

EARLY CLINICAL PREDICTORS OF MOTOR FUNCTION IN THE UPPER EXTREMITY ONE MONTH POST-STROKE

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Objective: To investigate factors within 3 days poststroke that could predict severe impairment in motor function in the upper extremity at one month poststroke.

Methods: This cross-sectional study included 104 patients with first-ever stroke and impaired motor function in the upper extremity. Initial impairment in motor function, demographic data, type of stroke and stroke risk factors were chosen as possible predictors. Severe impairment in motor function was defined as ≤31p according to the Fugl-Meyer Assessment for Upper Extremity (FMA-UE). Logistic regression was used to predict severe impairment in motor function at one month post-stroke.

Results: Three possible prediction models were found, comprising stroke severity combined with grip strength and sex, finger extension or shoulder abduction. Models including grip strength or finger extension gave the most accurate predictions, with overall predictive ability 90.4% (95% confidence interval (95% CI) 0.847-0.961) and sensitivity 92.9% (95% CI 0.851-1.0) and 90.5% (95% CI 0.816-0.979), respectively.

Conclusion: Within 3 days post-stroke, severe impairment in motor function in the upper extremity at one month can be predicted using assessment of stroke severity in combination with grip strength, finger extension or shoulder abduction. This may facilitate early planning of rehabilitation for patients with impaired upper extremity in the stroke unit.

Key words: stroke recovery; upper extremity; paresis; prognosis.

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The total burden of stroke is increasing worldwide 1 (1). Frequent symptoms following stroke are aphasia, dysarthria, cognitive dysfunction, sensory deficits and motor deficits. Among the most common symptoms is limb impairment (2) with reduced function of the upper extremity reported in 48–88% of patients immediately after stroke (2-4). Impaired function in the upper extremity can lead to activity limitations, participation restrictions and reduced independence

in daily life (5). As a consequence, quality of life may be negatively affected (6). Recovery following upper extremity impairment takes place primarily in the first 3 months after stroke, particularly in the first month (3).

Early prediction of impairment is essential in order to plan appropriate rehabilitation. Clinical assessments are available for early prediction of recovery of upper extremity function (7, 8), as well as more advanced models (9). Variables that may have an effect on motor recovery are grip strength (10), ability to perform finger extension and shoulder abduction (7), stroke severity at onset (11), age (12), sex (13), location of stroke (14), type of stroke (15), and risk factors such as smoking (16), diabetes (16) and physical inactivity (17). Most previous studies of clinical predictors have been based on follow-ups 3–6 months post-stroke (18). Early prediction of motor function could be difficult to establish, particularly in a population with an initially more severe reduction in motor function (7, 8, 19).

The duration of treatment in a comprehensive acute stroke unit is limited. In Sweden the hospital stay poststroke is shorter than 8 days in the stroke unit (20), and the mean hospital stay (including rehabilitation) is 14 days (20). Approximately 15% of patients are transferred for further hospital-based rehabilitation (20). Early planning of rehabilitation needs to be facilitated and further knowledge about early prediction of motor function outcome after stroke is therefore essential for planning rehabilitation and for improving early stroke management.

The purpose of this study was to investigate factors that within 3 days post-stroke may predict severe impairment in motor function in the upper extremity at one month, which is an important factor to consider in rehabilitation planning.

METHODS

Study design, setting and participants

In this cross-sectional study, 117 patients with first-ever stroke, from a comprehensive stroke unit at Sahlgrenska University Hospital in Gothenburg, were consecutively included in Stroke Arm Longitudinal Study at the University of Gothenburg, the SALGOT study (21), during a period of 18 months (2009–2010) (Fig. 1). Inclusion criteria for the SALGOT study were: (i) firstever clinical stroke based on the World Health Organization's criteria (22); (ii) impaired upper extremity activity according to the Action Research Arm Test (ARAT) (≤56) (23) 3 days post-

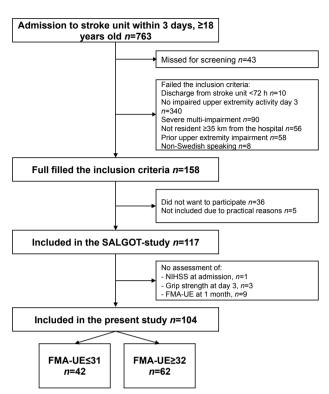


Fig. 1. Patient selection procedure in Stroke Arm Longitudinal Study at the University of Gothenburg (SALGOT) and flowchart of inclusion. NIHSS: National Institutes of Health Stroke Scale; FMA-UE: Fugl-Meyer Assessment of Upper Extremity.

stroke; (*iii*) admission to the stroke unit within 3 days of stroke onset; (*iv*) living within 35 km from the hospital and; (*v*) age 18 years or older. Exclusion criteria were: (*i*) upper extremity injury or disability of the upper extremity prior to stroke; (*ii*) multi-impairment or diminished physical condition prior to stroke; (*iii*) short life expectancy; and (*iv*) non-Swedish speaking.

