

Socioeconomic Factors Predicting Depression Differ in the Acute Stage and at 1 year After Ischemic Stroke or TIA

Ágnes Mirolovics, MD,*† Magdolna Bokor, MD, PhD,† Balázs Dobi,‡
Judit Zsuga, MD, PhD,§ and Dániel Bereczki, MD, PhD, DSc, FESO¶||

Introduction: Considerable depressive symptoms follow stroke in about one third of patients. Initial depressive symptoms may wane after the acute phase of stroke, but persisting depressive symptoms adversely affect rehabilitation and quality of life. We set forth to evaluate predictors of depressive symptoms with a focus on socioeconomic factors. *Methods:* We evaluated clinical features and socioeconomic characteristics in 233 consecutive patients with acute ischemic stroke or TIA. Depressive symptoms could be evaluated in 168 subjects in the acute phase with a repeated testing after a mean of 14.7 months via telephone interview in 116 patients. Survival status, scores on the Center for Epidemiologic Studies-Depression Scale (CES-D), Beck Depression Inventory (BDI) and disability (modified Rankin scale, mRS) were recorded. *Results:* In the acute phase, employment status ($p = 0.037$) and level of education ($p = 0.048$) whereas one year later dependency ($mRS \geq 3$, $p = 0.002$) and income ($p = 0.012$) were the significant predictors of the severity of depressive symptoms. A change from independent ($mRS \leq 2$) to dependent living predicted worsening depressive symptoms ($p = 0.008$), whereas improving to functional independence from an initially dependent condition was associated with diminishing depressive symptoms ($p = 0.077$ for CES-D and $p = 0.044$ for BDI) in the first year after an acute ischemic cerebrovascular event. *Conclusions:* Predictors of the severity of depressive symptoms differed in the acute phase and at follow-up. In addition to disability, education and employment status in the acute phase and income in the late phase predict the severity of depressive symptoms after ischemic stroke or TIA. **Key Words:** Stroke—Education—Employment Status—Income—Disability—Depression—Follow-up

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Introduction

The most prevalent psychiatric complication after stroke is depression. Clinically relevant depressive symptoms appear in about one third of cases after stroke.^{1,2}

The frequency of post stroke depression (PSD) is highest in the first year after stroke.³ In a recent Spanish survey of patients with TIA and minor stroke 43.9 % had post stroke

From the *János Szentágothai Doctoral School of Neurosciences, Semmelweis University, Budapest, Hungary; †Department of Neurology, National Institute of Psychiatry and Addictions Nyíró Gyula, Budapest, Hungary; ‡Department of Probability Theory and Statistics, Eötvös Loránd University, Budapest, Hungary; §Department of Health Systems Management and Quality Management in Health Care, Faculty of Public Health, University of Debrecen, Debrecen, Hungary; ¶Department of Neurology, Semmelweis University, Budapest, Hungary; and ||MTA-SE Neuroepidemiological Research Group, Budapest, Hungary.

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Corresponding author. E-mail: bereczki.daniel@med.semmelweis-univ.hu.

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depression (PSD) at 10 days after the cerebrovascular event and 8.6 % of patients had PSD 12 months later.⁴ Severity of depressive symptoms often changes in the first year after stroke. Berg et al reported that 46% of those who were depressive during the first 2 months were also depressive at 12 and/or 18 months after stroke. Only 12% of patients were depressive for the first time at 12 or 18 months.⁵

Depression in the first 3 months after stroke is a risk for early case fatality.⁶ Yuan et al reported poor outcome in those who had higher depression scores in the acute phase after stroke,⁷ and post stroke depressive symptoms were associated with worse functional outcome even in those treated with antidepressant medication.⁸ The Bergen Stroke Study confirmed that depression both before and after stroke are predictors of mortality among stroke patients,⁹ and results from the South London Stroke Registry also proved that depression is an independent predictor of poor health outcomes.¹⁰ On the other hand, a lower rate of depression was associated with return to work at 1 year in the South London Stroke Registry.¹¹ Although the adverse effect of depression on stroke outcome has long been acknowledged, attention to recognize depressive symptoms after stroke is insufficient, and depression is undertreated in this patient population.¹²

Depression following stroke is predicted by several factors, of which physical disability, stroke severity and cognitive impairment were the most consistent ones.¹³ In our previous study we found that depressive symptoms may persist long after stroke, and scores on the depression scales at 4 years after stroke correlated with both stroke severity and depressive scores in the acute phase.¹⁴ Pre-stroke socioeconomic factors may also contribute to PSD.¹⁵ Living alone and having few social contacts have been found to predict depression.^{16,17} We previously found that disadvantaged socioeconomic environment is associated with worse outcome after stroke,¹⁸ and we assume that socioeconomic deprivation after stroke is also related to persistent depressive symptoms, thus exaggerating the adverse effect of disadvantaged socioeconomic environment on stroke outcome.

