

## ORIGINAL ARTICLE

# ADMISSION VARIABLES ASSOCIATED WITH INDEPENDENT AMBULATION AT TIME OF DISCHARGE FROM A COMPREHENSIVE STROKE UNIT

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## ABSTRACT

**The aim:** To identify admission variables associated with Functional Ambulation Classification (FAC) 1 to 4 (unable to walk without assistance) at time of discharge (dFAC<5) from a comprehensive stroke unit (CSU).

**Materials and methods:** Patients admitted to CSU at Oberig Clinic, Kyiv, Ukraine, August 01, 2012 to July 31, 2018, were screened for study selection criteria. Association of qualifying patients' data with FAC score at CSU discharge was retrospectively assessed by univariate and multivariate logistic regression, odds ratios (OR) and 95% confidence intervals (95% CI) using MedCalc v. 19.1.

**Results:** The study cohort (442 of 492 admitted patients) had median age: 65.8 years, gender: 43% female, stroke-type: 84% ischemic strokes, median baseline NIHSS total score: 10. Estimated time from stroke onset to CSU admission was from less-than-24-hours to over-180-days. The univariate logistic regression analysis, revealed 28 variables significantly ( $p<0.05$ ) related to dFAC<5; while in multivariate analysis only 4 admission variables were significantly ( $p<0.05$ ) associated with dFAC<5: age (OR= 1.07; 95% CI 1.03-1.10, on average, for each additional year,  $p<0.001$ ), baseline NIHSS score (OR= 1.15; 95% CI 1.08-1.22, on average, with a 1-point increase in the total score,  $p<0.001$ ), initial FAC score (OR= 0.40; 95% CI 0.31–0.52, on average, with a 1-point decrease in the score,  $p<0.001$ ), and very late CSU admission (over 180 days; OR= 5.7; 95% CI 1.9–17.1,  $p=0.002$ ).

**Conclusions:** Four admission variables may be independently associated with dFAC<5 and provide opportunity for improving CSU outcomes and mitigating risk for inability to ambulate without assistance after CSU discharge.

**KEY WORDS:** Stroke, comprehensive stroke unit, admission variables, outcome, ambulation, prognostication

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## INTRODUCTION

Stroke is the second leading cause of death and the most common cause of disability in Europe [1, 2]. Up to one-third of patients with acute stroke die within the first month of stroke onset, and about a third of survivors become dependent lifelong [3-5]. High-quality medical assistance can improve outcomes. However, the optimal model for acute and subacute in-hospital stroke care has not been fully defined [6]. Admission to a comprehensive stroke unit (CSU) where acute care is combined with skilled nursing and early interdisciplinary rehabilitation is associated with a reduction in case-fatality, morbidity, and disability [7, 8]. The Action Plan for Stroke in Europe 2018–2030 emphasizes rehabilitation as a treatment element that is important in helping people with functional disabilities return home and to their communities [9]. The ability to ambulate in the community is important for independence, well-being, and participation in social roles. Independent ambulation is the most desired goal for most stroke victims, and one of the most frequent reasons for inpatient rehabilitation referral [10, 11]. Therefore, it is traditionally a key goal of post-stroke rehabilitation [12-14].

The possibility to predict a potential motor recovery after stroke, especially the ability for locomotion, may facilitate

the selection of effective individualized rehabilitation strategies [15]. As average lengths of stay poststroke at inpatient rehabilitation facilities in the United States are less than three weeks, service delivery must be efficient, and clinicians must make quick and accurate prognostic decisions shortly after admission [10]. Early prediction of outcomes is essential for (1) setting realistic and attainable therapeutic goals, (2) facilitating proper discharge planning, and (3) anticipating the need for specific durable medical equipment, home modifications, and community support [16]. Establishment of a clinical decision rule that can provide an estimate of a clinical outcome such as discharge walking ability may decrease inaccurate predictions (delayed discharges, last-minute home renovations, unnecessary durable medical equipment). With the limited lengths of stay, knowledge of how assessment results at admission predict walking ability at discharge, determining the factors that influence self-walking recovery, and correctly predicting the degree of patient mobility after rehabilitation would be extremely useful to clinicians, caregivers, and payers [17-19]. There is growing interest in using demographic, clinical, and neurological variables to predict functional outcomes after stroke [20]. However, no

systematic reviews to identify predictors for walking after stroke have been reported [21].

