Psychopathological evaluation and use of the Hospital Anxiety and Depression Scale in a sample of Brazilian patients with post-stroke depression

Vinicius S. P. Pedroso[1,2], Érica L. M. Vieira[1,2], André R. Brunoni[3], Edward C. Lauterbach[4], Antônio L. Teixeira[1,2,5]

[1] *Stroke Branch, Neuroscience Division, Interdisciplinary Laboratory of Medicinal Investigation, School of Medicine, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil.*
[2] *Graduate Program in Neuroscience, Institute of Biological Sciences, UFMG, Belo Horizonte, MG, Brazil.*
[3] *Interdisciplinary Center for Applied Neuromodulation (CINA), University Hospital, University of São Paulo (USP), São Paulo, SP, Brazil.*
[4] *Department of Psychiatry and Behavioral Sciences, Mercer University School of Medicine, Macon, GA, United States.*
[5] *Neuropsychiatry Program, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX, United States.*

Received: 11/3/2016 – **Accepted:** 11/11/2016
DOI: 10.1590/0101-60830000000102

Abstract

Background: Depression is the most frequent psychiatric complication of stroke and is often undetected or inadequately treated. **Objective:** This study aimed to characterize psychopathological aspects of Brazilian patients admitted to an acute stroke unit, and to evaluate the performance of the Hospital Anxiety and Depression Scale (HADS) in detecting cases of depression. **Methods**: This was a cross-sectional study. Sixty consecutive patients admitted to an acute stroke unit were assessed with the National Institutes of Health Stroke Scale, the Modified Rankin Scale, the Functional Independence Measure, the Mini International Neuropsychiatric Interview-Plus, the HADS, the Mini Mental State Examination (MMSE) and the Pathological Laughing and Crying Scale. **Results**: Prevalence of depression was 26.7%. Patients with post-stroke depression were more likely to present diabetes ($p < 0.01$) and had greater disability ($p < 0.001$) and cognitive impairment ($p < 0.001$) in comparison to non-depressed patients. Depressed patients showed worse performance specifically on tasks of attention/calculation and language of the MMSE. ROC curve analysis of HADS provided a cutoff value of 6 for detecting depression (sensitivity: 83.3%; specificity: 83.3%). The depression subscale of HADS (HADS-D) presented sensitivity of 100% and specificity of 99.17%. **Discussion**: HADS-D showed good performance in screening for depressive symptoms after acute stroke.

Pedroso VSP et al. / Arch Clin Psychiatry. 2016;43(6):147-50

Keywords: Post-stroke depression, Hospital Anxiety and Depression Scale, Mini Mental State Examination, depression, acute ischemic stroke.

Introduction

Stroke is a major cause of death and disability worldwide[1]. Mood disorders, especially depression, are commom in stroke-survivors and are associated with morbidity and mortality[2,3]. A recent meta-analysis showed that the prevalence of depression any time after stroke was 29% and that more than half of stroke survivors will be affected by depression at some point[4,5]. Despite this, mood disorders after stroke are frequently undetected or inadequately treated[6]. Untreated post-stroke depression (PSD) lenghtens hospital stays, impairs functional outcome and elevates mortality[7,8].

Early assessment for possible neuropsychiatric disorders in acute stroke units could allow prompt intervention and provide valuable information for the referral of patients. Stroke survivors often report that their physical needs are prioritised over their psychological ones and this is a relevant issue, since many patients will probably not receive this type of evaluation after discharge[7].

The gold-standard method for psychiatric diagnosing is a standardized clinical interview by an experienced clinician. However, this is time consuming and mostly unavailable on neurological or medical wards. Therefore, there is a need for valid and reliable screening instruments in order to find vulnerable or at risk patients. Hospital Anxiety and Depression Scale (HADS), a simple instrument developed to identify caseness of anxiety and depression among patients in nonpsychiatric hospital clinics, could be potentially useful for screening depressive disorders after stroke[9].

