

PROGNOSIS FOR PATIENTS WITH NEGLECT AND ANOSOGNOSIA WITH SPECIAL REFERENCE TO COGNITIVE IMPAIRMENT

Peter Appelros,^{1,2} Gunnel M. Karlsson,¹ Åke Seiger^{2,3} and Ingegerd Nydevik^{2,3}

From the ¹Departments of Neurology and Geriatrics, Örebro University Hospital, Örebro, ²Neurotec Department, Karolinska Institutet, ³Stockholms Sjukhem, Stockholm, Sweden

Objective: To describe prognosis in patients with unilateral neglect, anosognosia, or both, within a community based stroke cohort.

Methods: Patients ($n = 377$) were evaluated at baseline for the presence of neglect and anosognosia. After 1 year, the level of disability was established in survivors. Predictors for death and dependency were examined in multivariate analysis. The following independent variables were used: age, consciousness, hemianopia, arm paresis, leg paresis, sensory disturbance, aphasia, neglect, anosognosia, diabetes mellitus, cardiovascular disease, pre- and post-stroke cognitive impairment.

Results: Age, consciousness and sensory disturbance predicted death. Post-stroke cognitive impairment, neglect, hemianopia, arm paresis and age predicted dependency.

Conclusion: Neglect in the acute phase, which occurs in patients irrespective of pre-stroke cognitive level, negatively affects disability after 1 year. Anosognosia more often occurs in patients who are cognitively impaired before the stroke. These patients often are ADL-dependent already, or become dependent because of cognitive impairment, not because of anosognosia.

Key words: cerebrovascular disorders, epidemiology, prognosis, perceptual disorders.

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Correspondence address: Peter Appelros, Department of Neurology, Örebro University Hospital, SE-701 85, Örebro, Sweden. E-mail: peter.appelros@orebroll.se

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INTRODUCTION

In a previous paper (1) we examined the incidence of neglect and anosognosia after first-ever stroke and their relationship to dependency. Neglect has often been associated with an unfavourable long-term prognosis in terms of rehabilitation outcome, length of hospital stay and discharge to home (2–7). However, the generality of previous studies is limited because of subject selection methods. Often the sample has been drawn from admissions to hospitals or rehabilitation facilities. Furthermore, the studies tend to be small, and there may be no control group. Finally, data may not have been analysed with multi-

variate statistics, so it is difficult to be certain about the independence of predictors.

It is also known that anosognosia presents a risk for negative stroke rehabilitation outcome (8, 9) as well as for activities of daily living (ADL) function at hospital discharge (10). Results from a recent study have shown that patients with anosognosia in the acute phase of stroke had a poorer functional outcome after 1 year than patients who were aware of illness (11). Anosognosia has been associated with cognitive impairment and subcortical brain atrophy (12). Although the association between anosognosia and general cognition has been emphasized, it is not known how close their relationship is in an unselected group of patients.

Given the uncertain impact of neglect and anosognosia in the acute stage upon long-term outcome, especially with regard to cognitive decline, we decided to evaluate their impact upon mortality and dependency 1 year after a stroke event. This was accomplished within the frames of a population-based sample of first-ever stroke patients.

MATERIAL AND METHODS

Over a period of 1 year, from 1 February 1999 to 31 January 2000, 377 patients were identified as having a first-ever stroke in the municipality of Örebro, Sweden. The WHO diagnostic criteria were used (13). In the present study, patients with subarachnoidal haemorrhage were excluded due to their different aetiology and clinical course. The data collection was population-based, i.e. patients inside as well as outside the hospital were included. Cases were pursued as they occurred ("hot pursuit" method) (14). Several overlapping ways of finding patients were used. The procedure of ascertaining cases is explained in detail in a previous paper (15).

At baseline, an impairment evaluation according to the NIH stroke scale (NIHSS) was made (16). After the stroke diagnosis had been confirmed, an occupational therapist (GMK) performed the neglect and anosognosia testing 1–4 days after the event. If a patient then was too ill to co-operate, the occupational therapist would reiterate the tests up to 1 month after the event. In addition, an evaluation of ADL was performed according to the Katz ADL Index (KI) (17). The presence of pre-stroke dementia was established if these disabilities had been so severe as to interfere with everyday activities for at least 6 months, alternatively if there had been a confirmed diagnosis of dementia according to medical records. Information regarding living conditions and requirement for home assistance was acquired both at baseline and at the 1-year follow-up. We used the best available sources, either the patient, a next-of-kin, or another carer.