Functional Ambulation Classification (FAC) is a commonly used gait assessment scale that was first described by Holden et al. in the 1980s [22, 23]. Mehrholz et al. have shown that FAC has excellent reliability, along with good sensitivity, specificity, and prognostic value in stroke patients [24]. Our study aimed to identify admission variables associated with an inability to walk without assistance at the time of discharge (dFAC<5) from the Oberig Clinic CSU.

## MATERIALS AND METHODS

### PARTICIPANTS

Our CSU is an in-patient hospital unit at Oberig Clinic, Kyiv, Ukraine, that, since February 2010, has admitted, evaluated, and treated patients diagnosed with stroke per Canadian Stroke Best Practices (<https://www.strokebest-practices.ca/resources/professional-resources>). In consideration for admission to CSU, a qualified neurologist evaluated a patient for clinical diagnosis of stroke per the AHA/ASA definition of stroke, including verification with brain imaging [25]. On CSU admission, a patient began care per Canadian Stroke Best Practices, underwent ancillary imaging investigations, including neuroimaging (head multi-slice CT and/or 1.5T brain MRI), cerebral vessel imaging (contrast-enhanced CT or MR angiography), trans-thoracic echocardiography, 24-72 hour ECG monitoring and conventional laboratory tests, as well as assessment for interdisciplinary rehabilitation by qualified rehabilitation staff. During their CSU stay, patients were followed by a multidisciplinary team, including Neurologists, Nurses, Physical Therapists, Occupational Therapists, Logopaedics (Speech and Language Therapists), and Psychologists. The patient's family made the decision about discharge, usually based on the multidisciplinary team advice. All patients or their representatives signed an Informed Consent for care for their data collection and analysis, including entry into the database for study purposes.

In May 2010, our CSU launched a new database, and OC-CSU began to populate this database with pre-specified patient data. In June-July 2012, documentation of several other major assessment tools and outcomes was added to the database, including the FAC. From August 01, 2012, to July 31, 2018, 492 patients were admitted to the CSU and this database. In August 2018, we (YF and VH) closed the database, reviewed the available data, and then planned and performed the retrospective statistical assessment that is reported here.

During the screening, we included each patient with a complete data set in the database, i.e., 442 of 492 admitted patients. A patient was excluded if a patient did not have all qualifying data, died during CSU stay, did not ambulate before the stroke, or stayed for less than two days and thus was not adequately investigated. Some included patients were demented; the database had no patients with alternative features that prevented them from walking, e.g., bone

fractures, leg amputations, advanced Multiple Sclerosis, or Parkinson's disease.

### PREDICTOR VARIABLES

For each patient the following admission variables were also populated into our database: age, gender, stroke type, and TOAST classification subtype, cerebral infarction location (right middle cerebral artery, left middle cerebral artery or other) for ischemic stroke patients, hematoma location for intracerebral bleeding patients, vascular risk factors (history of atrial fibrillation, diabetes mellitus, hyperlipidemia, hypertension, previous stroke, smoking, alcohol abuse, obesity), premorbid and baseline modified Rankin scale (mRS) score, as well as admission National Institutes of Health Stroke Scale (NIHSS), Barthel Index (BI), FAC, Rivermead Mobility Index (RMI), Mini-Mental State Examination (MMSE), and Montreal Cognitive Assessment (MOCA) scores, baseline right arm, right leg, left arm and left leg scores in the respective NIHSS items, levels of consciousness (alert, drowsy, stuporous or comatose) and specific neurological deficits on admission (homonymous hemianopia, right-sided weakness, left-sided weakness, hemisensory loss, dysphagia or aphasia). Baseline laboratory test results that were retrospectively populated into our database included white cell count, erythrocyte sedimentation rate, creatinine, C-reactive protein (CRP), glycosylated hemoglobin (HbA1c), total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol.

For this study, we dichotomized the FAC score at discharge as follows: if the patient at time of CSU discharge had a FAC score of 5 or 6, the desired treatment outcome for the patient was achieved and the patient was classified as a 'non-event' (baseline model variable  $Y=0$ ), whereas if the FAC score ranged from 1 to 4, the desired outcome for this patient was not achieved. The patient was regarded as an 'event' (baseline model variable  $Y=1$ ).

