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ABSTRACT

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TIME COURSE AND PREDICTORS OF RECOVERY FROM LATEROPULSION AFTER HEMISPHERIC STROKE (PROSPECTIVE STUDY)

Introduction. In recent years, considerable attention has been paid to the abnormality of body verticality perception in stroke patients. Most often, misperception of body verticality is manifested in the form of lateropulsion and repulsion syndrome.

Objective: to study the timing of recovery from lateropulsion (pusher syndrome) and to determine the predictors of lateropulsion resolution in patients with hemispheric strokes.

Material and methods. We included in the study patients with hemispheric strokes occurring within the last month. 61 patients were diagnosed with lateropulsion and 9 patients with pusher syndrome, according to the Scale for Contraversive Pushing**.** After initial examination, patients were subsequently invited for a weekly examination until the body's verticality was normalized.

Results. Recovery time from pusher syndrome was significantly longer – 9.0 (95% confidence interval: 7.1–10.4) weeks compared to recovery time from lateropulsion – 5.9 (95% confidence interval: 5.5–6.3) weeks. Among all the studied factors, only spatial hemineglect was a significant independent predictor of a much longer resolution time of lateropulsion (hazard ratio 2.36; 95% confidence interval: 1.20–4.27). The mean duration of lateropulsion in patients with spatial hemineglect was 6.3 (95% confidence interval: 5.8–6.8) weeks, whereas in patients without spatial hemineglect, it was 4.8 (95% confidence interval: 4.3–5.4) weeks. In a subgroup of patients without spatial hemineglect, higher Fazekas scale values were a significant independent predictor of longer resolution time of lateropulsion (hazard ratio 2.38; confidence interval 95%: 1.25–4.48).

Conclusions. After hemispheric strokes recovery time from pusher syndrome is much longer than recovery from lateropulsion.

Recovery time from lateropulsion is determined by spatial hemineglect and leukoaraiosis severity.

Key words: hemispheric stroke, lateropulsion, pusher syndrome, recovery, predictors.

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ЧАСОВІ ХАРАКТЕРИСТИКИ ТА ПРЕДИКТОРИ РОЗРІШЕННЯ ФЕНОМЕНУ ЛАТЕРОПУЛЬСІЇ ПІСЛЯ ГЕМІСФЕРАЛЬНИХ ІНСУЛЬТІВ (ПРОСПЕКТИВНЕ ДОСЛІДЖЕННЯ)

Вступ. Останніми роками значна увага з боку науковців та клініцистів приділяється постінсультним порушенням сприйняття вертикальності тіла. В переважній більшості випадків порушення сприйняття вертикальності тіла проявляються у вигляді латеропульсії та синдрому відштовхування.

Мета: вивчити терміни відновлення після появи латеропульсії (синдрому відштовхування) та визначити предиктори розрішення латеропульсії у пацієнтів з півкульними інсультами.

Матеріал і методи. У дослідження були включені пацієнти з півкульними інсультами, що виникли протягом останнього місяця. У 61 пацієнта було діагностовано латеропульсію та у 9 пацієнтів – синдром відштовхування, згідно зі Scale for Contraversive Pushing. Після первинного обстеження пацієнтів запрошували на щотижневі огляди до моменту нормалізації вертикального положення тіла.

Результати. Час відновлення від синдрому відштовхування був достовірно довшим – 9,0 (95% довірчий інтервал: 7,1–10,4) тижнів порівняно з часом відновлення від латеропульсації – 5,9 (95% довірчий інтервал: 5,5–6,3) тижнів. Серед усіх факторів, що нами досліджувалися, лише просторовий гемінеглект був достовірним незалежним предиктором тривалішого часу розрішення латеропульсії (відношення ризиків 2,36; 95% довірчий інтервал: 1,20–4,27). Середня тривалість латеропульсії у пацієнтів з просторовим гемінеглектом становила 6,3 (95% довірчий інтервал: 5,8–6,8) тижня, тоді як у пацієнтів без просторового гемінеглекта вона становила 4,8 (95% довірчий інтервал: 4,3–5,4) тижня. У підгрупі пацієнтів без просторового гемінеглекту вищі показники церебрального лейкоареозу за шкалою Fazekas були достовірним незалежним предиктором тривалішого часу розрішення латеропульсії (відношення ризиків 2,38; довірчий інтервал 95%: 1,25–4,48).

