St. Cyril and St. Methodius University of Veliko Tarnovo
Center for Psychological Research and Counseling

1/2026

DOI: 10.54664/ENOF2802

EARLY DEPRESSION AFTER FIRST EVER MINOR STROKE — FREQUENCY, COURSE AND IMPORTANT RISK FACTORS — CASE-CONTROL STUDY

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Ethical approval: Written consent was received from patients the publication.
Conflict of interest and funding: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be considered as a potential conflict of interest.
Acknowledgement: We thank the patients and their families for their participation and consent.
Author contribution statement: All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Abstract: *Early post-stroke depression (PSD) is associated with poor outcome after a stroke. The aim of our study was to examine the risk factors, frequency and severity of early PSD after a minor stroke. Material and methods: We examined 109 post-stroke survivors with minor strokes and 112 control subjects. The control subjects were examined once, the stroke patients were examined on the 1st, 2nd, and 3rd day and in the 1st, 2nd and 3rd months after the incident via Hamilton Depression Rating Scale (HDRS). All results were interpreted at a 95% confidence level ($p < 0.05$).*

Results show that PSD was with high frequency during the first three days after the stroke and its prevalence and severity decreased over time to 30% by the 3rd month. It is associated with ageing, female gender, high-level formal education, loneliness, stroke severity and disability and number of vascular risk factors, but not with stroke location. This study shows that early post-stroke depression in patients with minor stroke is a common and multifactorial condition associated with a complex clinical course and several important risk factors.

Keywords: *early post-stroke depression, risk factors for post-stroke depression, minor stroke, vascular risk factors*

Introduciton

Strokes are among the leading causes for long-term disability and mortality all over the world [1]. One of the most important causes for post-stroke disability and poor prognosis is post-stroke depression (PSD), which is commonly underdiagnosed and undertreated [2]. The estimated prevalence of PSD is about 30% – 50% of all cases, although the frequency varies depending on the sample age, gender, race, other comorbidities and stroke severity [2], [3], [4], [5]. PSD can be divided into two separate groups: early (during the first 3 months after the stroke) and late (after the first 3 months) [6], [7]. Despite PSD being a well-known entity, relatively few studies are conducted among patients at early post-stroke stage [8], [6], [7], [9].

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Materials and Methods.

The aim of our study was to examine the risk factors, frequency and severity of early PSD after minor stroke.

We examined 109 patients (66.67±9.03-year-old; 67 males and 42 females) with minor stroke (The National Institutes of Health Stroke Scale - NIHSS≤3p.) and 112 Control subjects (66.70± 9.13 year-old; 69 males and 43 females) with similar vascular risk factors without stroke. The inclusion criteria for the study were: (1) age >50 y; (2) no previous history for depression, anxiety or other psychiatric disease; (3) no drug or alcohol abuse; (4) no other significant brain diseases such as traumatic brain disease, encephalitis, degenerative dementia, brain tumor or epilepsy; (5) no decompensation of any somatic disease during the last one year; (6) for stroke survivors – the stroke should be the first in life, NIHSS≤3p; modified Rankin scale (mRS) ≤2p.); (7) written informed consent.

After providing their informed consent, the subjects were divided into two groups: patients with minor stroke and control subjects.

All post-stroke survivors were examined via 21 Hamilton Depression Scale (HDS) on the 1st, 2nd, 3rd post-stroke day and in the 1st, 2nd and 3rd month. The control subjects were examined once with the same test.

The statistical analysis was done via descriptive analysis and paired t-test or Man/Whitney Test Statistics) via *Statgraphics 20 Plus* and SPSS 20. All results were interpreted at a 95% confidence level ($p < 0.05$).

Results

The demographic data of our subjects is summarized in Table 1. The demographic characteristics of our groups were similar. Most of our subjects were married men with upper-secondary school formal education. Among stroke survivors, the most frequent was the right middle cerebral artery (RMCA) stroke, followed by the left middle cerebral artery (LMCA) one. The least frequent was brainstem stroke.

Table 1. Demographic data

	Post-stroke survivors	Controls
N=	109	112
Age (y.)	66.67±9.03	66.70± 9.13
Male:female ratio	67:42	69:43
Marital Status Single:Married:Widows	4:83:22	5:86:21
Formal education: Basic/Upper-secondary/Higher	33:62:14	34:64:14
NIHSS (p)	1.98±0.63	NA
mRS (p.)	1.06±0.49	
With LMCA stroke: with RMCA stroke: with brainstem stroke	39:42:28	NA

Severity and frequency of depression: The results for the distribution and the severity of PSD are summarized in Table 2.

