Human & Veterinary Medicine
International Journal of the Bioflux Society HVM

OPEN ACCESS
Research Article

Incidence and predictive factors for poststroke depression

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Abstract. Aim: The purpose of this paper is to demonstrate an association between certain parameters and the risk of post-stroke depression, and to establish the incidence of post-stroke depression. Material and methods: This study involved 314 consecutive patients diagnosed with acute ischemic stroke. Of the 314 patients, two groups were formed: a depression group consisting of 82 patients diagnosed with post-stroke depression according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision and a control group of 234 patients where the diagnosis of depression was excluded. Patient demographics were observed. Brain imaging consisted in performing brain CT or MRI to confirm the diagnosis of stroke, the localization of the lesion, the degree of cerebral atrophy, and the existence of periventricular white mater lesions. Results: The incidence of post-stroke depression in our study was 19.33%. In univariate analysis patients with stroke located in the frontal lobe ($p<0.001$), the prefrontal cortex ($p<0.001$), the basal nuclei ($p=0.007$), the left hemisphere ($p<0.001$), who had white matter lesions ($p<0.001$) or cerebral atrophy ($p<0.001$), had a statistically significantly higher probability of being diagnosed with depression. The incidence of depression was lower in patients with stroke located in the parietal lobe ($p=0.02$). In multivariate analysis, the following variables had an independent contribution to the risk of developing depression: frontal lobe lesion (OR 2.4, $p=0.04$), prefrontal cortex lesion (OR 8.3, $p<0.001$), left hemisphere lesion (OR 7.4, $p<0.001$), periventricular lesion (OR 7.4; $p<0.001$). Conclusion : The risk of post-stroke depression may be influenced by the localization of stroke in the frontal lobe, the prefrontal cortex of the left hemisphere and the associated presence of periventricular white matter lesions.

Key Words: incidence, post-stroke depression, frontal lesion, left hemisphere lesion.

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Introduction

Post-stroke depression, an important complication of stroke, is rarely diagnosed and its treatment is unevenly administered. Mozaffarian et al (2016) stated that stroke is the third cause of mortality in the world, and the depressive disorder is the fourth cause of disability, but it is expected that in the not-too-distant future it will come second after cardiovascular disease.

There is a 15% risk of developing a depressive disorder throughout life in a healthy person, whereas in those with stroke this risk is double (Weg et al 1999). Estimates of prevalence may vary depending on the time elapsed from stroke to psychological evaluation. Patients evaluated during the sub-acute stage, who are in a transition period trying to adapt to post-stroke consequences, develop the depressive episode as a reflection of the major changes that have occurred. In fact, the highest prevalence of depressive episodes was reported in the first month after stroke (Aben et al 2006; Aben et al 2003; Andersen et al 1995; Bhogal et al 2004; Bour et al 2010). This depends on several risk factors: the presence of personal history of psychiatric pathology (Lisa et al 2017), HTA (Jiang et al 2014), increased levels of malondialdehyde (Jouyban et al 2017), modified 5-HTTLPR (Kohen et al 2008), Caucasian race (Ramasubbu et al 1998), past history of stroke (Eriksson et al 2004) and localization of stroke (Dam et al 1989).

In their study, Fingelkurts et al (2006) demonstrated via EEG (electroencephalogram) that patients with depression have abnormal activity in the prefrontal lobe and the limbic system. Among the most suggestive changes are as follows: the presence of theta waves in the frontal lobe and the frequency increase of alpha and beta waves. Since the first discussions about post-stroke depression (Robinson 1986), it has been suggested that when catecholamine neurons are affected the production and release of neurotransmitters during the regeneration process is reduced, and this does not happen only in the affected area, but also throughout the cerebral tissue. It is known that the region located in the anterior part of the frontal lobe is where the highest concentration of catecholaminergic fibres is found. This is consistent with the observation that injuries in the frontal region are the most vulnerable to the production of post-stroke mood disorders, namely to post-stroke depression.

