PAPER

Demographic and CT scan features related to cognitive impairment in the first year after stroke

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J Neurol Neurosurg Psychiatry 2004;**75**:1562–1567. doi: 10.1136/jnnp.2003.024190

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Received 23 July 2003
In revised form 23 January 2004
Accepted 23 January 2004

Objective: Little is known about the relation between stroke related features and cognitive performance over time when stroke patients with dementia or less severe cognitive disorders are considered separately. We aimed to study the features (computed tomography (CT) scan and demographic) that could be related to vascular cognitive impairment one, six, and 12 months after stroke.

Methods: A total of 176 patients with a first-ever brain infarct, a Mini Mental State Examination score ⩾15, age older than 40 years, and without pre-stroke dementia and other neurological or psychiatric disorders participated in this study. The following CT scan features were recorded: side of infarct, lacunar or territorial infarct, white matter lesions, silent infarcts, and brain atrophy. The demographic features studied were: age, level of education, and sex. Univariate and multivariate logistic regression analyses were performed to compare the three groups of patients (patients with dementia, patients with vascular cognitive impairment (VCI), and patients with vascular mild cognitive impairment (MCI)) with patients without cognitive disorders.

Results: At one month none of the variables were predictors of dementia; at six months older age (odds ratio (OR) 9.4), low education (OR 14.7), and territorial infarct (OR 10.6) predicted dementia; and at 12 months low education (OR 8.7) and pre-stroke cerebrovascular damage (OR 7.4) predicted dementia. Predictors of VCI were low education (OR 3.4) and territorial infarct (OR 2.4) at one month post stroke; older age (OR 4.3) and low education (OR 4.1) at six months; and older age (OR 3.5) at 12 months. Predictors of vascular MCI were low education (OR 4.96) and territorial infarct (OR 3.58) at one month; and older age and lower education at six months (OR 3.4 and 3.7, respectively) and at 12 months (OR 3.5 and 2.28, respectively).

Conclusions: Territorial infarct, older age, and low educational level are predictors of cognitive disorders after stroke.

The risk of dementia and other cognitive disorders increases after stroke. Stroke contributes to the development of cognitive disorders in nearly 20% of elderly patients.[1 2] Stroke related features such as multiple strokes, white matter lesions, left hemisphere infarct location, atrophy, and volume of infarcted tissue are associated with an increased risk of post-stroke dementia.[3–11] Age and level of education have also been reported as risk factors for vascular dementia (VaD).[7–9 12] Traditionally, patients with VaD have been compared with non-demented stroke patients to detect associations between stroke related factors and cognitive disorders (usually dementia). As such cognitive disorders less severe than dementia were not considered. However, milder cognitive disorders are more likely to occur after stroke than VaD.[13–17] These milder deficits, also called vascular mild cognitive impairment (MCI) or vascular cognitive impairment no dementia (CIND), may be barely perceptible in an early stage but may carry the risk of progression to more severe loss of cognitive functions.[18–20] If vascular MCI is a transition phase in the development of dementia it is important to identify the specific risk factors for this to attempt to prevent the progressive decline in cognitive function.[21 22] The few studies that investigated risk factors for cognitive decline in patients with either vascular MCI or VaD found older age, educational level, volume of infarcted tissue, and left hemispheric infarct location to be associated with cognitive impairment after stroke.[17 23–26] However, these studies did not differentiate between patients with dementia and patients with less severe cognitive disorders. Consequently, mechanisms related to post-stroke cognitive disorders without dementia have not been identified.

In the present study, we distinguished between patients with dementia and those with cognitive disorders without dementia (vascular MCI). Since the subgroups of patients were defined on the basis of their cognitive performance, the subgroups were homogeneous and generalisations about risk factors for vascular cognitive impairment could be made for these groups. Because little is known about the influence of stroke related risk factors on the development of cognitive impairment over time, we also monitored the cognitive abilities of our patient sample over one year.