Висновки. У пацієнтів з півкульними інсультами час відновлення від синдрому відштовхування є значно довший, ніж час відновлення від латеропульсії. Час відновлення після латеропульсації залежить від вираженості просторового гемінеглекту та ступеня церебрального лейкоареозу.

Ключові слова: гемісферальні інсульти, латеропульсія, синдром відштовхування, відновлення, предиктори.

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ABBREVIATIONS

CI – confidence interval
HR – hazard ratio
NIHSS – National Institute of Health Stroke Scale
PS – pusher syndrome
SCP – Scale for Contraversive Pushing
SHN – spatial hemineglect

INTRODUCTION / ВСТУП

The destruction of healthcare facilities and disrupted delivery of healthcare as a result of military operations in Ukraine require optimization of rehabilitation approaches for various diseases [1, 2, 3].

In recent years, among the various poststroke disorders of postural balance, considerable attention has been paid to the abnormality of body verticality perception. The latter is clinically manifested by deviation of the body axis in the frontal plane and possibly other symptoms. Lateral body tilt after hemispheric strokes occurs because of impaired graviception mechanisms due to a shift in the internal model of verticality in the opposite direction from the affected brain hemisphere [4, 5].

Today, the deficit of the active body orientation concerning gravity in the frontal plan is considered a continuum of postural disorders. It could be presented from mild forms – lateropulsion (isolated lateral tilt of the body axis) to severe forms – pusher syndrome (PS). PS, besides contralesional lateral body tilt, also includes active pushing of the unaffected arm or leg to the contralesional side and resistance to passive correction of posture [4, 6, 7].

Lateropulsion has a negative influence on balance and walkability after stroke and is associated with poor poststroke recovery and a longer rehabilitation duration [7, 8, 9].

It is known that chronic post-stroke disorders have certain peculiarities of the course over time, which requires prospective studies [10, 11]. However, to date, there are almost no prospective studies devoted to the temporal characteristics of recovery from lateropulsion after stroke. Also, the factors that may influence the resolution of lateropulsion are not well understood. At the same time, knowledge of the peculiarities of the course of lateropulsion, as well as the factors associated with prolonged periods of lateropulsion resolution, may be useful in choosing the right tactics for managing these patients.

Objective: to study the timing of recovery from lateropulsion (PS) and to determine the predictors of lateropulsion resolution in patients with hemispheric strokes.

Material and methods.

This study was approved by the Ethics Committee of Poltava State Medical University, in accordance with the Declaration of Helsinki (protocol №189/2020). The Declaration of Helsinki's guidelines were followed in the conduct of this study. Written informed consent was obtained for all patients before their inclusion in the study.

Criteria for inclusion of patients in the study:

- hemispheric strokes occurring within the last month;
- the presence of lateropulsion or PS at the first examination;
- written patient consent.

Criteria for exclusion of patients from the study:

- visual, vestibular, and proprioceptive disorders that distort the verticality perception;
- orthopedic and other neurological pathology that lead to passive or active changes in the body axis;
- decompensated somatic pathology;
- psychiatric and narcological pathology;
- use of drugs that disturb postural balance (anticonvulsants, sedatives, tranquilizers, neuroleptics, tricyclic antidepressants);
- impaired writing function, which does not allow for proper completion of the questionnaires.

For the diagnosis of lateropulsion and PS, we used the Scale for Contraversive Pushing (SCP). The SCP assesses 3 components during sitting and standing: the tilt of the body axis in the frontal plane, active pushing with healthy limbs in the opposite direction, and active resistance during posture correction. The total SCP score ranged from 0 to 6. Lateropulsion was diagnosed in cases of isolated body tilt in a sitting or standing position without pushing and resistance, which equals values ≥ 0.5 on the SCP. PS was diagnosed with a total score of SCP ≥ 3, provided that the value of each of the 3 components of SCP ≥ 1 [4].