The purpose of this paper is to demonstrate an association between certain parameters and the risk of post-stroke depression, and to establish the incidence of post-stroke depression.

Material and method

This is an observational, analytical, cross-sectional, prospective, case-control study.

Table 1. Characteristics of qualitative variables associated with the risk of post-stroke depression

Variable		Without depression	With depression	P
Age		67(60; 73)	65.5 (58.75; 74)	0.6
Gender		45 (19.2%)	20 (24.4%)	
	F			
	M	189 (80.6%)	62 (75.6%)	0.4
Environment	**R**	83 (35.5%)	34 (41.5%)	
	U	151 (64.5%)	48 (58.5%)	0.4
Frontal lobe lesion		27 (11.5%)	27 (32.9%)	<0.001
Prefrontal cortex lesion		13 (5.6%)	29 (35.4%)	<0.001
Basal nuclei lesion		84 (35.9%)	44 (53.7%)	0.007
Temporal lesion		102 (43.6%)	32 (39%)	0.5
Occipital lesion		64 (27.4%)	16 (19.5%)	0.2
Parietal lesion		58 (24.8%)	10 (12.2%)	0.02
Hemisphere	**R**	21 (9%)	35 (42.7%)	
	L	213 (91%)	47 (57.3%)	<0.001
White matter lesions		28 (12%)	43 (52.4%)	<0.001
Cerebral atrophy		53 (22.6%)	38 (46.3%)	<0.001

This study involved 599 consecutive patients diagnosed with acute ischemic stroke. Of these, 175 were excluded: 14 cases with a history of depression, 50 cases of coma and subsequent death, and 111 patients had global aphasia. Of the 424 patients, two groups were formed: a depression group consisting of 82 patients diagnosed with post-stroke depression according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth revised edition (DSM-IV TR) and the guidelines of Treatment and Diagnostic in Neurology, and a control group of 342 patients where the diagnosis of depression was excluded. Of these 342 witnesses, 108 were randomly excluded to obtain the homogeneity of the two groups in terms of age and gender. The study was conducted between 2009 and 2011 within the Emergency County Hospital in Cluj-Napoca, 2nd Neurology Clinic.

The Ethics Committee of "Iuliu Hatieganu" University of Medicine and Pharmacy approved the protocol of this study, and each patient signed the informed consent form.

Inclusion criteria were as follows:

- over 18 years of age
- clinical and imaging diagnosis of ischemic stroke

Exclusion criteria were as follows:

- patients who refused to participate in this study
- personal history of depression
- diagnosis of haemorrhagic stroke
- diagnosis of transient ischemic attack
- the presence of global aphasia
- comatose patients

Patient demographics were observed. Brain imaging consisted in performing brain CT or MRI to confirm the diagnosis of stroke, the localization of the lesion, the degree of cerebral atrophy, and the existence of periventricular white mater lesions. The psychological assessment consisted of using Beck's depression inventory with 21 items. This scale evaluates minor and major depression criteria. Evaluation was performed within the first 7-10 days of patient hospitalization and depending on the status of patients.

The statistical analysis was achieved using MedCalc Statistical Software version 17.6 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2017). Continuous data were expressed by median and 25th and 75th percentiles, and nominal data were characterized by frequency and percentage. Differences between groups were tested using the Man-Whitney test or the chi-square test, as appropriate. Multivariate binary logistic regression was used for assessing the independent association for some variables with presence of depression. A p value lower than 0.05 was considered statistically significant.

Results

Table 1 compares patients with depression with those without depression. Patients with stroke located in the frontal lobe, the prefrontal cortex, the basal nuclei,the left hemisphere, who had white matter lesions or cerebral atrophy, had a statistically significantly higher probability of being diagnosed with depression. The incidence of depression was lower in patients with stroke located in the parietal lobe.

