

Original article

Psychosocial predictors of depression and anxiety in Thai stroke caregivers

Chanatip Tongyonk^a , Sorawit Wainipitapong^a , Chavit Tunvirachaisakul^a ,
Aurauma Chutinet^b , Michael Maes^{a, c, *} , Thitiporn Supasitthumrong^a 

^aDepartment of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^bChulalongkorn Stroke Centre, King Chulalongkorn Memorial Hospital; Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University

^cDepartment of Psychiatry, Medical University Plovdiv, Plovdiv, Bulgaria; IMPACT Research Center, Deakin University, Geelong, Australia

Abstract

Background: Stroke is a leading cause of disability and places a considerable burden on caregivers worldwide. However, studies on the burden of stroke caregivers in Thailand remain limited.

Objective: This study aimed to identify characteristics of patients with ischemic stroke and their caregivers that may predict distress, depression, and anxiety symptoms in the caregivers.

Methods: The Hospital Anxiety and Depression Scale (HADS), Zarit Burden Interview (22-item ZBI), and Perceived Stress Scale (PSS-10) were used to measure the caregivers' burden, stress, depression, and anxiety symptoms. Furthermore, we used partial least squares structural equation modeling (PLS-SEM) to establish a multistep mediation model.

Results: Ninety-seven stroke patients and their caregivers were included in this study. The regression on ZBI-personal strain and stroke of other identified etiology explained 15.0% of the variation in the HADS depression score. We observed that the caregiver's underlying condition and the patients' National Institutes of Health Stroke Scale (NIHSS) explained 13.6% of the variation in the caregiver's overall ZBI score. The total ZBI score, the presence of lacunar circulatory infarction in the patients, and the caregiver's underlying condition explained 40.9% of the variation in the caregivers' overall PSS score. Moreover, PLS analysis revealed that the NIHSS and the caregiver's underlying medical condition had substantial indirect effects on the HADS score, mediated by the ZBI score.

Conclusions: The patient's disability, reliance, cognition, and stroke phenotypes, as well as the caregiver's health condition and burden, account for a considerable portion of variation in the stress and depression ratings in caregivers of patients with ischemic stroke. Therefore, screening ischemic stroke caregivers for the aforementioned risk factors is crucial.

Keywords: Anxiety, depression, ischemic stroke, mental problems, psychiatry, stress.

Introduction

Healthcare professionals need greater vigilance regarding diseases and their potential consequences, as the aging population worldwide, and in Thailand, continues to increase.⁽¹⁾ One of these age-related illnesses is ischemic stroke, the prevalence of which is anticipated to double by 2050 compared to 2010. Increased prevalence leads to an increase in disability-adjusted life years as a consequence of better acute ischemic stroke treatment.^(1, 2)

Stroke has various consequences that impact survivors and their families.⁽³⁻⁵⁾ Half of stroke survivors remain handicapped and require medical treatment for at least a year after the stroke.⁽⁶⁾ The majority of family members who become unskilled and unpaid informal caregivers are primarily female spouses and the patients' daughters.⁽⁷⁾

Among the most often reported pressures on stroke patients' caregivers are family changes, confinement, changes in personal goals, loss of autonomy, and anxiety about the future.⁽⁴⁾ The response to the stresses is governed by the degree of strain and the caregivers' coping mechanisms.⁽⁵⁾ Negative outcomes relate to passive and palliative coping techniques more than positive coping strategies.^(4, 5)

***Correspondence to:** Thitiporn Supasitthumrong, Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Email: thitiporn.s@chula.ac.th

Received: November 20, 2025

Revised: January 26, 2026

Accepted: February 28, 2026

Although caring activities may be rewarding, positive elements of caregiving have been noted, particularly among elder caregivers.⁽⁵⁾ Caregivers may experience emotional anguish because of the difficulties they confront. However, although this discomfort tends to lessen with time, many caregivers might not seek therapy while they are experiencing stress, depression, and anxiety symptoms, which can lead to anxiety and drug misuse disorders, as well as suicide.⁽⁶⁻⁹⁾ Female sex, being a spouse, Caucasian race, degree of handicap, level of reliance, care duration of 13 hours a day, self-funded financial source, care load, task complexity, and presence of the patient's depressive symptoms are factors that predispose caregivers to depression and anxiety. Although there are certain differences, such as having a husband.⁽¹⁰⁻¹⁴⁾