Our aim was to identify post-stroke predictors (stroke related and demographic) of VCI (with or without dementia) at 1, 6, and 12 months after stroke, with special emphasis on brain abnormalities as visualised by computed tomography (CT).

PATIENTS AND METHODS

Patient selection

The Maastricht CODAS (COgnitive Disorders After Stroke) project is a prospective, observational study investigating the development of cognitive impairment after stroke, and identification of factors related to these disorders.

The study includes patients with a first-ever cerebral infarct who are older than 40 years (to exclude atypical stroke), have adequate post-stroke fluency in Dutch, and who have an initial Mini Mental State Examination (MMSE) ⩾15

Abbreviations: CODAS, COgnitive Disorders After Stroke; CI, confidence interval; CT, computed tomography; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; OR, odds ratio; VaD, vascular dementia; VCI, vascular cognitive impairment

(to ensure neuropsychological testing is possible). Exclusion criteria are severe aphasia and other neurological or major psychiatric disorders, which could lead to cognitive impairment other than the qualifying event. For this report patients with pre-stroke dementia were also excluded.

Consecutive stroke patients admitted to the University Hospital Maastricht or those who visited the outpatient neurological clinic between January 2000 and July 2001 participated in this study. During the inclusion period, 592 patients came to the hospital with a stroke. Of these 396 were excluded (89 were not first-ever strokes, 80 died within one month after stroke, 57 had a stroke located in the brainstem or cerebellum, 46 had MMSE <15, 35 refused to participate, 34 had severe aphasia, 20 had other neurological or psychiatric disorders, 9 were younger than 40 years, 9 lived too far from the hospital, 6 were admitted too long after their stroke, 6 were in a coma, and 5 were not native Dutch speaking). A total of 196 patients were eligible for the CODAS study. Of these 18 had a haemorrhagic stroke and two patients had dementia before stroke and were consequently excluded.

Stroke was diagnosed by an experienced neurologist according to standardised, well accepted criteria described elsewhere.[27] All patients had at least one brain CT scan. In most patients (n = 93, 52.9%), CT was performed at admission or one day later (median 1 day, range 0–150 days). If a patient had a second scan on which lesions were more clearly seen, this was used.

Patient data were entered into the Maastricht Stroke Register (MSR), a prospective databank containing clinical information of all stroke patients treated in the University Hospital Maastricht.[27] The data included patient's age (high: 70 years and older, and low: younger than 70 years, based on the median split), sex, and level of education (low: primary education and vocational education, high: all other educational levels). All patients were tested neuropsychologically within one month of stroke (mean (SD) 1.07 (0.3) months), and again at six months (mean 6.06 (0.41)) and 12 months (mean 12.08 (0.36)). CT scanning was not repeated at follow up.

To define whether patients had a cognitive disorder, they were compared with a control group from the MAastricht Aging Study (MAAS).[28] This population based study focuses on determinants of normal cognitive ageing and covers the full adult life-span of initially healthy individuals. Normative data from this study were stratified according to age, sex, and educational level. Impairment was defined as a score below the 10th percentile of the control group from MAAS; this cut-off is in line with clinical practice.