Muscle strength was assessed on a 5-point scale. Spatial hemineglect (SHN) was investigated using the bell test (critical value – missed 6 or more bells on one half). Upper limb apraxia was diagnosed using the test of upper limb apraxia. Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS).

Cognitive disorders were diagnosed using the Montreal Cognitive Assessment Scale (cut-off score < 26 points). Anxiety and depressive disorders were determined by the Hospital Anxiety and Depression Scale with anxiety and depression subscale scores ≥ 11. Fatigue was assessed using the Fatigue Severity Scale (critical value ≥ 4 points).

Cerebral infarcts, depending on their localization, were divided into cortical-subcortical and subcortical ones. The volumes of cerebral infarcts were calculated on T-2 weighted magnetic resonance images and computed tomography images using the irregular ellipse formula [12]. Quantitative characteristics of leukoaraiosis were analyzed on magnetic resonance images in fluid attenuated inversion recovery mode using the visual Fazekas scale; the total Fazekas scale value was calculated as the sum of periventricular and subcortical leukoaraiosis. For morphometric assessment of internal and external brain atrophy, we calculated the bifrontal index, bicaudate index, maximum diameter of the third ventricle, and cortical atrophy index [13].

After inclusion in the study, patients were subsequently invited for a weekly examination until the body's verticality was normalized.

The Kaplan–Meier method was used to assess the time of resolution of lateropulsion and PS. The log-rank test was used to compare time to recovery from lateropulsion and PS. A stepwise multivariate Cox regression with a 95 % confidence interval (CI) was used to determine predictors of time to recovery from lateropulsion. For hazard ratio (HR) calculation, we included all variables that had $p < 0.1$ in the univariate Cox model into the multiple Cox model. A significance level of 0.05 was used for all tests.

Results

A total of 70 patients were included in the study, of whom 61 (87 %) were diagnosed with lateropulsion and 9 (13 %) with PS.

During observation, 10 patients, for various reasons (refusal of repeated examinations, death, change of residence), stopped participating in the study until the lateropulsion or PS was resolved.

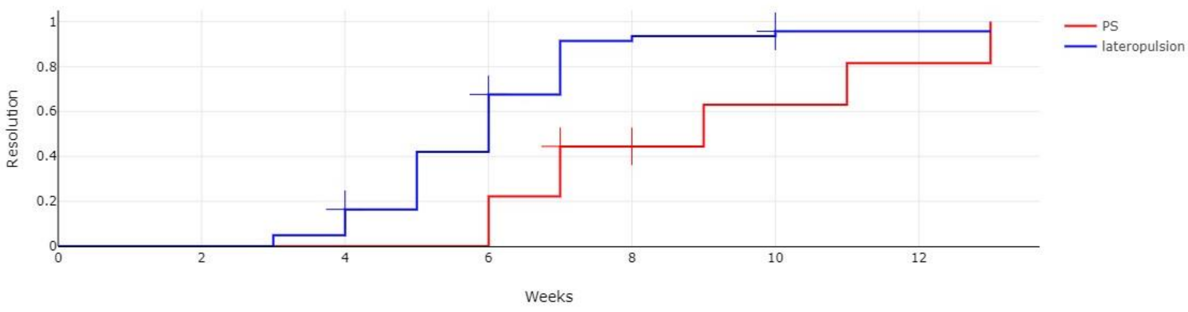

Figure 1 – Kaplan–Meier curve of time to the resolution of lateropulsion and PS

The mean recovery time from lateropulsion was 5.9 (95 % CI: 5.5–6.3) weeks, and the mean recovery time from PS was 9.0 (95 % CI: 7.1–10.4) weeks. Using the log-rank test, it was found that the time to resolution of PS was significantly longer than the time to resolution of lateropulsion ($\chi 2=9.62$, $p=0.002$).

The next step was to determine the factors associated with the timing of recovery from lateropulsion only because the limited number of PS cases was not enough for adequate statistical analysis.