Despite the central role caregivers play in stroke recovery, their psychological distress is frequently overlooked by healthcare professionals. Routine follow-up care often emphasizes secondary prevention and physical rehabilitation, while neglecting the emotional and psychosocial consequences that caregivers experience.⁽¹⁵⁾ This oversight can result in caregivers becoming "the next patient," as chronic stress, anxiety, and depression accumulate without intervention.⁽¹⁶⁾ Previous studies have shown that caregivers face a severe burden due to a lack of respite care, minimal institutional support, and the hidden nature of emotional strain. Interventions such as psychoeducation, counseling, and community-based support have demonstrated potential to reduce caregiver distress and improve outcomes. Therefore, integrating caregiver-focused psychosocial screening and support into the aftercare of patients with stroke is not only necessary but urgent.

Caregivers' assessments should extend beyond burden to include systematic screening for depression and anxiety.^(4, 7, 17) Brief interventions, such as telephone or online problem-solving support, education, and counseling, have been shown to reduce caregiver strain and psychological symptoms.⁽⁷⁾ Standardized tools, including the Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire, Center for Epidemiologic Studies Depression Scale, Geriatric Depression Scale, and Hamilton Anxiety Rating Scales, can effectively identify caregivers who are at risk.^(9, 11, 12, 17, 18) A 2017 meta-analysis reported that

40.2% of stroke caregivers experienced depression and 21.4% experienced anxiety; however, most of these studies were conducted in Western countries. To address this gap, we examined predictors of distress, depression, and anxiety among caregivers of patients with ischemic stroke in Bangkok, Thailand.⁽¹⁴⁾

Materials and methods

Research methods

This research is a descriptive cross-sectional study. Participants completed a self-reported questionnaire that included demographics, the Thai-HADS, the Zarit Burden Interview (22-item ZBI), and the Thai Perceived Stress Scale (PSS-10). Clinical data were obtained from patients' electronic medical records, including clinical diagnoses, cognitive evaluations, impairment assessments, and dependence assessments. The Institutional Review Board of Chulalongkorn University's Faculty of Medicine in Bangkok, Thailand, gave ethical clearance for this study (IRB No. 532/63). Informed consent was obtained from all individual participants, including patients and caregivers prior to enrollment, in accordance with the Declaration of Helsinki and institutional guidelines.

Study participants

The study included dyads of caregivers and their patients with ischemic stroke who had previously been hospitalized and were now undergoing follow-up visits at the stroke clinic at King Chulalongkorn Memorial Hospital in Bangkok, Thailand. Dyads who attended a follow-up appointment between October 1, 2022, and March 31, 2023, were invited to participate in the study. Caregivers who were relatives and provided the majority of day-to-day care were eligible if they were between the ages of 18 and 70, fluent in Thai, cared for patients with ischemic stroke diagnosed using ICD-10 criteria (I63 or I69.3), had been providing care for at least 4 weeks, and provided care for more than 8 hours per day. The dyads provided informed consent for data to be collected from questionnaires and electronic medical records. No participant (patient or caregiver) was included more than once. Participants were excluded if the care was financially reimbursed or if the patients resided in nursing homes or long-term care facilities.

Number of participants

The number of participants was determined prior to research commencement. A total of 85 individuals was required, which provided a power of 0.8, an alpha error of 0.05, and four predictors.

Instruments

Burden and stress

The 10-item PSS was used to assess the perceived stress.⁽¹⁹⁾ A Cronbach's alpha score of 0.85 was obtained after translating the rating scale into Thai.⁽²⁰⁾ The ZBI was created to measure caregivers' subjective hardship.⁽²¹⁾ The ZBI dimensions have been researched in the Asian population and have shown characteristics that correspond with patients' illness severity: personal strain, role strain, and concern about caregiving performance.⁽²²⁾ A Cronbach's alpha of 0.86 was found for the 22-item ZBI when translated into Thai.⁽²³⁾

Anxiety and depressive symptoms

The HADS was created to identify those who are at risk of developing depression or anxiety symptoms.⁽²⁴⁾ Its use has been broadened with high validity to include somatic, psychiatric, primary care, and even the general population.^(24, 25) Using an 8-point cut-off for each illness, HADS has a sensitivity and specificity of approximately 0.8 for each disorder.⁽²⁶⁾ The scale has been translated into Thai and has a Cronbach's alpha of 0.82 for depression and 0.85 for anxiety.