Computed tomography

The following features were recorded from the CT scan: side of the symptomatic infarct (left or right hemisphere); stroke type (lacunar or territorial infarct); presence of white matter lesions; presence of silent infarcts; and brain atrophy (for definitions see de Jong *et al*[27]). White matter lesions were defined as focal or diffuse hypodensities in the periventricular or deep white matter, not involving the cortex, with ill defined margins differentiating them from infarction.[29] The presence of white matter lesions around frontal or occipital ventricular horns or in the centrum semi ovale was rated separately. No effort was made to quantify the degree of white matter lesion density in these different sites, as this might be influenced by the tuning of the scanning and a certain degree of variability in the procedure of making hard copies of the scans. Silent brain infarction was defined as a low density area on the CT scan, compatible with infarction but without a history of stroke (as noted from the patient's history, from the family, or any other accessible information). Also, the symptoms of the stroke at entry into the study had to be anatomically incompatible with such silent infarcts. Old infarcts can usually be distinguished from new ones because they are more hypodense, and there may be signs of surrounding tissue loss such as retraction of brain structures towards the infarct. The degree of atrophy was scored in a semiquantitative way (none, mild, moderate, and severe), according to the criteria of Leys *et al*.[30] In short, CT scans of four patients were selected by three experts during a consensus meeting as example scans for the four categories: no, mild, moderate, or severe brain atrophy. The CT scans of the study patients were graded into one of these categories by visual comparison with the example scans. Silent infarcts or white matter lesions, or both were defined as ''pre-stroke cerebrovascular damage''. Two neurologists examined the CT scans independently. They were unaware of the neurological signs and the neuropsychological data. In case of a difference, consensus was reached by discussion. Interrater agreement (consensus reached by discussion was left out) of the classification of patients by stroke features on CT scan was excellent, with $\kappa = 0.88$ for symptomatic side, 0.85 for type of stroke, 0.60 for white matter, 0.79 for silent infarcts, and 0.69 for atrophy.

Patient groups

Cognitive functioning was assessed using a neuropsychological test battery described elsewhere.[13] Memory, mental speed, interference susceptibility, orientation, language, praxis, and abstract thinking were assessed based on the criteria of Roman *et al*.[31]

''Dementia'' was diagnosed independently by a neuropsychiatrist and a neuropsychologist according to the DSM IV criteria, based on all available data such as a questionnaire about daily functioning,[32] clinical information from a neuropsychologist, and cognitive profile. In five patients there was disagreement about the final diagnosis and these patients were classified as not demented. ''Vascular MCI'' was diagnosed when patients had at least one cognitive deficit. Our definition of MCI is somewhat broader than the traditional one of Petersen *et al*, which focused on amnestic disorders. We used their amplified criteria.[33 34] The group ''vascular cognitive impairment'' (VCI) had patients with both dementia or vascular MCI. Patients without cognitive disorders were assigned to the ''no cognitive disorder'' group. At each assessment, patients were re-evaluated for cognitive deficits and reassigned to one the four groups (dementia, VCI, vascular MCI, or no cognitive disorder) independent of the classification at other assessments.

Statistical analysis

Statistical analyses were performed using SPSS version 10. Demographic and CT features were compared for three different models: (i) patients with dementia versus patients without cognitive deficits; (ii) patients with VCI versus patients without cognitive deficits; and (iii) patients with vascular MCI versus patients without cognitive deficits.

For categorical variables χ^2 and Fisher's exact test were used; a two-sample Student's *t*-test was used for continuous variables. Logistic regression analyses were conducted to determine the predictability of the CT and demographic variables of dementia, VCI, and vascular MCI. Variables which distinguished ($p<0.05$; two-tailed) between the groups in the univariate analyses were entered in a multiple logistic regression model. If either white matter lesions or silent infarcts significantly predicted the outcome group, we entered ''pre-stroke cerebrovascular damage'' into the multiple logistic regression model.

Missing data were imputed according to a standard procedure as described by Tabachnick and Fidell.[35] Data

Table 1 Baseline demographic and clinical variables of the four patient groups of the study

	Dementia	VCI	Vascular MCI	No cognitive disorder
Number	17	142	125	34
Mean (SD) age	78.2 (6.6)	69.0 (12.3)	67.7 (12.4)	63.6 (12.8)*
Sex (M/F)	9/8	78/64	69/56	23/11
Education (L/H)	10/7	89/53	79/46	11/23*
Mean (SD) MMSE score	19.8 (2.3)	24.8 (3.5)	25.5 (3.1)	28.3 (1.5)*
Hypertension (pr/ab)	10/5	79/43	89/38	18/13
Diabetes (pr/ab)	13/2	104/20	91/18	30/3
Cholesterol (pr/ab)	8/0	70/19	62/19	25/3
Heart failure (pr/ab)	10/4	104/20	94/16	29/4
Current smoking (pr/ab)	6/5	52/43	46/38	18/10

*p<.05.
M, male; F, female; L, low; H, high; pr, presence; ab, absence; MCI, mild cognitive impairment; VCI, vascular cognitive impairment.

imputation was performed if there was at least one other test available within a specific cognitive domain and if the missing test was administered on an earlier or later assessment period.

