Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke

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Abstract

Objective: The aim of the present study was to examine the predictive value of cognitive impairment in the acute phase after stroke as a risk factor for long-term (six to ten months after stroke) depressive symptoms (DS) and a reduced quality of life (QOL), independent of demographic and neurological predictors.

Methods: We evaluated 143 patients within the first 3 weeks post-stroke. Predictor variables included domain-specific cognitive function, demographic data, vascular risk factors, lesion characteristics, and clinical factors. Predictor variables associated with long-term DS (Montgomery Åsberg Depression Rating Scale ≥ 7) and QOL (Stroke-Specific Quality of Life Scale) were identified with multiple logistic and linear regression.

Results: Long-term DS were independently predicted by cognitive impairment at baseline, DS at baseline, female sex, diabetes mellitus, and previous TIA(s). Cognitive impairment, increasing age, and functional dependence predicted a reduced QOL, whereas hypercholesterolaemia predicted a better QOL. Among all cognitive disorders, unilateral neglect was the greatest risk factor for DS after 6 months, whereas a disorder in visual perception and construction affected QOL the most.

Conclusions: Cognitive impairment and vascular risk factors are important predictors of long-term DS and QOL after stroke. The prognostic value of cognition suggests a reactive component in the development or continuation of long-term DS.

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Keywords: Stroke; Depressive symptoms; Cognitive impairment; Quality of life

1. Introduction

Depression is a common complication after stroke and is associated with increased mortality [1], poor functional outcome [2], and decreased quality of life [3]. Over the past 20 years conflicting findings have been reported regarding the association between cognitive impairment and depres-

sive pathology after stroke. Whereas most studies have reported an association with cognitive impairment [4–6], others did not find such an association [7], or were able only to show that this association held in patients with left hemisphere damage [8–10]. The majority of these studies have assessed *post-stroke depression* based on the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) and/or using self-rating scales such as the Beck Depression Inventory. However, communication difficulties and severe cognitive impairment may complicate the assessment of depression in patients who recently suffered a stroke. Consequently, the diagnostic approach often has resulted in the exclusion of

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patients with severe cognitive impairment (e.g. [6,11]). This emphasises the importance of administering observational methods in acute stroke patients with cognitive impairment. One recent study demonstrated that the presence of observer-rated depressive symptoms at 6 months post-stroke is closely related to the presence of dementia at 6 months [5]. Currently, it is still unclear whether cognitive impairment early after stroke is a risk factor of depressive symptoms in the longer term, independent of other well-known medical and demographic predictors.

In addition to emotional and cognitive disturbances, stroke patients frequently report a reduced subjective health perception or 'quality of life' (QOL) [3]. In the few studies that examined the relative contribution of cognitive performance in the prediction of QOL after stroke, either no significant association was found [12], or a selective association with aphasia was reported [13]. However, none of these studies examined cognitive functioning by means of an extensive neuropsychological examination tapping distinct cognitive functions, although specific cognitive disorders might affect quality of life after stroke differently.

In the present study, we aimed (i) to test whether acute cognitive impairment is an independent risk factor of DS 6 months after stroke, and (ii) to examine its relation with long-term QOL. Furthermore, we examined which specific cognitive deficits in the early phase of stroke were associated with DS and a reduced QOL after 6 months. To this end, we used a sensitive neuropsychological examination covering a broad range of cognitive domains, which has been shown to demonstrate a good predictive validity with respect to long-term domain-specific cognitive impairment [14].