Ischemic stroke classification

The Oxfordshire Stroke Project Classification (OSPC) and the Trial of ORG 10172 in Acute Stroke Treatment (TOAST classification) were used in this investigation to categorize patients according to phenotype and etiology, respectively. Total anterior circulation infarcts (TACI), partial anterior circulation infarcts, posterior circulation infarcts, and lacunar infarcts (LACI) are the four types of stroke classified by the OSPC.⁽²⁷⁾ Furthermore, each subtype varies in terms of the damaged region of the brain, the result of thrombolysis, risk of recurrent stroke, disability, functional outcome, and mortality rate.⁽²⁸⁾ The TOAST classification was used to offer data on etiologies such as large-artery atherosclerosis, cardioembolism, small-vessel occlusion, and stroke of unknown etiology.⁽²⁹⁾

Disability and reliance

The Barthel Index (BI) was used to assess the dependence of patients with stroke. In contrast, the modified Rankin Scale (mRS) and National Institutes

of Health Stroke Scale (NIHSS) were used to evaluate the degree of impairment and neurological dysfunction. As no single test can assess all areas of disability and reliance, it has been determined that a combination of BI, mRS, and NIHSS is adequate for assessing daily activities, global disability, and neurological impairment.⁽²⁹⁾ Although it is not universally agreed upon, the cut-off values for a favorable result are 95 for BI and 2 for mRS.

Cognitive ability

To identify cognitive deficits and dementia, the Thai Mental Status Examination (TMSE) and the Montreal Cognitive Assessment-Thai (MoCA) were used.^(30 - 33)

Statistical analysis

The required sample size (97 patients with stroke and their caregivers) was calculated using the statistical software G*Power version 3.1, based on a multiple linear regression model with four predictors. The parameters specified were an alpha level of 0.05, statistical power of 0.80, and a medium effect size of $f^2 = 0.15$, following Cohen's conventional criteria for effect size estimation.

Data were expressed as the mean $\pm$ standard deviation (SD) and percentage (%). Pearson's product-moment correlation coefficient was used to analyze intercorrelations between the variables. Multiple regression analysis was used to identify the most significant biomarkers associated with rating scale scores, while adjusting for demographic variables (e.g., age and education). We used a stepwise automated technique with a p-to-enter threshold of 0.05 and a p-to-remove threshold of 0.06. R^2 changes, multivariate normality (as measured by Cook's distance and leverage), homoscedasticity (as measured by the White and modified Breusch-Pagan tests), and multicollinearity (as measured by tolerance and the variance inflation factor) were all investigated. All regression analysis results were bootstrapped (5,000 samples), and the latter are shown if the findings were not concordant. All tests were two-tailed, with a significance level of $P \leq 0.05$. All statistical analyses were performed using IBM SPSS for Windows, version 25, 2017. Smart Partial Least Squares (SmartPLS) path analysis was applied to examine multistep mediated routes between explanatory factors (e.g., patients' NIHSS and stroke phenotype, as well as patients' ZBI scores and socio-demographic data)

and dependent variables (e.g., patients' PSS and HADS scores). The HADS score is the outcome variable, with all other factors serving as direct or indirect explanatory variables. Only when the inner/outer models met the following quality criteria did we perform complete SmartPLS analysis with 5,000 bootstrap samples: a) Confirmatory tetrad analysis confirmed that the latent vectors were not misspecified as reflective models; b) the overall fit of the pathway model was adequate with standardized root mean square residual (SRMR) = 0.08; c) the outer model latent vector loadings were >0.666 at $P = 0.001$; and d) the latent vectors showed adequate construct validity. Following that, we performed a full PLS path analysis with 5000 bootstrap samples, calculating the path coefficients (with P -values), outer model loadings, and specific indirect and total effects. Moreover, we employed blindfolding and PLSpredict with 10-fold cross-validation to evaluate the model's prediction performance.⁽³⁴⁾ Compositional invariance was examined using predicted-oriented segmentation analysis, multigroup analysis, and measurement invariance assessment.