Neglect was assessed using a reduced version of the Behaviour Inattention Test (18), the Baking Tray Task (BTT) (19) and 2 tests of personal neglect (20, 21). Neglect was diagnosed when there was a positive result on any of the tests. A questionnaire was used to assess anosognosia (12). This questionnaire addresses anosognosia for hemiplegia and anosognosia for hemianopsia. For a short description of each

Table I. Katz ADL Index level pre-stroke, and 1–4 days and 1 year post-stroke

Katz level	Pre-stroke n (%)	1–4 days post-stroke n (%)	1 year post-stroke n (%)
A	286 (76)	134 (36)	166 (44)
B	26 (7)	10 (3)	25 (7)
C	19 (5)	10 (3)	16 (4)
D	17 (5)	7 (2)	3 (1)
E	2 (1)	39 (10)	5 (1)
F	6 (2)	52 (14)	31 (8)
G	2 (1)	87 (23)	7 (2)
Dead	–	10 (3)	124 (33)
Missing	19 (5)	28 (7)	–

test and the procedure, we refer to our earlier paper (1). Nineteen of the 377 patients were discovered through death certificates, and 9 patients denied consent. A further 64 patients were not able to perform any of the tests due to the severity of stroke, low level of cognition, aphasia and/or apraxia.

After 1 year, population statistics was checked for patient survival. Survivors were asked to take part in a follow-up interview and an examination. The examination took place either at the hospital or in the patient's home according to the wishes of the patient. A single doctor (PA) assessed all the patients. At the follow-up visit a new evaluation was performed according to the KI. This evaluation was performed by means of a structured interview. Also, information was retrieved about each patient's KI level before the event. At the 1-year follow-up, we also assessed cognition with the Mini Mental State Examination (MMSE) (22). A few of the survivors ($n = 7$) with anosognosia at baseline were re-evaluated with the anosognosia questionnaire at the 1-year follow-up.

Confidence intervals for proportions were calculated using the method described by Newcombe & Altman (23). Multiple logistic regression and bivariate correlation were calculated using the SPSS package, version 11.5.

Ethics

Before entering the study, patients were asked orally for consent. They also received an information letter. In some cases, when a patient's ability to communicate was restricted, consent by next of kin was obtained. The Human Ethics Committee of the Örebro County Council approved the study. The local Data Inspection Board approved the data register.

RESULTS

In the acute phase of the disease, 23% of the testable patients

(65/279) had neglect. Neglect was more common in right hemisphere damage (32%) than in left hemisphere damage (17%). Seventeen percent (48/276) of the patients had anosognosia, which also was somewhat more common in right hemisphere damage (21%) than in left (13%). Patients who were testable had somewhat lower mean age (75 years compared with 77 years for the whole cohort), had lower case fatality (3% compared with 18%), and had less neurological impairment (6 points compared with 9 points on the NIHSS) (1).

Sixty-nine of the patients died within the first 28 days (18%), and a total of 124 patients had died within 1 year (33%). Table I shows the distribution of different KI levels before, 1–4 days after, and 1 year after the stroke event. Nine patients denied consent to take part in the follow-up consultation. However, they accepted to give information regarding their ADL status by telephone, or through relatives.

Data were analysed using univariate and multivariate regression in order to determine predictors for death and dependency after 1 year. The following explanatory variables were used: age, level of consciousness as measured with NIHSS items 1a, 1b and 1c, visual fields as measured with NIHSS item 3, paresis of arm as measured with NIHSS item 5, paresis of leg as measured with NIHSS item 6, sensory function as measured with NIHSS item 8, language as measured with NIHSS item 9, neglect, anosognosia, diabetes mellitus, cardiovascular disease (other than stroke), and pre-stroke cognitive impairment. For the regression model with regard to dependency, we also used post-stroke cognitive impairment as an explanatory variable.

All variables except age were dichotomized. The outcome variable was dichotomized to either independent (KI level A) or dependent (KI levels B–G). The result of the individual NIHSS items was dichotomized as normal (0 point), or not normal (1 point or more). One point on any of the sub-tests in NIHSS items 1, 5, and 6 lead to coding "not normal". Neglect, anosognosia, diabetes mellitus, cardiovascular disease, and pre-stroke cognitive impairment were coded either as present or not present. Post-stroke cognitive impairment was defined as a MMSE <24.