2. Methods

2.1. Subjects

The patient population in this study was selected from consecutive patients with a first-ever symptomatic stroke admitted to stroke units of three hospitals in The Netherlands (University Medical Centre Utrecht, Tweesteden Hospital Tilburg, St.-Elisabeth Hospital Tilburg) between February 2002 and January 2003 (see also [14,15] for two studies on the same cohort). Only patients with a first-ever ischaemic stroke or primary intracerebral haemorrhage were included. Diagnosis of stroke was based on both the presence of acute neurological symptoms and a compatible lesion on CT or MRI scan. Exclusion criteria were: (1) pre-existing depression as diagnosed by general practitioner/psychiatrist, or history that might influence outcome, i.e. history of drug abuse, pre-existent dependence in activities of daily living, or pre-existent dementia (as defined by a score of 3.6 or higher on the short Informant Questionnaire on Cognitive Decline in the Elderly — IQCODE Dutch

Version) [16], (2) patients older than 85 years, and (3) patients who could not be examined within the first 21 days post-stroke due to severe disturbances in consciousness or inability to comprehend task instructions. No restrictions were used with respect to the level of cognitive impairment caused by the stroke. This is particularly important to note as previous studies often excluded patients with severe cognitive impairment. Consequently, we included also those patients who would fulfil criteria for post-stroke dementia. However, we consider it unreliable to classify patients as such in the early phase post-stroke, as the term 'post-stroke dementia' suggests that the syndrome is irreversible while typically the opposite is true in patients who suffered a first stroke. For example, with respect to their cognitive functions a high number of patients recover to a great extent in the first months after the stroke [14].

Finally, patients who suffered a recurrent stroke or who developed comorbidity that might affect outcome (i.e. cancer, myocardial infarction, CABG, or psychiatric illnesses) between the first and the second examination were excluded from follow-up examination. Fig. 1 presents a chart showing the number of patients who were in- and excluded.

The Ethics Committee of each participating hospital approved the study protocol. Written informed consent was obtained from each subject.

2.2. Predictor variables

2.2.1. Demographic factors

On admission, we evaluated demographic factors including age (years), level of education (scored with 7 categories ranging from 1: did not finish primary school to 7: university degree, and dichotomised at the median) [15], and sex.

2.2.2. Vascular risk factors

Recorded vascular risk factors comprised previously diagnosed and treated diabetes mellitus, hypertension, hypercholesterolaemia, transient ischaemic attack (TIA), smoking during the last 5 years, and alcohol consumption of more than 2 units per day.

2.2.3. Clinical scales and neuropsychological assessment

All clinical variables were assembled at the same time as the cognitive assessments and within 3 weeks post-stroke (mean interval, 7.8 ± 4.2 days post-stroke). Stroke severity was assessed with the National Institutes of Health Stroke Scale (NIHSS) [17] and categorised as mild if NIHSS ≤ 7 [18]. Functional dependence was assessed with the modified Barthel Index (MBI) [19] and categorised as present if MBI < 19 [20]. Cognitive impairment at baseline was assessed with a neuropsychological examination covering 7 cognitive domains, i.e. abstract reasoning, visual memory, verbal memory, executive functioning, visual perception and construction, language, and unilateral neglect. The neuro-
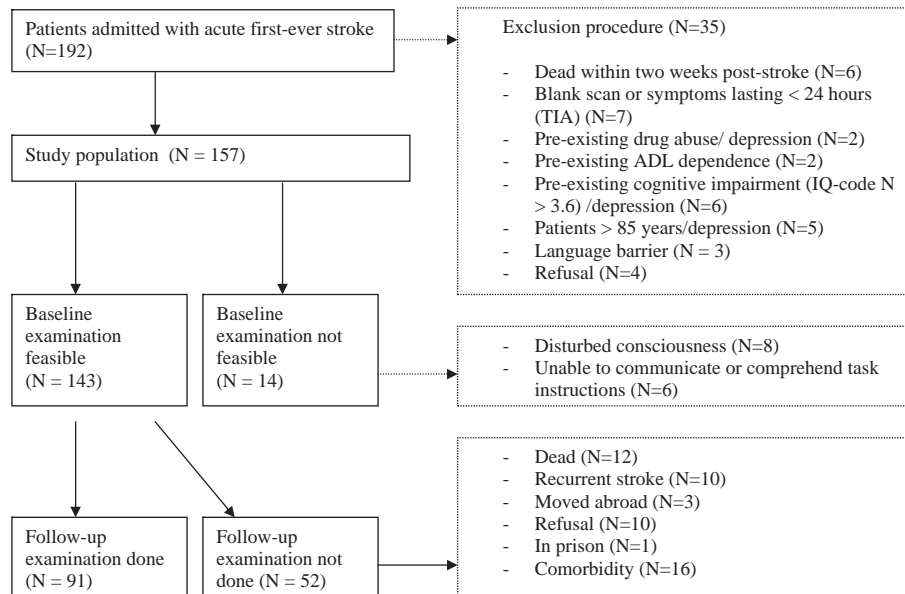
Fig. 1. Flowchart of patient inclusion.