RESULTS

A total of 176 patients (101 men (57.3%), 75 women (42.7%), average (SD) age 67.9 (12.5) years) were examined one month after stroke (table 1). Of the included patients, 100 patients (56.8%) had a low educational level. Mean (SD) MMSE score was 25.5 (3.5). Ninety patients (51.1%) had no symptomatic ischaemic lesions on CT. At the time of CT evaluation, the CT scans of 11 patients (6.2%) could not be retrieved from the radiological department archives. Clinical data were used to categorise these patients and those without a CT scan, as having lacunar or territorial brain infarction (67 were classified as lacunar, 34 as territorial). Ninety nine patients (56.3%) had lacunar stroke and 77 (43.7%) had territorial stroke. Ninety six (54.5%) patients had a stroke in the right hemisphere, 78 (44.3%) in the left hemisphere, and two (1.2%) patients in both hemispheres. Thirty six (20.5%) patients had white matter lesions, 110 (62.5%) had atrophy, and 57 patients (32.4%) had at least one silent infarct.

At six months after stroke, 4 patients (2.3%) had died and 13 (7.4%) refused to participate further, 4 (2.3%) refused to be reassessed (although for this time only; they were reassessed at 12 months) and 1 patient (0.6%) was not traceable. At 12 months after stroke, a further 5 (3.2%) patients had died and 9 (5.8%) refused to participate. Patients who did not complete the study did not differ from those who remained in the study with respect to baseline MMSE score, age, educational level, and sex. Table 1 shows the distribution of the demographic and clinical variables at baseline for the four groups.

At six months after stroke 13 patients were demented, 99 were diagnosed as vascular MCI and 42 did not had any cognitive deficits. At 12 months after stroke 14 patients were demented, 85 were diagnosed as vascular MCI and 45 did not had any cognitive deficits. At six months after stroke three patients progressed from ''vascular MCI'' to ''dementia'', and nine patients progressed from ''no cognitive disorder'' to ''vascular MCI''. At 12 months after stroke, three patients progressed from ''vascular MCI'' to ''dementia'' and seven patients progressed from ''no cognitive impairment'' to ''vascular MCI''. Patients who deteriorated were more often women ($\chi^2 = 4.5$, df = 1, p = 0.03). The other variables (age, level of education, stroke type, side of the infarct, white matter lesions, asymptomatic infarcts, and atrophy) were not different between the patients who deteriorated and those who did not.

Older age, territorial infarct, silent infarcts, pre-stroke cerebrovascular damage, and atrophy were associated with dementia one month after stroke (table 2). At six months, older age, lower educational level, territorial infarct, and pre-stroke cerebrovascular damage were associated with dementia. At 12 months, the same variables plus silent infarcts were associated with dementia (table 2).

At one month after stroke, lower educational level and territorial infarcts were associated with VCI; at six months older age, lower educational level, territorial infarct, and atrophy were associated with VCI; and at 12 months older age, female sex, lower educational level, white matter lesions, pre-stroke cerebrovascular damage, and atrophy were associated with VCI (table 3).

At one month after stroke, lower educational level and territorial infarcts were associated with vascular MCI; at six months older age, lower educational level, and territorial infarct were associated with vascular MCI; and at 12 months older age, female sex, lower educational level, white matter lesions, and pre-stroke cerebrovascular damage were associated with vascular MCI (table 4).

In all the univariate analyses, age was also graded in other categories (60 *v* <60; 70 *v* <60, 80 *v* <60). This did not change the associations.