### STATISTICAL ANALYSIS

To quantify the degree of influence of admission variables on the risk of event logistic regression models were constructed and analyzed. The predictive value of the models was characterized by its sensitivity (the proportion of correctly predicted 'events') and specificity (the percentage of correctly predicted 'non-events') [26]. A 95% confidence interval (95% CI) was calculated for these values. The ability of the models to distinguish between the two groups 492 patients were checked for by constructing and analyzing the operating characteristics curve (ROC – Receiver Operating Characteristic curve analysis) with calculating the area under the ROC curve (AUC – Area under the ROC curve) and its 95% CI. The model is considered adequate if there is a statistically significant difference in the value of the AUC from 0.5 [26]. The impact of the factors was estimated by the odds ratio (OR), for which 95% of CIs were also calculated [26]. To select the minimal set of pre-

**Table 1.** Characteristics of a 4-factor logistic regression model for predicting the risk of not recovering independent ambulation (FAC 5 or 6) at discharge from the CSU

Factors	Model coefficient, $b \pm m$	p value for difference of model coefficient from 0	OR (95% CI)
Age, years	0.064±0.015	<0.001	1.07 (1.03–1.10)
Less than 24 hours		Reference	
1-7 days	-0.55±0.51	0.29	-
Time delay from estimated time of stroke onset to time of CSU admission			
8-14 days	-0.80±0.64	0.21	-
15-30 days	0.46±0.54	0.39	-
31-60 days	-0.15±0.60	0.81	-
61-180 days	-0.06±0.63	0.92	-
More than 180 days	1.75±0.56	0.002	5.7 (1.9–17.1)
Baseline NIHSS total score	0.14±0.03	<0.001	1.15 (1.08–1.22)
Initial FAC score	-0.92±0.13	<0.001	0.40 (0.31–0.52)

Notes: CSU - Comprehensive Stroke Unit. FAC - Functional Ambulation Classification. NIHSS - National Institutes of Health Stroke Scale.

dictors strongly and independently associated with the risk of being an 'event,' the stepwise method was used. In this method, variables are sequentially entered into the model. After entering each variable in the model (if  $p < 0.1$ ), the possibility to remove variables that became non-significant (if  $p > 0.2$ ) is checked. The optimal decision threshold for the model was determined by achieving maximum sensitivity and specificity using the Youden index [27]. The significance level for all tests was 0.05. Statistical analysis of the data was performed using the package MedCalc v. 19.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2019).

## RESULTS

### PATIENT CHARACTERISTICS

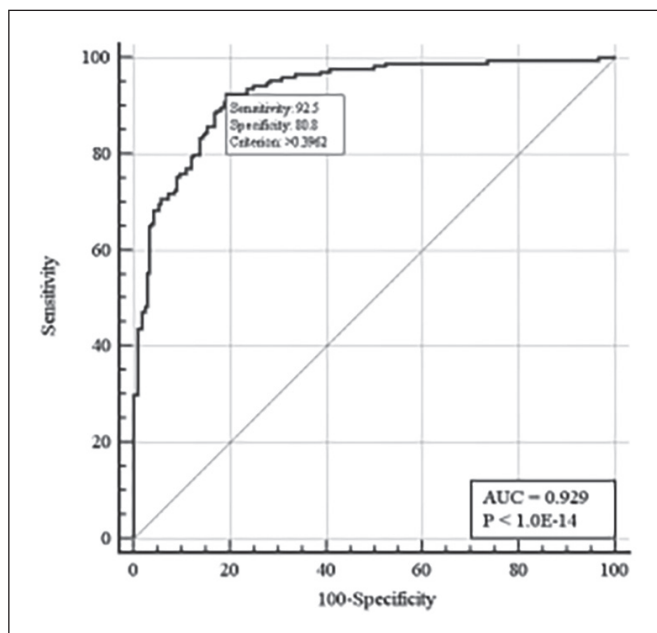
Of all 492 patients admitted to the CSU during the study period, 442 patients were enrolled in the study. The study cohort age ranged from 28.1 to 95.7 years (median of 65.8 years, interquartile interval 17.6 years); 188 (42.5%) were women; 69 (15.7%) patients had an intracerebral hemorrhage, and 373 (84.3%) had an ischemic stroke. The total admission NIHSS score ranged from 0 to 36 (median 10, interquartile interval 11). Time from estimated stroke onset to CSU admission ranged from less than 24 hours to over 180 days in the following distribution: 0 to 24 hours in 92 (20.8%) patients, 25 hours to 7 days in 100 (22.6%) patients, 8 to the 14 days in 36 (8.2%) patients, 15 to the 30 days in 61 (13.8%) patients, 31 to the 60 days in 37 (8.5%) patients, 61 to 180 days in 44 (9.9%) patients, and over 180 days in 72 (16.2%) of the study participants.