Three additional inclusion criteria were used in the current study: (*i*) attainable score of stroke severity, assessed with National Institutes of Health Stroke Scale (NIHSS) at stroke onset (24); (*ii*) assessment of grip strength with a handheld dynamometer (JAMAR, Sammons Preston Rolyan, Bolingbrook, USA) (25) 3 days post-stroke; and (*iii*) assessment of upper extremity function according to Fugl-Meyer Assessment for Upper Extremity (FMA-UE) (26) 3 days and one month post-stroke. This resulted in a study population of 104 patients (Fig. 1).

Ethical approval for the SALGOT study was received from the Regional Ethical Review Board in Gothenburg. All patients, or their next of kin, provided informed written consent for participation. The STROBE guideline for cohort studies (http://strobe-statement.org/index.php?id=available-checklists) was followed in this report.

Clinical assessments and procedures

On arrival at hospital stroke severity was assessed by physicians, according to the National Institutes of Health Stroke Scale (NIHSS) (24). The maximum score is 46 points, with a higher score representing a more severe stroke (24).

At 3 days post-stroke, the level of physical activity prior to stroke was evaluated by the patients according to a 6-graded ordinal scale for estimating physical activity, which is a modified

version of the 4-graded physical activity scale by Saltin-Grimby (27). A lower level of activity gives a lower score.

At 3 days and at one month post-stroke, grip strength and upper extremity function were assessed in accordance with a standardized protocol (21) by 3 experienced and trained physiotherapists, who were not involved in the care or rehabilitation of the patients. Grip strength in the paretic hand was assessed in pounds with a handheld dynamometer (JAMAR) (25, 28). In the test procedure of grip strength, standardized instructions were followed and the mean of 3 trials was used. Patients rested their arm and hand on a table during the assessment to increase their ability to participate even with low muscle strength. Motor function in the upper extremity was assessed with FMA-UE (26), divided into 4 subscales, including items scoring 0–2 on an ordinal scale. The maximum score is 66 and indicates normal motor function (26). From the assessment of FMA-UE at 3 days only 2 items, finger extension and shoulder abduction, were used. The majority of the assessments were performed in a test room at Sahlgrenska University Hospital. If the patient was unable to travel, the assessments were performed in the patient's home, nursing home or on the hospital ward. Participants received individually adjusted, functional task-specific rehabilitation from the first day in the comprehensive stroke unit according to standard routine. Demographic data (age, sex, smoking habits, diabetes, type of stroke and hand dominance) were collected from the patient charts and the Swedish Stroke Register, a national quality register for stroke.

Variables and data handling

The study population was divided into 2 groups based on the results of the FMA-UE (26) at one month: patients with severe upper extremity impairment (\leq 31 p FMA-UE), corresponding to no or poor function (29) and those with less severe upper extremity impairment (\geq 32 p FMA-UE), corresponding to the ability to perform a drinking task with the paretic arm (8, 30).

Physical activity level was recalculated into a dichotomous variable based on previous studies on physical activity affecting stroke outcome (17, 31): 1-3 = low to moderate physical activity; and 4-6 = regular physical activity or training. Items for finger extension and shoulder abduction in the FMA-UE were recalculated into dichotomous variables: 0 = not able and 1-2 = able. In the statistical analyses stroke severity (NIHSS) was treated as a continuous variable. Patients who were not able to perform the grip strength test at 3 days due to lack of grip function were scored 0.

Statistical methods

Descriptive statistics were used for demographic data. To analyse differences between groups χ^2 test, Mann–Whitney U test or independent t-test were used, depending on the level of the data, with p < 0.05 as statistically significant level.

Based on previous literature, the following possible clinical predictors for the outcome variable severe impairment in motor function (\leq 31p FMA-UE) at one month were selected: age (12), sex (13), hand dominance (14), type of stroke (ischaemic or haemorrhage) (15), stroke severity (NIHSS) (11), grip strength (JAMAR) at 3 days (10), finger extension at 3 days, shoulder abduction at 3 days (7), physical activity (17), smoking and diabetes (16). Spearman's rank-order correlation (rho) was used to control for multicollinearity between the independent variables. If correlations were rho \geq 0.8, the variables were not used in the same logistic regression analysis and parallel analyses were performed.