Table 1 – Univariate Cox proportional hazards regression analysis for predictors of duration of recovery from lateropulsion

Variable	HR (95 % CI)	p
age (years)	1.00 (0.96–1.03)	0.90
male gender	0.96 (0.56–1.66)	0.88
degree of paresis (points)	1.16 (0.90–1.49)	0.25
SHN	2.48 (1.35–4.57)	0.004
upper limb apraxia	1.38 (0.71–2.69)	0.35
aphasias	1.44 (0.79–2.62)	0.23
NIHSS (points)	0.96 (0.88–1.04)	0.29
ischemic stroke	1.30 (0.40–4.22)	0.67
right-hemisphere stroke	1.82 (1.00–3.34)	0.05
primary stroke	0.95 (0.40–2.23)	0.91
cognitive impairments	1.04 (0.61–1.79)	0.89
anxiety disorders	1.12 (0.61–2.07)	0.72
depression disorders	0.94 (0.50–1.80)	0.86
fatigue	0.73 (0.38–1.40)	0.35
subcortical stroke	0.70 (0.38–1.29)	0.25
stroke volume (cm^3)	1.00 (1.00–1.00)	0.35
leukoaraiosis (points)	1.19 (0.93–1.52)	0.15
bifrontal index	1.04 (0.98–1.09)	0.19
bicaudate index	0.96 (0.89–1.04)	0.36
maximum diameter of the third ventricle (mm)	1.01 (0.99–1.02)	0.40
cortical atrophy index	0.92 (0.77–1.09)	0.31

As shown in Table 1, according to the univariate Cox regression analysis, SHN was a significant predictor of longer resolution time of lateropulsion. In the multivariate Cox regression analysis, SHN remained a significant independent predictor of longer resolution time of lateropulsion (HR 2.36; CI 95 %: 1.20–4.27, p=0.01), whereas the right-hemispheric strokes had an HR of 1.52 (CI 95 %: 0.81–2.86, p=0.19).

The mean duration of lateropulsion in patients with SHN was 6.3 (95 % CI: 5.8–6.8) weeks, whereas in patients without SHN, it was 4.8 (95 % CI: 4.3–5.4) weeks. Using the log-rank test, we found that the recovery time from lateropulsion in patients with SHN was significantly longer than in patients without SHN ($\chi 2=13.0$, $p < 0.001$).

Thus, it can be assumed that lateropulsion in the presence (or absence) of SHN is a different phenomenon in terms of resolution features. So, the next step was to determine factors that can affect the timing of lateropulsion in the presence (or absence) of SHN.

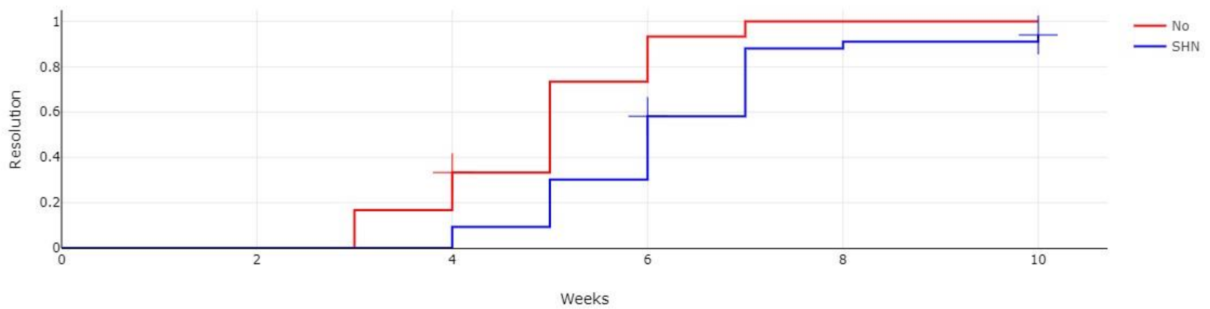

Figure 2 – Kaplan Meier curve of time to resolution of lateropulsion depending on the presence (absence) of SHN

Table 2 – Univariate Cox proportional hazards regression analysis for predictors of duration of recovery from lateropulsion depending on the presence (or absence) of SHN

