



## CLINICAL AND FUNCTIONAL DIFFERENCES BETWEEN RIGHT AND LEFT STROKE WITH AND WITHOUT CONTRALATERAL SPATIAL NEGLECT

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**Objective:** To examine the clinical and functional characteristics associated with contralateral spatial neglect in right compared with left subacute stroke, and to investigate the correlations between neglect severity and stroke severity, functional ability and outcome.

**Methods:** Cross-sectional study comparing neurological impairment and disability. The same data-set was used in part 2 of this study.

**Results:** Contralateral neglect was present in 79.7% of right stroke and 68.3% of left stroke rehabilitants, and was, on average, equally mild. Left stroke rehabilitants with neglect had higher stroke severity, cognitive and total disability and dependence level and more impaired sphincter control than right stroke rehabilitants with neglect, while the occurrence of depression, motor and sensory impairment was similar. Rehabilitants with neglect, irrespective of stroke side, had higher stroke severity, cognitive, motor and total disability and dependence level than rehabilitants without neglect.

**Conclusion:** In left and right stroke rehabilitants with equally mild neglect, those with left stroke had higher stroke severity, cognitive and total disability and dependence level. Neglect severity correlated with right or left stroke severity and functional ability, moderate to severe neglect correlated significantly more with functioning. Neglect severity was independently associated with functional outcome in right stroke.

**Key words:** clinical characteristics; functioning; inpatient; outcome; subacute rehabilitation; severity; spatial neglect; stroke laterality.

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Stroke is a leading cause of functional impairment worldwide. Annually, approximately 16.9 million people have their first stroke (1, 2). Approximately one-third of stroke patients present lifelong disability (2, 3). Hemi-spatial neglect is a complex and puzzling syndrome, defined as a failure to attend to the contralateral side of personal, peri- or extra-personal space (4). In a recent national registry study neglect was found in 30% of all stroke patients admitted to hospital (5). Among stroke

### LAY ABSTRACT

Contralateral spatial neglect (inattention) occurred in 79.9% of rehabilitants with right and 68.3% of those with left stroke at admission to rehabilitation, and was, on average, equally mild. Rehabilitants with left stroke and neglect had higher stroke severity and higher cognitive-communicative and overall disability and dependence level and more impaired sphincter control than those with right stroke and neglect, while the occurrence of depression, and motor and sensory impairment was largely similar. Rehabilitants with neglect, irrespective of stroke side, had higher stroke severity and higher cognitive, motor and overall disability than those without neglect. Neglect severity was related to right or left stroke severity and functional ability, moderate to severe neglect was significantly more related to functioning. Neglect severity was independently related to functional outcome in rehabilitants with right stroke.

rehabilitants the occurrence has been found to increase to 80% (6, 7), being most common in the immediate post-stroke and subacute phase (7, 8) and usually more common and severe after right compared with left brain damage (4, 7, 9–11), although in different studies the occurrence varies widely, depending on the methods used to assess neglect, the criteria applied in patient selection including age, and the time after stroke onset (4, 10, 12). Even if up to 77% of left brain-damaged stroke rehabilitants have been found to show at least some behavioural neglect (4), most studies on neglect have concentrated mainly on right-sided brain lesions (6, 13), or some studies have been conducted in mixed populations with lesions on either side (7, 8, 14–16). In these studies hemi-spatial neglect has been linked with higher stroke severity and high motor, sensory and cognitive impairment and disability in activities of daily living (ADL) (5, 7, 8, 17–21). However, little is known about left stroke with neglect (14), and studies aiming at comparing clinical and functional differences between right and left stroke patients with neglect are lacking. In addition, the correlations between severity of neglect and both neurological impairment and disability level require clarification (22).

In order to extend previous stroke research on the correlation of spatial neglect with various clinical and functional factors and their connection with stroke laterality, the aim of this study was to investigate the clinical characteristics and functional ability in ADL associated with right and left subacute stroke with and without

neglect, and, secondly, to investigate the correlation between contralateral neglect severity and stroke severity, functional ability and outcome in right and left stroke.

### PATIENTS AND METHODS

A total of 173 consecutive, previously independent, patients, aged over 16 years, with first-ever, radiologically confirmed, unilateral, either right or left hemispheric stroke, were included in this cross-sectional study between August 2015 and February 2019. The patients were mostly referred to the neurological rehabilitation unit from the acute stroke unit of the same university hospital. Sometimes the patient had to wait after the acute stroke unit care on a general ward for stabilization of the medical condition before intensive rehabilitation, or due to lack of capacity of the rehabilitation unit. Because of the intensive programme and high costs of multidisciplinary rehabilitation it is necessary to assess which patients are most suited for admittance to inpatient rehabilitation ward and which patients would be better taken care of at home with possible outpatient therapies or in a skilled nursing facility (23, 24). For admission to our rehabilitation ward, patients had to be able to sit in a wheelchair for a minimum of 30 min.

A multidisciplinary team evaluation included assessments made by a neurologist, a physiotherapist, an occupational therapist, a speech and language therapist, a neuropsychologist, a social worker, a rehabilitation planner, rehabilitation nurses and, when necessary, also other consultants. Intensive comprehensive inpatient rehabilitation programme consisted of combined coordinated meetings with these rehabilitation specialists 5 days a week according to patients' individual needs, in addition to constant daily rehabilitative nursing.

Exclusion criteria were: current major medical, neurological or psychotic condition, in addition to stroke ( $n = 1$ ), patients with infra-tentorial or bilateral lesions or with a radiological finding of a previous stroke or other brain damage or with brain injury without radiological findings ( $n = 55$ ), those with ipsilateral (1 patient with right hemisphere infarct) or bilateral ( $n = 3$ ) neglect, delay in admission to rehabilitation from stroke onset over 1 year ( $n = 2$ ), and medical reasons for interrupted rehabilitation ( $n = 5$ ).