### UNIVARIATE ANALYSIS

As the first stage of the analysis, logistic regression models were constructed to predict the risk of failing to achieve independent ambulation at discharge for each of the 41 factors. After CSU treatment, 197 (44.6%) patients were

unable to walk without assistance (FAC score was from 1 to 4 at discharge).

Per univariate analysis, a statistically significant association with the risk  $dFAC < 5$  was found for 28 variables. In particular, the likelihood of  $dFAC < 5$  significantly increased with age (OR= 1.05 95% CI 1.03–1.07, on average, for each additional year,  $p < 0.001$ ). Likewise, the odds of  $dFAC < 5$  was higher in female (OR= 1.6 95% CI 1.1–2.4,  $p=0.01$ ) compared to male patients. The risk of  $dFAC < 5$  was significantly greater in atherosclerotic (OR= 3.4; 95% CI 1.2–9.5,  $p=0.02$ ) and cardioembolic (OR= 5.1; 95% CI 1.8–14.2,  $p=0.002$ ) subtypes of ischemic stroke and in intracerebral hemorrhage (OR= 7.2; 95% CI 2.4–21.3,  $p < 0.001$ ) compared with the lacunar ischemic stroke. In this analysis, the time from estimated stroke onset to the CSU admission had no significant impact on the risk of  $dFAC < 5$ . Among vascular stroke risk factors, the probability of not achieving the FAC score of 5 or 6 was significantly increased only by atrial fibrillation (OR= 1.8; 95% CI 1.2–2.7,  $p=0.005$ ), whereas history of stroke, hypertension, diabetes, hyperlipidemia, smoking, alcohol abuse, and obesity had no statistically significant association with the endpoint of interest. However, a pre-morbid mRS score had a significant correlation with the odds of requiring assistance while walking: OR= 1.30; 95% CI 1.04–1.61, on average, for each additional point,  $p=0.02$ . Furthermore, highly significant association with the primary outcome was revealed for baseline scores of all on major assessment scales used in stroke: mRS (OR= 5.1; 95% CI 3.7–7.0, on average, for each additional point,  $p < 0.001$ ), BI (OR= 0.95; 95% CI 0.94–0.96, on average, for each additional point,  $p < 0.001$ ), NIHSS (OR= 1.26; 95% CI 1.20–1.31, on average, for each additional point,  $p < 0.001$ ), RMI (OR= 0.65; 95% CI 0.60–0.70 with a 1-point increase in the total score,  $p < 0.001$ ), MMSE (OR= 0.91; 95% CI 0.89–0.93, on average, with a 1-point increase in the total score,  $p < 0.001$ ) and MOCA (OR= 0.91; 95% CI 0.89–0.93, on average, for each additional point,  $p < 0.001$ ). Decreased level of consciousness at presentation also had a highly significant



**Fig. 1.** ROC curve of a 4-factor logistic model for predicting the risk of failure to regain the ability to walk independently after the in-patient treatment for stroke (FAC score of 5 or 6 at CSU discharge).

negative impact on the likelihood of independent walking at discharge: OR= 6.5; 95% CI 3.6-11.7,  $p < 0.001$ . Each of the above-mentioned neurological deficits on admission was highly significantly ( $p < 0.01$ ) associated with lack of to walk unassisted at discharge: OR= 4.31, 95% CI 2.78–6.69; OR= 1.90, 95% CI 1.30–2.77; OR= 1.55, 95% CI 1.06–2.27; OR= 2.52, 95% CI 1.71–3.70; OR= 5.56, 95% CI 3.31–9.33; and OR= 1.66, 95% CI 1.13–2.45 for homonymous hemianopia, right-sided weakness, left-sided weakness, hemisensory loss, dysphagia and aphasia, respectively. In univariate analysis, the dFAC<5 risk was the greater, the more pronounced was limb weakness on admission as assessed by the NIHSS scale (1.7 to 2.4, on average, for each additional point in the respective item,  $p < 0.001$  for each of the four extremities). Of the laboratory blood assessments, only inflammatory markers significantly correlated with dFAC<5: ESR (OR= 1.02; 95% CI 1.01–1.03, on average, for each additional mm per hour,  $p < 0.001$ ), C-reactive protein (OR= 1.03; 95% CI 1.02-1.05, on average for every additional 1 mg per L,  $p < 0.001$ ) and, to a lesser extent, leukocyte count (OR= 1.07; 95% CI 1.00-1.13,  $p = 0.04$ ), creatinine, glycosylated hemoglobin, cholesterol, and its fractions were not statistically significantly associated with dFAC<5.

