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ORIGINAL ARTICLE

Factors of Hamilton Depression Rating Scale (17 items) at 2 weeks correlated with poor outcome at 1 year in patients with ischemic stroke

Huaiwu Yuan · Ning Zhang · Chunxue Wang · Ben Yan Luo · Yuzhi Shi · Jingjing Li · Yong Zhou · Yilong Wang · Tong Zhang · Juan Zhou · Xingquan Zhao · Yongjun Wang

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Abstract There was fewer paper about the relation between the Hamilton Depression Rating Scale (17 Items, HDRS-17) factors and stroke outcomes. Our aim was to investigate the influence of total score and factors of HDRS-17 on outcome of ischemic stroke at 1 year. A total of 1,953 patients with acute ischemic stroke were enrolled into a multicentered and prospective cohort study. The HDRS-17 was used to assess symptoms at 2 weeks after ischemic stroke. The Modified Ranking Scale (mRS) scores of 3–6 points and 0–2 points were regarded as poor outcome and benign outcome, respectively. At 1 year, 1,753 (89.8 %) patients had mRS score data. After adjusting for the confounders, patients with a total HDRS-17 score of ≥8 had a worse outcome at 1 year (OR = 1.62, 95 % CI 1.18–2.23). Symptoms of suicide (OR = 1.89, 95 % CI 1.27–2.83), decreased or loss of interest of work (OR = 1.89, 95 % CI 1.38–2.58), retardation (OR = 1.74, 95 % CI 1.27–2.38), psychic anxiety (OR = 1.72, 95 % CI 1.26–2.34), and agitation (OR = 1.61, 95 % CI 1.08–2.40) increased the risks for poor outcome by >60 %, respectively. Depressed mood, somatic anxiety, somatic symptoms-gastrointestinal, and early insomnia also increased the risk for poor outcome by nearly 50 %, respectively. A total HDRS-17 score of ≥8, and suicide, decreased or loss of interest of work, anxiety, agitation, retardation, depressed mood, somatic anxiety, somatic symptoms-gastrointestinal, and early insomnia of the HDRS-17 factors at 2 weeks after ischemic stroke increase the risk for poor outcome at 1 year.

Keywords Depression · Cerebrovascular disorders · Outcome assessment · Prospective study · Cohort studies

Introduction

Stroke has become the leading cause for disability and death in China [5]. Patients with ischemic stroke even had a worse functional outcome as compared with patients with hemorrhagic stroke [8, 21]. Previous studies reported 33 % patients with stroke were accompanied with depressive symptoms [14]. Depression increased the risk for poor outcomes of disability and death in patients with stroke, and some studies indicated that the higher score of the Hamilton Depression Rating Scale (HDRS) [6], the greater risk for poor outcomes in stroke patients [16, 17, 19]. The HDRS is usually used to evaluate depressed mood. Most studies concentrated on the association between the total score and the poor outcomes of stroke, not the relation between the HDRS factors and stroke outcomes. Although Robert et al. [22] reported that mental retardation could increase the risk for death among ordinary population, few studies reported the influence of retardation on patients'

H. Yuan and N. Zhang contribute to this paper equally.

H. Yuan · N. Zhang · C. Wang (✉) · Y. Shi · J. Li · Y. Zhou · Yilong Wang · T. Zhang · X. Zhao · Yongjun Wang
Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, No. 6 Tiantanxili, Dongcheng District, Beijing 100050, China
e-mail: snowsen@126.com

H. Yuan
e-mail: yhw0202@hotmail.com

H. Yuan · B. Y. Luo
Department of Neurology, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

J. Zhou
Department of Neurology, Beijing Daxin District Hospital, Capital Medical University, Beijing, China

poor outcomes after stroke. Agitation is a common symptom in patients with stroke [7]. Nevertheless, there are few studies to investigate the association between agitation and stroke outcomes. Further studies on the relation between stroke outcomes and depressed mood and accompanied symptoms after stroke are needed to help clinicians to recognize and control risk factors and further improve outcomes in post-stroke patients.