#### Demographic variables

Demographic data, including age, sex, marital status, educational level and working status, were collected (Table I).

#### Independent variables

The independent admission variables included, firstly, neglect (presence and severity) as the main variable and, secondly, other independent variables that can affect functioning: type of lesion (infarction vs haemorrhage), stroke severity, severity of paresis and aphasia, presence of sensory impairment, apraxia and depres-

sion, time since stroke onset, number of comorbidities, Charlson Comorbidity Index (Table II). Clinical data (e.g. 10<sup>th</sup> revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnosis, date of diagnosis, date of admission and discharge, 24 h National Institutes of Health Stroke Scale (NIHSS) score after possible thrombolysis and/or thrombectomy, comorbidities) were collected from the hospital patient charts. The total number of comorbidities was counted, a procedure previously used to categorize comorbidities (25), and the Charlson Comorbidity Index was calculated (26). The presence of depression and apraxia were based on the clinical judgement of the team.

#### Scales

An occupational therapist assessed the level of possible spatial neglect of each rehabilitant at admission, using the Catherine Bergego Scale (CBS). The CBS is a measure of functional neglect in spontaneous behaviour in personal, peri- and extra-personal space. It is based on direct observation of 10 real-life situations, i.e. grooming, dressing, eating, mouth cleaning, gaze orientation, knowledge of limbs, auditory attention, moving (collisions), spatial orientation, and finding personal belongings. It captures mild neglect better than traditional paper-and-pencil tests. A total score of 1–10 is classed as mild, 11–20 moderate, and 21–30 severe neglect (4, 27, 28).

A neurologist assessed the neurological status of subjects, including the NIHSS score at admission. The NIHSS is a scale of key components of a standard neurological examination used to assess stroke severity from 0 to 42 ("normal functioning" – "coma"). Total scores 1–4 mean mild, 5–15 moderate, 16–20 severe, and 21–42 very severe stroke (29).

#### Functional variables

Functional variables included admission FIM total score and motor and cognitive sub-score, dependence level, domain scores, and FIM item scores main locomotion and stairs separately (Table III). The discharge FIM total score was chosen as the main outcome variable because it covers a large number of items and measures outcome in stroke (Tables III, V and VI).

#### FIM instrument

As part of our formal rehabilitation programme, a rehabilitation nurse, trained and accredited in accordance with Uniform Data System standards as a Functional Independence Measure (FIM®) rater, assessed the level of functioning of each rehabilitant at admission and discharge using an electronic FIM tool (FIM® version 5.2, Amherst, NY, USA). The FIM is a measure of physical and cognitive disability and dependence in 18 items, including 4 motor (self-care, sphincter control, transfer and locomotion) and 2 cognitive (communication and social cognition) domains. The domain locomotion consists of the items main locomotion

**Table I.** Demographic data of the four rehabilitant subgroups.

Variables at admission	Right-sided stroke		Left-sided stroke		p
	With neglect n = 55	Without neglect n = 14	With neglect n = 71	Without neglect n = 33	
Age, years, median (IQR) range	65.1 (56.2, 71.2) 33.6–82.4	57.6 (51.1, 67.2) 36.4–81.4	66.5 (56.1, 74.3) 16.3–83.5	60 (56.1, 71.4) 25.6–77.9	0.3
Education, years, median (IQR) range	11 (9, 14) 6–22	9.5 (9.0, 12.0) 6.0–16.0	10 (9, 13) 6–20	12 (9, 14) 6–25	0.4
Gender female, n (%)	25 (45.4)	8 (57.1)	29 (40.8)	13 (39.4)	0.7
Cohabiting, n (%)	30 (54.6)	10 (71.4)	45 (63.4)	19 (57.6)	0.6
Still working, n (%)	18 (32.7)	6 (42.9)	23 (32.4)	18 (54.6)	0.1

IQR: interquartile range.

and stairs. Each item is measured on a 7-point scale, ranging from 1 (total assistance) to 7 (complete independence). The total score ranges from 18 to 126, motor sub-score from 13 to 91, and cognitive sub-score from 5 to 35 (<http://udsmr.org>).

Participants signed a written informed consent. The same data-set was used in part 2 of this study (30). A proportion of the participants were also included in a previous study (31).

The ethics committee of the University of Turku and Turku University Hospital approved the study (19.5.2015, 73/2015). The ethical standards of the World Medical Association Helsinki Declaration of 1975, as revised in 1983, were followed.

### Statistical analysis

Categorical variables were described using frequencies and percentages and, for continuous variables, medians with range of values and interquartile range (IQR) percentiles were used. Comparisons between the 4 rehabilitant subgroups for continuous variables were carried out using the non-parametric Kruskal–Wallis test, and, for pairwise comparisons, the Mann–Whitney *U* test with Bonferroni correction was used. Difference on Hodges–Lehmann estimate for median difference was used. With categorical variables comparisons between subgroups were assessed with  $\chi^2$  test, or, in the case of small cell frequencies, Fisher's exact test. Spearman's correlation coefficient was used to test the correlation between CBS score, varying from 0 to 29 in the present study, and, firstly, NIHSS score and, secondly, FIM total score, motor and cognitive sub-score and dependence level at admission. When examining the significance of the mild vs moderate to severe neglect on neurological and functional status, we chose to selectively include only the rehabilitants with neglect (CBS  $\geq 1$ ). Correlations of 0–0.29 were considered weak, 0.30–0.49 moderate, 0.50–0.69 strong, and 0.70–1.00 very strong. Among rehabilitants with neglect (CBS  $\geq 1$ ), linear associations between discharge FIM total score and variables potentially having an impact on outcome were investigated. The factors found to have a significant bivariate association with discharge FIM score were included as independent variables in a linear multiple regression model with discharge FIM score as a dependent variable. Residuals were checked to justify the analysis. Possible multicollinearity was checked; correlation coefficient  $\geq 0.8$  and/or tolerance value  $< 0.1$  was considered a sign of multicollinearity. Again, we chose to exclude participants with a normal CBS score (=0) in order to focus selectively on the impact of neglect severity as a predictive factor. *p*-values below 0.05 (2-tailed) were considered statistically significant. Statistical analyses were performed using SAS 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

