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PREDICTORS OF INDEPENDENT WALKING RECOVERY AFTER STROKE IN PATIENTS ADMITTED TO AN INTEGRATED STROKE UNIT

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Walking unassisted is a key goal of post-stroke rehabilitation. The study aimed to determine the predictors of independent walking at the time of hospital discharge. Uni- and multivariate regression models were built on the basis of demographic, clinical, and laboratory data of 442 study participants (median age was 65.8 years, 43 % were women, 84 % – with cerebral infarction). In a univariate analysis, the subtype of stroke, age and sex of the patient, atrial fibrillation, stroke severity, disability, motor, and cognitive impairment, and elevated levels of inflammatory markers during hospitalization were significantly associated with the dependence while walking. Multivariate analysis revealed only four independent predictors: patient's age, the severity of initial neurological deficits, initial assessment of gait function, and very late onset of rehabilitation. If the reliability of the prognostic model is confirmed, its use can contribute to realistic treatment goals and optimal preparation for hospital discharge.

Key words: cerebral stroke, post-stroke rehabilitation, walking, stroke unit, prediction of treatment outcomes, prognostic models.

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ПРОВІСНИКИ ВІДНОВЛЕННЯ НЕЗАЛЕЖНОЇ ХОДЬБИ ПІСЛЯ ІНСУЛЬТУ У ПАЦІЄНТІВ, ЯКІ ПЕРЕБУВАЛИ НА ЛІКУВАННІ В ІНТЕГРОВАНОМУ ІНСУЛЬТНОМУ БЛОЦІ

Ходьба без сторонньої допомоги є ключовою ціллю реабілітації після інсульту. Метою дослідження було визначити предиктори незалежної ходьби на момент виписки. На основі демографічних, клінічних та лабораторних даних 442 учасників дослідження (середній вік 65,8 року, 43 % жінок, 84 % з інфарктом мозку) були побудовані одно- та багатофакторні регресійні моделі. При однофакторному аналізі значущий зв'язок із залежністю при ходьбі мали підтип інсульту, вік та стать пацієнта, фібриляція передсердь, тяжкість інсульту, функціональних обмежень, рухових і когнітивних порушень та підвищений рівень маркерів запалення при госпіталізації. Багатофакторний аналіз виявив лише чотири незалежних провісника: вік пацієнта, тяжкість початкового неврологічного дефіциту, початкова оцінка функції ходи та дуже пізній початок реабілітації. Якщо валідність прогностичної моделі буде підтверджена, її використання може сприяти реалістичним цілям лікування та оптимальній підготовці до виписки.

Ключові слова: мозковий інсульт, постінсультна реабілітація, ходьба, інсультний блок, прогнозування результатів лікування, прогностичні моделі.

The study is a fragment of the research project "Determining the features of the course and consequences of stroke in patients of various ages, taking into account genetic and infectious factors and comorbidity", state registration No. 0118U003695.

Stroke is the second leading cause of death and the leading cause of permanent disability among adults worldwide [7]. Up to 35 % of patients with acute cerebral stroke die within a month of the onset of the disease, and up to 75 % of survivors have some restrictions on everyday life, and about a third become dependent on outside help [13]. High-quality medical care can reduce the severity of stroke consequences, but the optimal model for organizing stroke care in a hospital has not yet been determined [12]. Staying in an integrated stroke unit (ISU), where treatment is combined with comprehensive secondary prevention, skilled nursing care and persistent interdisciplinary rehabilitation, is associated with reduced mortality and disability in stroke [3]. These conclusions were based on research data, mostly conducted in developed countries. Little is known about the results of inpatient stroke treatment using different models of stroke care in developing countries, and in Ukraine in particular.

