Cognitive Functioning after Stroke: A One-Year Follow-Up Study

Sascha M.C. Rasquin, Jan Lodder, Rudolf W.H.M. Ponds, Ieke Winkens, Jelle Jolles, Frans R.J. Verhey

Departments of Psychiatry and Neuropsychology and Neurology, University Hospital Maastricht, Maastricht, The Netherlands

Key Words
Dementia, post stroke • MCI, post stroke • Cognitive functioning, post stroke

Abstract
Cognitive disorders after stroke are one of the main causes of disability in daily activities. The main aim of this study was to investigate the frequency of post-stroke dementia, post-stroke mild cognitive impairment (MCI) and post-stroke amnestic MCI at different times after first-ever stroke; 196 patients were included in the study. In addition, cognitive disorders and their clinical course were studied. Frequency of post-stroke dementia was about 10% at all evaluation times; most patients had post-stroke MCI. Of the cognitive functions investigated, mental speed and calculation were most frequently affected. Performance on almost all cognitive tests was improved 6 and 12 months after stroke. Thus, while the frequency of post-stroke dementia is low, the frequency of post-stroke MCI is high, but improvement of cognitive function is possible.

Introduction
Stroke can have dramatic consequences for patients and their environment. Besides physical handicaps, cognitive disorders can also contribute to disability in everyday life [1]. Most studies of cognitive disorders after stroke report vascular dementia (VaD) as the main outcome [2–4]; 8–26% of stroke patients develop a dementia syndrome within 12 months [5–7]. The variation in prevalence rates is attributable to different patient populations and to differences in diagnostic criteria [8]. One of the problems with the current criteria (DSM-IV, NINDS-AIREN, ADDTC, and ICD-10) for VaD is that they are largely based on the definition of Alzheimer-type dementia. For instance, all criteria (except the ADDTC) require a memory disorder for the diagnosis of dementia; however, stroke may primarily affect other cognitive functions [9]. For example, stroke affects the performance on tasks involving mental speed [10, 11] even more than memory performance [12]. Thus when studying the cognitive consequences of stroke, it is important to investigate a broad range of cognitive functions and not solely dementia.

To emphasize this broader approach, Bowler and Hachinski [13] introduced the concept of vascular cognitive impairment (VCI). VCI describes a whole range of cognitive impairments from the lowest level of cognitive impairment to dementia caused by vascular brain damage.
Few data exist about the prevalence of the milder forms of cognitive impairment, also called vascular cognitive impairment no dementia (CIND) or vascular mild cognitive impairment (MCI) [14–18]. The concept of MCI originally focused on memory disorders, whereas CIND is not limited to one cognitive domain.

The purpose of this longitudinal study was to investigate the prevalence of dementia and other cognitive disorders at different times after stroke and changes in cognitive functioning with time.

Material and Methods

Study Population
Participants of this study took part in a larger study called ‘Cognitive Disorders after Stroke’ (CODAS). CODAS is a longitudinal, prospective clinical study aimed at investigating cognitive functioning, risk factors for cognitive impairment and the course of cognitive functioning after stroke [12]. Patients with a first-ever cerebral stroke not located in the brainstem or cerebellum were assessed clinically and neuropsychologically at 1, 6, 12 and 24 months after stroke. For this report the data of the first three assessments were available.

Patients who were admitted to the hospital or who visited the outpatient clinic of the Academic Hospital Maastricht between January 2000 and August 2001 because of a stroke were asked to participate in this study. An experienced neurologist diagnosed stroke based on clinical findings and data, supported by a CT scan evaluated by an experienced radiologist.

Strokes were stratified in three categories: (1) ischaemic or haemorrhagic stroke, side of the stroke, stroke on clinical findings and data, supported by a CT scan evaluated by the latter two clinicians. An experienced neurologist diagnosed stroke based on clinical findings and data, supported by a CT scan evaluated by an experienced radiologist.

Inclusion criteria were: first-ever cerebral stroke, age 40 years, fluency in Dutch, no other neurological or psychiatric disorders, and a Mini Mental State Examination (MMSE) score ≥ 15 (to exclude patients with severe cortical deficits and retain a group of patients who could be tested reliably).

One hundred and ninety-six patients were included (mean age 68.5 years; 107 men and 89 women). Cognitive functioning was compared with that of a control group taken from the Maastricht Aging Study (MAAS), a study of healthy older volunteers from the region of South Limburg which investigates the features predisposing to normal cognitive aging. Norm tables are stratified according to age, sex, and level of education [20]. In the MAAS project, healthy subjects were recruited from the registration network of general practitioners. The population is representative of the Limburg and Dutch populations with respect to demographic characteristics (age, gender, educational level and type of health care) [20].