Since the number of regression analyses was quite large (nine variables, three measurements periods and three groups) resulting in 81 analyses, it could be argued to correct

Table 2 Patients with dementia compared with patients without a cognitive disorder: univariate analyses

	1 month post stroke				6 months post stroke				12 months post stroke			
	N (%)	OR	CI	p*	N (%)	OR	CI	p*	N (%)	OR	CI	p*
Older age	15 (88.2)	12.1	2.4 to 61.8	**0.00**	10 (76.9)	8.3	1.9 to 35.7	**0.01**	10 (71.4)	6.2	1.6 to 23.2	**0.01**
Sex (female)	8 (47.1)	1.9	0.6 to 6.1	0.31	7 (53.8)	2.1	0.6 to 7.4	0.25	7 (50.0)	2.8	8 to 9.5	0.11
Education (low)	10 (58.8)	2.9	0.9 to 9.9	0.08	10 (76.9)	7.4	1.8 to 31.6	**0.01**	10 (71.4)	4.1	1.1 to 15.2	**0.03**
Stroke type (territorial)	10 (58.8)	4.0	1.2 to 13.6	**0.03**	9 (69.2)	5.6	1.5 to 21.8	**0.01**	10 (71.4)	4.5	1.2 to 16.8	**0.02**
Side (left)	9 (52.9)	2.8	0.7 to 7.4	0.18	7 (53.8)	1.8	0.5 to 6.4	0.35	8 (57.1)	2.1	0.6 to 7.2	0.23
White matter lesions (pr)	3 (20.0)	1.8	0.3 to 9.4	0.48	3 (23.0)	1.8	.4 to 8.5	0.46	1 (8.3)	0.9	0.1 to 8.5	0.90
Silent infarcts (pr)	10 (66.7)	4.0	1.1 to 14.6	**0.04**	8 (61.5)	3.2	.9 to 11.6	0.08	8 (66.7)	5.6	1.4 to 22.5	**0.01**
PSCVD (pr)	11 (73.3)	4.8	1.3 to 18.5	**0.02**	12 (80.0)	6.5	1.6 to 26.6	**0.02**	8 (66.7)	5.6	1.4 to 22.5	**0.01**
Atrophy (pr)	13 (92.9)	9.2	1.1 to 79.9	**0.05**	12 (92.3)	7.8	.9 to 66.5	0.06	11 (91.7)	7.7	.9 to 65.2	0.06

*p values in bold indicate association with dementia.
OR, odds ratio; pr, present; PSCVD, pre-stroke cerebrovascular damage

Table 3 Patients with vascular cognitive impairment compared with patients without a cognitive disorder: univariate analyses

	1 month post stroke				6 months post stroke				12 months post stroke			
	N (%)	OR	CI	p*	N (%)	OR	CI	p*	N (%)	OR	CI	p*
Older age	79 (55.6)	2.0	0.9 to 4.4	0.07	66 (58.9)	3.5	1.7 to 7.7	**0.00**	58 (58.8)	3.5	1.6 to 7.4	**0.00**
Sex (female)	64 (45.1)	1.7	0.8 to 3.8	0.18	54 (48.2)	1.7	0.8 to 3.5	0.17	49 (49.5)	2.7	1.2 to 5.8	**0.01**
Education (low)	89 (62.7)	3.5	1.6 to 7.8	**0.00**	71 (63.4)	3.9	1.8 to 8.2	**0.00**	61 (61.6)	2.6	1.3 to 5.5	**0.01**
Stroke type (territorial)	68 (48.9)	2.6	1.1 to 5.9	**0.03**	55 (49.2)	2.4	1.1 to 5.2	**0.02**	46 (46.5)	1.6	0.8 to 3.3	0.22
Side (left)	67 (47.5)	1.8	0.8 to 4.0	0.14	51 (45.9)	1.3	0.6 to 2.8	0.45	45 (45.9)	1.3	0.7 to 2.8	0.42
White matter lesions (pr)	32 (24.4)	2.3	0.8 to 7.2	0.14	25 (24.3)	1.9	0.8 to 5.1	0.19	25 (26.3)	3.4	1.1 to 10.5	**0.03**
Silent infarcts (pr)	46 (35.1)	1.1	0.5 to 2.4	0.85	36 (34.9)	1.1	0.5 to 2.3	0.85	35 (36.8)	1.6	0.7 to 3.7	0.23
PSCVD (pr)	60 (45.8)	1.5	0.7 to 3.3	0.33	46 (44.7)	1.3	0.7 to 2.7	0.47	45 (47.4)	2.5	1.1 to 5.6	**0.02**
Atrophy (pr)	93 (75.6)	2.2	0.9 to 5.1	0.07	73 (77.7)	2.3	1.0 to 5.1	**0.05**	68 (78.2)	2.5	1.1 to 5.6	**0.03**