In our single center prospective study with one-year follow-up we evaluated predictors of depressive symptoms in the acute phase and at 1 year after ischemic stroke or transient ischemic attack (TIA). The primary endpoint of our study was the presence of depressive symptoms at 1 year after the index cerebrovascular event. Secondary endpoints were depressive symptoms immediately after ischemic stroke/TIA, and the change (i.e. improvement or worsening) of depressive symptoms by comparing CES-D scores at discharge from hospital and at follow-up one year later. We hypothesized that in addition to functional disability, some socioeconomic factors like education level, employment status, income, and living conditions, may also affect depressive symptoms both in the acute stage and at one year after the acute event.

Methods

Patients

Data of consecutive patients admitted for acute cerebrovascular disease between February 2013 and April 2014 to the Department of Neurology of the Nyíró Gyula National Institute of Psychiatry and Addictions, Budapest, Hungary were prospectively collected. The department is responsible for the neurological care of the 13th district of Budapest, as well as the citizens of two other Hungarian towns: Pilisvörösvár and Csobánka. These areas cover approximately 133,000 people. We enrolled consecutive 250 inpatient cases with acute cerebrovascular disorder who were admitted to our department during the 13-month period of our study except for those who were admitted after intravenous thrombolysis (IVT) or mechanical thrombectomy (MT) at a primary stroke center. Of the 250 patients 89 (35.3%) were originally admitted to a primary stroke center, but being ineligible for IVT or MT, were transferred further to the department of the study, according to the regional patient admission rules.

Data collection

We collected information using healthcare data and a *structured questionnaire* within the first week of hospitalization. The same neurologist performed both the patient examination and data collection. We recorded stroke severity on admission by the National Institutes of Health Stroke Scale (NIHSS),¹⁹ as well as the affected brain hemisphere, presence of speech disturbance and routine laboratory values. We also recorded the presence of hypertension, diabetes mellitus, atrial fibrillation (AF), heart disease, other arrhythmia, peripheral vascular disease, psychiatric disease, liver and lung disease. We recorded data on alcohol consumption, smoking, regular medications, type of the earlier stroke, treatment of AF if present, the pre-stroke modified Rankin scale score (mRS), the CHA₂DS₂VASc score,²⁰ the HAS-BLED score,²¹ admission brain CT scan results (no change, ischemic or hemorrhagic lesion or subarachnoid hemorrhage), blood pressure and heart rate. Comorbidity was measured by summing the observed comorbid conditions and medications, effectively creating a comorbidity-polypharmacy score (CPS,²²). It needs to be noted that data assessment focused on stroke-relevant conditions, therefore information on comorbidity was incomplete, and we also had limited information on depression in the patients' medical history.

Regarding sociodemographic data we recorded the type of residence (stand-alone house, apartment in building made of brick, panel apartment houses built of concrete – i.e. the main urban housing built in the soviet era, also called Larsen-Nielsen-type building –, and other type: retirement home, homeless shelter), marital state, level of education, profession, employment status, property ownership, monthly income per capita, and number of children.

Additional information relating to hospital stay and discharge were also recorded, such as the TOAST classification²³ of the stroke, the findings of carotid duplex scan and of echocardiography; medication use on the ward (anticoagulants, antihypertensives, antidiabetics, statins); and condition at discharge (survival status and mRS score). To evaluate the severity of depressive symptoms we used the Center for Epidemiologic Studies Depression Scale (CES-D scale)²⁴ and the Beck Depression Inventory (BDI) 13 item short form.²⁵ In our primary analyses we used results of the CES-D as it has been shown to be a reliable tool after stroke in a systematic review of PSD studies.²⁶

A one-year follow-up assessment with a mean of 13.9 months from the stroke event was performed via telephone interview. Survival status, new stroke event, scores on the depression scales and mRS were recorded. Depression scale scores in the acute phase were available for 168 patients, of those repeated scoring was possible in 116 patients with a mean follow-up of 14.7 months. In patients with lack of communication (aphasia or severe general condition), we gained information from family members or from medical documentation.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the Ethics Committee of Semmelweis University, Budapest, Hungary, and with the 1964 Helsinki declaration and its later amendments. The study was approved by the Ethics Committee of Semmelweis University, Budapest, Hungary (No: TUKEB 8/2013), and written consent was obtained from the patients.