This study is to explore the relation between the total HDRS-17 score with symptoms represented by each factor and outcomes of ischemic stroke.

Methods

A multicentered prospective cohort study was conducted among 56 secondary or tertiary hospitals from April 2008 to April 2010 in China to investigate the morbidity, risk factors, therapeutic status of post-stroke depression (PSD), and the influence of PSD on patients' clinical outcomes after stroke. Study protocol and related information can be found in the previous published papers [26]. This current study was a subgroup analysis to investigate the influence of a total HDRS-17 score and its factors at 2 weeks after ischemic stroke on the patients' poor outcome, which was measured by modified Rankin Scale (mRS) [25] at 1 year. The study was approved by the Medical Ethics Committee of Beijing Tiantan Hospital affiliated to Capital Medical University, and was conducted in compliance with the Declaration of Helsinki Guidelines for Protection of Human Subjects.

Subjects and baseline data

Patients who met the following inclusion criteria were recruited into this study: (1) having acute stroke defined by World Health Organization (WHO) criteria [10]; (2) within 14 days after initial stroke; (3) aged $\geq$18 years old; (4) could finish examinations; (5) written informed consent provided by the patient or their legal guardian. The exclusion criteria included: (1) acute hemorrhagic stroke; (2) missing HDRS-17 data at 2 weeks after stroke; (3) lost to follow up within 1 year after stroke; (4) no written informed consent provided by the patient or their legal guardian.

Baseline data were collected and measured from consecutive patients with acute ischemic stroke at admission, including: demographic features (age and gender); vascular risk factors including histories of hypertension (defined as having previous history or taking antihypertensive drugs), mellitus diabetes (previous history or taking lower glucose drugs), hyperlipidemia (previous history or taking lower lipid drugs), previous stroke, and cardiovascular diseases; smoking (current smokers); the National Institutes of Health Stroke Scale (NIHSS) score [11], systolic pressure, and diastolic pressure at admission; stroke types and present intervention data (i.e., stroke related treatment, antidepressants, stroke education).

HDRS-17 evaluation at 2 weeks after ischemic stroke

Patients were evaluated with the HDRS-17 at 2 weeks after stroke by neurologists who received psychiatric training. The factors of HDRS-17 include depressed mood, feelings of guilt, suicide, insomnia-early, insomnia-middle, insomnia-late, work and interest, retardation, agitation, anxiety-psychic, anxiety-somatic, somatic symptoms-gastrointestinal, somatic symptoms-general, genital symptoms, hypochondriasis, loss of weight, and insight. The score of every factor ranges from 0 to 4, and 0 is defined as "asymptomatic" and 1–4 is defined as "symptomatic" [2]. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, fourth edition) was used to diagnose PSD. Aphasia and unilateral neglect were also assessed by neurologists at 2 weeks [11]. All investigators received the standardized training to ensure to correctly use the HDRS-17 and DSM-IV.

Outcomes at 1 year after ischemic stroke

Outcomes of patients were obtained via phone or face-to-face follow-up at 1 year after stroke. The mRS score of 3–6 was defined as poor outcome and the mRS of 0–2 was defined as benign outcome. All follow ups were abided by standardized follow-up agreement and were implemented by physicians who received standardized training in each center. The outcome assessors were blind to patients' baseline data.