Diagnosis of Post-Stroke Cognitive Disorders

Post-Stroke Dementia. Dementia was diagnosed independently by an experienced neuropsychiatrist and a neuropsychologist according to DSM-IV criteria. Both clinicians are experts in the field of dementia. The diagnosis was based on all available data, including information about medical history, structured interview with an informant, clinical observation and test performances. Interference with daily activities due to cognitive deficits was assessed by the Interview for Deterioration in Daily Life in Dementia (IDDD) [21]. The diagnosis of VaD was based on NINDS-AIREN criteria [22]. When there was a disagreement between the two clinicians, the final diagnosis was negative; this was the case in 5 patients. Agreement between the two clinicians was excellent ($k = 0.88; p = 0.00$).

In order to determine whether dementia was present before the stroke, a proxy of the patient was asked whether the patient met, in retrospect, each of the criteria for dementia of the DSM-IV (i.e. whether any signs of memory disorder, aphasia, apraxia, agnosia or executive dysfunction existed before the stroke, and whether these cognitive impairments interfered with daily activities).

Post-Stroke MCI. Post-stroke MCI was diagnosed when patients fulfilled the following criteria: (1) cognitive disorder in at least 1 of the following cognitive functions: memory, language, orientation, mental speed, attention, praxis, executive functioning, calculation and visuospatial functioning; (2) no interference of the cognitive disorders with daily activities as assessed by the IDDD, and (3) no dementia. These criteria are largely based on the criteria of MCI [23].

Post-Stroke Amnestic MCI. Patients with the following features were classified as post-stroke amnestic MCI: memory disorder only; the memory disorder did not interfere with daily activities as assessed by the IDDD, and no dementia. These criteria are based on the recent adapted criteria for MCI [23].

Assessment of Neuropsychological Functioning

CAMCOG. This is the cognitive part of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX), a standardized instrument for the diagnosis and gradation of dementia in the elderly. The CAMCOG can be subdivided into 10 subscales: orientation, language expression, language understanding, memory (long and short term), attention, calculation, praxis, abstract thinking and abstract perception. The Dutch version of the CAMCOG was used [24], which has been shown to be well accepted and sensitive for the detection of cognitive disorders in stroke patients [25].

Auditory Verbal Learning Test (AVLT). This test is used to measure episodic memory. The variable of interest is the number of words recalled after each trial and after a 20-min delay [26]. To minimise the influence of a learning effect, we used parallel versions of the AVLT.

Concept-Shifting Task (CST). This test is derived from the Trail-Making Test and is used to measure the ease of shifting between two concepts. The variable of interest is the time needed to complete each of the four subtests [27].

Stroop Colour Word Test. The Stroop test is a test of selective attention and interference susceptibility. The variable of interest is the time needed to complete each of the four subtests [27].

Calculation. This test is part of the Groninger Intelligence Test (GIT) and involves the correct completion of as many sums as possible in 1 min. It measures arithmetic skills [29].

Mental Rotation. This mental rotation test is also part of the GIT. It requires the subject to indicate which two-dimensional shapes from a larger set are needed to exactly fill up a given space on the test page. This test measures visuospatial abilities [29]. Normative data were available for all psychometric tests used in this study, except for the CAMCOG.

Cognitive Domains

Nine cognitive domains were formed based on the neuropsychological test battery: memory, mental speed, executive functioning, verbal fluency, visuospatial functioning, language expression, language understanding, attention and interference susceptibility. The variable of interest is the number of words recalled after each trial and after a 20-min delay [26]. To minimise the influence of a learning effect, we used parallel versions of the AVLT.

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orientation, attention, language, praxis, visuospatial abilities, and calculation. These cognitive domains (except for mental speed) are based on the cognitive domains mentioned in the NINDS-AIREN criteria for VaD.

Three cognitive functions were selected based on data in the literature: memory, mental speed, and executive functioning [30]. Compound scores were derived for these three cognitive functions. Patient scores were converted to standardized scores with the following formula: \( Z = (\text{patient score} - \text{norm score})/\text{standard deviation} \) from the norm group. Memory was calculated from the mean of the Z scores of the total score after five trails and the recall score after 20 min. For mental speed the mean of the Z scores of the CST I/II/0 and STROOP 1 was used. The mean of the Z interference scores from the Stroop and CST was used to define the cognitive domain ‘executive functioning’. The interference scores of the Stroop and CST were defined by the following formula: part III = mean (part I + part II). A score lower than the 10th percentile (a cut-off commonly used in clinical practice) compared with the norm group defined a cognitive disorder. To define improvement or deterioration on cognitive tests, the Reliable Change Index (RCI) was used [31]. The RCI can be used to determine whether a change observed in a subject is clinically significant. The amount of change between two measurement times is divided by the standard measurement of the difference (this can be conceived as the random error in the sample survey) [32]. A score exceeding the range of –1.96 to 1.96 reflects a significant change [31].