## MULTIVARIATE ANALYSIS

Stepwise rejection/addition of factors in a multivariate logistic regression model found four admission variables to have an independent association with dFAC<5: baseline FAC and the NIHSS scores, age, and time from stroke onset to the CSU admission (table I).

Per multivariate logistic regression, only 4 factors that had a statistically significant association with 'event' can

be considered predictors of the lack of ability to walk unassisted at discharge from the CSU (table I). In particular, the risk of inability to walk without assistance increased with age (OR= 1.07; 95% CI 1.03-1.10, on average, for each additional year,  $p < 0.001$ ). Baseline NIHSS (OR= 1.15; 95% CI 1.08-1.22, on average, with a 1-point increase in the total score,  $p < 0.001$ ) and initial FAC (OR= 0.40; 95% CI 0.31–0.52, on average, with a 1-point increase in the score,  $p < 0.001$ ) scores had a statistically significant and independent influence on the risk of not achieving independent ambulation. In addition to that, the likelihood of walking unassisted at CSU discharge significantly decreased when the patient was admitted to the CSU later than 180 days after the onset (OR= 5.7; 95% CI 1.9–17.1,  $p = 0.002$ , less than 24 hours used as reference).

The logistic regression model based on the selected set of four variables proved adequate (chi-square = 267.1 at 9 degrees of freedom,  $p < 0.001$ ). Fig. 1 shows the operating characteristics curve of the model. The area under the operating characteristics curve AUC = 0.93 (95% CI 0.90 – 0.95) shows excellent consistency of the prediction model and the strong association of this set of factors with the risk of dFAC<5. Sensitivity of this test is 92.5% (95% CI 87.6 – 96.0) and specificity= 80.8% (95% CI 74.7 – 85.9) for the optimal (by the Youden index) criterion value

## DISCUSSION

In this retrospective cohort study, we analyzed data of stroke patients of different ages with various stroke types and severity, who received evidence-based treatment and rehabilitation at different stages of the disease (from acute to chronic). This allowed for the assessment of the variables associated with dFAC<5.

Univariate logistic regression analysis showed a significant relationship between the risk of dFAC<5 and numerous demographic, clinical and laboratory characteristics such as age, gender, stroke subtype, history of atrial fibrillation, initial severity of neurological deficits, motor and cognitive impairment, and disability along with elevated serum inflammation markers at presentation. Multivariate logistic regression found four variables to be independently statistically significant associated with the event (dFAC<5). Both analyses identified patient age and the initial severity of the stroke-related neurological deficit (the total NIHSS score) as well as the initial FAC score predictive value for dFAC<5. On the other hand, multivariate logistic regression analysis also showed a significant negative influence of the very late start of rehabilitation activities, which was not revealed in the univariate analysis.

The authors of several other studies have also demonstrated an association between ambulation in patients after stroke and patient age as well as the severity of the initial neurological deficits (including the decreased level of consciousness and pronounced sensory-motor impairment of the affected limbs) [28-34]. Prognostic value of hemianopia, urinary incontinence, poor torso control, and sitting balance, among other factors, has also been reported [16, 33]. Kwakkel et al. have emphasized the importance of time delay from stroke onset to the examination by a rehabilitation specialist [35, 36]. Unfortunately, the results of these studies and

our study are difficult to compare due to discrepancies in patient characteristics, treatment settings and timing, rehabilitation interventions, and ways of evaluating the outcomes.

The strengths of this study include its rather large sample size, evidence-based treatments, patient evaluation by a multidisciplinary team as well as the use of valid assessment tools and modern statistical methods. Our study was limited by its observational nature and retrospective design, which did not allow full control of potentially confounding factors, bias, and error. Also, various lengths of patients stay on the CSU for different reasons did not always allow achievement of the best possible functional outcome in each case.

Further research should focus on the creation of a prognostic model to assess the likelihood of restoration of independent walking at the time of discharge from the hospital and to validate its validity in different settings. In conclusion, a prospective study to validate the predictive nature of the identified variables for stroke patients' ability to ambulate after CSU admission is needed.

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