Statistical analysis

Categorical variables were represented by frequency or percentage, and the χ^2 test was used to compare them. The *t* test was used to compare continuous variables that were represented by mean $\pm$ standard deviation. The Mann–Whitey test was used to compare the continuous variables that were represented by median (inter-quartile range). The multivariate logistic regression model was used to explore the real relations between the HDRS-17 factors and poor outcome after adjusting for the potential confounders (i.e., age, gender, and variables that showed the significant difference between patients with poor outcome and benign

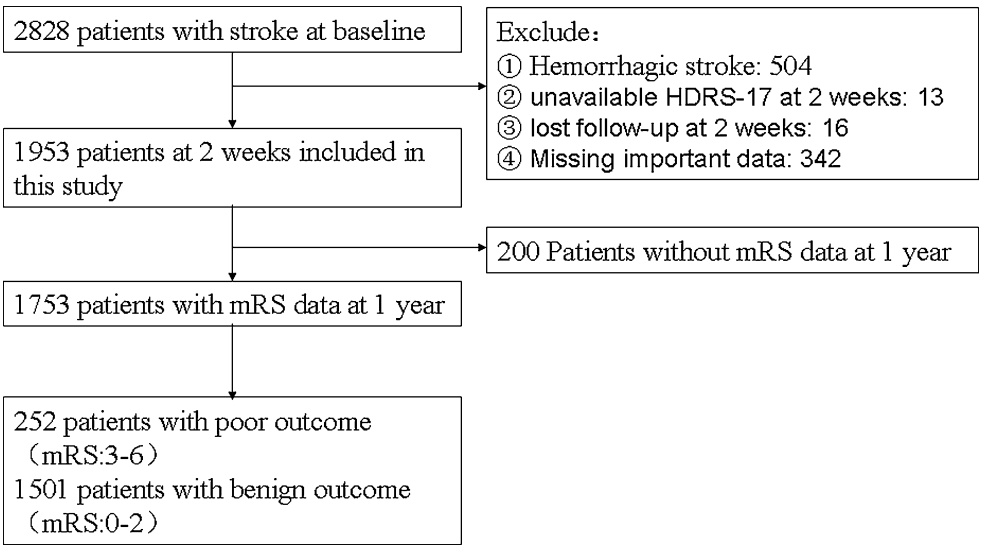

Fig. 1 Patients inclusion chart. *HRSD*-17 Hamilton Depression Rating Scale (17-items), *mRS* modified Ranking Scale

outcome at 1 year after stroke). A two-sided significance level of $\alpha = 0.05$ was assumed. All data were analyzed using SPSS17.0 (SPSS Inc., Chicago, USA).

Results

Among 2,828 patients who met the inclusion criteria, 504 patients with hemorrhagic stroke, 13 patients lacked of HDRS-17 data at 2 weeks, 26 patients lost follow up at 2 weeks after stroke, 342 patients missed important information, and therefore leaving 1,953 patients in our study (Fig. 1). There were 1,753 (89.8 %) patients having mRS data at 1 year. Among these patients, 1,172 (66.9 %) patients were male, aged 60.7 ± 11.5 years old; and 581 (33.1 %) patients were female, aged 64.6 ± 11.1 years old.

Baseline patients characteristics

Compared with patients with benign outcome, patients with poor outcome at 1 year were older (65.8 ± 11.4 vs. 61.4 ± 11.4 years, $P = 0.000$); having a higher NIHSS score at admission (8 [4–11] vs. 3 [2–6], $P = 0.000$); and having a greater proportion of history of stroke (33.3 vs. 23.4 %, $P = 0.001$), history of cardiovascular diseases (32.9 vs. 22.5 %, $P = 0.000$), taking lower glucose drugs (34.9 vs. 27.0 %, $P = 0.010$), and aphasia at 2 weeks (20.2 vs. 14.6 %, $P = 0.022$), unilateral neglect at 2 weeks (3.2 vs. 0.6 %, $P = 0.000$), antidepressants at 2 weeks (13.9 vs. 5.3 %, $P = 0.000$). Meanwhile, patients with poor outcome had a lower proportion of stroke education (81.3 vs. 86.8 %, $P = 0.021$) (Table 1).