*p values in bold indicate association with vascular cognitive impairment (VCI).
OR, odds ratio; pr, present; PSCVD, pre-stroke cerebrovascular damage.

the significance level to prevent type 1 errors. However, since the adjusted p value would have become very small ($p_{adj.}<0.0006$), the probability of finding a significant effect at all would have been reduced to an extremely low level. Because of the explorative character of the present study, it was decided not to adjust the p level, but both interpret the significance of the statistical tests and judge whether the observed effects were clinically relevant with care.

Multivariate analyses using logistic regression were performed to identify factors that were independently associated with cognitive impairment after stroke (table 5). In model I (''dementia'' *v* ''no cognitive disorder'' at one month after stroke) the variables included were age, location (territorial or lacunar) infarct, pre-stroke cerebrovascular damage, and atrophy. No independent predictors of dementia could be identified. Older age, lower educational level, and territorial infarct location were independently associated with dementia at six months after stroke. Older age and pre-stroke cerebrovascular damage were independently correlated with dementia at 12 months after stroke.

In model II (''VCI'' *v* ''no cognitive disorder'') lower educational level and territorial infarct were independently correlated with VCI at one month after stroke. Both older age and lower educational level were independently correlated with VCI at six months after stroke. Older age was independently correlated with VCI at 12 months after stroke. In model III (''vascular MCI'' *v* ''no cognitive disorder''), lower educational level and territorial infarct location were independently correlated with vascular MCI at one month after stroke. Both older age and lower educational level were independently correlated with vascular MCI at six and 12 months after stroke.

DISCUSSION

We investigated specific characteristics (stroke related and demographic) that could be related to dementia, VCI, and vascular MCI at one, six, and 12 months after stroke, with special emphasis on neuroimaging data. In all the group, older age and lower educational level were found to be important predictors after stroke. Moreover, territorial as opposed to lacunar stroke was also a predictor at one month after stroke.

Other studies of post-stroke dementia have reported similar risk factors,[7–10 12] however, these studies identified several stroke related risk factors for dementia, whereas we identified only territorial infarction. Territorial infarction might be associated with cognitive impairment because of the importance of these regions for higher cerebral cognitive functioning.[3 23 36] Most studies found white matter lesions and atrophy to be independent contributors to post-stroke dementia,[5 8 10 37–40] whereas we did not. One reason for this discrepancy is that we used CT instead of magnetic resonance imaging which is more sensitive. However, most hospital patients with stroke have a CT on admission, and as such the data presented here are of clinical relevance. Another reason is that few patients (20.5%) had white matter lesions in our study, whereas in other studies more than half of the patients had such lesions.[5 9 38] The low number of patients with white matter lesions in our study could be a consequence of the exclusion of patients with MMSE <15. It is quite possible that some of these excluded patients had insidiously progressing cognitive decline before stroke, which is related to white matter lesions.[7 41 42] Thus our exclusion of patients with severe cognitive impairments may have resulted in the exclusion of patients with white matter lesions.