Variable	**SHN present**		**SHN absent**	
	HR (95 % CI)	p	HR (95 % CI)	p
age (years)	1.00 (0.96–1.04)	0.83	0.99 (0.92–1.07)	0.86
male gender	0.82 (0.43–1.58)	0.55	1.43 (0.49–4.21)	0.51
degree of paresis (points)	1.21 (0.89–1.63)	0.22	1.18 (0.70–1.98)	0.53
upper limb apraxia	1.09 (0.42–2.81)	0.86	1.03 (0.36–2.91)	0.96
aphasias	1.65 (0.80–3.37)	0.17	1.08 (0.37–3.18)	0.89
NIHSS (points)	0.95 (0.86–1.05)	0.32	1.06 (0.87–1.29)	0.56
ischemic stroke	1.61 (0.38–6.81)	0.52	0.33 (0.04–2.79)	0.31
right-hemisphere stroke	1.09 (0.42–2.81)	0.86	2.72 (0.90–8.26)	0.08
primary stroke	0.94 (0.28–3.13)	0.92	0.52 (0.14–1.90)	0.32
cognitive impairments	0.96 (0.50–1.86)	0.91	0.56 (0.18–1.75)	0.33
anxiety disorders	0.96 (0.45–2.04)	0.91	1.72 (0.59–5.06)	0.32
depression disorders	0.67 (0.29–1.53)	0.34	2.56 (0.81–8.11)	0.11
fatigue	0.45 (0.19–1.10)	0.08	1.37 (0.48–3.89)	0.55
subcortical stroke	0.80 (0.37–1.73)	0.57	0.61 (0.22–1.72)	0.35
stroke volume (cm^3)	1.00 (1.00–1.00)	0.35	1.00 (1.00–1.00)	0.61
leukoaraiosis (points)	0.86 (0.64–1.17)	0.35	2.77 (1.41–4.74)	0.01
bifrontal index	1.05 (0.99–1.12)	0.12	0.96 (0.86–1.09)	0.56
bicaudate index	0.99 (0.90–1.08)	0.79	0.98 (0.81–1.18)	0.80
maximum diameter of the third ventricle (mm)	1.00 (0.99–1.02)	0.71	0.99 (0.95–1.02)	0.47
cortical atrophy index	0.96 (0.78–1.16)	0.65	0.85 (0.57–1.24)	0.39

As shown in Table 2, according to univariate Cox regression analysis, in cases of SHN, none of the factors had significant associations with the timing of lateropulsion resolution. In patients without SHN, higher Fazekas scale values were significant predictors of longer resolution time of lateropulsion. In the multivariate Cox regression analysis, higher Fazekas scale values in patients without SHN remained a significant independent predictor of longer resolution time of lateropulsion (HR 2.38; CI 95 %: 1.25–4.48, p=0.01), whereas right-hemispheric stroke had an HR of 1.55 (CI 95 %: 0.42–5.74, p=0.51).

For a detailed analysis of recovery from lateropulsion in patients without SHN, we dichotomized this cohort into two subgroups, depending on the Fazekas scale values (< 3 points and ≥ 3 points).

The mean time to recovery from lateropulsion in patients with a Fazekas scale score of < 3 was 4.0 (95 % CI: 3.3–4.7) weeks, whereas in patients with a Fazekas scale score of ≥ 3 the mean time to recovery from lateropulsion was 4.8 (95 % CI: 4.3–5.4) weeks. Using the log-rank test, it was found that the time for resolution of lateropulsion in patients with higher Fazekas scale values was significantly longer than the time in patients with lower Fazekas scale values (χ^2=7.5, p=0.01).

Discussion

We found that after hemispheric strokes, the recovery time from PS is significantly longer than the recovery time from lateropulsion. From the literature data, the duration of lateropulsion varies considerably in individual patients and is up to 20 weeks after the stroke [14]. To date, only one study has shown that the duration of lateropulsion is much longer in patients with higher initial SCP scores [15]. Logically, more severe disorders of graviception mechanisms require a more prolonged period for their resolution.