psychological test battery is described in detail elsewhere [15]. Test scores on individual tasks were transformed into z-scores based on means and standard deviations of healthy controls (without neurological, psychiatric, or cognitive history). Subsequently, z-scores of tasks belonging to the same cognitive domain were averaged. Patients with disturbances in at least one cognitive domain (z-score < − 1.65) were classified as having cognitive impairment at baseline [15]. DS severity at baseline was assessed with the Montgomery Åsberg Depression Rating Scale (MADRS) [21], and DS were classified as present if MADRS ≥ 7 according to standardised criteria [22]. This cut-off value has also been used to indicate the presence of DS in stroke patients [5,23].

2.2.4. Lesion characteristics

An experienced stroke neurologist (HBvdW) who was blind to the clinical data determined stroke type and location from CT or MRI. In addition, he recorded the presence of silent infarcts [24] and white matter lesions (scored as present if patients obtained a score > 0 on the 'Van Swieten scale') [25]. Lesion volume was calculated by manual tracing of the lesion on each slice showing the infarct or haemorrhage, followed by multiplying the lesion area by the slice thickness in all slices showing the lesion [26].

2.3. Outcome measures

Follow-up assessment was carried out after a minimum of 6 and a maximum of 10 months, dated from the baseline assessment (mean interval, 7.5 ± 1.3 months). Two distinct types of outcome were used, i.e. long-term DS and QOL. Long-term DS were classified as present if MADRS ≥ 7 at follow-up [5,22,23].

QOL was assessed with the Stroke-Specific Quality of Life Scale (SS-QOL) [27], which is a disease-specific quality of life measure that consists of 49 items encompassing 12 domains (Social role, Mobility, Energy, Language, Self-care, Mood, Personality, Thinking, Upper Extremity Use, Family Role, Vision, and Work/Productivity). Each item is ranked on a 5-point Likert scale. The summary score of this scale is an unweighted average of the 12 domains with higher scores indicating better QOL. The summary score was used as the second outcome measure in this study.

2.4. Statistical analyses

First, to determine whether any selection bias had occurred between patients who were re-examined at follow-up and those who were not, we performed Student t-tests for continuous data, Mann–Whitney U tests for ordinal data, and χ^2 analyses for categorical data on the baseline characteristics of patients. Next, we performed a forward stepwise logistic regression analysis with presence of DS in the long term as the dependent variable to determine independent baseline predictors of DS after the first 6 months. We performed a forward stepwise linear regression analysis with SSQOL as the dependent variable to determine independent baseline predictors of QOL after the first 6 months. Potential predictors for both analyses were selected from a series of univariate analyses, with a $p \leq 0.1$ level as a screening criterion. Finally, non-parametric Mann–Whitney U tests were performed to examine associations between specific cognitive disorders at baseline and outcome in the long term. Because of the large number of non-parametric analyses, only p-values ≤ 0.01 were considered significant.

3. Results

3.1. Potential selection bias

Of the 143 patients included at baseline, 91 (64%) were re-examined at follow-up. Patients not included at follow-up were significantly older $[t(141)=2.4; p<0.05]$, and more of these patients demonstrated white matter lesions $[\chi^2(1)=7.04; p<0.01]$ than the included patients. No difference was found with respect to other demographic factors, vascular risk factors, or the prevalence of DS or cognitive impairment at baseline. Characteristics of patients included for follow-up are shown in Table 1.