The results of the univariate and multivariate analyses are given in Table II. Age, lowered consciousness at baseline and

Table II. Predictors of death or dependency 1 year after a stroke event (95% CIs)

Predictor	Odds ratios for death (univariate)	Odds ratios for death (multivariate)	Odds ratios for dependency (univariate)	Odds ratios for dependency (multivariate)
Age	1.07 (1.05–1.10)	1.10 (1.05–1.15)	1.08 (1.04–1.11)	1.05 (1.01–1.09)
Consciousness	13.3 (7.2–25)	3.2 (1.6–6.6)	4.4 (2.5–7.6)	
Hemianopia	5.1 (3.2–8.1)		3.4 (1.8–6.4)	3.8 (1.6–9.4)
Arm paresis	3.4 (1.9–6.2)		2.1 (1.2–3.9)	2.9 (1.3–6.6)
Leg paresis	3.6 (2.1–6.2)		2.0 (1.1–3.5)	
Sensory disturbance	3.5 (2.2–5.4)	2.5 (1.3–5.1)	1.3 (0.7–2.4)	
Aphasia	3.6 (2.3–5.7)		1.7 (0.9–3.1)	
Neglect	2.7 (1.4–5.1)		4.0 (2.0–7.8)	3.9 (1.6–9.3)
Anosognosia	5.3 (2.7–11)		12 (4.3–33)	
Diabetes mellitus	1.0 (0.6–1.7)		1.3 (0.7–2.5)	
Cardiovascular disease	1.2 (0.8–2.0)		1.3 (0.7–2.3)	
Pre-stroke cognitive impairment	6.4 (3.2–13)		7.1 (1.9–26)	
Post-stroke cognitive impairment	–	–	7.6 (4.0–14)	5.9 (2.7–13)

Table III. Bivariate correlations (Pearson) between neglect, anosognosia, pre- and post-stroke cognitive impairment

	Anosognosia	Pre-stroke cognitive impairment	Post-stroke cognitive impairment
Neglect	0.36	0.05	0.15
Anosognosia		0.38	0.49
Pre-stroke cognitive impairment			0.46

impaired sensory functions were the best predictors of death within 1 year. Post-stroke cognitive impairment, neglect, visual fields, arm function and age were the best predictors of dependency after 1 year.

Correlation coefficients between neglect, anosognosia, pre- and post-stroke cognitive impairment are given in Table III. There are strong correlations between anosognosia and both pre- and post-stroke cognitive impairment, but only weak correlations between neglect and cognitive impairment.

The relationships between neglect, anosognosia and cognitive impairment on one hand, and the need for a sheltered living and need for home help service on the other, are shown in Table IV.

After 1 year 7 of 27 survivors with anosognosia at baseline were re-tested using the same method. None showed anosognosia at the later date.

DISCUSSION

Within a community-based stroke study, we have shown that neglect, but not anosognosia, in the acute phase of stroke, is a valid predictor of dependency after 1 year. Neither of them are independent predictors of death within the first year. Not unexpectedly, post-stroke cognitive impairment is a predictor of dependency.

Although insensitive to small degrees of change, and with known "floor" and "ceiling" effects, the KI is simple to use, and is still much used in Sweden. There is a high degree of agreement between KI and the Barthel Index (24). The KI has, as the Barthel Index, often been used as an interview index, although its validity as such is poorly documented (25). For the purpose of the present study, however, we feel that this use can be justified, because the scale can adequately classify stroke survivors as dependent or independent (24).

At present, we have no commonly used multivariate statistical

method that fully takes advantage of ordinal data. For logistic regression, transformation into multiple independent variables ("dummying") could be an alternative, but in this case that would yield too many variables. Therefore, we have chosen to dichotomize data. This technique may reduce some wealth of detail from the calculations, but in our case the cut-offs were natural, i.e. paresis—no paresis; diabetes—no diabetes, so that a minimum of serendipity was used.

Not many test instruments exist for anosognosia. To our knowledge, the instrument that we used was the best available at the time the study started. It might have been an advantage to register anosognosia for hemiplegia and anosognosia for hemianopsia separately, but the fact that these conditions can be double-dissociated was recently highlighted (11). However, the overwhelming majority of the anosognosia patients in our study had anosognosia for hemiplegia.