Most stroke survivors experience a gradual recovery of impaired functions [2]. Recovery from a stroke is a complex biological process, the pace and trajectory of which is influenced by many factors [6]. The ability to move independently plays an important role in returning to a normal lifestyle, patient well-being, and performing social roles, so it is traditionally considered one of the key goals of post-stroke rehabilitation [5]. The ability to walk unassisted is the goal of treatment, which is most often mentioned by patients, and the most common reason for referring a patient to a rehabilitation facility [4]. After rehabilitation in the hospital, 60–80 % of patients can walk independently, but in 10–20 % of patients gait function is not restored enough, and they need outside help when walking [15]. Safe walking, especially outdoors, requires not only good motor skills and endurance, but also appropriate cognitive abilities that

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allow you to adapt to changing environmental conditions, various visual and auditory stimuli, the appearance of obstacles, the movement of other objects, and other factors [10].

The Functional Ambulation Classification (FAC), which distinguishes 6 levels of walking, is widely used to assess gait function in stroke patients. They are rated from 1 point (unable to walk) to 6 points (walks independently on flat and uneven surfaces) [14]. FAC has excellent reliability, as well as a good level of sensitivity, specificity, and prognostic value in stroke patients [8]. Predicting the possibility of resuming independent walking is important for determining realistic and achievable treatment goals, as well as for appropriate preparation for patient's discharge (adaptation of the apartment, purchase of aids, organization of care, etc.). Given the limited length of patients' stay in rehabilitation institutions, it is useful to identify factors that predict the resumption of independent walking and the degree of patient's mobility [1].

The purpose of the study was to determine independent predictors of recovery of independent walking before discharge from hospital in stroke patients who were hospitalized in an integrated stroke unit.

Material and Methods. 1. Sampling of the study. The study was performed in the Stroke Center (SC) – a Department of a General Hospital (Medical Center Universal Clinic "Oberig"). The study enrolled stroke patients who were consecutively admitted to the SC during 2010–2018.

The study included 442 patients with cerebral stroke who had assessments of walking function on the FAC scale before and after treatment. The age of patients ranged from 28 to 96 years (median age – 65.8 years, interquartile range – 57.5–75.1 years). There were 188 female patients (42.5 %). Intracerebral hemorrhage was diagnosed in 69 (15.7 %) patients, and 373 (84.3 %) patients had a brain infarction.

2. A set of analyzed indicators. The defined data set of each patient was entered into a special database. Age and gender of the patient, type and subtype of stroke, localization of brain infarction, premorbid evaluation according to the modified Rankin scale (mRS), vascular risk factors (atrial fibrillation, diabetes mellitus, dyslipidemia, hypertension, a history of stroke, smoking, alcohol abuse, obesity), scores on scales at hospitalization (National Institutes of Health Stroke Scale – NIHSS, Barthel Index – BI, FAC, mRS, Rivermead Mobility Index – RMI, Mini-Mental State Examination – MMSE, Montreal Cognitive Assessment – MOCA), as well as assessment of the strength of the right arm, right leg, left arm and left leg in the corresponding NIHSS sections), impaired consciousness, laboratory indicators at admission (white blood cells count, erythrocyte sedimentation rate, creatinine, C–reactive protein, glycosylated hemoglobin, total cholesterol, low and high-density lipoprotein cholesterol in the blood). Patients who did not have data on the assessment of gait function were excluded from the study. The FAC score was considered as a result of the analysis before discharge: if it was 5–6 points, the effect of treatment for the patient was considered achieved; if 1–4 points, it was not achieved.

3. Statistical analysis. The method of constructing and analyzing logistic regression models was used to quantify the degree of influence of factor traits on the risk of incomplete recovery of gait function in patients after stroke according to FAC. The prognostic quality of the models was assessed by indicators of sensitivity (share of correctly predicted "cases") and specificity (share of correctly predicted "non-cases"). The corresponding 95 % confidence interval (95 % CI) was calculated for these values. The adequacy of the models was assessed by the method of construction and analysis of ROC (Receiver Operating Characteristic curve) while calculating the area under the ROC curve (AUC – Area under the ROC curve) and its 95 % CI. The model is considered adequate with a statistically significant difference between the AUC value and the 0.5 value. The influence of factor characteristics was assessed by the value of the odds ratio (OR), for which 95 % CI was calculated. The $\alpha_{кр}$ =0.05 critical significance level was accepted for all tests. Statistical analysis of data and processing of research results were performed using the package MedCalc v. 19.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2019).