In Brazil, where stroke is the leading cause of death, it is estimated that survivors reach 2.5 million individuals and there is virtually no information on the profile of neuropsychiatric disorders in these patients[10]. Despite limited data on this topic, we recently reviewed Brazilian studies that assessed the prevalence of depression after stroke in different settings and found rates ranging from 20 to 59%[10]. However, there is very limited evidence on the use of screening instruments in this population.

Therefore, the objective of this study was to characterize psychopathological aspects of Brazilian patients admitted to an acute stroke unit, and to evaluate the performance of the HADS in detecting cases of depression in this sample of patients.

Methods

This was a cross-sectional study, in which consecutive patients with a diagnosis of acute ischemic stroke admitted to the Stroke Unit of the Hospital Municipal Odilon Behrens, Belo Horizonte, Brazil, underwent neuropsychiatric evaluation during the first week after stroke. We included patients of both genders, older than 45 years of age and who consented to participate. Individuals with hemorrhagic stroke, active infectious diseases, autoimmune diseases, acute recent myocardial infarction, dementia, decreased level of consciousness (Glasgow Coma Scale < 14), severe aphasia or who underwent recent neurosurgery were excluded.

In a semi-standardized interview, we collected data on sociodemographic and clinical characteristics of the participant. These variables were used to calculate the Framingham Risk Score for cardiovascular disease[11]. Stroke severity was quantified by using the National Institutes of Health Stroke Scale (NIHSS)[12] and disability was assessed with the Modified Rankin Scale (mRS)[13] and the Functional Independence Measure (FIM)[14]. Subsequently, patients were interviewed by a trained psychiatrist using the Mini International Neuropsychiatric Interview-Plus (MINI-Plus) – Brazilian version 5.0.0 to provide formal psychiatric diagnosis[15]. Finally, patients underwent psychopathological evaluation, through the use of HADS[9], Mini Mental State Examination[16] and Pathological Laughing and

Address for correspondence: Vinicius S. P. Pedroso. Laboratório Interdisciplinar de Investigação Médica (LIIM), sala 281, Faculdade de Medicina, Universidade Federal de Minas Gerais. Av. Alfredo Balena, 190, Santa Efigênia – 30130-100 – Belo Horizonte, MG, Brazil. Phone: +55 (31) 3409-8073. E-mail: viniciuspietra@yahoo.com.br

Crying Scale (PLACS)[17]. Two weeks after the evaluation, patients were contacted by phone to ensure the stability of the diagnosis of depression in that period of time, based on the MINI-Plus mood disorders section.

Demographic and clinical variables between participants with and without the diagnosis of depression were compared by chi-square test, Mann-Whitney U test and Spearman correlation analysis. Receiver Operating Characteristic (ROC) curve analysis was calculated to identify optimal cut-off values for the diagnosis of depression with the HADS. Commom language effect size (CLES) statistic was calculated according to the equation CLES = U/mn[18]. The level of significance was set at $p < 0.05$.

The study was approved by the local research ethics committee.

Results

Sociodemographic and clinical features

Sixty patients were enrolled in the study. Diagnosis of depression made by the use of MINI-Plus reached a prevalence of 26.7%. Diagnosis made in the stroke unit remained stable in all cases after two weeks. Two groups were divided based on the presence of depression, and their demographic and clinical features were compared (Table 1). No differences were observed with respect to age and gender. Depressed patients exhibited higher rate of diabetes, but did not differ in relation to the average values of body mass index (BMI) and waist circumference, as well as to the Framingham risk score. There were no differences regarding the presence of other medical comorbidities such as hypertension, dyslipidemia, obesity, myocardial infarction, smoking, heart failure or coronary artery disease (data not shown). Depressed patients showed higher mRS values on admission as well as worse functional performance as assessed by the FIM. A trend of higher score in NIHSS was observed among patients with depression, but this difference did not reach statistical significance ($p = 0.062$).