### Statistical Analyses

Statistical analyses were performed with the statistical package for Social Sciences, version 10. Descriptive statistics were used to define the number of patients with one of the cognitive disorders or cognitive impairments. The number of patients that improved or deteriorated was also analyzed with descriptive statistics. Differences between groups at baseline with regard to CT variables were calculated if there was at least one other test available for the same cognitive function, how to impute the data. Data imputation was performed if there was at least one other test available for the same cognitive domain and if the missing test had been administered during at least one of the three assessments evaluated here. For instance, at baseline (1 month) CST and Stroop data were missing in 22.4 and 23.4% of the cases, respectively. In 28.9 and 16.9% of these cases imputation took place; in 12.8% of the patients AVLT data were missing, and in 8.0% the AVLT data were imputed. The rate of missing data at the 6-month assessment was somewhat lower (12.2% for the CST I–III, and 17.4% for the Stroop 1–3), and imputation was performed in 9.5 and 16.7%, respectively. At 12 months after stroke data were comparable to imputation at 6 months after stroke.

### Results

During the inclusion period, 592 stroke patients were admitted to the hospital. Of these, 196 were eligible for the CODAS study, 80 died within 1 month after stroke and another 316 were excluded (89 were not first-ever strokes, 57 had a stroke located in the brainstem or cerebellum, 46 had MMSE scores < 15, 34 had severe aphasia, 20 had comorbid neurological or psychiatric disorders, 6 were in a coma, 5 were non-native Dutch speakers, 9 were younger than 40 years, 9 lived too far from the hospital, 6 were admitted too long after their stroke and 35 refused to participate). Six months after stroke, 172 patients (87.4%) could be tested and 159 (80.4%) were assessed at 12 months. Main reasons for drop-out were refusal or death. Patients who dropped out did not differ from patients who remained in the study in terms of baseline MMSE (6 months: \( t = 0.29, p = 0.78 \); 12 months: \( t = -1.59, p = 0.11 \)), age (6 months: \( t = 1.1, p = 0.26 \); 12 months: \( t = 1.1, p = 0.27 \)), education (6 months: \( \chi^2 = 2.4, p = 0.17 \); 12 months: \( \chi^2 = 1.4, p = 0.23 \)) or sex (6 months: \( \chi^2 = 2.9, p = 0.08 \); 12 months: \( \chi^2 = 0.09, p = 0.77 \)).

Table 2 describes the prevalence rates of post-stroke dementia, post-stroke MCI and post-stroke amnestic MCI.

Two patients appeared to have been demented before stroke, they were excluded from the analyses because we were interested in the prevalence of dementia after stroke. Twenty-four patients (12.2%) developed dementia within 1 year after stroke. Of these, 15 (62.5%) had evidence of

### Table 1. Patient characteristics at baseline, mean MMSE scores for the 3 measurements and stroke-related characteristics

<table>
<thead>
<tr>
<th>Baseline data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>196</td>
</tr>
<tr>
<td><strong>Education received, low/high</strong></td>
<td>110/86</td>
</tr>
<tr>
<td><strong>Sex, M/F</strong></td>
<td>107/89</td>
</tr>
<tr>
<td><strong>Age, mean (SD), years</strong></td>
<td>68.4 (12.5)</td>
</tr>
<tr>
<td><strong>MMSE-1 score, mean (SD)</strong></td>
<td>25.1 (5.4)</td>
</tr>
<tr>
<td><strong>MMSE-2 score, mean (SD)</strong></td>
<td>25.1 (5.5)</td>
</tr>
<tr>
<td><strong>MMSE-3 score, mean (SD)</strong></td>
<td>25.2 (5.6)</td>
</tr>
<tr>
<td><strong>Territorial/lacunar/haemorrhagic, % (n = 194)</strong></td>
<td>39.2/52.6/8.2</td>
</tr>
<tr>
<td><strong>Side: left/right/both, % (n = 190)</strong></td>
<td>41.6/56.8/1.6</td>
</tr>
<tr>
<td><strong>White matter lesions present, % (n = 181)</strong></td>
<td>24.9</td>
</tr>
<tr>
<td><strong>Silent infarcts present, % (n = 179)</strong></td>
<td>35.2</td>
</tr>
<tr>
<td><strong>Atrophy present, % (n = 187)</strong></td>
<td>70.1</td>
</tr>
</tbody>
</table>

SD = Standard deviation; MMSE-1, -2, -3: taken at 1, 6 and 12 months.