Statistical analysis

We analyzed the relationship between discharge and follow-up depression using correlation analyses (Pearson, Kendall and Spearman). Linear regression was used for the analysis of the continuous depression scales. This included models for the discharge scores, follow-up scores and their differences. First, all potential covariates were included into univariate regression models to check their effects on the response variable. The multiple regression models then were built the following way: we defined a set of important control variables which were included in all models of a given dependent variable. These were sex, age, admission NIHSS and discharge mRS. We then assessed the effect of all other possible covariates one-by-one, controlled by the previously set variables. Covariate selection was based on the relevance and validity of the variables, and significance at least at the 0.1 level was secondary support information. In this last step we also considered the viability of the overall model, the effect of similar variables and interaction terms. We also aimed to synchronize models with similar dependent variables. Automatized tools such as stepwise regression were considered but discarded due to small sample size and missing data.

The overall effect of categorical variables with more than two levels in multivariate models was tested with likelihood-ratio test. (The individual effect of the levels is also displayed, see the “p-value (overall)” column in the relevant tables.) The goodness of fit of the linear regression models was tested using statistical and visual tools, namely the Shapiro-Wilks test and the quantile-quantile plot.

R version 3.6.2 was used for data analysis with packages ggplot2, gridExtra, survival, survminer, MASS, generalhoslem, psych, rms, stringr and questionr.

Results

Of the 250 consecutively included patients, there were 187 cases of ischemic stroke, 46 cases of transient ischemic attack, 16 cases of intracerebral hemorrhage, and 1 case of subarachnoid hemorrhage. In our analyses we include those 233 patients who had acute ischemic cerebrovascular disease (i.e. ischemic stroke or TIA). Depressive symptoms could be evaluated in 168 subjects in the acute phase with a repeated testing after one year (mean of 14.7 months from the stroke event) via telephone interview in 116 patients. The patient flow chart is presented in Fig. 1.

We found evidence of pre-stroke depression in 27 patients. Pre-stroke depression had significant effect on discharge depression. However, due to incomplete information in many patients, pre-stroke depression was not included in the final models as this uncertainty would have introduced serious bias in the models. We found no significant effect of CPS in any of our models, thus the comorbidity-polypharmacy score was excluded from the analysis.

Baseline features

Basic features of the study population at baseline are presented in Table 1. Patients whose depression could be assessed using the CES-D scale were significantly younger on average than patients with missing CES-D data. This is true for both baseline and follow-up values (67.9 ± 13.5 (n = 168) vs. 76.4 ± 11.7 (n = 65) years, $p < 0.001$ and 67.0 ± 13.6 (n=116) vs. 73.6 ± 12.7 (n = 117) years, $p < 0.001$ respectively using Welch's t-test). The 8.5 years difference in mean ages in the acute phase and the 6.6 years difference at one year suggests that older age is associated with either more reluctance or less physical or mental capacity due to the acute stroke or other comorbidities to cooperate in the evaluation of the severity of depressive symptoms.

Findings at discharge

At discharge 67% of the initial study population were independent, whereas 86% of those with initial depression screening and 87% of those with repeated CES-D scoring were independent at discharge. 119 of the 213 patients with follow-up mRS data were independent.