The incidence of post-stroke depression in our study was 19.33%. To determine the independent influence of the variables on the risk of depression we used the binary logistic regression (table 2). The presence or the absence of depression was considered as the dependent variable. The data triggering statistical significance in univariate analysis were considered as independent variables. The following variables had an independent contribution to the risk of developing depression: frontal lobe lesion (OR 2.4, p=0.04), prefrontal cortex lesion (OR 8.3, p<0.001), left hemisphere lesion (OR 7.4, p<0.001), periventricular lesion (OR 7.4; p<0.001).

Table 2. Multivariate binary logistic regression for the risk of post-stroke depression

Variable	B	P	OR	95% C.I.for OR	
				Lower	Upper
Frontal lobe lesion	0.9	0.04	2.4	1	5.9
Prefrontal cortex lesion	2.1	<0.001	8.3	3.2	21.2
Basal nuclei lesion	0.3	0.3	1.4	0.7	2.8
Parietal lobe lesion	-0.2	0.6	0.8	0.3	1.9
Left hemisphere	2	<0.001	7.4	3.3	16.4
Associated white matter lesions	2	<0.001	7.4	3.5	16
Cortical and subcortical cerebral atrophy	0.5	0.1	1.6	0.8	3.3

Discussions

In our study, we analysed the correlation between the existence of certain ischemic lesions and the occurrence of post-stroke depression, as well as the existence of other factors that could influence the incidence of post-stroke depression. According to the established protocol, one out of five patients experienced post-stroke depression. Lu et al (2017) indicated 11.1 cases of post-stroke depression in 1,000 people with stroke. Salinas et al (2017) assessed 1,424 patients and noticed that 21.4% developed post-stroke depression. This varied according to ischemic stroke localization, there fore when occurring in the anterior circulation depression appeared in 31.4% of cases and in 16.1% of the cases with white matter lesions. Yang et al (2015) found 40 patients with post-stroke depression out of a total of 116, which was correlated with the localization of the lesion, especially right insular or left putamen involvement. Yuan et al (2012) showed that 3 out of 10 patients developed post-stroke depression, which is 481 (28.1%) of 1,713 patients.

In our study, cases involving associated periventricular white matter lesions have a greater risk of post-stroke depression (53.8%). In their study, Kim et al (2011) emphasized that 47.8% of cases with vascular lesions in the periventricular white matter were diagnosed with post-stroke depression. On a group of 243 participants, Wu et al (2014) demonstrated that silent white matter lesions in basal ganglia were associated with a high risk of depression (p=0.01). Chenfei et al (2016) showed that focal white matter lesions syndrome in the cingulate gyrus were associated with the onset of post-stroke depression.

In 32.9% of cases, frontal lobe lesions were associated with the onset of post-stroke depression, which was also supported by studies by Tang et al (2011) and Vataja et al (2004). Metoki et al (2016) showed a16.9% incidence of post-stroke depression in a group of 421 patients, with the highest risk in case of frontal or temporal lobe lesions. In our study, patients with temporal lobe lesions did not have a statistically significant risk of developing depression, as opposed to those with prefrontal cortex lesions. This was confirmed by Vataja et al (2001) on a group of 109 patients, where the risk of post-stroke depression was associated with the presence of lesions of the prefrontal cortex, especially in the left hemisphere, and the presence of cerebral atrophy did not correlate with post-stroke depression. Using mice with lesions of the left prefrontal cortex, Vahid-Ansari et al(2016) demonstrated the correlation between this localization and the onset of post-stroke depression, however associated with a significant degree of anxiety.

Gender distribution shows a prevalence of depression in males (75.6%). This was also confirmed by Sarfo et al (2017) in their study on 200 patients, where depression was found in 52.5% of men, with a 36.5% incidence of post-stroke depression. In a group of 73 stroke patients, Gyagenda et al (2015) observed a 31.5% prevalence of depression, without being influenced by the patient's area of origin (urban/rural). In our study, 63% of patients come from the urban area, but this does not correlate with the risk of post-stroke depression. In a longitudinal observational study on a group of 89 patients, Ortega-Barrioet al (2013) demonstrated that the patient's are of origin does not statistically influence the risk of post-stroke complications, including depression.