HDRS-17 total score and factors at 2 weeks after ischemic stroke

Compared with patients with benign outcome at 1 year, patients with poor outcome had a higher total score of HDRS-17 (7 [3–12] vs. 4 [1–7], $P = 0.000$) (Table 2). Except for genital symptoms, hypochondriasis and insight, the detection rates of other 14 factors in patients with poor outcome obviously increased: depressed mood (53.8 vs. 32.5 %, $P = 0.000$), feelings of guilt (45.2 vs. 31.0 %, $P = 0.000$), suicide (23.2 vs. 8.8 %, $P = 0.000$), early insomnia (52.6 vs. 35.7 %, $P = 0.000$), middle insomnia (38.6 vs. 29.5 %, $P = 0.004$), late insomnia (45.2 vs. 33.2 %, $P = 0.000$), decreased or loss of interest of work (44.8 vs. 22.5 %, $P = 0.000$), retardation (46.8 vs. 23.5 %, $P = 0.000$), agitation (22.3 vs. 10.3 %, $P = 0.000$), psychic anxiety (46.4 vs. 29.9 %, $P = 0.000$), somatic anxiety (51.2 vs. 32.8 %, $P = 0.000$), somatic symptoms-gastrointestinal (32.4 vs. 17.1 %, $P = 0.000$), somatic symptoms-general (39.6 vs. 28.6 %, $P = 0.000$), loss of weight (24.1 vs. 16.7 %, $P = 0.005$) (Table 2).

Relation between HDRS-17 total score and poor outcome

Among 1,753 patients with the mRS data at 1 year, there were 252 (14.4 %) patients with poor outcome. Compared with patients having a total HDRS-17 score of <8 at 2 weeks, patients with a total score of HDRS-17 ≥8 had a higher proportion of having poor outcome at 1 year (24.5 vs. 10.5 %, $P = 0.000$). After adjusting for age, gender, and other significantly different variables at baseline between the poor outcome group and benign outcome

Table 1 Comparisons of baseline characteristics between patients with benign outcome and poor outcome at 1 year after ischemic stroke onset

Characteristics[a]	Benign outcome[b]	Poor outcome[b]	*P*
Age, mean ± SD (y)	61.4 ± 11.4	65.8 ± 11.4	0.000
Female	485 (32.3)	96 (38.1)	0.071
History of diabetes	379 (25.2)	77 (30.6)	0.076
History of hyperlipidemia	346 (23.1)	53 (21.0)	0.479
History of hypertension	986 (65.7)	174 (69.0)	0.297
Smoking	683 (45.5)	112 (44.4)	0.755
History of stroke	351 (23.4)	84 (33.3)	0.001
History of cardiovascular disease	338 (22.5)	83 (32.9)	0.000
SBP at admission, mean ± SD, mmHg	150.8 ± 23.3	88.4 ± 13.8	0.989
DBP at admission, mean ± SD, mmHg	88.4 ± 13.8	87.7 ± 13.4	0.437
NIHSS score at admission, median (IQR)	3 (2–6)	8 (4–11)	0.000
Intravenous thrombolysis	40 (2.7)	5 (2.0)	0.527
Anticoagulation	260 (17.3)	44 (17.5)	0.957
Antiplatelet	1,445 (96.3)	242 (96.0)	0.855
Taking antihypertensive drugs	826 (55.0)	136 (54.0)	0.754
Taking lower lipid drugs	1,012 (67.4)	163 (64.7)	0.392
Taking lower blood glucose drugs	406 (27.0)	88 (34.9)	0.010
Having stroke education	1,303 (86.8)	205 (81.3)	0.021
Taking antidepressants at 2 weeks	80 (5.3)	35 (13.9)	0.000
Aphasia at 2 weeks	219 (14.6)	51 (20.2)	0.022
Unilateral neglect at 2 weeks	9 (0.6)	8 (3.2)	0.000

SD standard deviation, *y* year, *IQR* interquartile range, *NIHSS* national institutes of health stroke scale, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

[a] Data are given as number (percentage) unless specific representations were indicated

[b] Poor outcome was defined as a mRS of 3–6, and benign outcome indicated a mRS of 0–2

group (including history of stroke, history of cardiovascular diseases, NIHSS score at admission, taking lower glucose drugs, stroke education, and antidepressants, aphasia, unilateral neglect), the risk of having poor outcome at 1 year increased 62 % (OR = 1.62, 95 % CI 1.18–2.23) when compared with patients whose total HDRS-17 score of <8 at 2 weeks (Fig. 2).