## RESULTS

Of the 173 consecutive stroke rehabilitants who fulfilled the inclusion criteria, 126 (72.8%) were affected by contralateral neglect, 79.7% of those with right and 68.3% of those with left stroke. Of those with neglect, neglect was mild in 65.4% of those with right, and 81.7% of those with left stroke, moderate in 20.0% and 12.7%, and severe in 14.5% and 5.6%, respectively. Four subgroups were formed, those with right-sided stroke with ( $n=55$ ) and without ( $n=14$ ) neglect and those with left-sided stroke with ( $n=71$ ) and without ( $n=33$ ) neglect. No statistically significant differences were found in demographic data between the 4 subgroups (Table I).

**Table II.** Clinical characteristics of the four rehabilitant subgroups with between-group differences using Kruskal–Wallis test. Difference on Hodges–Lehmann estimate for median difference. All pairwise comparisons are Bonferroni corrected.

Variables at admission	Right-sided stroke		Left-sided stroke		Right stroke with vs left stroke with neglect		Left stroke with vs without neglect		Difference between medians (95% Confident limits) , <i>p</i>	
	With neglect (group 1), <i>n</i> = 55	Without neglect (group 2) <i>n</i> = 14	With neglect (group 3) <i>n</i> = 71	Without neglect (group 4) <i>n</i> = 33	Right stroke with vs without neglect	Left stroke with vs without neglect	Right stroke with vs left stroke with neglect	Left stroke with vs without neglect	Right stroke with vs left stroke with neglect	Left stroke with vs without neglect
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>p</i>	<i>p</i>	<i>p</i>	<i>p</i>	<i>p</i>	<i>p</i>
Infarction (vs hemorrhage)	34 (61.8)	11 (78.6)	47 (66.2)	21 (63.6)	0.7					
Severity of stroke: 24 h NIHSS, median (IQR) range	11 (7, 16) 3–28	5 (2, 8) 1–13	16 (11, 22) 5–34	8 (5, 15) 3–23	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Admission NIHSS, median (IQR) range	7 (5, 10) 1–20	2 (1, 3) 0–12	11 (7, 14) 3–22	3 (1, 5) 0–12	<0.0003	<0.0003	<0.0003	<0.0003	<0.0003	<0.0001
Time since stroke onset, median (IQR) range	36 (23, 62) 6–130	44.5 (16, 83) 3–169	37 (17, 72) 6–199	25 (18, 43) 7–139	0.3	0.3	0.3	0.3	0.3	0.3
Length of stay, median (IQR) range	29 (18, 44) 3–90	13.5 (8, 27) 4–32	35 (20, 46) 4–91	15 (11, 21) 3–36	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Neglect (CBS score 0–29) , median (IQR) range	5 (2, 14) 1–29	0	5 (2.5, 8) 1–25	0	<0.0001	<0.0001	<0.0001	<0.0003	<0.0003	1 (–1, 3) 1.0
Number of comorbidities, median (IQR) range	1 (1, 2) 0–6	1.5 (1, 2) 0–4	1 (1, 2) 0–4	1 (0, 2) 0–4	0.2	0.2	0.2	0.2	0.2	0.2
Charlson index, median (IQR) range	0 (0, 1) 0–3	0 (0, 1) 0–2	0 (0, 1) 0–3	0 (0, 0) 0–2	0.3	0.3	0.3	0.3	0.3	0.3
Presence of paresis, <i>n</i> (%)	45 (81.8)	4 (28.6)	56 (78.9)	8 (24.2)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Severity of paresis, median (IQR) range	2 (1, 5) 0–8	0 (0, 2) 0–5	4 (1, 7) 0–8	0 (0, 0) 0–8	0.01	0.01	0.01	0.01	0.01	0.01
Presence of sensory impairment, <i>n</i> (%)	37 (67.3)	5 (35.7)	42 (59.1)	12 (36.4)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Presence of apraxia, <i>n</i> (%)	6 (10.9)	0 (0, 0)	46 (64.8)	12 (36.4)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Presence of aphasia, <i>n</i> (%)	4 (7.3)	1 (7.1)	63 (88.7)	22 (68.8)	0.5	0.5	0.5	0.5	0.5	0.5
Severity of aphasia, <i>n</i> (%)	3 (75/1.25/0.0)	1 (100/0/0.0)	28 (44.4/24.38.1/11.17.5)	14 (63.6/7.31.8/14.5)	0.5	0.5	0.5	0.5	0.5	0.5
Presence of depression, <i>n</i> (%)	3 (5.5)	0 (0, 0)	8 (11.3)	2 (6.1)	0.4	0.4	0.4	0.4	0.4	0.4

IQR: interquartile range; NIHSS: National Institutes of Health Stroke Scale, CBS: Catherine Bergego Scale, FIM: Functional Independence Measure; Severity of aphasia: mild to moderate/severe/global.



**Table III.** Functioning assessed with FIM of the four rehabilitant subgroups with between-group differences using Kruskal-Wallis test. Difference on Hodges-Lehmann estimate for median difference. All pairwise comparisons are Bonferroni corrected.