Table 1. Sociodemographic and clinical features in a sample of 60 patients with acute ischemic stroke

Sociodemographic and clinical features			
	% or mean (standard deviation)		*p* value
	Depression (n = 16)	No depression (n = 44)	
Age (years)	61.07 (5.7)	65.38 (9.41)	0.069[b]
Gender (% male)	75.00	68.18	0.504[a]
Diabetes (%)	56.25	20.45	< 0.01[a]
BMI (kg/m²)	25.43 (3.06)	26.70 (4.87)	0.206[b]
Waist circumference (cm)	95.47 (10.41)	97.60 (14.41)	0.398[b]
Framingham risk score	22 (0.85)	21 (3.80)	0.404[b]
mRS	2.93 (0.88)	2.16 (0.93)	< 0.05[b]
NIHSS	5.67 (4.21)	3.22 (2.34)	0.062[b]
FIM	103.67 (14.12)	117.00 (9.93)	< 0.001[b]

[a] Chi-square; [b] Mann-Whitney U test.

Psychopathological features

Table 2 presents the comparison of psychopathological characteristics between depressed and non-depressed patients. Patients with depression had poorer performance on the MMSE. Specifically, patients with PSD performed worse attention/calculation and language tasks ($p = 0.001$ and 0.049, respectively). Concerning the use of the HADS, depressed patients had higher scores in the total score and in the depression subscale, but did not differ in the anxiety subscale. In the assessment of involuntary emotional expression disorder (IEED) by the PLACS, no differences were observed between the groups, although there was a trend towards higher scoring among depressed patients. There was a positive correlation between the total scores of HADS and the PLACS (rho = 0.322, $p = 0.025$).

Table 2. Psychopathological features in a sample of 60 patients with acute ischemic stroke

Psychopathological features				
	Mean (standard deviation)		*p* value	Effect size
	Depression (n = 16)	No depression (n = 44)		
MMSE				
Orientation	8.40 (1.59)	9.31 (0.79)	0.058	0.35
Registration	3.00 (0.00)	3.00 (0.00)	1.00	0.50
Attention and calculation	1.80 (0.94)	3.33 (1.68)	0.001	0.23
Recall	1.93 (0.70)	2.24 (1.09)	0.067	0.35
Language	6.87 (1.06)	7.38 (0.89)	0.049	0.34
Copying	0.40 (0.51)	0.53 (0.50)	0.375	0.43
Total	22.40 (1.96)	25.79 (2.90)	< 0.001	0.17
HADS				
Total	13.50 (4.23)	5.69 (3.36)	< 0.001	0.88
HADS Depression	10.08 (2.64)	2.36 (2.10)	< 0.001	0.93
HADS Anxiety	3.42 (2.15)	3.33 (2.50)	0.744	0.50
PLACS				
Total	5.40 (7.06)	1.91 (4.80)	0.059	0.60
Crying	2.60 (5.40)	1.16 (3.49)	0.714	0.50
Laughing	1.80 (3.75)	0.38 (1.43)	0.105	0.55

Receiver Operating Characteristic (ROC) curve analysis

Based on the diagnosis made by MINI Plus and evaluation with the HADS, a ROC curve analysis was made to determine the optimal cutoff point of the scale. Figure 1 shows the resulting ROC curve. The HADS consists of 14 items, of which 7 make up a subscale of depression and 7 make up a subscale of anxiety. The areas under the curve (AUC) were respectively 0.928 and 0.979 for HADS Total and HADS Depression (HADS-D). There was no association between the anxiety subscale and the diagnosis of depression ($p = 0.748$). There was no correlation between the HADS-D and the HADS Anxiety (HADS-A) subscales ($p = 0.438$). The total score and the depression subscale were significantly associated with the diagnosis of depression ($p < 0.001$). The depression subscale exhibited the best performance. The cut-off values chosen based on ROC curve analysis were 10 for the total scale and 6 for the subscale of depression. These cutoffs have led to sensitivity of 83.3% and specificity of 83.3% for the total scale (accuracy: 0.83) and sensitivity of 100% with specificity of 99.17% for the subscale of depression (accuracy: 0.94).