Results of the study and their discussion. The overall NIHSS score at admission ranged from 0 to 36 points (median – 10 points, interquartile range – 5–16 points). The time from stroke onset to admission to the SC was from 0 to 24 hours in 92 (20.8 %) patients, in 100 (22.6 %) – from 25 hours to 7 days, in 36 (8.2 %) – from the 8th to the 14th day, in 61 (13.8 %) – from the 15th to the 30th day, in 37 (8.5 %) – from the 31st to the 60th day, in 44 (9.9 %) – from the 61st to the 180th day and in 72 (16.2 %) – later than 180 days.

Univariate analysis. At the first stage of the analysis, logistic regression models were performed to predict the risk of not achieving the desired treatment effect (1–4 points on the FAC scale before discharge from SC) for each of the 35 factor's features. The desired treatment effect was not achieved in 197 (44.6 %) patients.

According to the results of single-factor analysis, a statistically significant association ($p < 0.05$) with the risk of not resuming independent walking at the time of discharge from the SC had 20 factor's

features. In particular, the risk of failure to achieve the desired effect of treatment was significantly higher 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 to lacunar subtype of ischemic stroke. The probability of maintaining dependence on outside help when walking after treatment in SC significantly increased with age (by OR 1.05 95 % CI 1.03–1.07, on average, for each additional year, p<0.001). The probability of non–renewal of independent walking was higher in female patients of SC (OR 1.6 95 % CI 1.1–2.4, p=0.01) compared with males. The time from the onset of the disease to the hospitalization in the SC did not have a significant effect on the risk of not achieving the desired effect of treatment. Among vascular risk factors, only atrial fibrillation (OR 1.8; 95 % CI 1.2–2.7, p=0.005) significantly increased the probability of failure to achieve the desired functional treatment outcome, while a history of stroke, hypertension, diabetes mellitus, dyslipidemia, smoking, alcohol abuse, and obesity did not have a statistically significant effect. A significant association with the probability of maintaining gait dependence on outside help was found in the mRS score before the stroke (OR 1.30; 95 % CI 1.04–1.61, on average, for each additional mRS point, p=0.02) and especially scores on the primary scales after the admission to SC: mRS (OR 5.1; 95 % CI 3.7–7.0, on average, for each additional mRS point, p<0.001), BI (OR 0.95; 95 % CI 0.94–0.96, on average, with a decrease in the total score for each point, p<0.001), NIHSS (OR 1.26; 95 % CI 1.20–1.31, on average, with an increase in the total score for each point, p<0.001), RMI (OR 0.65; 95 % CI 0.60–0.70 with a decrease in the total score for each point, p<0.001), 0.65 (0.60–0.70), MMSE (OR 0.91; 95 % CI 0.89–0.93, on average, with a decrease in the total score for each point, p<0.001) and MOCA (OR 0.91; 95 % CI 0.89–0.93, on average, with a decrease in the total score for each point, p<0.001). The presence of impaired consciousness in the patient during hospitalisation to the SC had a very significant negative impact on the probability of restoring independent walking at the time of discharge (OR 6.5; 95 % CI 3.6–11.7 p<0.001). The risk of remaining in need of assistance during walking after treatment in the SC increased significantly with more severe weakness (higher score) of the muscles of the limbs in the relevant sections of the NIHSS scale (OR from 1.7 to 2.4, on average, for each additional score in the corresponding section of the scale, p<0.001 for each of the four limbs). Of the laboratory parameters, only inflammatory markers had a significant direct connection with the lack of the desired effect of treatment: ESR (OR 1.02; 95 % CI 1.01–1.03, on average, for each additional 1 mm/hr, p<0.001), C-reactive protein level (OR 1.03; 95 % CI 1.02–1.05, on average, for every 1 mg/L, p<0.001) and, to a lesser extent, the white blood cells count (OR 1.07; 95 % CI 1.00–1.13, p=0.04). However, neither creatinine nor glycosylated haemoglobin, nor lipid profile was significantly affected.