Results

Characteristics of patients with ischemic stroke and their caregivers

The surveys were completed and analyzed by 97 dyads of patients with ischemic stroke and caregivers. **Table 1** shows the dyad features. The majority of caregivers were in their forties, with an average age of 46.2 ± 14.6 years. Daughters (27.8%) and spouses (25.8%) were the most prevalent caretakers, reflecting the fact that two-thirds of them (66.0%) were female. They provided care despite being employed (77.3%), and only a tiny proportion (12.4%) were healthcare workers. Furthermore, almost one-third (34.0%) were affected by medical disorders such as hypertension, dyslipidemia, and diabetes. Furthermore, almost three-quarters (77.3%) were unaided, despite the average number of household members being 4.1 ± 1.8 .

The majority of patients with ischemic stroke (53.7%) were middle to late adult males with a mean age of 63.3 ± 12.7 . Approximately half of them had LACI (62.9%) according to the Oxford classification

or small-vessel occlusion (44.3%) according to the TOAST classification, with a severity of "mild stroke" according to the NIHSS, as their mean NIHSS score was 1.56 ± 2.7 . Their cognition test results indicated the possibility of mild cognitive impairment but not dementia, as their mean MoCA and TMSE were 21.2 ± 6.3 and 26.3 ± 3.8 , respectively. The dyads' mean monthly family income was $55,026.0 \pm 67,431.0$, which was approximately double the Bangkok average. A significant proportion of the dyads' medical treatment is not self-funded (95.8%).

Burden, stress perception, and depression and anxiety symptoms

According to the HADS, the mean scores for depression and anxiety symptoms among family caregivers were 3.3 ± 3.1 and 4.3 ± 3.4 , respectively. Using a HADS cut-off score of 8 in each subscale, 7.2% and 17.5% of caregivers had indications of clinically significant depression and anxiety symptoms, respectively. The caregivers' stress and load, as measured by the PSS-10 and ZBI-22, were 9.9 ± 6.4 and 15.7 ± 11.2 , respectively.

Depressive and anxiety symptom predictors

Table 2 reveals that the TACI and strokes of other identified origin were linked with HADS depression. Caregiving assistance was linked to HADS distress, and ZBI was associated with the occurrence of aphasia and NIHSS. Furthermore, strokes of unknown cause were linked to the PSS. Furthermore, caregiver work in health care was associated with sadness and anxiety on the HADS, as well as PSS. Furthermore, the caregiver's underlying medical conditions were linked to all four outcomes. **Table 3** shows the findings of the multiple regression analysis.

The regression model, including total ZBI, lacunar circulation infarcts, and caregivers' underlying condition (all of which were positively associated), explained 40.9% of the variation in the patients' PSS scores. The regression of the ZBI-personal strain domain score on stroke of other identified etiology (both positively linked) explained 15.0% of the variation in the HADS score. We discovered that regression on the caregiver's underlying medical conditions and the patients' NIHSS score (both positively associated) explained 13.6% of the variation in the overall ZBI score.

Table 1. Descriptive statistics of demographics, patient's factors, and caregiver's factors.

Factors		Participants, no. (%)
Patient	Overall	97 (100.0)
	Age (mean [SD], years)	63.3 [12.7]
	Gender	Female
		45 (46.3)
	Ethnicity	Thai
		81 (83.5)
	Education	12 years and above
		45 (46.4)
	Financial coverage	Universal coverage
		38 (39.2)
		Social security
		11 (11.3)
		Government officer benefits
		44 (45.4)
	Oxford classification	TACI
		7 (7.2)
		PACI
		18 (18.6)
		LACI
		61 (62.9)
		POCI
		11 (11.3)
Caregivers	TOAST classification	LAA
		32 (33.0)
		Cardioembolism
		9 (9.3)
		Small vessel occlusion
		43 (44.3)
		Stroke of other determined etiology
		4 (4.1)
		Stroke of undetermined etiology
		9 (9.3)
	Aphasia	Present
		5 (5.2)
	NIHSS (mean [SD])	1.6 [2.7]
	TMSE (mean [SD])	26.3 [3.8]
	MoCA (mean [SD])	21.2 [6.3]
	mRS (mean [SD])	1.3 [1.3]
	BIS (mean [SD])	91.4 [17.6]
	Age (mean [SD], years)	46.2 [14.6]
	Gender	Female
		66 (66.0)
Outcomes	Ethnicity	Thai
		84 (86.6)
	Education	Bachelor's degree and above
		56 (57.7)
	Prior health-care training	
		12 (12.4)
	Occupation	Employed
		75 (77.3)
	Underlying disease	Present
		33 (34.0)
	Relations to patient	Wife
		25 (25.8)
		Husband
		11 (11.3)
		Daughter
		27 (27.8)
		Son
		12 (12.4)
		Other relatives
		22 (22.7)
	Duration of caregiving (mean [SD], months)	13.3 [13.6]
	Hours of caregiving per day (mean [SD])	13.9 [8.4]
	Assistance in caregiving	
		22.0 (22.7)
	Number of assistants in caregiving (mean [SD])	1.3 [0.7]
	Number of household members (mean [SD])	4.1 [1.8]
	Household income (mean [SD])	55,026.0 [67,431.0]
	HADS-Depression (mean [SD])	3.2 [3.0]
	HADS-Anxiety (mean [SD])	4.3 [3.3]
	PSS-10 (mean [SD])	9.9 [6.3]
	ZBI-22-Overall (mean [SD])	15.7 [11.1]
	ZBI-22-Personal strain (mean [SD])	3.5 [3.6]
	ZBI-22-Role strain (mean [SD])	9.9 [7.8]
	ZBI-22-Worries about caregiving performance (mean [SD])	1.4 [1.3]