We found that the presence of SHN is associated with a significantly longer time to normalize body verticality. There is evidence of a longer duration of lateropulsion in patients with SHN [15], although there is evidence of the absence of this pattern [16]. SHN could impair perception of the subjective visual vertical in the frontal plane [17], resulting in a contralateral tilt of the body axis [18]. Probably, lateropulsion has significant differences in resolution patterns, depending on the presence (or absence) of SHN. An indirect evidence of the latter statement may be a phenomenon that in the presence of SHN, none of the studied factors were associated with prolonged recovery time from lateropulsion.

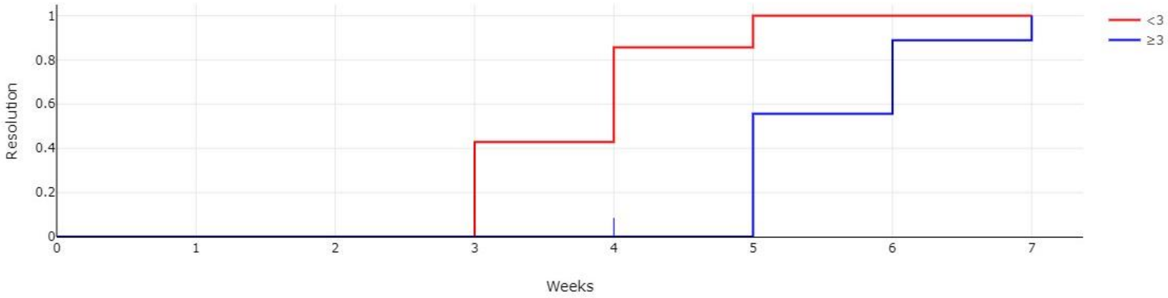

Figure 3 – Kaplan Meier curve of time to resolution of lateropulsion in patients without SHN depending on Fazekas scale values

In patients without SHN, the recovery time from lateropulsion is directly associated with leukoaraiosis severity, according to the Fazekas scale.

According to Japanese researchers, the presence of cerebral lesions on neuroimaging (strokes, silent cerebral infarctions, microhemorrhages, white matter hyperintensity, dilated perivascular spaces) is associated with more prolonged recovery time from lateropulsion (without taking into account SHN). The duration of lateropulsion in patients with conditionally minor neuroimaging abnormalities was 62.0 (95 % CI, 56.2–67.8) days, while in patients with significant abnormalities, the duration of lateropulsion was 94.0 (95 % CI, 77.0–111.1) days [19]. Probably, more severe cerebral damages are associated with a slower poststroke recovery from lateropulsion. It is known that the degree of leukoaraiosis determines the course of other chronic poststroke complications, in particular, poststroke fatigue [20].

It should be noted that we did not find any differences in the duration of lateropulsion depending on the affected cerebral hemisphere. Although, some studies have shown that in right-hemispheric strokes, the resolution of lateropulsion is significantly longer than in left-hemispheric strokes [6, 16]. The perception of verticality and control of body position relative to gravity is a highly lateralized right-hemispheric function [5]. In addition, SHN occurs significantly often in right hemispheric lesions [21]. Probably, the longer duration of lateropulsion in right-hemispheric strokes can be partially explained by the frequent simultaneous presence of SHN.

From a practical point, our findings can help clinicians in predicting the recovery time from lateropulsion and in rational planning of rehabilitation approaches.

CONCLUSIONS / ВИСНОВКИ

1. After hemispheric strokes recovery time from PS is significantly longer than recovery time from lateropulsion.

2 The presence of SHN is associated with a significantly longer recovery time from lateropulsion.

3. In patients without SHN, recovery time from lateropulsion is directly associated with the severity of cerebral leukoaraiosis due to the Fazekas scale.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Further research is needed to find out what factors influence the time characteristics of recovery from lateropulsion and PS in patients after stroke.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

The authors confirm their contribution to the paper as follows: study conception and design: I. Delva and O. Oksak; data collection: O. Oksak; analysis and interpretation of results: I. Delva, O. Oksak and M. Delva; draft manuscript preparation: I. Delva, O. Oksak and M. Delva. All authors reviewed the results and approved the final version of the manuscript.

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