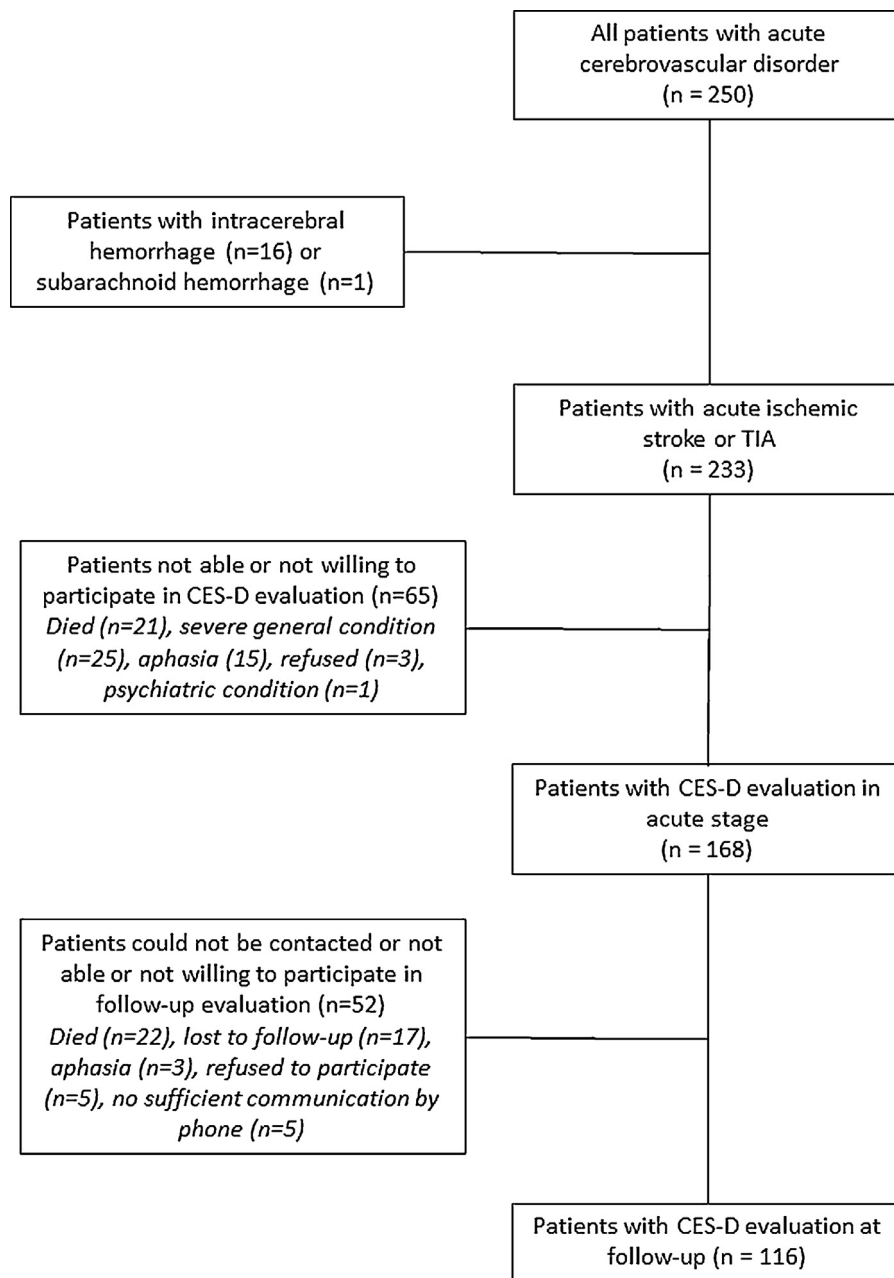


Fig. 1. Patient flowchart.

Multiple linear regression was used for the analysis of predictors of discharge CES-D (Table 2). According to the Shapiro-Wilk test ($p = 0.104$) and the normal Q-Q plot of the residuals, the model has an acceptable fit. Using the algorithm described in the Statistical analysis section, we found that employment, education and income should be included in the model on top of the control variables. Other socio-economic variables were also considered and tested but were

eventually discarded. The variables in this model also proved to be important in other models of this study.