Relation between HDRS-17 factors at 2 weeks after ischemic stroke and poor outcome at 1 year

After adjusted age, gender, and other potential confounders that were significantly different between the poor outcome group and good outcome group at the baseline (including history of stroke, history cardiological diseases, the NIHSS score at admission, lower blood glucose drugs, stroke education, and antidepressants, aphasia, unilateral neglect), the multivariate logistic regression analysis showed that the following nine symptoms represented by the HDRS-17 factors increased the OR of poor outcome at 1 year (listing from the highest to lowest OR): suicide (OR = 1.89, 95 % CI 1.27–2.83), decreased or loss of interest of work (OR = 1.89, 95 % CI 1.38–2.58), retardation (OR = 1.74, 95 % CI 1.27–2.38), psychic anxiety (OR = 1.72, 95 % CI 1.26–2.34), agitation (OR = 1.61, 95 % CI 1.08–2.40), depressed mood (OR = 1.54, 95 % CI 1.13–2.11), early insomnia (OR = 1.50, 95 % CI 1.11–2.04), somatic anxiety (OR = 1.47, 95 % CI 1.08–2.01), and somatic symptoms-gastrointestinal (OR = 1.44, 95 % CI 1.02–2.04) (Fig. 2). The Other HDRS-17 factors did not obviously increase the OR of poor outcome at 1 year (Fig. 2).

Discussion

Our study found, that the OR of the poor outcome at 1 year in patients with a total HDRS-17 score of ≥8 increased 62 % when compared with patients with a total HDRS-17 score of <8. Among the HDRS-17 factors, the OR for the poor outcome in patients with suicide or decreased or loss of interest of work increased up to 89 %. The OR for the poor outcome in patients with retardation and psychic anxiety obviously increased 74 and 72 %, respectively. The OR for the poor outcome in patients accompanied with agitation increased 61 %. The OR for the poor outcome in patients with depressed mood, early insomnia, somatic anxiety, and somatic symptoms-gastrointestinal increased 54, 50, 47, 44 %, respectively.

In our study, the OR (1.89) for poor outcome at 1 year in patients with decreased or loss of interest of work or suicide is close to many studies reported that decreased or loss of interest of work was the main symptom of PSD [4], [13]. The DSM-IV defined decreased or loss of interest of work as one of the core symptoms of depression. In our study,

Table 2 Comparisons of HDRS-17 factors at 2 weeks after ischemic stroke between patients with benign outcome and poor outcome at 1 year

HDRS-17[a]	*n* (%)	Benign outcome[b]	Poor outcome[b]	*P*
HDRS-17, median (IQR)	1,731 (100)	4 (1–7)	7 (3–12)	0.000
Depressed mood	621 (35.5)	486 (32.5)	135 (53.8)	0.000
Feelings of guilt	578 (33.1)	465 (31.0)	113 (45.2)	0.000
Suicide	190 (10.9)	132 (8.8)	58 (23.2)	0.000
Insomnia-early	667 (38.2)	535 (35.7)	132 (52.6)	0.000
Insomnia-middle	539 (30.9)	442 (29.5)	97 (38.6)	0.004
Insomnia-late	611 (35.0)	498 (33.2)	113 (45.2)	0.000
Work and interest	449 (25.7)	337 (22.5)	112 (44.8)	0.000
Retardation	468 (26.8)	351 (23.5)	117 (46.8)	0.000
Agitation	210 (12.0)	154 (10.3)	56 (22.4)	0.000
Anxiety-psychic	563 (32.3)	447 (29.9)	116 (46.4)	0.000
Anxiety-somatic	618 (35.4)	490 (32.8)	128 (51.2)	0.000
Somatic symptoms-gastrointestinal	336 (19.3)	255 (17.1)	81 (32.4)	0.000
Somatic symptoms-general	525 (30.1)	426 (28.6)	99 (39.6)	0.000
Genital symptoms	567 (32.7)	486 (32.7)	81 (32.7)	0.995
Hypochondriasis	296 (17.0)	246 (16.5)	50 (20.1)	0.160
Loss of weight	310 (17.8)	250 (16.7)	60 (24.1)	0.005
Insight	276 (15.9)	227 (15.3)	49 (19.8)	0.076