The following procedure (Fig. 2) was applied for analysis with each of the variables that correlated rho ≥ 0.8 . Univariate logistic regressions were performed in order to identify possible predictors for further analyses, with the significance level set at p < 0.25 (Wald test). All significant predictors from the univariate regression analyses were submitted to a first multivariate analysis, ruling out the variables that were non-significant; p > 0.25(Wald test). This was continued until a final model with only significant variables at level p < 0.05 (Wald test) was obtained. Predictors that correlated (rho $\geq 0.5 - \leq 0.8$) and were considered clinically relevant were controlled for an interaction effect, and were included if they contributed significantly (p < 0.05) to the model. All previously ruled out variables were re-inserted, one at a time to check for significant contribution with p < 0.05 (Wald test). The sensitivity (%), specificity (%), positive predictive value, negative predictive value and overall prediction ability, including the 95% exact confidence intervals of the models were calculated. Models are presented with unstandardized coefficient, p-value and the odds ratio with a 95% confidence interval. The goodness of fit of the logistic regression models were tested using receiver operating characteristics curves (ROC curves) and Nagelkerke R square was obtained for each model. Statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS version 21.0, for Windows).

RESULTS

There were no significant differences between the original SALGOT population (n=117) and the patients who met the inclusion criteria (n=104) (Fig. 1) regarding age (p=0.576), sex (p=0.642), stroke severity (p=0.989) or upper extremity function at 3 days (p 0.215).

Demographic data and assessments at 3 days and at one month post-stroke are summarized in Table I. Patients with severe impairment in motor function (FMA-UE \leq 31) at one month had a significantly ($p\leq$ 0.05) more severe stroke at onset (NIHSS: mean 13, SD 5.6) and a significantly lower value of grip strength 3 days post-stroke (mean 0.7, SD 3.23). There was also a significantly higher proportion of patients with severe

Table I. Demographics at 3 days and at one month post-stroke

	All subjects $n = 104$	FMA ≤ 31 at 1 month $n = 42$	FMA > 31 at 1 month n = 62	<i>p</i> -value 0.05
Sex, M/W (%)	55/45	60/40	52/48	0.426
Age, years, mean (SD)	69	71	67	0.123
Location of stroke, %				
Right	53	60	47	
Left	42	40	44	
Bilateral	3	0	5	
Cerebellum	1	0	2	
Brain stem	1	0	2	
Ischaemic/haemorrhage, %	83/17	79/21	86/14	0.361
NIHSS, median	7	13	4	< 0.001
(q1-q3)	(3-13)	(9-18)	(3-7)	
Dominant arm affected, %	45	41	48	0.426
Smoking, no/yes, %	81/19	86/14	77/23	0.275
Diabetes, no/yes, %	89/12	88/12	89/11	0.923
Physical activity high/low	35/65	28/72	39/61	0.280
GS day 3, pounds mean	24.1	0.7	40.0	< 0.001
(SD)	(29.86)	(3.23)	(29.42)	
FE day 3, able/not able, %	56/44	7/93	89/11	< 0.001
SA day 3, able/not able, %	47/53	5/95	76/24	< 0.001

FMA-UE: Fugl Meyer Assessment of Upper Extremity; NIHSS: National Institutes of Health Stroke Scale; GS: grip strength; FE: finger extension; SA: shoulder abduction.

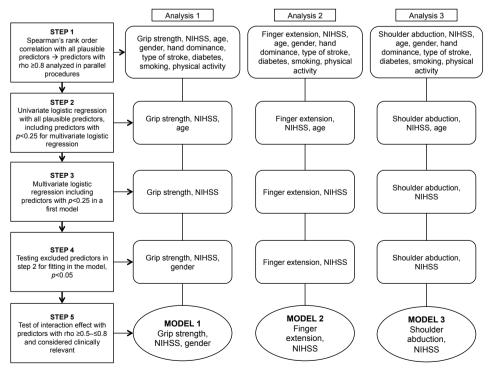


Fig. 2. Logistic regression analysis procedure. NIHSS: National Institutes of Health Stroke Scale.