It is previously known that anosognosia correlates with total lesion size (26), and that it is associated with subcortical brain atrophy, as well with a low post-stroke score on the Mini-Mental State Examination (12). Results from the present study show that anosognosia also correlates with pre- and post-stroke cognitive impairment. Taken together, this strengthens the impression that anosognosia above all is associated with diffuse brain damage, even though it may be associated with some localised lesions, notably in the temporoparietal junction, thalamus and basal ganglia (12). Anosognosia is also more common in right-sided lesions (1, 10, 26). The fact that anosognosia seems to be associated with diffuse brain damage and low cognition, may in some cases make the evaluation of the condition more difficult.

Our results confirmed the reports of others regarding the significance of consciousness in the acute stage for both death (27, 28) and dependency (28, 29) after 1 year. One previous study has also noted an association between sensory loss and death within 1 year (29). Also the effect of age is corroborated by previous studies.

Several authors have studied the influence of neglect on long-term functional outcome. For a comprehensive review, we refer to Ferro and co-workers (30). Additional studies have appeared in the last years (6–7, 31–33). Due to limited patient selection and lack of controls, the external validity of many of these studies may be questioned. Also, many of them did not use multivariate analysis, and therefore confounding may be a problem. Although one large well-designed study failed to show that neglect had any independent influence on short-term

Table IV. Place of living and need of home assistance before and after the stroke, % (95 % CIs) (n = 253)

Patient category	Living in service flat or nursing home		Need of home assistance	
	Pre-stroke	Post-stroke	Pre-stroke	Post-stroke
All	4.7 (2.7–8.1)	21 (16–26)	22 (17–27)	59 (53–65)
Neglect	2.2 (0.4–12)	40 (26–56)	20 (11–34)	82 (69–91)
Anosognosia	15 (5.9–33)	52 (34–69)	48 (31–66)	96 (82–99)
Post-stroke cognitive impairment	21 (10–37)	71 (54–83)	59 (42–74)	97 (85–99)

functional outcome (34), most previous studies have shown that neglect has an unfavourable influence upon overall prognosis in terms of functional outcome (6, 7), improvement on rehabilitation (35), length of hospital stay and discharge to home (5, 36).

The impact of anosognosia on death and dependency has been little studied. Pedersen et al. (10) found that anosognosia independently increased the risk of dying during hospital stay. In the present study, anosognosia was significantly associated with death after 1 year in univariate analysis, but not in multivariate analysis. Even if our calculations did not make use of the same set of explanatory variables, it may well be that anosognosia is a predictor of death in the acute phase, but not in the long term. Although the number of patients who were re-tested in our study was small, the results are not inconsistent with that anosognosia tends to disappear within months (8, 11), which may explain the lack of such an association. The negative role of anosognosia in stroke rehabilitation has been emphasized (8–10), but our results could not confirm the results of others (11) that anosognosia at baseline has an independent impact upon dependency after 1 year.

Patients with neglect had greater needs for a sheltered living and home assistance after event. Patients with anosognosia and post-stroke cognitive impairment had greater such needs both before and after the stroke. This strengthens the thesis that the last-mentioned group more often has pre-existing brain damage. The reason for their greater needs 1 year after a stroke seems to be cognitive decline, not anosognosia.

Our study has the advantage of a population-based material, which should minimize selection bias and enhance external validity. We have confirmed the observations of others, that neglect has a strong influence upon dependency in stroke survivors after 1 year. Although it was not the primary aim of the study, our results are not in disagreement with the fact that anosognosia disappears within the first year. Anosognosia does not seem to have an independent influence upon functional outcome after 1 year. Their relationship in univariate analysis may be explained by confounding, the intervening factor being diffuse brain damage, expressed by cognitive impairment.

In conclusion, it seems that neglect often follows stroke in a previous healthy brain and has serious long-term consequences upon the patient's ADL performance. Anosognosia more often occurs in patients who are cognitively impaired before the stroke. Anosognosia often resolves spontaneously. Patients with anosognosia are often ADL-dependent previously, or become dependent because of cognitive impairment. Rehabilitation efforts and research should probably be directed towards neglect rather than anosognosia, because anosognosia often disappears and does not seem to affect dependency independently.

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