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Table 2. Number of patients and prevalence rates (percentages) of VaD, post-stroke MCI and post-stroke amnestic MCI

<table>
<thead>
<tr>
<th>Months</th>
<th>1</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cognitive disorders</td>
<td>34 (17.5)</td>
<td>36 (18.6)</td>
<td>40 (20.6)</td>
</tr>
<tr>
<td>VaD</td>
<td>21 (10.8)</td>
<td>15 (7.7)</td>
<td>15 (7.7)</td>
</tr>
<tr>
<td>Post-stroke MCI</td>
<td>138 (71.1)</td>
<td>119 (61.3)</td>
<td>100 (51.5)</td>
</tr>
<tr>
<td>Post-stroke amnestic MCI</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>2 (1.0)</td>
</tr>
</tbody>
</table>

Table 3. Cognitive functioning at 1, 6 and 12 months: percentages of people with (w) or without (w/o) cognitive impairments

<table>
<thead>
<tr>
<th>Months</th>
<th>1</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>w/o</td>
<td>w</td>
<td>w/o</td>
<td>w</td>
</tr>
<tr>
<td>CAMCOG</td>
<td>55.7</td>
<td>44.3</td>
<td>66.5</td>
</tr>
<tr>
<td>Memory</td>
<td>75.6</td>
<td>24.4</td>
<td>83.4</td>
</tr>
<tr>
<td>Speed</td>
<td>39.8</td>
<td>60.2</td>
<td>46.4</td>
</tr>
<tr>
<td>Executive</td>
<td>67.9</td>
<td>32.1</td>
<td>75.7</td>
</tr>
<tr>
<td>Orientation</td>
<td>89.7</td>
<td>10.3</td>
<td>92.9</td>
</tr>
<tr>
<td>Attention</td>
<td>68.0</td>
<td>32.0</td>
<td>65.5</td>
</tr>
<tr>
<td>Language</td>
<td>64.9</td>
<td>35.1</td>
<td>71.8</td>
</tr>
<tr>
<td>Praxis</td>
<td>68.6</td>
<td>31.4</td>
<td>77.1</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>63.5</td>
<td>36.5</td>
<td>77.2</td>
</tr>
<tr>
<td>Calculation</td>
<td>47.9</td>
<td>52.1</td>
<td>57.4</td>
</tr>
</tbody>
</table>

CVD on CT scan and developed dementia within 3 months after stroke, thus fulfilling the criteria of probable VaD. The other 9 patients were diagnosed as possible VaD, since 6 patients (25.0%) had a negative scan and 3 (12.5%) developed dementia after 3 months. Seven patients were demented at baseline, but were no longer considered to be demented later on in the study. Only 3 patients who were not demented at 1 or 6 months became demented later on. Most patients were classified as having post-stroke MCI, whereas very few (0.5, 0 and 1.3% for each measurement time) were classified as having post-stroke amnestic MCI. During the one-year follow-up, 30 patients deteriorated to a more severe cognitive deficit compared to an earlier measurement period. Patients who deteriorated were older (t = 2.7, p = 0.01) and had lower baseline MMSE scores (t = –2.6, p = 0.01) than patients who did not deteriorate, but there was no difference in stroke-related variables, education and sex.

Patients with dementia at baseline had more often territorial infarcts, white matter lesions, silent infarcts and atrophy on CT scan compared with patients with post-stroke MCI and patients without cognitive disorders, but these differences were not significant. Patients with dementia had significantly more often a stroke in the left hemisphere compared with patients without any cognitive disorder, while patients with post-stroke MCI were intermediate (52.4, 32.2 and 40.9%, respectively). Because of the low number of patients with amnestic MCI, this group was omitted from these analyses.

Table 3 presents the number of patients with impairment of one or more cognitive functions at each measurement time. Mental speed and calculation were the cognitive functions that were most often disturbed.

Table 4 shows the changes in performance on the cognitive tests. In the period 1–6 months, more people showed performance improvement than deterioration. This was also the case for the period 6–12 months, except for the CST I–III, calculation and mental rotation tasks, in which more patients showed performance deterioration than performance improvement. In both comparisons (6 vs. 1 month and 12 vs. 6 months), the performance of most patients did not change.