We found that those who had not been employed before their stroke scored 5.5 higher on average on the CES-D scale than those who had been employed at the time of their stroke (Table 2). Also, compared to those with 8 years or less education, patients in the higher education group scored 1.8–5.6 less on average on the CES-D scale. Only the effect

Table 1. Baseline features of the study population

Feature	All patients at baseline (n=233)	Patients with baseline depression evaluation (168/233)	Baseline values of those with follow-up depression evaluation (116/233)
Age (mean±SD)	70.3±13.6	67.9±13.5	67.0±13.6
Male	109/233	85/168	55/116
Female	124/233	83/168	61/116
N available for monthly net income	190/233	168/168	116/116
0-50 thousand HUF	27/190	24/168	16/116
50-100 thousand HUF	74/190	62/168	41/116
100-150 thousand HUF	52/190	46/168	34/116
150-200 thousand HUF	27/190	26/168	17/116
more than 200 thousand HUF	10/190	10/168	8/116
N available for level of education	191/233	168/168	116/116
Elementary school or less	38/191	34/168	21/116
Vocational training	60/191	49/168	33/116
Secondary school graduation	59/191	52/168	37/116
College/university degree	34/191	33/168	25/116
Discharge mRS (median and IQR)	2 (1-5)	1 (1-2)	1 (1-2)
Independent at discharge (mRS2)	157/233	145/168	101/116
Baseline CES-D score (mean±SD)	-	16.5±9.8	14.9±9.5

At the time of the study the exchange rate was around 300 HUF for 1 EUR.

mRS: modified Rankin scale score, CES-D: Center for Epidemiologic Studies Depression Scale.

Table 2. Predictors of discharge CES-D

Reference category	Variable	Coefficient	95% C.I.	p-value	Overall p-value	N
	(Intercept)	16.5	8.3 – 24.8	<000.1		168
Male	Sex - female	2.4	-0.6 – 5.4	0.117		83
	Age	0.010	-0.133 – 0.154	0.888		168
mRS: 0-2	Admission NIHSS	-0.34	-0.96 – 0.28	0.281		168
	Discharge mRS 3-6	4.6	-0.5 – 9.6	0.078		23
Active	Employment - Inactive	5.5	0.4 – 10.6	0.037		140
Elementary school or less	Vocational training	-1.8	-6.0 – 2.4	0.403	0.048	49
	Secondary school grad.	-5.6	-9.9 – -1.4	0.011		52
	College/university degree	-4.9	-10.2 – 0.3	0.066		33
Monthly net income per person 0-50 thousand HUF	50-100 thousand HUF	-3.8	-8.4 – 0.9	0.112	0.556	62
	100-150 thousand HUF	-3.3	-8.2 – 1.7	0.200		46
	150-200 thousand HUF	-2.3	-8.0 – 3.4	0.427		26
	over 200 thousand HUF	-4.6	-12.2 – 2.9	0.231		10

Active work status: full or part-time occupation. Inactive work status: unemployed, retired, supported by others. Overall p-values for multilevel factors are displayed on the right side of the “p-value” column.

At the time of the study the exchange rate was around 300 HUF for 1 EUR.

of secondary school education and the overall effect of the education variable ($p = 0.048$) were statistically significant. Patients with higher-than-the-lowest income also showed milder depression on average but none of these effects were significant at the $p < 0.05$ level.

Only disability at discharge ($mRS \geq 3$) showed some statistically detectable ($p < 0.1$) effect of the non-socio-economic variables. Patients with disability showed higher

CES-D scores on average. None of the other variables in this model showed a significant effect on discharge depression measured by CES-D.

In summary, at discharge after the acute event, the level of education and prior employment status are the major predictors of the severity of depressive symptoms, whereas current disability has only a marginal effect and income has no significant effect at all on the CES-D scale.

Table 3. Predictors of follow-up CES-D

Reference category	Variable	Coefficient	95% C.I.	p-value	Overall p-value	N
	Intercept	18.2	9.0 – 27.5	<000.1		116
Male	Sex - female	3.1	-0.4 – 6.6	0.087		61
	Age	0.038	-0.116 – 0.191	0.632		116
	Admission NIHSS	-0.68	-1.37 – 0.02	0.058		116
0-2	Discharge mRS 3-6	-2.0	-10.0 – 6.0	0.631		15
0-2	FUP mRS 3-6	12.8	4.7 – 20.8	0.002		13
Active	Employment - Inactive	2.9	-2.7 – 8.6	0.315		96
Elementary school or less	Vocational training	1.4	-3.5 – 6.4	0.570	0.083	33
	Secondary school	-3.9	-8.8 – 1.0	0.118		37
	College/university degree	-2.6	-8.4 – 3.3	0.390		25
Monthly net income per person 0-50 thousand HUF	50-100 thousand HUF	-8.2	-13.4 – -2.9	0.003	0.012	41
	100-150 thousand HUF	-10.5	-16.3 – -4.6	<000.1		34
	150-200 thousand HUF	-8.3	-14.9 – -1.7	0.016		17
	over 200 thousand HUF	-9.3	-17.4 – -1.1	0.028		8

Active work status: full or part-time occupation, Inactive work status: unemployed, retired, supported by others. Overall p-values for multilevel factors are displayed on the right side of the “p-value” column.