Table 2. Distribution and severity of early PSD over time

	HDS (p)	% depressed
Controls	7.73±3.50 (5-15)	12%
Post - stroke survivors		
1st day	11.16±4.49 (7-15)	49%
2nd day	12.90±6.32 (8-16)	55%
3rd day	13.31±5.79 (7-16)	57%
p (1, 2, 3 day)	>0.05	
p (1, 2, 3rd day; C)	0.0001	
1st month	11.06±2.90 (6-15)	45%
2nd month	9.55±3.85 (6-15)	44%
3rd month	8.13±3.69 (6-14)	30%
p (3rd day,1 month)	0.0001	
p (3rd day, 2month)	0.0028	
p (3rd day, 3 month)	0.0034	
p (3rd month, controls)	0.0004	

None of our subjects had severe depression. About 12% of our control subjects had depression (HDS≥10p.). Depression was found with 57% of patients during the first three days after the stroke, although it was most frequent on the third day. The frequency of early depression decreased gradually to 30% of all cases by the 3rd month. The severity of depression after the 3rd day also decreased over time. However, the severity and frequency of depression even in the third month after the stroke were higher than those of the controls.

Relation Between Early PSD and Other Factors.

Depression was strongly associated with age, female sex, lack of partnership, high-level education, level of disability and stroke severity (see table 3).

Table 3. Relation between early PSD and some of its risk factors.

	P=
Age (y.)	0.0001
Female vs male	0.0039
Single/widow vs married	0.0049
Higher education vs basic/upper-secondary	0.02359
Stroke severity – NIHSS (p.)	0.0358
Level of disability (mRS p.)	0.0007
Stroke localization	>0.05
Number of vascular risk factors	0.0229

It was also associated with the number of vascular risk factors (hypercholesterolemia, diabetes mellitus or insulin resistance, arterial hypertension, ischemic heart disease, atrial fibrillation and carotid atherosclerosis). It was not associated with the stroke localization.

Discussion

Early PSD is a serious medical condition, that can worsen post-stroke outcome and prognosis [2], [6], [10]. Nevertheless, it is frequently underestimated [6]. Our study shows that about 57% of patients develop PSD during the first three days after the minor stroke, although the frequency of PSD gradually decreases over time to 40% in the 3rd month. Thus, nearly 50% of all cases developed only transient depressive symptoms and improve to normal mood even without treatment, which was suggested from some previous studies [10], [9]. However, the frequency of early PSD prevails regarding depression among control subjects with similar vascular risk factors. Yet there was no patient with HDS>16p. so all patients with PSD had only mild signs of depression. Very similar results are obtained from previous studies [11], [6], [9]. Interestingly, the frequency of depression (but not its severity) increases over the first three days after the incident, which might be associated with the disease awareness and its limitations, feeling of loneliness during the hospital admission and the specificity of hospital atmosphere (reactive depression) or might be associated with the hypothalamus-pituitary axis and functional brain changes after the acute stroke [3], [12].

The frequency of early PSD is associated with some demographic factors as ageing, female gender, higher education and loneliness. Ageing is associated with cerebral ischemia, post-stroke disability and impaired neuroplasticity, as well as development of cognitive impairment and depression [13]. It is also associated with factors, leading to reactive depression such as fatigue, loneliness and frailty [14]. Unfortunately, all these factors along with the development of depression can have cumulative effect on functional outcome after stroke, therefore it is important to identify them, particularly in cases with poor family environment (widows, single elderly, no relatives, etc.). Such patients are at risk of abandonment and poor medication compliance. PSD is well known to be more prevalent in women than men, which is associated with many hormonal and environment factors [15]. Higher education is associated with lower levels of depression among elderly that have physical activity [16]. Nevertheless, our results show that highly educated post-stroke survivors are more frequently depressed than those with lower education, which could be explained by specific socio-demographic factors in our country, as well as their self-awareness and the feeling of increased social dependence. The surprising association between higher education and depression is found also among college students [17].

PSD is also associated with stroke severity and level of post-stroke disability [2], [10], [4], [5]. Despite the fact that all our patients are with minor stroke, such association is also obtained from our study.

We failed to find any association with lesion localization and early PSD. Lack of relationship between left and right stroke and depression is suggested from other authors [18]. However, some depressive signs are associated with lesions at specific brain zones such as orbitofrontal cortex, dorsolateral prefrontal cortex, pre- and post-central gyri and basal ganglia (motivational deficits), dorsal thalamus, anterior insula and somatosensory cortex (sadness), dorsolateral prefrontal cortex (changes in concentration and cognitive decline) and insula, parietal operculum and amygdala lesions (somatic syndromes) [19].

Our study shows that vascular risk factors play important role for early PSD development. Li et al. [20] have found that diabetes mellitus and hypertension are associated with PSD development. However, the exact mechanism of their impact remains unclear although they are associated with small vessel disease leading to disconnection and neurotransmitter imbalance [21].

Conclusion

This study shows the complexity, multi-etiology and high frequency of early PSD among patients with minor stroke. It highlights the complex mechanism of its development as reactive and functional entity, as well as its specific natural course and some of its important risk factors.

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