Discussion

Few patients would appear to become demented after stroke (12%), although other studies have reported higher rates of dementia prevalence (18–26%) 3 months after stroke [6, 34, 35]. The lower prevalence rate in our study could be due to the fact that we excluded people who had a second stroke or an MMSE <15 (7.7% patients, n = 46). The other studies included patients with severe cognitive deficits other than aphasia [6, 34, 35]. If we had not excluded the patients with severe cognitive deficits at baseline and if we assume that these patients would have been demented, the proportion of patients with post-stroke dementia would be 27.8%, which is similar to that of other studies [6, 34, 35]. In our sample, the percentage of patients with pre-stroke dementia is low compared to others who found a prevalence of 16.3% of pre-stroke dementia [36, 37]. This is probably also related to the exclusion of patients with an MMSE score <15.

Most research into cognitive disorders after stroke is focused on the development of dementia, but other, less severe cognitive disorders could also be present. These other cognitive disorders may be mild in an early stage but may carry long-term risks of dementia and as such are
clinically relevant and should be investigated. The term ‘MCI’ is often used to describe this transitional phase and is mostly used to describe the development of Alzheimer’s disease. The traditional term MCI, which focused on memory disorders only, has been replaced by other concepts such as ‘amnestic MCI’ [23]. We found only 2 patients with post-stroke amnestic MCI, and thus it is doubtful whether this concept is applicable to a pre-dementia stage after stroke. The traditional concept of MCI has been further adapted to include disturbances of cognitive functions other than memory [23], and this new concept would appear more appropriate to describe the transitional phase into dementia development, especially in post-stroke dementia. In our study almost 65% of the patients had multiple cognitive deficits, but not so severe as to warrant a diagnosis of dementia. Thus cognitive deficits after stroke (including subtle deficits) are frequent, and in fact more frequent than may be thought in daily practice. As these cognitive deficits may cause impairments in daily activities to some extent, this figure may point towards a problem hidden so far [1].

The patients investigated had relatively few memory disturbances. Mental speed and calculation were the most frequently disturbed cognitive functions, which has also been found by other researchers [11, 38, 39]. These results suggest that in investigations of the early stage of VaD the emphasis should not be solely on memory but should include other cognitive disorders.

The prognosis of dementia in our study was not always unfavourable; one third of the patients who were demented at baseline were no longer considered to be demented later on in the study, most (5/ 7) because of the fact that they no longer fulfilled the criterion of interference of daily life activities. The patients also improved – or at least did not deteriorate – on most neuropsychological tests. This has consequences for the way patients are informed directly after stroke. The prognosis regarding the development of cognitive disorders after stroke is in general favourable and recovery is possible. Desmond et al. [40] also found improvement in 12.5% of his stroke patients 1 year after stroke. Schmidt et al. [41] found that 24% of patients with a first-ever cerebral stroke had an improved performance 6 months after stroke. Ballard et al. [42] found that even 50% of the patients had improved 15 months after stroke, with improvement defined as a 2-point increase on the MMSE. The influence of treatments such as cognitive rehabilitation, blood pressure regulation or cholesterol regulation on improvement is not known. However, it should be remembered that the condition of some patients deteriorated or that they developed cognitive disorders and did not show improvement, which could be the consequence of increasing brain damage due to silent infarcts [43]. Patients who are older and had a lower baseline MMSE were at greater risk of deterioration. Stroke-related factors were not related to decline.

One shortcoming of our study is that the diagnosis of dementia was not based on direct clinical contact with the patient. However, all data necessary for the diagnosis of dementia were available, and information was collected in a structured and highly standardized approach, including informant’s reports on daily functioning, clinical observation by trained research psychologists, and neuropsychological testing. A second point to address is that patients were tested 3 times, which could have led to a learning effect. Although this effect could not be ruled out,
it is of minimal consequence for the Stroop after the second administration and this also holds for the CST. Moreover, in the last part of the CST there seems to be no learning effect, and the AVLT parallel versions largely prevent a learning effect [44].

One advantage of our study is that we had a representative patient population in which the patients were tested neuropsychologically almost directly after their stroke, for the first time at 1 month. Most studies investigate cognitive performance 3 months after stroke [6, 38, 45]. If cognitive performance is tested later than that, damage can be so severe that it renders treatment ineffective.

In conclusion, few patients become demented after stroke, and most cognitive disturbances are in the field of mental speed and calculation. While improvement is possible, some patients will experience no improvement or might even deteriorate. Future research features should investigate aspects that influence the course of cognitive disorders after stroke. Research that is not restricted to dementia after stroke but encompasses the whole range of cognitive disorders can serve as a starting point for treatment and rehabilitation.

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