Among the limitations of the study we mention the relatively modest number of patients, the lack of psychological assessments prior to acute stroke, and the lack of imaging evaluation prior to the onset of stroke.

Conclusions

The risk of post-stroke depression may be influenced by the localization of stroke in the frontal lobe, the prefrontal cortex of the left hemisphere and the associated presence of periventricular white matter lesions.

References

Aben I, Lodder J, Honig A, Lousberg R, Boreas, A, & Verhey F. Focal or generalized vascular brain damage and vulnerability to depression after stroke: a 1-year prospective follow-up study. Int.Psychogeriatr 2006;18(1):19-35.

Aben I, Verhey F, Strik J, Lousberg R, Lodder J & Honig A. A comparative study into the one year cumulative incidence of depression after stroke and myocardial infarction. J Neurol Neurosurg Psychiatry 2006;74(5):581-585.

Andersen G, Vestergaard K, & Ingeman-Nielsen M. Post-stroke pathological crying: frequency and correlation to depression. European Journal of Neurology 1995;2(1):45-50.

Bhogal SK, Teasell R, Foley N, & Speechley M. Lesion location and poststroke depression: systematic review of the methodological limitations in the literature. Stroke 2004;35(3):794-802.

Bour A, Rasquin S, Aben I, Boreas A, Limburg M, & Verhey F. A one-year follow-up study into the course of depression after stroke. J Nutr Health Aging 2010;14(6):488-493.

Chenfei Ye, Jun Wu, Xuhui Chen, Changle Zhang, Hengtong Li, Shuai Mao, Ma HT. Structural changes of cingulate cortex in post stroke depression. Conf Proc IEEE Eng Med Biol Soc 2016;2016:1099-1102.

Dam H, Pedersen HE, Ahlgren P.Depression among patients with stroke. Acta Psychiatr Scand 1989;80(2):118-24.

Eriksson M, Asplund K, Glader EL, Norrving B, Stegmayr B, Terént A, et al; Riks-Stroke Collaboration Self-reported depression and use of antidepressants after stroke: a national survey. Stroke 2004;35(4):936-41.

Fingelkurts AA, Fingelkurts AA, Rytsälä H, Suominen K, Isometsä E, Kähkönen S. Composition of brain oscillations in ongoing EEG during major depression disorder. Neurosci Res 2006;56(2):133-44.

Gyagenda JO, Ddumba E, Odokonyero R, Kaddumukasa M, Sajatovic M, Smyth K, Katabira E. Post-stroke depression among stroke survivors attending two hospitals in Kampala Uganda. Afr Health Sci 2015;15(4):1220-31.

Jiang XG, Lin Y, Li YS. Correlative study on risk factors of depression among acute stroke patients. Eur Rev Med Pharmacol Sci 2014;18(9):1315-23.

Jouyban A, Khoubnasabjafari M. Comments on "Malondialdehyde: A novel predictive biomarker for post-stroke depression". J Affect Disord 2017;225:52-53.

Kim JT, Park MS, Yoon GJ, Jung HJ, Choi KH, Nam TS, et al. White matter hyperintensity as a factor associated with delayed mood disorders in patients with acute ischemic stroke. Eur Neurol 2011;66(6):343-9.

Kohen R, Cain KC, Mitchell PH, Becker K, Buzaitis A, Millard SP, et al. Association of serotonin transporter gene polymorphisms with poststroke depression. Arch Gen Psychiatry 2008;65(11):1296-302.

Lisa A, Babkair. Risk Factors for Poststroke Depression: An Integrative Review. J Neurosci Nurs 2017;49(2):E1-E2.