Variables, n, % or median (IQR) range	Right-sided stroke		Left-sided stroke		p	Right stroke with vs without neglect difference between medians (95% Confident limits) , p	Left stroke with vs without neglect difference between medians (95% Confident limits) , p	Right stroke with neglect vs left stroke with neglect
	with neglect (group 1) n=55	without neglect (group 2) n=14	with neglect (group 3) n=71	without neglect (group 4) n=33				
At admission								
FIM dependence level	5.0 (3, 5) 2-7	6.0 (5, 6) 3-7	4.0 (2, 5) 1-6	6.0 (5, 6) 2-6	<0.0001	1 (1,2) 0.003	2 (1, 2) <0.0003	1 (0, 1) 0.03
FIM total	90 (68, 101) 50-126	119 (96, 124) 66-126	74.0 (50, 95) 18-116	114 (106, 120) 49-124	<0.0001	25 (11, 36) 0.001	35 (23, 46) <0.0003	14 (4, 23) 0.008
FIM motor	62 (41, 75) 24-91	87 (71, 90) 33-91	50 (32, 73) 13-91	86 (81, 90) 30-92	<0.0001	20 (8, 30) 0.003	29 (19, 41) <0.0003	7 (-1, 15) 0.3
Self-care (mean)	4.7 (3.5, 5.8) 2.3-7	6.9 (5.5, 7) 3.2-7	3.8 (2.8, 5.7) 1-7	6.8 (6.3, 7) 1.8-7	<0.0001	1.7 (0.7, 2.5) 0.002	2.3 (1.5, 3.3) <0.0003	0.5 (0, 1.2) 0.1
Sfincter control	6 (4, 7) 1-7	7 (6.5, 7) 3.5-7	4.5 (1.5, 7) 1-7	7.0 (6.5, 7) 1-7	<0.0001	0.5 (0, 1.5) 0.05	2 (0.5, 3.5) <0.0003	1 (0, 2) 0.03
Transfers	5 (3, 6) 1-7	6.7 (6, 7) 1.3-7	4.0 (2, 6) 1-7	7.0 (6, 7) 3-7	<0.0001	1.3 (0.7, 2.7) 0.006	2 (1.3, 3) <0.0003	0 (-0.3, 1) 1.0
Locomotion: walking, wheeling or both	5 (4, 6) 1-7	6 (6, 7) 2-7	5 (3, 6) 1-7	6 (6, 7) 3-7	<0.0001	1 (0, 2) 0.03	1.5 (1, 2) <0.0003	0.5 (0, 1) 1.0
Ambulatory/sedentary/both	22 40/28 50.9/5 9.1	11 78.6/0 0.0/3 21.4	28 39.4/40 56.3/3 4.2	27 81.8/6 18.2/0 0.0	0.0003			
Stairs	1 (1, 4) 1-7	6 (1, 6) 1-7	1 (1, 3) 1-7	6 (5, 7) 1-7	<0.0001	4 (3, 5) 0.007	4 (3, 5) <0.0003	0 (0, 0) 1.0
FIM cognitive	29 (27, 32) 11-35	34 (30, 35) 25-35	24 (17, 28) 5-35	29 (25, 31) 10-34	<0.0001	3 (1, 6) 0.01	5 (2, 7) 0.002	6 (4, 8) <0.0003
Communication	6 (5, 7) 2-7	7 (6, 5, 7) 5.5-7	4 (2, 5, 5) 1-7	5.5 (5, 6.5) 1-7	<0.0001	0.5 (0, 1) 0.1	1.25 (0.5, 2) 0.006	2 (1.5, 2.5) <0.0003
Social cognition	6 (5, 6.3) 1.7-7	6.8 (5.7, 7) 4.7-7	5.3 (3.7, 6) 1-7	6.0 (5.0, 6.3) 1.7-7	0.0001	0.8 (0.3, 1.3) 0.02	0.7 (0, 1) 0.4	0.7 (0.3, 1) 0.02
At discharge								
FIM total	107 (87, 115) 39-126	121 (108, 125) 71-126	103 (66, 114) 18-125	119 (113, 123) 47-126	<0.0001	12 (6, 21) 0.004	15 (9, 24) <0.0003	5 (-1, 12) 0.3

Clinical characteristics and functioning of the 4 subgroups with significant between-group differences are shown in Tables II and III. Rehabilitants with right and left stroke had, on average, equally mild neglect (CBS median 5 in both subgroups), but those with left stroke had a more severe stroke and lower FIM total score and cognitive sub-score including lower score in the FIM domains sphincter control, communication and social cognition and higher overall dependence level. No differences were found between the 2 neglect subgroups in FIM motor sub-score or motor domain or item scores. The occurrence of depression, sensory impairment, presence and severity of paresis and ambulatory ability were largely similar in the 2 neglect sub-groups, but aphasia and apraxia were more common in those with left stroke. Compared with those without neglect, rehabilitants with neglect, irrespective of stroke side, had a more severe stroke, more often sensory impairment, paresis and more severe paresis, less often ambulatory ability, and higher overall, motor and cognitive disability.

Spearman correlations between neglect severity (CBS score at admission, range 0-29, median 3,  $n=173$ ) and stroke severity (admission NIHSS) and level of functioning and dependence (admission FIM) in those with right ( $n=69$ ) or left ( $n=104$ ) stroke are shown in Table IV. Moderate to very strong correlations were found.