At the time of the study the exchange rate was around 300 HUF for 1 EUR.

Findings at follow-up

For the follow-up CES-D score we created a linear regression model similar to the one we used at discharge (Table 3). According to the Shapiro-Wilk test ($p = 0.452$) and the normal Q-Q plot of the residuals, the model has an acceptable fit.

Patients from all income categories had significantly milder follow-up depression on average than those in the lowest category: those who were in any of the higher income categories had between 8.2 and 10.5 lower average scores on the CES-D scale than the financially most disadvantaged group (Table 3).

Work status and education lost the significance of the effects that were seen at discharge. It can be noted though, that the overall effect of education was close to significance with a $p = 0.083$.

Women tended to have higher CES-D scores on average than men, but this effect failed to reach the level of statistical significance ($p = 0.087$). Using the $p < 0.05$ critical value only current disability ($p = 0.002$) and income (overall $p = 0.012$) showed a significant effect on follow-up depression measured by CES-D. In other words, loss of independence and poverty are the major predictors of the severity of depressive symptoms at one year after the index acute event.

The effect of change in dependent status between discharge and follow-up

Of those with follow-up CES-D, 15 patients were dependent ($mRS \geq 3$) at discharge, and 4 of them improved to achieve independence by one year. On the other hand, by one year 2 patients who had been independent at

discharge deteriorated to a dependent condition. Discharge mRS was not a predictor of depressive symptoms one year later ($p = 0.631$). However, follow up disability had a significant effect on the follow-up CES-D score ($p = 0.002$). Those who were dependent at follow-up scored on average 12.8 points higher on the CES-D scale than those who were independent at the 1-year follow-up.

We created new variables which measure the difference between the follow-up and the discharge depression scores. We analyzed these new variables with the previous set of covariates in linear regression models. Results for CES-D difference can be seen in Table 4.

We found that CES-D difference is only influenced significantly in this model by follow-up disability status ($p = 0.008$). Compared to patients who were independent (i.e. $mRS \leq 2$) both at discharge and follow-up, those who became dependent (i.e. $mRS \geq 3$) at follow-up had on average a 10.2 higher increase in the CES-D score.

Sensitivity analyses using the results by the BDI to evaluate severity of depressive symptoms

In addition to CES-D, we also evaluated depressive symptoms of the patients by the BDI. The results of these models should be interpreted with caution as all of these showed mild to moderate problems with the model fit according to the Shapiro-Wilk tests ($p < 0.05$) and the normal Q-Q plots.

We found that the level of education ($p = 0.014$), current disability ($p = 0.033$) and the second-to-lowest income category ($p = 0.043$, compared to the lowest) were predictors of the severity of acute depressive symptoms evaluated by the BDI at discharge (Supplementary Table 1).

Table 4. Predictors of changes in CES-D

Reference category	Variable	Coefficient	95% C.I.	p-value	Overall p-value	N
	(Intercept)	0.80	-7.61 – 9.21	0.852		116
Male	Sex - female	-2.1	-5.2 – 1.1	0.209		61
	Age	0.057	-0.083 – 0.197	0.425		116
	Admission NIHSS	-0.15	-0.78 – 0.48	0.641		116
0-2	Discharge mRS 3-6	-6.6	-13.9 – 0.6	0.077		15
0-2	FUP mRS 3-6	10.2	2.9 – 17.5	0.008		13
Active Elementary school or less	Employment - Inactive	-2.0	-7.1 – 3.2	0.458	0.939	96
	Vocational training	1.4	-3.1 – 5.9	0.550		33
	Secondary school	0.5	-3.9 – 5.0	0.816		37
	College/university degree	1.0	-4.3 – 6.3	0.721		25
Monthly net income per person 0-50 thousand HUF	50-100 thousand HUF	-1.7	-6.4 – 3.1	0.500	0.496	41
	100-150 thousand HUF	-3.5	-8.8 – 1.8	0.198		34
	150-200 thousand HUF	-4.9	-10.9 – 1.1	0.110		17
	over 200 thousand HUF	-4.4	-11.8 – 3.0	0.247		8

Active work status: full or part-time occupation, Inactive work status: unemployed, retired, supported by others. Overall p-values for multilevel factors are displayed on the right side of the “p-value” column.

