke, previous dementia, or mixed dementia were excluded, the correlates remained the same.

As in other studies, we found a relationship between age and dementia. Atrial fibrillation as a risk factor for PSD was reported by other authors. Speculatively, regularization of cardiac rhythm and the use of oral anticoagulants in patients with atrial fibrillation might reduce the risk of PSD, but this hypothesis is a subject for a randomized trial.

Depressive disorders, including both major depression and other less severe but nonetheless clinically significant depressions, are common comorbidities, components, or complications of dementia. Depression has been considered a risk factor for the expression of Alzheimer’s disease in later life.

Values are ORs (with 95% CIs in parentheses).
*Cases without missing data introduced in the model/total number of cases in the group.
†Questionnaire on cognitive decline in the elderly assessing mental decline before stroke.
‡CNS at discharge.
and may be part of its preclinical phase.\textsuperscript{44} We found a relationship between the antecedent of psychiatric disease and the risk of PSD, but when prestroke demented patients were excluded, the strength of this association decreases, perhaps because some of these cases have a degenerative origin.

From our 24 patients with nephropathy, 13 (54\%) were demented after stroke. They had a 3-fold risk of PSD, probably because most of them had an extensive arteriolar-sclerosis affecting multiple organs.\textsuperscript{45}

Cognitive decline previous to the stroke was also a predictor of PSD. In the study of Inzitari et al.,\textsuperscript{7} the prestroke level of handicap, assessed by the Rankin Scale,\textsuperscript{46} was an independent determinant of PSD. Two aspects of prestroke disability were measured in our series, and previous cognitive decline according to the Spanish version of the IQCODE\textsuperscript{20} but not previous functional state according to Barthel Index\textsuperscript{19} was found to be an independent predictor of dementia even when patients with prestroke dementia were excluded. The cognitive status before the stroke has been assessed in only a few studies, such as those of Hénon et al.,\textsuperscript{14} who examined prestroke dementia, and Pohjasvaara et al.,\textsuperscript{15} who examined prestroke cognitive decline. They found a significant effect of cognitive decline previous to the stroke on the incidence of dementia in all poststroke cases. The present study demonstrates that mild cognitive decline is also an independent risk factor of dementia after stroke, because previously demented cases have been prospectively diagnosed at the acute stage of stroke and excluded from the analyses. This is an important finding because these cases can be identified in primary care facilities among patients with vascular risk factors, and preventive measures can be applied.

It is evident that PSD is frequent (occurring in \textasciitilde 30\% of cases) and is not determined by a single factor; several factors combine to exceed the critical threshold for normal cognition. PSD is not a nosological entity but a heuristic concept that is useful in guiding research in the prevention and management of vascular dementia. The heterogeneity of PSD may be the cause of the disparity of risk factors in different series. We have identified some already described risk factors for PSD (age, atrial fibrillation, and severity of stroke) and others not previously described (nephropathy, previous depression, and previous cognitive decline). Some of these factors can be preventable, especially if there is screening for mild cognitive decline.

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