In further analysis, mild neglect (left and right CBS range 1-10, median 3,  $n=94$ ) correlated slightly more strongly with admission NIHSS (Spearman  $r=0.35$ ,  $p=0.0005$ ) than with FIM total score ( $r=-0.28$ ,  $p=0.007$ ), but moderate to severe neglect (left and right CBS range 11-29, median 16,  $n=32$ ) correlated significantly more strongly with FIM ( $r=-0.46$ ,  $p=0.009$ ) than with NIHSS ( $r=0.23$ ,  $p=0.2$ ). When analysing the 2 sides separately, the corresponding correlations of mild neglect with FIM and NIHSS in right stroke (median CBS 3,  $n=36$ ) were  $r=-0.22$ ,  $p=0.20$  and  $r=0.38$ ,  $p=0.02$ , and in left stroke (median CBS 4,  $n=58$ )  $r=-0.27$ ,  $p=0.04$  and  $r=0.31$ ,  $p=0.02$ , respectively, and of moderate to severe neglect in right stroke (median CBS 16,  $n=19$ )  $r=-0.64$ ,  $p=0.003$  and  $r=0.16$ ,  $p=0.52$  and in left stroke (median CBS 16,  $n=13$ )  $r=-0.49$ ,  $p=0.09$  and  $r=0.42$ ,  $p=0.15$ , respectively.

**Table IV.** Spearman's correlation coefficients between neglect severity (CBS 0-29) and measures of stroke severity (NIHSS) and functioning (FIM) at admission

	CBS 0-29	
	Right stroke (n=69)	Left stroke (n=104)
NIHSS	0.68**	0.70**
FIM total	-0.64**	-0.62**
Motor	-0.62**	-0.60**
Cognitive	-0.39*	-0.41**
Dependence level	-0.62**	-0.59**

\* $p<0.001$ , \*\* $p<0.0001$ .

CBS: Catherine Bergego Scale; FIM: Functional Independence Measure; NIHSS: National Institutes of Health Stroke Scale.

Results of bivariate linear regression analysis between discharge FIM total score and neglect severity (admission CBS score range 1–29) and potential confounding factors in right and left stroke separately are shown in Table V. Age, stroke severity, functioning (FIM), severity of neglect and paresis, presence of apraxia and depression, time since stroke and Charlson Comorbidity Index were found to be associated with discharge FIM total score. CBS score was found to explain 41.9% of the variance of the discharge FIM total score in those with right and 17.3% in those with left stroke; the corresponding figures for admission FIM total score were 64.1% and 69.0%, respectively.

Multiple linear regression analysis was applied to test the association between discharge FIM total score and variables significantly associated with FIM in bivariate analysis (Table VI). Admission functional ability, age and time since stroke onset were found to be independently associated with outcome in both neglect subgroups, severity of neglect in those with right stroke and presence of depression in those with left stroke and neglect. No significant multicollinearity was found. The factors significantly associated with FIM in multivariate analysis explained 79.8% of the variance of discharge FIM score in rehabilitants with right and 81.2% in those with left stroke.

In addition, associations between length of stay as a dependent variable and the above-mentioned variables potentially affecting outcome (Table V) were investigated: of the variables associated with length of stay in bivariate analyses (severity of neglect, admission FIM motor or total score, education, 24 h and admission NIHSS and severity of paresis), education, admission FIM motor or total, and admission NIHSS score were independently associated with length of stay in both right and left stroke, but not neglect severity ( $CBS \geq 1$ ). Spearman correlations coefficients between  $CBS \geq 1$  and length of stay analysed separately in the 3 discharge categories (home without or with service or institutionalized) and in the entire population ( $n = 173$ ) were 0.09, 0.14, 0.15 and 0.24, respectively.

## DISCUSSION

The occurrence of neglect in the rehabilitant population in this study was high in both right and left stroke (79.7% vs 68.3%), almost as high as in a previous study using a battery of tests to detect neglect (85% vs 77.3%) (4). This is not surprising, as CBS has been

**Table V.** Results of bivariate regression analysis between admission neglect severity and other potential factors affecting outcome (discharge FIM total score)

Variables	Right stroke (n=55)			Left stroke (n=71)		
	$\beta$	R-Square	<i>p</i>	$\beta$	R-Square	<i>p</i>
Demographic variables						
Age	-0.66	0.18	0.001	-0.62	0.08	0.02
Sex, female	1.85	0.002	0.7	-4.55	0.01	0.5
Education in years	-0.17	0.001	0.8	0.90	0.01	0.4
Stroke severity						
NIHSS 24 hour	-2.37	0.47	<0.0001	-2.63	0.34	<0.0001
Admission	-2.64	0.26	<0.0001	-3.16	0.28	<0.0001
Functioning at admission						
FIM total	0.76	0.64	<0.0001	0.85	0.67	<0.0001
Motor	0.75	0.55	<0.0001	0.91	0.58	<0.0001
Cognitive	1.70	0.20	0.0007	2.23	0.39	<0.0001
Dependence level	12.66	0.63	<0.0001	14.61	0.65	<0.0001
Severity of neglect (CBS 1–29)						
Severity of neglect (CBS 1–29)	-1.50	0.42	<0.0001	-1.91	0.17	0.0003
Severity of paresis	-3.37	0.32	<0.0001	-4.20	0.24	<0.0001
Severity of aphasia		0.02	0.5		0.06	0.2
No	reference					
Mild	12.49		0.3	1.29		0.9
Moderate to severe	10.16		0.6	-5.33		0.6
Global				-18.68		0.1
Presence of apraxia	-23.06	0.14	0.006	-15.45	0.07	0.02
Presence of sensory impairment						
Presence of sensory impairment	6.38	0.002	0.3	0.93	0.0003	0.9
Presence depression	-3.92	0.002	0.7	-41.62	0.24	<0.0001
Timing and comorbidities						
Time since stroke at admission						
Time since stroke at admission	-0.18	0.07	0.04	-0.34	0.31	<0.0001
Length of stay	-0.16	0.02	0.3	-0.10	0.004	0.6
Number of comorbidities	-3.70	0.05	0.1	-4.93	0.03	0.1
Charlson Comorbidity Index						
Charlson Comorbidity Index		0.13	0.02		0.05	0.2
No risk factors	reference					
1–2 risk factors	-14.34		0.009	-5.52		0.4
$\geq 3$ risk factors	10.26		0.6	-35.09		0.08