At follow-up the only significant effect on depression measured by BDI was the loss of independence from discharge to follow-up ($p = 0.001$, Supplementary Table 2).

When analyzing the BDI score difference, we found that compared to patients who were independent (i.e. $mRS \leq 2$) both at discharge and follow-up, those who were independent at discharge but became dependent (i.e. $mRS \geq 3$) at follow-up had on average a higher increase in the BDI score ($p = 0.003$, Supplementary Table 3). However, dependency at discharge *per se* also had a significant negative effect on follow-up BDI score ($p = 0.044$).

Those patients who were dependent at discharge (i.e. $mRS \geq 3$), but were independent at follow-up (i.e. $mRS \leq 2$) had a greater decrease in their BDI score compared to patients who were independent at both discharge and at follow-up. In other words, *decreasing* mRS scores between discharge and follow-up entail decreasing BDI scores on average. It is important to note that this analysis focuses on the difference between scores and not the value of the score itself as in previous analyses.

Discussion

Summary of the results

In a prospective study of 233 consecutively admitted patients with acute ischemic cerebrovascular disorders we could evaluate depressive symptoms in 168 patients in the acute phase, whereas repeated examination at 1 year was possible in 116 subjects. In univariate analysis severity of depressive symptoms (as measured by CES-D) was associated with age, level of education, employment status, income, housing condition and disability both at discharge and at follow-up. We found similar results when depressive symptoms were evaluated by the Beck Depression Inventory.

In multivariable analysis in the acute phase level of education and prior employment status are the major predictors of the severity of depressive symptoms. Whereas at one year after the index event the actual level of disability and financial competence were the significant predictors of the severity of depressive symptoms. One year after the index event, depressive symptoms worsened in those who became dependent after the initial independent condition at discharge, whereas those who were initially dependent but improved to be able to care for themselves at 1 year after the index event had decreasing severity of depression.

Predictors of depressive symptom severity in the acute stage/at discharge from hospital

Regarding employment status in our study those who had not been employed before their acute cerebrovascular event scored higher on the CES-D scale compared to those who had been employed. Further, compared to those with no more than 8 years of education, higher education level was associated with less severe depressive symptoms. In a systematic review those with post-stroke depression were found to have fewer years of education than those without post-stroke depression.²⁷ Patients with long-term education in general, may develop better self adjustment abilities.²⁸ In addition to employment status and level of education, only discharge mRS had a tendency for association with the severity of depressive symptoms: those with more severe disability at discharge scored higher on the CES-D scale ($p = 0.07$) in the acute phase.

In the acute phase of stroke, severity of depressive symptoms were found to relate mostly to age, stroke severity, pre-stroke depression and female gender.^{29–31} In a Hong Kong Chinese study employment status before stroke was associated with depression in acute stroke.³² Broomfield

et al examined those with a diagnosis of stroke and TIA. They found that those with TIA had similar rates and predictors of mood disorder as those with stroke.³³

Predictors of the severity of depression after one year after stroke

When evaluating predictors of severity of depressive symptoms at 1 year after the acute event, we found that those in the lowest income category had significantly higher depression score than those in higher income categories. Compared to the results at discharge, employment status and education lost their effect on CES-D by one year after the index event.

In the year after an acute cerebrovascular event, the level of disability was generally found to be a strong predictor of the severity of depressive symptoms with corresponding results in Asian, European and American populations.^{34–38} Similarly to the conclusions of a review by Robinson and Spaletta³⁹ we also found that functional impairment was a consistent predictor of the severity of post stroke depressive symptoms at one-year after the index event.