Table 1
Predictors of long-term depressive symptoms

	Entire group	Presence of DS at follow-up		
	N=91	No DS (N=43)	DS (N=48)	p
Demographic characteristics				
Age (years), mean±S.D.	61.6±13.2	60.8±13.1	62.3±13.3	0.57
Female sex	48.4	32.6	62.5	0.01*
High education	41.8	51.2	33.3	0.09*
Lesion characteristics				
% PICH/all strokes	7.7	4.7	10.4	0.30
Lesion location involving				
Frontal lobe	13.2	7	18.8	0.10*
Parietal lobe	17.6	16.3	18.8	0.76
Temporal lobe	19.8	18.6	20.8	0.79
Occipital lobe	14.3	14.0	14.6	0.93
Striatum	19.8	11.6	27.1	0.07*
Caudate nucleus	7.7	2.3	12.5	0.07*
Thalamus	11.0	9.3	12.5	0.63
Internal capsule	25.3	25.6	25.0	0.95
Lesion volume (ml), mean±S.D.	13.6±22.3	8.9±12.8	17.7±27.7	0.05*
Lesion site				0.08*
Left supratentorial	42.5	48.8	37.0	
Right supratentorial	43.7	31.7	54.3	
Infratentorial	13.8	19.5	8.7	
Silent infarct(s)	15.7	20.5	11.4	0.25
White matter lesions	15.4	16.3	14.6	0.82
Vascular risk factors				
Hypercholesterolaemia	17.8	20.9	14.9	0.45
Hypertension	41.1	44.2	38.3	0.57
Diabetes mellitus	12.2	4.7	19.1	0.04*
Previous TIA(s)	14.4	4.7	23.4	0.01*
Smoking	41.1	37.2	44.7	0.47
Alcohol>2 units/day	17.8	25.6	10.6	0.06*
Clinical variables in early phase				
Cognitive Impairment	41.8	25.6	56.3	0.01*
DS	49.5	34.9	62.5	0.01*
NIHSS >7	75.8	81.4	70.8	0.24
mBI <19	56.0	53.5	58.3	0.64

Values are within-group percentages and means±standard deviations. Some within-group percentages are based on incomplete samples due to small amounts of missing data.

* Variables with $p \leq 0.1$ are entered in multivariate analyses. Abbreviations: PICH=primary intracerebral haemorrhage; DS=depressive symptoms; mBI=modified Barthel Index; NIHSS=National Institutes of Health Stroke Scale.

Table 2
Predictors of long-term depressive symptoms: stepwise logistic regression analysis

Independent baseline predictors	DS at follow-up	
	O.R.	95%CI
Female gender	4.41	1.5–13.1
Diabetes mellitus	10.0	1.5–67.0
Previous TIA(s)	6.2	1.0–37.6
DS at baseline	3.3	1.1–9.7
Cognitive impairment at baseline	3.4	1.2–9.7
R-square	0.42	
GOF	p=0.29	

Values are Odds Ratios (O.R.) and 95% Confidence Intervals (C.I.). Abbreviations: DS=depressive symptoms; GOF=Hosmer and Lemeshow goodness-of-fit.

Eleven patients (12%) received antidepressant medication between stroke onset and follow-up.

3.2. Determinants of DS after the first 6 months

In the early phase after stroke, 45 patients (49.5%) demonstrated DS, whereas 30 of these patients continued to show DS in the long term. When considering the patient population as a whole, 48 patients (52.7%) demonstrated DS after the first 6 months. There was no significant difference in the prevalence of DS at baseline and follow-up (McNemars test: $p=0.7$). Univariate associations between potential predictor variables and DS after the first 6 months are shown in Table 1. Results of the multiple stepwise logistic regression analysis are summarised in Table 2. At 6 months, DS were independently associated with cognitive impairment and DS in the acute stage of stroke, female sex, pre-existent diabetes mellitus, and pre-existent TIA(s). Results were similar when linear regression was applied with the continuous MADRS scores at follow-up as the dependent variable or when antidepressant medication was taken into account as a predictor variable (data not shown).