FIM: Functional Independence Measure; NIHSS: National Institutes of Health Stroke Scale; CBS: Catherine Bergego Scale. If association between FIM total score and categorical variable with multiple classes was not statistically significant, estimates between classes are not reported.

found to be a more sensitive method to assess neglect than any single paper-and-pencil test (4). Even if the mean level of neglect in the current study population was equally mild in both right and left stroke, more moderate and severe cases of neglect were found

**Table VI.** Results of multiple linear regression analysis with the variables significant in bivariate analysis for FIM total score at discharge

Variables at admission:	Right stroke n=55		Left stroke n=71		Right and left stroke n=126	
	$\beta$	<i>p</i>	$\beta$	<i>p</i>	$\beta$	<i>p</i>
CBS score (1–29)	-0.74	0.002	-0.44	0.1	-0.54	0.002
FIM motor score	0.46	0.001	0.47	<0.0001	0.46	<0.0001
FIM cognitive score	0.92	0.009	0.85	0.003	1.03	<0.0001
NIHSS score	0.22	0.7	-0.23	0.7		0.6
Severity of paresis	0.26	0.7	-1.06	0.08		0.5
Presence of depression			-12.90	0.02	-9.30	0.02
Presence of apraxia	-8.74	0.09	-3.16	0.4		0.1
Age	-0.30	0.003	-0.35	0.02	-0.34	0.0007
Time since stroke	-0.12	0.005	-0.12	0.003	-0.12	<0.0001
Charlson index						
No risk factors	reference					
1–2 risk factors	-1.99	0.5				
$\geq 3$ risk factors	-4.45	0.7				

Variables with empty spaces are not included in the multiple regression analysis. FIM: Functional Independence measure; CBS: Catherine Bergego Scale; NIHSS: National Institutes of Health Stroke Scale.

among those with right stroke. The finding of higher occurrence and more severe cases in association with right compared with left stroke is in agreement with previous studies (4, 7, 9–11).

When comparing the clinical and functional differences between the 2 subgroups with neglect, rehabilitants with left stroke had a more severe stroke and higher cognitive and total disability and dependence level, but no significant difference was found in motor or sensory functions or the presence of depression. Aphasia and apraxia were significantly more common in those with left brain damage; it is noteworthy that difficulties in communication explain a large part of the FIM cognitive sub-score besides social cognition. In the only previous study primarily aiming at comparing functioning between populations with unilateral left or right hemi-neglect, left neglect was found to be more frequent and severe than right neglect, while motor and cognitive functioning (cognitive ability, communication, motor strength, mobility, and self-care) was largely equal in these 2 groups. Physical independence at admission was similar in rehabilitants with left, right and no neglect. The results of the current study cannot be directly compared with this retrospective study, because of several differences in the populations studied; in the previous study, 29% of 84 rehabilitants, 31 with right and 53 with left hemineglect had ipsilateral or bilateral neglect compared with the current study population with only contralateral lesions, the left-sided neglect was, on average, more severe than in our population, physical independence was similar in rehabilitants with left, right or no neglect at admission to rehabilitation, and patients with problems in understanding were excluded (11). Nevertheless, the previous finding of physical sequelae in functioning and independence being largely comparable in rehabilitants with mild left- and right-sided hemi-neglect is in agreement with our results.

Past studies on neglect have concentrated on comparing patients with neglect to those without neglect, especially in connection with right stroke. Hemi-spatial neglect has been linked with higher severity of stroke and more severe motor, sensory and cognitive impairment and disability in ADL (5, 7, 8, 17–21). The findings of the current study show that this applies to both right and left stroke: those with neglect had a more severe stroke, more often sensory impairment, paresis and more severe paresis, less often ambulatory ability, and higher overall, motor and cognitive disability and dependence level in daily activities than those without neglect.

Neglect appeared to be mild in most of our rehabilitants (74.6% of those with neglect), significantly less often moderate (15.9%) or severe (9.5%). Irrespective of stroke side, the correspondence of neglect severity with stroke severity (NIHSS) was strong to very strong,

and with functioning (FIM) moderate to strong. On closer analysis, in both right and left stroke moderate to severe neglect (CBS >10) correlated significantly more strongly with FIM than with NIHSS; mild neglect (CBS 1–10), on the other hand, correlated slightly more strongly with NIHSS. Moderate to strong correlations have also been found previously between neglect and both FIM and NIHSS (20, 22, 31). In a previous study, neglect correlated slightly more strongly with FIM than with NIHSS during the first year post-stroke (22), which is in agreement with our finding concerning moderate to strong neglect (CBS >10). As CBS is a more sensitive method to detect neglect than conventional assessments used in the previous study, milder cases of neglect were most probably included in our population than in the previous study; this is also supported by the fact that the mean severity of stroke was lower in our population. Nevertheless, the stronger correlation of more severe neglect with FIM than with NIHSS can be seen as an indication that clinically significant neglect influences functional outcome. In accordance with this assumption is the fact that attentional training for disabling neglect has been found to improve functional independence (behaviour), but not neurological status (33).