Table II. Multivariate logistic regression for severe impairment in motor function in the upper extremity at one month post-stroke

	Predictor	Unstand. coefficient	<i>p</i> -value	OR (95% CI)	Nagelkerke R square
Model 1	Grip strength ^a	-0.155	0.003	0.86 (0.772-0.950)	0.791
	NIHSS	0.189	0.009	1.21 (1.048-1.393)	
	Sex	-1.511	0.049	0.22 (0.049-0.992)	
Model 2	Finger extension ^a	4.534	< 0.001	93.17 (17.522-495.361)	0.782
	NIHSS	0.194	0.001	1.21 (1.082-1.362)	
Model 3	Shoulder abduction ^a	3.760	< 0.001	42.97 (7.953-232.154)	0.672
	NIHSS	0.175	0.001	1.19 (1.073-1.323)	

^aAssessed day 3.

Coding: sex: 0: male, 1: female; finger extension: 0: able, 1: not able; shoulder abduction: 0: able, 1: not able; outcome: less severe impairment in motor function: 0, severe impairment in motor function: 1.

OR: odds ratio; CI: confidence interval; NIHSS: National Institutes of Health Stroke Scale.

impairment in motor function (FMA-UE \leq 31) who were not able to perform finger extension 3 days post-stroke (93%) and shoulder abduction 3 days post-stroke (95%). There were no significant differences between patients with FMA-UE \leq 31 and those with FMA-UE \geq 32, one month after stroke with regards to sex, age, type of stroke, handedness, physical activity level prior to stroke, smoking prior to stroke or diabetes.

Grip strength, finger extension and shoulder abduction at 3 days correlated strongly (rho > 0.8) and were analysed in 3 parallel analysis procedures. Interaction effects were controlled for between stroke severity

and grip strength (rho 0.544) and stroke severity and shoulder abduction (rho 0.566), but no statistical interaction effect was shown.

In the first analysis, a model including grip strength at 3 days, stroke severity and sex had the best predictive ability (model 1). In the second analysis, a model including finger extension at 3 days and stroke severity had the best predictive ability (model 2). In the third analysis, a model including shoulder abduction at 3 days and stroke severity had the best predictive ability (model 3). The inclusion of predictors is shown in Fig. 2 and all the models are shown in Table II.

The predictive abilities of the models are shown in Table III, indicating that both models 1 and 2 had excellent predictive abilities. This is shown in Fig. 3 with area under the curve (including 95% CI interval) using ROC curves, in model 1 0.96 (0.928–0.995), and in model 2 0.97 (0.941–0.996). As shown in Table III, model 1 had a higher sensitivity and higher negative predictive value (NVP) and model 2 had a higher specificity and higher positive predictive value (PPV).

Table III. Predictive properties of the models for predicting severe impairment in motor function in upper extremity at one month post-stroke

	FMA-UE ≤ 31 at one month post-stroke					
	Model 1 (95% CI)	Model 2 (95% CI)	Model 3 (95% CI)			
Sensitivity %	92.9 (0.851-1.0)	90.5 (0.816-0.979)	85.7 (0.752-0.963)			
Specificity %	88.7 (0.808-0.966)	90.3 (0.830-0.977)	82.3 (0.727-0.918)			
PPV %	85.0 (0.744-0.950)	86.4 (0.762-0.955)	76.6 (0.645-0.887)			
NPV %	94.8 (0.891-1.0)	93.3 (0.870-0.996)	89.5 (0.815-0.974)			
Overall %	90.4 (0.847-0.961)	90.4 (0.847-0.961)	83.7 (0.765-0.908)			

FMA-UE: Fugl Meyer Assessment of Upper Extremity; 95% CI: 95% exact confidence interval; PPV: positive predictive value; NPV: negative predictive value; model 1: grip strength, stroke severity and sex; model 2: finger extension and stroke severity; model 3: shoulder abduction and stroke severity.

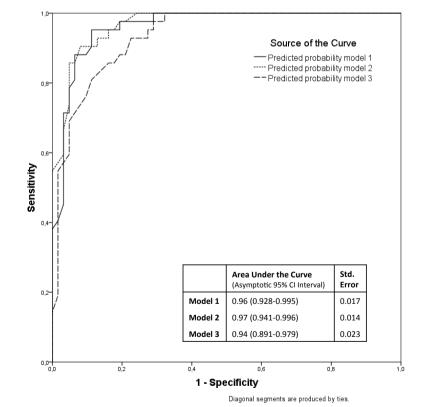


Fig. 3. Illustration of the prediction probabilities of models 1, 2 and 3 to predict severe impairment in motor function in the upper extremity (FMA-UE \geq 32 points) at one month post-stroke using receiver operating characteristic (ROC) curves. Model 1: grip strength, stroke severity and sex; model 2: finger extension and stroke severity; model 3: shoulder abduction and stroke severity.