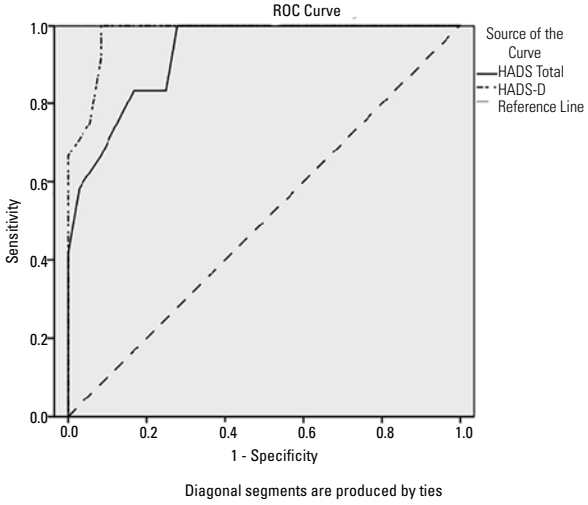

Figure 1. ROC curve analysis of HADS in a sample of 60 patients with acute ischemic stroke.

Discussion

To our knowledge, this is the first study to evaluate the potential of HADS in the screening of PSD in Brazil. We found a prevalence of 26.7% of PSD in the acute phase, which is in agreement with the international literature and confirms the high frequency of mood disorders associated with stroke[19].

Carod-Artal *et al*. found that PSD was the stronger predictor of low health related quality of life in Brazilian stroke survivors[20]. This fact points to the importance of detection and intervention in such cases. For this reason, we evaluated the use of HADS in screening for PSD. In a review of the literature, the threshold values identified for optimal balance between sensitivity and specificity for HADS showed little variability, and were close to 8, defined as the cut-off for 'possible cases' by the original authors of the scale[21]. This threshold was found for HADS-A and HADS-D in the general population as well as in patients with medical conditions[21]. However, studies evaluating its use in stroke patients suggested that the cutoff values could be lower for PSD detection[22]. In this way, cut-points ranging from 4 through 8 for the HADS-D have been proposed in stroke[23]. In the present study, we found the value of 6 as optimal cutoff point for the depression subscale. This value led to a sensitivity of 100% and a specificity of 99.17%. Wichowicz and Wieczorek found a cutoff value of 7 in a sample of 75 Polish stroke patients, with sensitivity of 90.0% and specificity of 92.2% for the HADS-D[24]. Tang *et al*. also found cutoff values of 6/7 in 100 Chinese patients, though with sensitivity of 88% and specificity of 53%[25].

Patients with depression in our sample tended to be more severely disabled, evidenced by higher scores on the mRS on admission and lower scores on the FIM. Several factors have been associated with PSD, such as previous history of psychiatric disorders, female gender, family history of depression, and cerebrovascular risk factors, among others[10,26]. Among those, physical disability, stroke severity and cognitive impairment have been more consistently associated with PSD. In accordance with these data, we found that patients with PSD had worse performance on the MMSE. Cognitive performance in PSD was assessed by a series of studies, and there is evidence that PSD affects problem solving, verbal and visual memory, language, visuospatial processes, attention and psychomotor speed[10]. For instance, in a cohort of 143 patients who were followed up to 10 months after a stroke, Nys *et al.* found that early cognitive impairment independently predicted long-term depressive symptoms. Moreover, cognitive deficits were related to worse quality of life[27]. In our sample, patients with PSD presented poorer performance specifically in attention/calculation and language tasks, in accordance with the previous findings mentioned above.