In agreement with the wider literature (34, 35), the current study found that admission functional status, age and time (delay) from stroke onset to rehabilitation were independent predictors of discharge functional ability, and this applied to both neglect subgroups. Previous research has shown that admission FIM score is the single most significant predictor of outcome (36) and FIM variance at discharge (32). In a previous study among patients with right stroke, neglect severity was shown to be an independent predictor affecting functional recovery (31). Recently, unilateral neglect has been included in a predictive outcome tool for rehabilitants with severe stroke (34). In the current population, especially in those with right stroke, neglect severity predicted independently discharge functional status, but not length of stay, which may be a more biased outcome variable by dependency on, for example, domestic situation and organization of rehabilitation services. Of the neglect subgroups, those with right stroke had milder degree of stroke severity and disability than those with left stroke, but the mean neglect severity was equal in the 2 subgroups; thus, the impact of other factors than functional ability, such as neglect severity, may potentially explain a greater proportion of the outcome in those with right stroke. In addition, the right stroke subgroup had more cases with clinically significant moderate to severe neglect (34.5% vs 18.3%) although the mean severity of neglect did not differ between the 2 subgroups. Advanced age has also previously been found to be a risk factor for poor functional outcome after stroke (36–38), but



also for the presence and severity of neglect (12). In accordance with the results of depression being a predictor of outcome in the subgroup with left stroke and neglect, previous research has shown that depression was associated with outcome and was more common in those with left stroke (39).

### Study limitations

This study has some limitations. Although the number of participants was limited, it was adequate for the purpose of this research. In addition, no data were missing in this prospective study. Although a wide range of consecutive patients, with severity levels varying from NIHSS 0–22 and FIM 18–126, were included in the study, the most and the least disabled patients were not admitted to intensive inpatient rehabilitation, which narrows the generalizability of the results to the entire stroke population. In addition, rehabilitants with first-ever unilateral hemispheric lesions in one facility only were included; thus, the results may not be representative to all stroke rehabilitants. The application of cross-sectional study design does not allow confirmation of causal relationships of disability, i.e. whether they are based on the disease itself or its secondary consequences. When comparing the current results with studies using conventional paper-and-pencil tests to assess neglect, the current population probably includes more rehabilitants with mild neglect, as the functional assessment used in the current study is more sensitive to detect neglect. The FIM may not capture all consequences of neglect, but it covers the most important ADL and is widely accepted as a functional tool in stroke rehabilitation.

### Conclusion

When comparing right and left stroke rehabilitants with equally mild neglect those with left stroke had higher stroke severity and higher cognitive and total disability and dependence level. Rehabilitants with neglect, irrespective of stroke side had not only higher stroke severity and higher cognitive and total disability and dependence level, but also higher motor disability than those without neglect. Severity of neglect correlated with right or left stroke severity and functional ability, moderate to severe neglect significantly more with functioning. Severity of neglect was independently associated with functional outcome in rehabilitants with right stroke.

*The authors have no conflicts of interest to declare.*

## REFERENCES

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Bur-

- den of Disease Study 2010. *Lancet* 2014; 383: 245–255.
2. Grysiewicz RA, Thomas K, Pandey DK. Epidemiology of ischemic and hemorrhagic stroke: incidence, prevalence, mortality, and risk factors. *Neurolog Clin* 2008; 26: 871–895.
3. Singh RJ, Chen S, Ganesh A, Hill MD. Long-term neurological, vascular, and mortality outcomes after stroke. *Int J Stroke* 2018; 13: 787–796.
4. Azouvi P, Bartolomeo P, Beis JM, Perennou D, Pradat-Diehl P, Rousseaux M. A battery of tests for the quantitative assessment of unilateral neglect. *Resto Neurol Neurosci* 2006; 24: 273–285.
5. Hammerbeck U, Gittins M, Vail A, Paley L, Tyson SF, Bowen A. Spatial neglect in stroke: identification, disease process and association with outcome during inpatient rehabilitation. *Brain Sci* 2019; 9: 374.
6. Stein MS, Kilbride C, Reynolds FA. What are the functional outcomes of right hemisphere stroke patients with or without hemi-inattention complications? A critical narrative review and suggestions for further research. *Disabil Rehabil* 2016; 38: 315–328.
7. Chen P, Chen CC, Hreha K, Goedert KM, Barrett AM. Kessler Foundation Neglect Assessment Process uniquely measures spatial neglect during activities of daily living. *Arch Phys Med Rehabil* 2015; 96: 869–876.
8. Nijboer T, van de Port I, Schepers V, Post M, Visser-Meily A. Predicting functional outcome after stroke: the influence of neglect on basic activities in daily living. *Front Hum Neurosci* 2013; 7: 182.
9. Stone SP, Halligan PW, Greenwood RJ. The incidence of neglect phenomena and related disorders in patients with an acute right or left hemisphere stroke. *Age Ageing* 1993; 22: 46–52.
10. Bowen A, McKenna K, Tallis RC. Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. *Stroke* 1999; 30: 1196–1202.
11. Ten Brink AF, Verwer JH, Biesbroek JM, Visser-Meily JMA, Nijboer TCW. Differences between left- and right-sided neglect revisited: a large cohort study across multiple domains. *J Clin Exp Neuropsychol* 2017; 39: 707–723.
12. Gottesman RF, Kleinman JT, Davis C, Heidler-Gary J, Newhart M, Kannan V, et al. Unilateral neglect is more severe and common in older patients with right hemispheric stroke. *Neurology* 2008; 71: 1439–1444.
13. Chen P, Hreha K, Fortis P, Goedert KM, Barrett AM. Functional assessment of spatial neglect: a review of the Catherine Bergego scale and an introduction of the Kessler foundation neglect assessment process. *Top Stroke Rehabil* 2012; 19: 423–435.
14. Jehkonen M, Laihosalo M, Kettunen JE. Impact of neglect on functional outcome after stroke: a review of methodological issues and recent research findings. *Restor Neurol Neurosci* 2006; 24: 209–215.
15. Nijboer TC, Kollen BJ, Kwakkel G. The impact of recovery of visuo-spatial neglect on motor recovery of the upper paretic limb after stroke. *PLoS One* 2014; 9: e100584.
16. Chen P, Hreha K, Kong Y, Barrett AM. Impact of spatial neglect on stroke rehabilitation: evidence from the setting of an inpatient rehabilitation facility. *Arch Phys Med Rehabil* 2015; 96: 1458–1466.
17. Appelros P, Karlsson GM, Seiger A, Nydevik I. Neglect and anosognosia after first-ever stroke: incidence and relationship to disability. *J Rehabil Med* 2002; 34: 215–220.
18. Buxbaum LJ, Ferraro MK, Veramonti T, Farne A, Whyte J, Ladavas E, et al. Hemispatial neglect: Subtypes, neuroanatomy, and disability. *Neurology* 2004; 62: 749–756.
19. Katz N, Hartman-Maeir A, Ring H, Soroker N. Functional disability and rehabilitation outcome in right hemisphere damaged patients with and without unilateral spatial neglect. *Arch Phys Med Rehabil* 1999; 80: 379–384.
20. Cherney LR, Halper AS, Kwasnica CM, Harvey RL, Zhang M. Recovery of functional status after right hemisphere stroke: relationship with unilateral neglect. *Arch Phys Med*