Table 4 Patients with vascular mild cognitive impairment, compared to patients without a cognitive disorder: univariate analyses

	1 month post stroke				6 months post stroke				12 months post stroke			
	N (%)	OR	CI	p*	N (%)	OR	CI	p*	N (%)	OR	CI	p*
Older age	64 (51.2)	1.7	0.8–3.7	0.18	56 (56.6)	3.3	1.5–7.1	**0.00**	48 (56.5)	3.2	1.5–6.9	**0.03**
Sex (female)	69 (55.2)	1.7	0.8–3.8	0.19	47 (47.4)	1.6	0.8–3.4	0.20	42 (49.4)	2.7	1.2–5.9	**0.01**
Education (low)	46 (36.8)	3.6	1.6–8.0	**0.02**	61 (61.6)	3.6	1.7–7.7	**0.00**	51 (60.0)	2.5	1.2–5.2	**0.02**
Stroke type (territorial)	67 (53.8)	2.4	1.0–5.6	**0.04**	53 (53.5)	2.2	1.1–4.7	**0.04**	49 (57.6)	1.3	0.6–2.8	0.45
Side (left)	58 (46.8)	1.8	0.8–3.9	0.17	44 (44.9)	1.3	0.6–2.7	0.53	37 (44.0)	1.3	0.6–2.6	0.56
White matter lesions (pr)	29 (25.0)	2.4	0.8–7.5	0.13	22 (24.4)	1.9	0.7–5.2	0.19	24 (28.9)	3.9	1.2–12.0	**0.02**
Silent infarcts (pr)	36 (31.0)	0.9	0.4–2.1	0.80	28 (31.1)	0.9	0.4–1.9	0.79	27 (32.5)	1.4	0.6–3.1	0.47
PSCVD (pr)	49 (42.2)	1.3	0.6–2.9	0.55	36 (40.0)	1.1	0.5–2.3	0.84	37 (44.6)	2.3	1.0–5.1	**0.05**
Atrophy (pr)	80 (73.3)	1.9	0.8–4.6	0.13	61 (75.3)	1.9	0.9–4.5	0.10	57 (76.0)	2.2	0.9–5.1	0.06

*p values in bold indicate association with vascular mild cognitive impairment.
OR, odds ratio; pr, present; PSCVD, pre-stroke cerebrovascular damage.

Table 5 Multivariate logistic regression model containing univariate significant variables

	Dementia *v* no cognitive disorder			VCI *v* no cognitive disorder			V-MCI *v* no cognitive disorder		
	1 month OR (CI)	6 months OR (CI)	12 months OR (CI)	1 month OR (CI)	6 months OR (CI)	12 months OR (CI)	1 month OR (CI)	6 months OR (CI)	12 months OR (CI)
Older age	4.3 (0.5 to 12.9)	9.4* (1.3 to 65.7)	3.1 (0.60 to 15.6)		4.3* (1.6 to 11.3)	3.5* (1.4 to 8.9)		3.4* (1.5 to 7.8)	3.5* (1.5 to 8.2)
Sex (female)						1.8 (0.7 to 4.8)			1.8 (0.8 to 4.4)
Education (low)		14.7* (1.9 to 110.3)	8.7* (1.3 to 60.3)	3.4* (1.5 to 7.6)	4.1* (1.7 to 9.9)	2.0 (0.8 to 4.8)	4.96* (2.0 to 12.2)	3.7* (1.6 to 8.2)	2.28* (1.0 to 5.4)
Location (territorial)	2.6 (0.5 to 12.9)	10.6* (1.4 to 77.6)	6.2 (0.9 to 38.7)	2.4* (1.0 to 5.7)	2.1 (0.9 to 5.1)		3.58* (1.3 to 9.7)	2.01 (0.9 to 4.6)	
PSCVD	2.9 (0.6 to 15.1)	3.4 (0.5 to 21.5)	7.4* (1.1 to 47.2)			1.9 (0.7 to 5.4)			1.5 (0.6 to 3.8)
Atrophy	3.0 (0.3 to 37.5)				1.0 (0.4 to 3.0)	1.2 (0.5 to 3.2)			

*p<0.05.
CI, confidence interval; OR, odds ratios; PSCVD, pre-stroke cerebrovascular damage; VCI, vascular cognitive impairment; V-MCI, vascular mild cognitive impairment.