Although PSD patients exhibited higher scores on PLACS, there was no difference in the occurence of IEED between patients with and without depression. This may reinforce the view that PSD and IEED are distinct entities, even though they can present some degree of overlap[28]. Indeed, IEED is regarded as a risk factor for the development of PSD[19,29]. Accordingly, there was a positive correlation between the scores of PLACS and HADS.

Another aspect observed in our sample was the association between diabetes and PSD. Some studies have suggested a bidirectional association between diabetes and PSD, i.e. people with diabetes have increased risk of developing depressive symptoms and people with depression have increased risk of developing diabetes[30-32]. Micro and macrovascular complications due to diabetes were strongly related to the occurrence of depression in this group of individuals[33]. In a large cohort of 157,243 Danish patients with stroke, diabetes was found as a risk factor for PSD[34]. The findings of an association between the occurrence of a depressive syndrome in the elderly population and the presence of white matter lesions of vascular origin, particularly in the frontal regions, have led to the hypothesis of the existence of a "vascular depression", which would be linked to microangiopathy[35]. Based on that, one could speculate whether patients with diabetes are more susceptible to the development of depressive symptoms after a major vascular insult superimposed on chronic vascular microlesions.

In conclusion, we observed that HADS-D showed good performance in screening for depressive symptoms after acute stroke. Patients with PSD were more likely to present diabetes, and had greater disability and cognitive impairment in comparison to non-depressed patients. Future studies should focus on the longitudinal assessment of PSD patients to better define the contribution of each variable in the development of depressive symptoms after stroke, with the aim of designing effective interventions for treatment and rehabilitation.

Acknowledgements

This study was funded by *Fundação de Amparo à Pesquisa do Estado de Minas Gerais* (Fapemig) (APq-03539-13).

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics – 2013 update: a report from the American Heart Association. Circulation. 2013;127(1):e6-e245.
2. Broomfield NM, Quinn TJ, Abdul-Rahim AH, Walters MR, Evans JJ. Depression and anxiety symptoms post-stroke/TIA: prevalence and associations in cross-sectional data from a regional stroke registry. BMC Neurol. 2014;14:198.
3. Souza BPF, Torquato Jr MAA, Soares SMSR. Prevention of poststroke depression. Rev Psiq Clín. 2010;37(4):182.
4. Ayerbe L, Ayis S, Wolfe CD, Rudd AG. Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. Br J Psychiatry. 2013;202(1):14-21.
5. Ayerbe L, Ayis S, Crichton S, Wolfe CD, Rudd AG. The natural history of depression up to 15 years after stroke: the South London Stroke Register. Stroke. 2013;44 (4):1105-10.
6. Sagen U, Vik TG, Moum T, Mørland T, Finset A, Dammen T. Screening for anxiety and depression after stroke: comparison of the hospital anxiety and depression scale and the Montgomery and Asberg depression rating scale. J Psychosom Res. 2009;67(4):325-32.
7. Lees R, Stott DJ, Quinn TJ, Broomfield NM. Feasibility and diagnostic accuracy of early mood screening to diagnose persisting clinical depression/anxiety disorder after stroke. Cerebrovasc Dis. 2014;37(5):323-9.
8. Terroni LMN, Mattos PF, Sobreiro MFM, Guajardo VD, Fráguas R. Post-stroke depression: psychological, neuropsychological, HHA axis, localization of stroke aspects and treatment. Rev Psiq Clín. 2009;36(3):100-8.
9. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67(6):361-70.
10. Pedroso VSP, Souza LC, Brunoni AR, Teixeira AL. Post stroke depression: clinics, etiopathogenesis and therapeutics. Arch Clin Psychiatry. 2015;42(1):18-24.
11. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-53.
12. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke. 1989;20(7):864-70.
13. van Swieten J, Koudstaal P, Visser M, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988;19(5):604-7.
14. Riberto M, Miyazaki MH, Jucá SSH, Sakamoto H, Pinto PPN, Battistella LR. Validation of the Brazilian version of Functional Independence Measure. Acta Fisiatr. 2004;11(2):72-6.
15. Amorim P. Mini International Neuropsychiatric Interview (MINI): validation of a short structured diagnostic psychiatric interview. Rev Bras Psiquiatr. 2000;22(3):106-15.
16. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatric Res. 1975;12(3):189-98.
17. Robinson RG, Parikh RM, Lipsey JR, Starkstein SE, Price TR. Pathological laughing and crying following stroke validation of a measurement scale and a double-blind treatment study. Am J Psychiatry. 1993;150(2):286-93.
18. Acion L, Peterson JJ, Temple S, Arndt S. Probabilistic index: an intuitive non-parametric approach to measuring the size of treatment effects. Stat Med. 2006;25(4):591-602.