Lu CY, Huang HC, Chang HH, Yang TH, Chang CJ, Chang SW, Chen PC. Acupuncture Therapy and Incidence of Depression After Stroke. Stroke 2017;48(6):1682-1684.

Metoki N, Sugawara N, Hagii J, Saito S, Shiroto H, Tomita T, et al. Relationship between the lesion location of acute ischemic stroke and early depressive symptoms in Japanese patients. Ann Gen Psychiatry 2016;1;15:12.

Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation 2016;133:e38–e360.

Ortega-Barrio MÁ, Herce-Martínez MB, Valiñas-Sieiro F, Mariscal-Pérez N, López-Cunquero MÁ, Cubo-Delgado E. [Impact of rural or urban areas on disability after a stroke]. Enferm Clin 2013;23(5):182-8.

Ramasubbu R, Robinson RG, Flint AJ, Kosier T, Price TR. Functional impairment associated with acute poststroke depression: the Stroke Data Bank Study. J Neuropsychiatry Clin Neurosci 1998;10(1):26-33.

Robinson RG. Post-stroke mood disorders. Hosp.Pract.(Off Ed), 21(4), 83-89; 1986.

Salinas J, Ray RM, Nassir R, Lakshminarayan K, Dording C, Smoller J, et al Factors Associated With New-Onset Depression Following Ischemic Stroke: The Women's Health Initiative. J Am Heart Assoc 2017;1;6(2).

Sarfo FS, Jenkins C, Singh A, Owolabi M, Ojagbemi A, Adusei N, et al. Post-stroke depression in Ghana: Characteristics and correlates. J Neurol Sci 2017;379:261-265.

Tang WK, Lu JY, Chen YK, Chu WC, Mok V, Ungvari GS, Wong KS J. Association of frontal subcortical circuits infarcts in poststroke depression: a magnetic resonance imaging study of 591 Chinese patients with ischemic stroke. Geriatr Psychiatry Neurol 2011;24(1):44-9.

Vahid-Ansari F, Lagace DC, Albert PR. Persistent post-stroke depression in mice following unilateral medial prefrontal cortical stroke. Transl Psychiatry 2016;6(8):e863.

Vataja R, Leppävuori A, Pohjasvaara T, Mäntylä R, Aronen HJ, Salonen O, et al. Poststroke depression and lesion location revisited. J Neuropsychiatry Clin Neurosci 2004;16(2):156-62.

Vataja R, Pohjasvaara T, Leppävuori A, Mäntylä R, Aronen HJ, Salonen O, et al. Magnetic resonance imaging correlates of depression after ischemic stroke. Arch Gen Psychiatry 2001;58(10):925-31.

van de Weg FB, Kuik DJ, Lankhorst GJ. Post-stroke depression and functional outcome: a cohort study investigating the influence of depression on functional recovery from stroke. Clin Rehabil 1999;13(3):268-72.

Wu RH, Li Q, Tan Y, Liu XY, Huang J. Depression in silent lacunar infarction: a cross-sectional study of its association with location of silent lacunar infarction and vascular risk factors. Neurol Sci 2014;35(10):1553-9.

Yang S, Hua P, Shang X, Cui Z, Zhong S, Gong G, Humphreys GW. A significant risk factor for poststroke depression: the depression-related subnetwork. J Psychiatry Neurosci 2015;40(4):259-68.

Yuan HW, Wang CX, Zhang N, Bai Y, Shi YZ, Zhou Y, et al. Poststroke depression and risk of recurrent stroke at 1 year in a Chinese cohort study PLoS One 2012;7(10):e46906.

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Citation	Ilut S, Vacaras V, Fodoreanu L. Incidence and predictive factors for poststroke depression. HVM Bioflux 2017;9(3):98-101.
Editor	Ştefan C. Vesa
Received	13 August 2017
Accepted	23 August 2017
Published Online	23 August 2017
Funding	None reported
Conflicts/ Competing Interests	None reported