Next, we examined which specific cognitive disorders at baseline were associated with DS after 6 months. On the whole, 27.5% of patients demonstrated a disorder in visual perception and construction, 26.4% in executive functioning, 25.8% demonstrated neglect, 19.8% demonstrated a disorder in abstract reasoning, 18.7% in language, 17.6% in verbal memory, and 13.2% in visual memory. Univariate logistic regression analyses adjusted for age, sex, and education showed that patients with unilateral neglect in the first weeks of stroke demonstrated a high risk of showing DS after 6 months (O.R.=9.5; 95%CI=1.9–48.5), as did patients with visual memory disorders (O.R.=6.8; 95%CI=1.3–35.9), and language impairment (O.R.=4.9; 95%CI=1.2–19.5). With respect to visual perception/construction, there was a trend towards the development of long-term DS (O.R.=2.7; 95%CI=0.93–7.9). In multiple stepwise analysis, patients with unilateral neglect demon-

strated the greatest risk of showing DS after 6 months (O.R.=9.5; 95%CI=1.9–48.5).

3.3. Determinants of QOL after the first 6 months

Univariate associations between potential predictor variables and quality of life after the first 6 months are shown in Table 3. Four independent predictors of long-term QOL emerged, i.e. early cognitive impairment (beta=−0.261; $p=0.01$), older age (beta=−0.223; $p=0.02$), and ADL dependence in the early phase post-stroke (beta=−0.242; $p=0.02$) predicted a reduced QOL, whereas the presence of hypercholesterolaemia before the stroke predicted a better QOL (beta=0.194; $p=0.05$). The R-square in this multivariate model was 0.27.

Among cognitive disorders at baseline, early disorders in executive functioning (beta=−0.21; $p<0.05$), visual perception/construction (beta=−0.47; $p<0.001$), visual memory (beta=−0.37; $p<0.001$), and unilateral neglect (beta=−0.29; $p<0.01$) were risk factors for a reduced QOL after 6 months. In multiple stepwise analysis, an impairment in visual perception/construction was the strongest risk factor of a reduced QOL (beta=−0.44;

Table 3
Predictors of long-term QOL

	B	p value
Demographic characteristics		
Age	−0.28	0.008*
Female sex	−0.06	0.58
High education	0.29	0.005*
Lesion characteristics		
% PICH/all strokes	−0.10	0.33
Lesion location involving		
Frontal lobe	−0.10	0.33
Parietal lobe	0.12	0.27
Temporal lobe	−0.07	0.49
Occipital lobe	0.001	0.99
Striatum	−0.02	0.89
Caudate nucleus	−0.10	0.34
Thalamus	−0.17	0.10
Internal capsule	−0.22	0.69
Lesion volume	−0.22	0.04*
Silent infarct(s)	−0.05	0.67
White matter lesions	−0.04	0.74
Vascular risk factors		
Hypercholesterolaemia	0.21	0.04*
Hypertension	−0.10	0.37
Diabetes mellitus	−0.10	0.34
Previous TIA(s)	−0.06	0.58
Smoking	0.02	0.88
Alcohol >2 units/day	0.18	0.09*
Clinical variables in early phase		
Cognitive impairment	−0.39	0.001*
DS	−0.17	0.11
NIHSS >7	−0.219	0.038*
mBI <19	−0.336	0.001*

* Variables with p≤0.1 are entered in multivariate analyses. Abbreviations: PICH=primary intracerebral haemorrhage; DS=depressive symptoms; mBI=modified Barthel Index; NIHSS=National Institutes of Health Stroke Scale.