DISCUSSION

This study identified clinical factors that, at 3 days after stroke onset, were able to predict severe impairment in motor function at one month post-stroke. This was done through a combination of initial stroke severity and an assessment of either grip strength, finger extension or shoulder abduction. Stroke severity made an important contribution to the prediction model and the most accurate predictions were made combined either with assessment of grip strength (and sex) or finger extension at day 3. Patients with less severe impairment of motor function initially were more likely to be predicted correctly compared with those with initially severe impairment in motor function.

The prediction models used in this study were based on quick and simple clinical assessments that could be performed at the bedside. Immediately after stroke onset, patients often are tired (32) and the first prediction assessments of motor function should be quick and simple. To have tests that can be performed at the bedside is meaningful (8, 33), and in the comprehensive stroke unit, patients are seen early by a physiotherapist, which makes the assessments cost-effective, since the suggested tests require no extra equipment other than a hand-held dynamometer.

Impaired motor function after stroke may be difficult to predict, particularly in a population with severe impairment in motor function early after stroke onset (7, 8, 19, 34–36) which is in line with results from the present study. In the present study, the prediction of motor function of patients with initially severe impairment in motor function was less accurate than for those with an initially less severe impairment, as the PPV was lower in all models. As a result, the challenge of predicting the impairment in motor function for patients with initially severe impairment remains, and neuropsychological assessments may be useful to predict the patients with initially severe impairment of the upper extremity (33).

It has been shown previously that the initial severity of stroke is of importance in the prediction of upper extremity outcome (18), but now also in the short-term perspective at one month. The area under the curve in models 1 and 2 was similar, and the model including finger extension (model 2) could be interpreted as a better predictor for patients with initially severe impairment in motor function than the models including grip strength (model 1) and shoulder abduction (model 3), since it has higher PPV. The NIHSS comprises assessment of arm and shoulder function, but does not examine grip strength, which might explain why the model including shoulder abduction has lower predictive ability than the models including grip strength and finger extension. This also indicates that the arm

score in NIHSS may be too crude for the prediction of motor function impairment in an upper extremity.

Other prediction models have combined assessment of finger extension and shoulder abduction (7) (in the present study these variables correlated too strongly and were used in separate models) or have included neuropsychological assessments (34). The results of the present study indicate that grip strength may be as reliable as finger extension and shoulder abduction for predicting severe impairment in motor function at one month post-stroke. Grip strength may have an impact on motor function outcome (10, 37) as well as overall cardiovascular mortality (37). However, further research is needed in order to predict motor function outcome within the first days after stroke onset.

Patients in this study received standard Swedish healthcare and rehabilitation, which may influence the results, and should be taken into account when interpreting the findings of the study. The type of therapy, dose and intensity are eventual sources of variability that could be included in a prediction model.

The present study has some limitations. First, the number of participants (n=104) limited the number of variables that it was possible to include in the multivariate logistic regressions. Contrary to previous research, age, hand dominance, type of stroke, smoking, diabetes and physical activity did not affect the motor function outcome in this study. Reasons may be the changing stroke population (38) and the time-window for follow-up, since most previous studies are based on follow-up at 3-6 months (18) when recovery is more stable (3, 39). The lack of neurophysiological data is also a limitation, since it has been shown to be important in prediction models (33). Another limitation is the definition of severity in motor function. In the present study, patients with ≥32 points in FMA-UE are classified as having less severe impairment in motor function, although they may not have reached normal motor function (29). As there is no consensus on FMA-UE cut-offs, the ability to perform a drinking task was considered as clinically important to the patient, and therefore a cut-off of 32 was chosen. However, if a different cut-off had been used, this would have influenced the results. Likewise, the dichotomization of self-reported physical activity may influence the results, but the definitions of low, moderate and high physical activity level and the mechanisms underlying the effect of physical activity are unknown (31). Furthermore, the ordinal scale NIHSS is treated as a continuous variable. Alternative handling of the data was deliberated prior to the analysis; however, treating NIHSS as a continuous variable was considered the best way to handle the data. Another method could have been to dichotomize the NIHSS; however, since

the median at arrival was 7, the number of patients in the 2 groups would have been uneven, since 7 is not a commonly used cut-off.

In conclusion, when assessed early after stroke, finger extension, shoulder abduction and grip strength can predict severe impairment in motor function in the upper extremity at one month, but must be combined with an assessment of stroke severity for the most accurate predictions. As the length of hospital stay is limited and discharge planning starts early after stroke onset, this knowledge could facilitate early planning of rehabilitation at the stroke unit.

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