The studies referred to above examined dementia after stroke, and as such they neglected patients who did not meet the criteria for dementia but who nevertheless might have had cognitive impairments. Other investigators have investigated the association between cognitive disorders not restricted to dementia, and stroke related features, but few included multivariate analyses in the study design.[17 23–26] Schmidt *et al*[23] found multiple infarcts and temporal lobe infarction to be risk factors for cognitive disorders. Patel *et al*[26] reported left hemisphere infarction, older age, ethnicity, socioeconomic status, and stroke severity to be important contributors to the development of cognitive disorders after stroke. The only stroke related factor that contributed independently to VCI early after stroke in our study was territorial infarction. Unlike other studies we were able to diagnose more subtle cognitive deficits because of the use of an extensive and sensitive set of neuropsychological tests. Patients with only subtle cognitive deficits have either less brain damage or they might have brain damage in regions that are of less importance for cognitive functioning. This could explain why we found fewer associations between the CT scan features and cognitive disorders.

Although recent research has focused on post-stroke cognitive impairment not restricted to dementia, to our knowledge no studies have reported on cognitive disorders without dementia. We found that soon after stroke, territorial infarction, older age, and lower educational level were predictors of vascular MCI. The univariate analyses revealed that pre-existing vascular brain damage (white matter lesions or silent infarcts) became more important later. This could mean that with increasing time after the stroke the influence of the initial infarct decreases, and the influence of pre-existing brain damage becomes more important. In most stroke patients white matter lesions or silent infarcts progress over time, despite standard treatment, and consequently, cognitive functioning may decline.[29 43–45] We did not investigate whether the patients with cognitive decline had progressively increasing brain damage at six and 12 months, but in the future we plan to investigate the relation between accumulating brain damage and cognitive decline.

There are certain limitations to this study. First, only one third of the total stroke population admitted to the hospital during the inclusion period was included in the study. However, our series was not affected by referral bias, because the University Hospital Maastricht is the only hospital in that region. Secondly, to perform valid analyses with sufficient power we imputed data for some patients with missing data. This was done by an experienced neuropsychologist who decided, on the basis of the available data and the patients' neuropsychological profile, how to impute the data. Although this method is subjective, a comparison of this method with one based on regression analyses did not yield different results. We also compared for all analyses the database with the imputed data with the database without the imputed data and all conclusions were unchanged. Thirdly, because we excluded patients with MMSE <15 we may have excluded patients with specific stroke related features such as territorial infarction or white matter lesions. However, we studied cognitive decline in those patients for whom such decline might be most relevant, namely patients without any prior severe cognitive problems. Fourthly, infarct site and size might be relevant factors to study as independent predictors for post-stroke cognitive impairment. However, the fact that only about one half of the patients had an infarct visible on CT, which was mainly due to early scanning, forestalled such analysis. Another study also found visible lesions on CT within 48 hours after stroke in 50% of the patients.[46] Lastly, our study design could not rule out that some patients with dementia might have had mixed type instead of vascular type. Although white matter lesion are generally held to be caused by vascular insufficiency, they can also occur in patients with dementia of Alzheimer's type.[47] However, by excluding patients with MMSE <15 and patients with dementia before stroke, we made the likelihood of including such patients low.

Despite its limitations, this study is the first to investigate the relation between early CT scan features and post-stroke cognitive impairment on a longitudinal basis. Territorial infarction, older age, and lower educational level are important risk factors for cognitive disorders after stroke. Pre-stroke damage, as diagnosed from the CT scan, is probably related to cognitive disorders later after stroke.

ACKNOWLEDGEMENTS

We would like to thank I Winkens for the neuropsychological assessment, Prof Dr J Jolles for the imputation of missing data, and R Ponds for his contribution in the diagnosis of dementia.

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This study was supported by grants from the Adriana van Rinsum-Ponssen foundation.

Competing interests: SR has been reimbursed by SWOL for attending a conference.

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