Multivariate analysis and model building. Because of step-by-step selection, four factors were identified that have a statistically significant independent relationship with the preservation of the need for outside help when walking before discharge: initial FAC and NIHSS scores, age and time from the disease onset to hospitalisation to the SC (table 1).

Table 1

Characteristics of a 4-factor prognostic model to assess the risk of not achieving the desired treatment effect (FAC=1–4 points)

Factorial attribute		Model coefficient value, b±m	Significance level p difference of the model coefficient from 0	OR (95 % CI)
Age		0.064±0.015	<0.001	1.07 (1.03–1.10)
Time from estimated stroke onset to SC admission	Within 24 hours	Reference		
	1–7 days	–0.55±0.51	0.29	–
	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	–
	>180 days	1.75±0.56	0.002	5,7 (1,9–17,1)
NIHSS score*		0.14±0.03	<0.001	1.15 (1.08–1.22)
FAC score*		–0.92±0.13	<0.001	0.40 (0.31–0.52)

Notes. * – baseline (upon admission). OR – odds ratio. CI – confidence interval. SC – Stroke Center. FAC – Functional Ambulation Classification. NIHSS – National Institutes of Health Stroke Scale.

According to multivariate analysis, independent predictors of the need for assistance with walking at the time of discharge from the SC were only 4 factors that were significantly related to the failure to achieve the desired treatment outcome. In particular, the risk of failure to achieve the desired

result of treatment for independent walking increased with the age of the patient (OR 1.07; 95 % CI 1.03–1.10, on average, for each additional year, p<0.001). Initial NIHSS scores (OR 1.15; 95 % CI 1.08–1.22, on average, with an increase in the overall score per each point, p<0.001) and FAC scores (OR 0.40; 95 % CI 0.31–0.52, on average, with a decrease in the score per each point, p<0.001) had a statistically significant and independent effect on the risk of not achieving the desired treatment effect. The probability of independence in walking was significantly reduced in those cases when the patient was hospitalized to the SC later than 180 days from the onset of the disease (OR 5.7; 95 % CI 1.9–17.1, p=0.002).

The logistic regression model based on the selected set of features turned out to be adequate (chi-square=267.1 at 9 degrees of freedom, p<0.001). Fig. 1 shows the curve of operational characteristics of the constructed model.

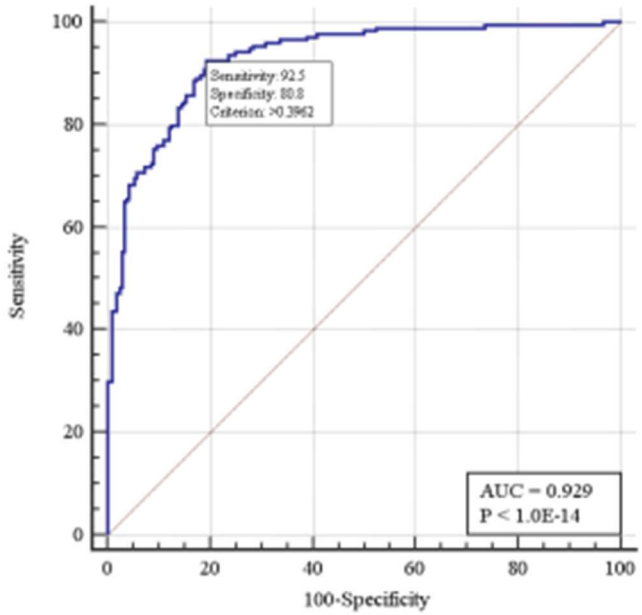

Fig. 1. ROC-curve of a 4-factors logistic model for predicting the risk of failure to achieve the desired treatment effect on the FAC scale (independent ambulation).