19. Chemerinski E, Robinson RG. The neuropsychiatry of stroke. Psychosomatics. 2000;41(1):5-14.
20. Carod-Artal FJ, Trizotto DS, Coral LF, Moreira CM. Determinants of quality of life in Brazilian stroke survivors. J Neurol Sci. 2009;284(1-2):63-8.
21. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
22. Tang WK, Wong E, Chiu HF, Ungvari GS. Rasch analysis of the scoring scheme of the HADS Depression subscale in Chinese stroke patients. Psychiatry Res. 2007;150(1):97-103.
23. Prisnie JC, Fiest KM, Coutts SB, Patten SB, Atta CA, Blaikie L, et al. Validating screening tools for depression in stroke and transient ischemic attack patients. Int J Psychiatry Med. 2016;51(3):262-77.
24. Wichowicz HM, Wieczorek D. Screening post-stroke depression using the Hospital Anxiety and Depression Scale. Psychiatr Pol. 2011;45(4):505-14.
25. Tang WK, Ungvari GS, Chiu HF, Sze KH, Yu AC, Leung TL. Screening post-stroke depression in Chinese older adults using the hospital anxiety and depression scale. Aging Ment Health. 2004;8(5):397-9.
26. Angelelli P, Paolucci S, Bivona U, Piccardi L, Ciurli P, Cantagallo A, et al. Development of neuropsychiatric symptoms in poststroke patients: a cross-sectional study. Acta Psychiatr Scand. 2004;110(1):55-63.
27. Nys GM, van Zandvoort MJ, van der Worp HB, de Haan EH, de Kort PL, Jansen BP, et al. Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. J Neurol Sci. 2006;247:149-56.
28. Pedroso VSP, Souza LC, Teixeira AL. Neuropsychiatric syndromes associated with stroke: review of the literature. J Bras Psiquiatr. 2014;63(2):165-76.
29. Carota A, Dieguez S, Bogousslavsky J. Psychopathology of stroke. Psychol Neuropsychiatr Vieil. 2005;3(4):235-49.
30. Golden SH, Lazo M, Carnethon M, Bertoni AG, Schreiner PJ, Diez Roux AV, et al. Examining a bidirectional association between depressive symptoms and diabetes. J Am Med Assoc. 2008;299(23):2751-9.
31. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes. Diabetes Care. 2001;24 (6):1069-78.
32. Raval A, Dhanaraj E, Bhansali A, Grover S, Tiwari P. Prevalence and determinants of depression in type 2 diabetes patients in a tertiary care centre. Indian J Med Res. 2010;132:195-200.
33. Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. J Affect Disord. 2012;142 Suppl:S8-21.
34. Jørgensen TS, Wium-Andersen IK, Wium-Andersen MK, Jørgensen MB, Prescott E, Maartensson S, et al. Incidence of Depression After Stroke, and Associated Risk Factors and Mortality Outcomes, in a Large Cohort of Danish Patients. JAMA Psychiatry. 2016;73(10): 1032-40.
35. Sneed JR, Culang-Reinlieb ME. The vascular depression hypothesis: an update. Am J Geriatr Psychiatry. 2011;19(2):99-103.