HDRS-17 Hamilton Depression Rating Scale (17-items), *n* sample size, *IQR* interquartile range

[a] Data are given as number (percentage) unless specific representations were indicated

[b] Poor outcome was defined as a mRS of 3–6, and benign outcome indicated a mRS of 0–2

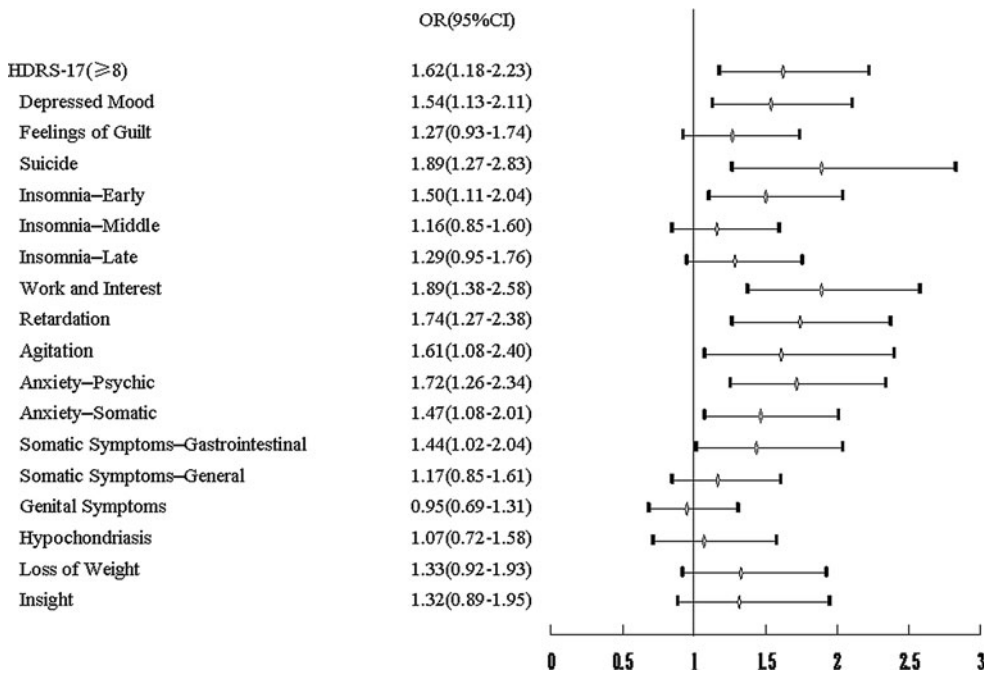

Fig. 2 Adjusted odds ratios (95 % confidence interval) of *HDRS*-17 factors at 2 weeks after ischemic stroke onset in relation to poor outcome at 1 year. *HDRS-17* Hamilton Depression Rating Scale (17-items). Adjusted potential confounders included age; gender; history of stroke; history cardiological diseases; the NIHSS score at admission; using lower blood glucose drugs, stroke education, and antidepressants, aphasia, unilateral neglect

compared with patients without decreased or loss of interest of work, PSD morbidity was obviously increased in patients with decreased or loss of interest of work. Hence, we speculated that the significant association between poor outcome and decreased or loss of interest of work might be mediated by PSD. We speculated suicide was closely related to poor outcome since suicide increased mortality. In our study, 26 patients died, but the cases of deaths caused by suicide were unclear because all-cause mortality was collected.