- Rehabil 2001; 82: 322–328.
21. Spaccavento S, Cellamare F, Falcone R, Loverre A, Nardulli R. Effect of subtypes of neglect on functional outcome in stroke patients. *Ann Phys Rehabil Med* 2017; 60: 376–381.
  22. Appelros P, Nydevik I, Karlsson GM, Thorwalls A, Seiger A. Recovery from unilateral neglect after right-hemisphere stroke. *Disabil Rehabil* 2004; 26: 471–477.
  23. Mees M, Klein J, Yperzeele L, Vanacker P, Cras P. Predicting discharge destination after stroke: a systematic review. *Clin Neurol Neurosurg* 2016; 142: 15–21.
  24. Hakkenes S, Hill KD, Brock K, Bernhardt J, Churilov L. Selection for inpatient rehabilitation after severe stroke: what factors influence rehabilitation assessor decision-making? *J Rehabil Med* 2013; 45: 24–31.
  25. Silva AG, Queiros A, Sa-Couto P, Rocha NP. Self-reported disability: association with lower extremity performance and other determinants in older adults attending primary care. *Phys Ther* 2015; 95: 1628–1637.
  26. Goldstein LB, Samsa GP, Matchar DB, Horner RD. Charlson Index comorbidity adjustment for ischemic stroke outcome studies. *Stroke* 2004; 35: 1941–1945.
  27. Azouvi P, Olivier S, de Montety G, Samuel C, Louis-Dreyfus A, Tesio L. Behavioral assessment of unilateral neglect: study of the psychometric properties of the Catherine Bergego Scale. *Arch Phys Med Rehabil* 2003; 84: 51–57.
  28. Klinke ME, Hjaltason H, Hafsteinsdottir TB, Jonsdottir H. Spatial neglect in stroke patients after discharge from rehabilitation to own home: a mixed method study. *Disabil Rehabil* 2016; 38: 2429–2444.
  29. Kasner SE. Clinical interpretation and use of stroke scales. *Lancet Neurol* 2006; 5: 603–612.
  30. Sinikka Tarvonen-Schröder, Tuuli Niemi, Mari Koivisto. Comparison of functional recovery and outcome at discharge from subacute inpatient rehabilitation in patients with right or left stroke with and without contralateral spatial neglect. *J Rehabil Med* 2020; 52: jrm00071.
  31. Tarvonen-Schröder S, Hurme S, Laimi K. The World Health Organization Disability Assessment Schedule (WHODAS 2.0) and the WHO Minimal Generic Set of Domains of Functioning and Health versus Conventional Instruments in subacute stroke. *J Rehabil Med* 2019; 51: 675–682.
  32. Di Monaco M, Schintu S, Dotta M, Barba S, Tappero R, Gindri P. Severity of unilateral spatial neglect is an independent predictor of functional outcome after acute inpatient rehabilitation in individuals with right hemispheric stroke. *Arch Phys Med Rehabil* 2011; 92: 1250–1256.
  33. Paolucci S, Antonucci G, Guariglia C, Magnotti L, Pizzamiglio L, Zoccolotti P. Facilitatory effect of neglect rehabilitation on the recovery of left hemiplegic stroke patients: a cross-over study. *J Neurol* 1996; 243: 308–314.
  34. Scrutinio D, Lanzillo B, Guida P, Mastropasqua F, Montillo V, Pusineri M, et al. Development and validation of a predictive model for functional outcome after stroke rehabilitation. *Stroke* 2017; 48: 3308–3315.
  35. Tarvonen-Schröder S, Matomäki J, Laimi K. Factors associated with outcomes of inpatient stroke rehabilitation. *Int J Ther Rehabil* 2018; 25: 34–40.
  36. Chumney D, Nollinger K, Shesko K, Skop K, Spencer M, Newton RA. Ability of Functional Independence Measure to accurately predict functional outcome of stroke-specific population: systematic review. *J Rehabil Res Dev* 2010; 47: 17–29.
  37. Wade DT, Hower RL. Stroke: Associations with age, sex, and side of weakness. *Arch Phys Med Rehabil* 1986; 67: 540–545.
  38. Jehkonen M, Ahonen JP, Dastidar P, Koivisto AM, Laippala P, Viikki J, et al. Visual neglect as a predictor of functional outcome one year after stroke. *Acta Neurol Scand* 2000; 101: 195–201.
  39. Ahn D-H, Lee Y-J, Jeong J-H, Kim Y-R, Park J-B. The effect of post-stroke depression on rehabilitation outcome and the impact of caregiver type as a factor of post-stroke depression. *Ann Rehabil Med* 2015; 39: 74–80.