The area under the curve of operational characteristics AUC=0.93 (95 % CI 0.90–0.95), which is evidence of the excellent consistency of the prediction model, and the strong association of this set of factors with the risk of lack of independent walking after treatment in the SC in the FAC assessment.

Therefore, this study collected and analysed data from a cohort of stroke patients of various types and severity hospitalised in SC at different stages of the disease (from the most acute to long-term) and received treatment that included sufficient interdisciplinary rehabilitation. This allowed us to identify factors associated with the lack of recovery of independent walking after the treatment.

The results of the univariate analysis showed a significant association of the risk of failure to achieve the desired effect of treatment with a large group of factor signs: stroke subtype, age and gender of the patient, the presence of atrial fibrillation, the overall severity of neurological deficits, motor and cognitive disorders and general functional failure, as well as an increased level of inflammatory markers in the blood during hospitalisation. Multivariate analysis identified only four independent predictors of the need for walking assistance. On the one hand, as in the case of univariate analysis, the patient's age and the initial severity of neurological deficits caused by stroke retained their prognostic value (overall NIHSS score). On the other hand, multivariate analysis revealed a negative effect of the initial assessment of walking function on the FAC scale and the very late start of rehabilitation measures, when more than 180 days passed from the onset of the disease to the SC admission.

The authors of several other studies also found an association between gait function in patients after stroke and the patient's age, the severity of initial neurological deficits (in particular, depression of consciousness and the degree of sensory-based motor disorders of the affected limbs), and life limitations [11, 15]. Kwakkel et al. [9] emphasised the importance of a short period from the disease onset to the examination of rehabilitation specialists and the beginning of rehabilitation activities. There are also reports of prognostic significance of homonymous hemianopsia, urinary incontinence, torso control, sitting balance and other factors [15]. Unfortunately, the results of these studies and our study are difficult to compare due to differences in patient characteristics, treatment duration, rehabilitation interventions, and methods for assessing mobility outcomes.

Future studies should focus on creating a predictive model to assess the probability of recovery of independent walking at the time of discharge from the hospital based on the initial characteristics of the patient and testing its validity in different health facilities and under different treatment conditions.

Conclusion

By analysing the data of a relatively large sample of patients who were hospitalised and received a sufficient amount of interdisciplinary rehabilitation during their stay, four predictors were identified

that had an independent statistically significant relationship (p<0.001) with the absence of independent walking at the time of discharge from the SC. The risk of dependence on outside help when walking directly depended on the patient's age (OR 1.07; 95 % CI 1.03–1.10, on average, for each additional year, p<0.001), the initial severity of the stroke, which was indicated by the NIHSS score (OR 1.15; 95 % CI 1.08–1.22, on average, with an increase in the overall score for every 1 point, p<0.001). The risk of remaining dependent on third-party walking assistance was inversely related to the severity of gait impairment after hospitalisation in the ISU according to the FAC (OR 0.40; 95 % CI 0.31–0.52, on average, with a decrease in the score for every 1 point, p<0.001), and in cases where the patient was hospitalised in the SC later than 180 days from the onset of the disease (OR 5.7; 95 % CI 1.9–17.1, p=0.002). Suppose the predictive value of these predictors is confirmed in other independent studies. In that case, it may help set realistic goals and make optimal decisions about the duration of treatment and preparation of the patient for discharge.

References

1. Bland MD, Sturmoski A, Whitson M, Connor LT, Fucetola R, Huskey T, Corbetta M, Lang CE. Prediction of discharge walking ability from initial assessment in a stroke inpatient rehabilitation facility population. Arch Phys Med Rehabil. 2012 Aug; 93(8): 1441–1447. DOI: 10.1016/j.apmr.2012.02.029.