Table 4
SS-QOL domains affected by specific cognitive deficits

SS-QOL domains	Cognitive deficits at baseline			
	Visual memory	Visual perception/ construction	Unilateral Neglect	Executive function
Mobility		X		
Energy		X	X	
Upper extremity		X		
Work	X	X	X	X
Mood		X		
Self-care	X	X	X	
Social relations		X		
Family relations		X	X	
Vision		X		
Language				
Personality		X	X	
Thinking				

X indicates Mann–Whitney U tests with p-values ≤0.01.

$p<0.001$). Post hoc analyses revealed that patients with a deficit in visual perception/construction reported the most complaints in terms of the number of affected SS-QOL domains, followed by patients with unilateral neglect at baseline (Table 4).

4. Discussion

A first important finding of this study is that cognitive impairment in the early phase of stroke is an independent risk factor of DS and a reduced QOL after 6 months. Until now, acute cognitive impairment after stroke has been studied mainly with global screening instruments intended to detect dementia, e.g. the Mini-Mental State Examination [28] or the CAMCOG [29]. Whereas antidepressant treatment has been shown to reduce cognitive impairment after stroke suggesting that depression causes a great deal of cognitive impairment after stroke (the so-called 'dementia of depression' or 'pseudo-dementia') [30,31], our results suggest that early cognitive impairment after stroke may also predict the presence of DS in the long term. More specifically, patients with unilateral neglect, higher-level visual disorders, and language impairment in the early phase of stroke were at high risk of showing DS in the long term, with acute neglect being the most important cognitive risk factor. There are no previous reports of a direct link between neglect and depression/depressive symptoms. However, our study is the first to examine the potential association between specific cognitive disorders and depressive symptoms in patients with stroke. One study [32] reported a close association between right posterior stroke and depression in the long term and the authors suggested that visual perceptual impairment may have played a role in the aetiology of depression in these patients. Similarly, it has been demonstrated that perceptual/attentional networks in the brain overlap with neural networks involved in mood [33], which may explain why specifically those cognitive

disorders seem closely related to DS in our patient sample. Interestingly, two previous reports [34,35] suggested that there is a dissociation between depressive behaviour and the subjective experience of depression, and that particularly patients with anosognosia for hemiplegia might be unaware of the fact that they are depressed ('anosognosia for depression'). Anosognosia for hemiplegia is a condition which is strongly associated with neglect in the acute phase of stroke [36]. Whereas sickness insight in these patients is typically limited in the early phase of stroke, models of anosognosia for hemiplegia propose that subjects discover their deficit when they engage in activities that confront their disability [35]. In our study, patients with acute higher-level visual disorders and unilateral neglect subjectively reported a reduction in QOL after 6 months, at the physical level as well as at the mental and social level. This confirms that patients were aware of (at least some of) their limitations by that time.

In addition to cognitive impairment, we identified several other independent predictors of DS and QOL after stroke. The presence of DS in the acute stage post-stroke emerged as an independent predictor of DS after 6 months. This finding is particularly important given the possibility of effective pharmacological treatment of depression in patients with stroke [37]. Moreover, it has been shown that antidepressant treatment is more effective early after stroke as compared to treatment at later stages [38]. Antidepressant treatment has been shown to improve functional outcome [2] and to decrease mortality after stroke [39]. Interestingly, a recent clinical study suggested that depressed stroke patients with comorbid cognitive impairment demonstrated a greater resistance to antidepressant treatment in the long term [40]. However, placebo-controlled clinical trials are warranted to evaluate the differential effects of antidepressant treatment in depressed patients with and without cognitive impairment. Furthermore, two vascular risk factors emerged as independent predictors of DS, namely pre-existent TIA(s) and a history of diabetes mellitus (either type 1 or type 2). The finding that diabetes mellitus is a risk factor for the presence of depressive pathology after stroke has been reported before, but this association was found solely in patients with a stroke in the left hemisphere [8]. According to some authors, diabetes is a risk factor for DS through a biological mechanism linking the metabolic changes of diabetes to changes in the brain structure or function [41]. Our study also showed that females have a greater risk of showing DS 6 months after stroke than males, in line with most studies. Similarly, this finding has been consistently reported in subjects without brain damage, but it remains unclear whether the determinants of this sex difference are biological or social [42]. We did not find a relation between the location of the lesion and the presence of DS after 6 to 10 months. Similarly, we did not find a relation between DS and lesion location in a previous study in the acute phase of stroke (<3 weeks post-stroke) [4]. Hence, we cannot confirm the neurobiological