We found that the OR for poor outcome at 1 year after ischemic stroke increased more than 70 % in patients with anxiety or retardation. Kengo et al. reported that generalized anxiety disorder significantly affected patients with stroke on their daily living ability and extremities rehabilitation, similar to the findings by Acharya et al. [1, 9]. Our study indicates that physicians need to actively identify the accompanied anxiety mood and suicide trend after ischemic stroke, which may help to improve stroke prognosis. Our study found that retardation increased the risk of poor outcome at 1 year in patients with ischemic stroke. As far as we know, there were few reports on the influence of retardation about stroke outcomes. Robert et al. [22] reported that risk for death in patients with mild and moderate mental retardation increased 153 % of that in the ordinary population, the risk for death of patients with severe mental retardation increased 173 % of that in the ordinary population, and the risk in all patients with mental retardation increased 159 %. Their conclusion of mental retardation increasing death risks in the ordinary population was in consistence with our results that retardation increased the risk for poor outcome at 1 year in patients with ischemic stroke. Many studies reported that the suicide risk in patients with mental retardation was higher than that in the ordinary population [20]. In our study, it is proved that suicide thoughts or action was an independent risk factor for poor outcome at 1 year in patients with ischemic stroke, and suicide might be one of the important causes of retardation that increased poor outcome in patients with ischemic stroke. In addition, like decreased or loss of interest, retardation was one of main symptoms of PSD [13]. More patients with retardation met the diagnosis criteria of PSD than patients without retardation, so, the relation between retardation and ischemic stroke outcome may be mediated partially by PSD. The result, that the OR for poor outcome in patients with retardation increased by 74 %, suggested that retardation played an important role in influencing depression to worsen stroke outcome.

There were few studies that reported the association between agitation and stroke outcomes. Compared with patients without agitation, patients with agitation after stroke had thalamic-pituitary-adrenal axis function disorder [7], which might regulate up sympathetic nerve activity, raise hypertension, aggravate atherosclerosis, and further aggravate encephalic ischemia [3]. McManus et al. [15] reported a low infusion in patients with agitation might be severer, which obviously aggravated nerve functional deficiency. It is worthy of attention that the possibility of poor prognosis of patients with agitation increased by 61 % in our study.

Depressed mood is the core symptoms for depression [2]. In our study, PSD morbidity in patients with depressed mood was obviously higher than that in patients without depressed mood, which might be one of manifestations that PSD increased the poor outcome in patients with stroke [17].

Clinicians and investigators had already observed that insomnia was a common symptom among patients with stroke. Leppävuori et al. [12] reported, among 277 patients with ischemic stroke, 157 (56.7 %) had insomnia symptom at 3–4 months after stroke. In our study, early insomnia, middle insomnia, and late insomnia in the HDRS-17 totally accounted for 41.9 %, which was similar to the Leppävuori et al. study, and also they significantly increased the risk of poor prognosis, respectively. Insomnia might bring severe psychic and somatic problems. In a cross-sectional study, Tang et al. found that insomnia symptom increased the risk for suicide by 70 % at 3 months in patients after stroke [24]. Besides, insomnia after stroke would aggravate clinical symptoms, delay recovery of nerve functions [18], and decrease life of quality of patients with stroke [23]. Thus, clinicians need to pay attention and take active interventions to insomnia problem after stroke.

Conclusion

A total HDRS-17 score of $\geq$8 at 2 weeks after ischemic stroke significantly increased the risk for poor outcome at 1 year. Among the HDRS-17 factors, suicide, decreased or loss of Interest of work, anxiety, agitation, and retardation could obviously increase risk of poor outcome at 1 year. In addition, depressed mood, somatic anxiety, somatic symptoms-gastrointestinal, and early insomnia could cause aggravation on ischemic stroke outcome.

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Conflict of interest The authors declare no conflicts of interest.

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