2. Blennerhassett JM, Levy CE, Mackintosh A, Yong A, McGinley JL. One-Quarter of People Leave Inpatient Stroke Rehabilitation with Physical Capacity for Community Ambulation. J Stroke Cerebrovasc Dis. 2018 Dec;27(12):3404–3410. DOI: 10.1016/j.jstrokecerebrovasdis.2018.08.004.

3. Chan DK, Cordato D, O'Rourke F, Chan DL, Pollack M, Middleton S, Levi C. Comprehensive stroke units: a review of comparative evidence and experience. Int J Stroke. 2013 Jun; 8(4):260–4. DOI:10.1111/j.1747-4949.2012.00850.x).

4. Cramer SC. Recovery After Stroke. Continuum (Minneap Minn). 2020 Apr; 26(2):415–434. doi: 10.1212/CON.0000000000000838.

5. Danks KA, Pohlig RT, Roos M, Wright TR, Reisman DS. Relationship Between Walking Capacity, Biopsychosocial Factors, Self-efficacy, and Walking Activity in Persons Poststroke. J Neurol Phys Ther. 2016 Oct; 40(4): 232-8. DOI: 10.1097/NPT.0000000000000143.

6. Feng W, Belagaje SR. Recent advances in stroke recovery and rehabilitation. Semin Neurol. 2013 Nov; 33(5): 498–506. DOI:10.1055/s-0033-1364215.

7. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2017 Feb 3; 120(3): 439–448. DOI: 10.1161/CIRCRESAHA.116.308413.

8. Hömberg V. Rehabilitating Walking Ability After Stroke. Dtsch Arztebl Int. 2019 Mar 8;116(10):174. doi: 10.3238/arztebl.2019.0174a.

9. Kwakkel G, Kollen BJ. Predicting activities after stroke: what is clini¬cally relevant? Int J Stroke. 2013 Jan; 8(1):25–32. DOI: 10.1111/j.1747-4949.2012.00967.x.

10. Pournajaf S, Goffredo M, Agosti M, Massucci M, Ferro S, Franceschini M; Italian Study Group on Implementation of Stroke Care (ISC Study). Community ambulation of stroke survivors at 6 months follow-up: an observational study on sociodemographic and sub-acute clinical indicators. Eur J Phys Rehabil Med. 2019 Aug; 55(4): 433–441. DOI: 10.23736/S1973-9087.18.05489-8.

11. Stinear CM. Prediction of motor recovery after stroke: advances in biomarkers. Lancet Neurol. 2017 Oct; 16(10):826–836. doi: 10.1016/S1474-4422(17)30283-1.

12. Sun Y, Paulus D, Eyssen M, Maervoet J, Saka O. A systematic review and meta-analysis of acute stroke unit care: what's beyond the statistical significance? BMC Med Res Methodol. 2013 Oct 28; 13: 132. DOI:10.1186/1471-2288-13-132.

13. Townsend N, Wilson L, Bhatnagar P, et al. Cardiovascular disease in Europe: epidemiological update 2016. Eur Heart J. 2016; 37: 3232–3245. DOI:10.1093/eurheartj/ehw334.

14. Tsang RC, Chau RM, Cheuk TH, Cheung BS, Fung DM, Ho EY, et al. The measurement properties of modified Rivermead mobility index and modified functional ambulation classification as outcome measures for Chinese stroke patients. Physiother Theory Pract. 2014 Jul; 30(5):353–9. doi: 10.3109/09593985.2013.876563.

15. Veerbeek JM, Van Wegen EE, Harmeling-Van der Wel BC, Kwakkel G; EPOS Investigators.Is accurate prediction of gait in nonambulatory stroke patients possible within 72 hours poststroke? The EPOS study. Neurorehabil Neural Repair. 2011 Mar-Apr;25(3):268–74. DOI: 10.1177/1545968310384271.

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