A metaanalysis in stroke patients reported that education level, income, and age showed significant effects on depressive symptoms.⁴⁰ Assessing depressive symptoms after stroke should consider the interaction of gender, economic status, education level, history of depression and the presence/absence of a spouse.⁴¹

In a Polish study⁴² predictors for the presence of symptoms suggestive of depression at 3 months after stroke were low level of socioeconomic situation, education, low income, greater severity of stroke, and worse functional status. Socioeconomic deprivation was found to be a predictor of post stroke depression in a study in Ghana,⁴³ and a systematic review had similar conclusion in the sub-Saharan region: PSD was significantly associated with low education, cognitive impairment, physical disability, poor quality of life, and divorced marital status.⁴⁴ The Rotterdam study found that symptomatic cerebrovascular disease increases the vulnerability to late-life depression and the risk of depression after TIA is similar to that after stroke.⁴⁵

Predictors of improving or worsening of depression in the first year after stroke

We found that CES-D difference between discharge and follow-up at 1 year was only influenced significantly in our model by the level of dependency tested in a binary manner: patients with $mRS \leq 2$ were considered to be able to live independently, whereas those with $mRS \geq 3$ needed help from others in everyday activities. We found that those who turned dependent from an independent condition at discharge presented more severe depressive symptoms at one year, and vice versa, those who improved from the dependent condition at discharge to be able to live an independent life one year later, had less severe depressive symptoms at follow-up compared to discharge.

The effect of functional improvement on the change of depressive symptoms remains controversial: whereas better functional recovery was associated with improved mood in a study by Torrisi et al,⁴⁶ results were inconclusive as to whether improvement of depression was independently associated with functional recovery at 12 weeks.⁴⁷

When assessing the factors influencing the difference between the follow-up and discharge CES-D score with multiple linear regression, we found that only the dependent state of the patient (measured by mRS) had a significant effect. Namely, patients who transitioned from independent to dependent state (i.e. from discharge $mRS \leq 2$ to follow-up $mRS \geq 3$) showed significantly more increase in their depressive symptoms (i.e. CES-D score) between discharge and follow-up than those patients who were independent in the whole study period. We also found that improvement from discharge $mRS \geq 3$ to follow-up $mRS \leq 2$ significantly lowered the CES-D score between discharge and follow up compared to those patients who were independent in the whole study period (i.e. both discharge and follow-up $mRS \leq 2$). It is important to note that as both the discharge and follow-up depression data were required for this analysis, only survivors (i.e. both discharge and follow-up $mRS < 6$) were included in this model.

The strengths of our study are the repeated evaluation of patients in the acute stage and one year later, the use of two tools (the CES-D and the BDI) to evaluate severity of depressive symptoms, and the detailed evaluation of socioeconomic features of individual patients. Our study has several limitations. As a single center study the number of patients is relatively small. Admitting patients ineligible for reperfusion therapy in acute stroke may result in some selection bias, as in another study we found that those who had reperfusion therapy were more satisfied after stroke than those without thrombolysis [Szócs et al, Budapest, unpublished data, August 2020]. We had limited data on comorbidity, therefore the Charlson comorbidity index could not be calculated. Although some studies indicated that depression in the acute phase of stroke is related to pre-stroke depression, the history of pre-stroke depression was not obtained systematically in all patients in our study. As no accurate information was available on lifetime prevalence of depression in our patients, the effect of pre-stroke depression could not be evaluated. Further, the evaluation of socioeconomic factors was based on the report of the patients and caregivers, and was not confirmed by independent sources. Finally, restricting the analysis of outcome to those with follow-up CES-D evaluation may have resulted in some selection bias.

Based on multivariate testing we conclude that different socioeconomic factors predict severity of depressive symptoms in the acute phase and at one year after the event. Immediately after the acute cerebrovascular event level of education and employment status, whereas one year later income and the level of disability predict the severity of depressive symptoms. Finally, the change in

dependence status between the acute stage and the follow-up predicted changes in the severity of depressive symptoms in both directions: patients independent at discharge but dependent 1 year later had increasing severity of depressive symptoms, whereas an improvement in depressive symptoms could be observed in those who became independent at one year after a dependent condition in the acute phase.

Data availability

The datasets generated for this study are available on request to the corresponding author.

Author contributions

DB designed and supervised the study. AM performed patient examination and data collection. BD performed statistical analysis of the data. AM and BD drafted the manuscript. JZ and MB edited the manuscript for important intellectual and clinical content. All authors read and approved the final version of the manuscript.

Declaration of Competing Interest

None declared.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.jstrokecerebrovasdis.2020.105241](https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105241).

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