model put forward by Robinson and his research group (which states that post-stroke depression is caused by left anterior lesions and/or lesions in the underlying basal ganglia), neither in the acute phase nor in the chronic phase [32,37,43–46]. This may be due to the fact that we assessed *depressive symptoms* rather than *post-stroke depression*. However, a systematic review [47] and more extensive studies on determinants of post-stroke depression (e.g. [34]) could not demonstrate this relation neither. Although the role of lesion location on the pathogenesis of post-stroke depression might still be identified by prospective studies on very large cohorts, together with innovative neuroimaging methods, the prognostic value of cognition in our study suggests a reactive component in the development or continuation of long-term DS. DS may develop as a psychological reaction to the loss of previous capacities. In line with this suggestion, patients with long-term DS still demonstrated more cognitive impairment at 6 months than patients without long-term DS (data not shown). Finally, in the present study cognitive impairment and DS at baseline but not stroke severity and functional dependence predict DS in the long term. This is probably due to the fact that neurological functions improve considerably after the acute phase, whereas cognitive deficits and DS remain present in a greater number of patients. For example, in a previous study from our group [15], we showed that the majority of patients from our study demonstrated an intact bADL after 6 to 10 months, whereas 31% of patients still demonstrated cognitive impairment in the long term.

In studies testing outcome after stroke it is important to incorporate measures like QOL, as stroke may lead to a broad range of impairments and a wide spectrum of symptom severity. Disease-specific measures, such as the SS-QOL [27], may be especially valuable because they are more sensitive than generic measures to meaningful changes in QOL after stroke. Similar to previous work on determinants of QOL [3,13], we found that age and functional dependence were important predictors of a low quality of life. Furthermore, pre-existent hypercholesterolaemia independently predicted a better quality of life after 6 months. High cholesterol levels in the acute phase of stroke have been associated with a better functional outcome at 1 month post-stroke [48]. Alternatively, this association may be explained by the use of statins by these patients. Recent studies suggest that the long-term use of statins among patients with coronary artery disease is associated with a reduced risk of depression, anxiety, and hostility [49]. An ongoing trial seeks to ascertain the beneficial or adverse effects of statins on a set of noncardiac endpoints in elderly patients, including cognition, mood, and behaviour [50].

Two limitations of the present study should be addressed. First, as the aim of this study was to include patients with severe cognitive impairment to examine the relation with DS, we administered an observer-rated scale to reliably assess DS in both the early stage post-stroke and after 6

months. The advantage of the MADRS is that (i) it does not draw heavily on somatic symptoms, (ii) it has good psychometric properties, and (iii) it consists of a small number of items. Given that the MADRS score may be influenced by physical symptoms or problems with concentration or sleeping in the early phase of stroke (like any other depression measure), we added the presence of early DS as a covariate in the multivariate regression analyses to examine the *independent* contribution of cognition in the prediction of long-term DS. A drawback of using the MADRS, however, is that we cannot extrapolate our results to the post-stroke depression literature as it is currently unclear how depressive symptoms relate to post-stroke depression. Second, we did not assess potential emotional confounders such as catastrophic reactions [51], apathy [52], or anxiety [53], although the presence of these disorders might have affected the MADRS or SSQOL scores to some extent.

In conclusion, cognitive impairment in the first weeks after stroke is an important risk factor of long-term depressive symptoms and a reduced quality of life. Our findings may assist caregivers in the early detection and treatment of patients at risk for adverse emotional outcome after stroke. As there may be differences in the effects of antidepressants in patients with and without cognitive impairment after stroke, future studies are warranted to examine the relation between depression/depressive symptoms and cognitive impairment in more detail.

Acknowledgements

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