BIS, Barthel Index; HADS, hospital anxiety and depression score; LAA, large artery atherosclerosis; LACI, lacunar circulation infarction; MoCA, Montreal cognitive assessment; NIHSS, National Institute Stroke Scale; mRS, modified Rankin Scale, POCI, Posterior circulation infarction; PSS-10, Perceived stress scale-10 item; TACI, total anterior circulation infarction; SD, standard deviations; TMSE, Thai Mental Status Examination; ZBI-22: Zarit burden interview-22 item.

Table 2. Intercorrelation analysis matrix.

	HADS-D	HADS-A	ZBI	PSS	TACI	SOD	Aphas.	NIHSS	Cg's HC career	Cg's UD	Asst. in cg.	
												1.00
HADS-D	1											0.75
HADS-A	0.676	1										0.50
ZBI	0.233	0.259	1									0.25
PSS	0.172	0.112	0.572	1								0.00
TACI	-0.244	0.022	0.045	0.017	1							-0.25
SOD	0.258	0.075	-0.076	-0.217	-0.058	1						-0.50
Aphas.	0.063	0.163	0.279	0.084	0.115	-0.048	1					-0.75
NIHSS	0.109	0.150	0.242	-0.041	0.096	0.045	0.388	1				-1.00
Cg's HC career	-0.195	-0.230	-0.051	-0.124	0.016	-0.078	-0.088	-0.015	1			
Cg's UD	0.191	0.217	0.321	0.336	0.052	-0.039	0.325	0.087	-0.204	1		
Asst. in cg.	0.091	0.219	0.063	-0.008	-0.056	-0.112	0.096	0.108	0.021	-0.077	1	

Aphas, aphasia; Asst, assistance; Cg, caregiver; HADS, hospital anxiety and depression score; HADS-A, HADS anxiety; HADS-D, HADS depression; HC, health-care; NIHSS, National institute of health stroke scale; PSS, perceive stress scale; TACI, total anterior circulation infarction; SOD, stroke of other determined etiology; UD, underlying disease; ZBI, Zarit burden interview.

Table 3. Multiple regression analyses with the Perceived Stress Scale (PSS), Depressive domain on Hospital and Depression Score (HADS-D) and Zarit Burden Interview (ZBI) scores as dependent variables.

Dependent variables	Explanatory variables	β	t	P	F model	df	P	R ²
PSS	Model							
	ZBI (Total)	0.54	6.35	<0.001	20.76	3/90	<0.001	0.409
	Lacunar circulation	0.24	2.96	0.004				
	Infarction	0.17	2.01	0.047				
	Caregiver's U/D							
HADS-D	Model							
	ZBI persstrain	0.28	2.89	0.005	8.03	2/91	0.001	0.150
	SOD	0.28	2.87	0.005				
ZBI	Model							
	Caregiver's U/D	0.28	2.89	0.005	7.14	2/91	0.001	0.136
	NIHSS	0.22	2.21	0.030				

Cg's U/D, Caregiver's underlying disease; HADSdep, HADS depression; NIHSS, the National Institute Stroke Scale; ZBIpersstrain, ZBI personal strain; ZBI (Total), total score of ZBI.

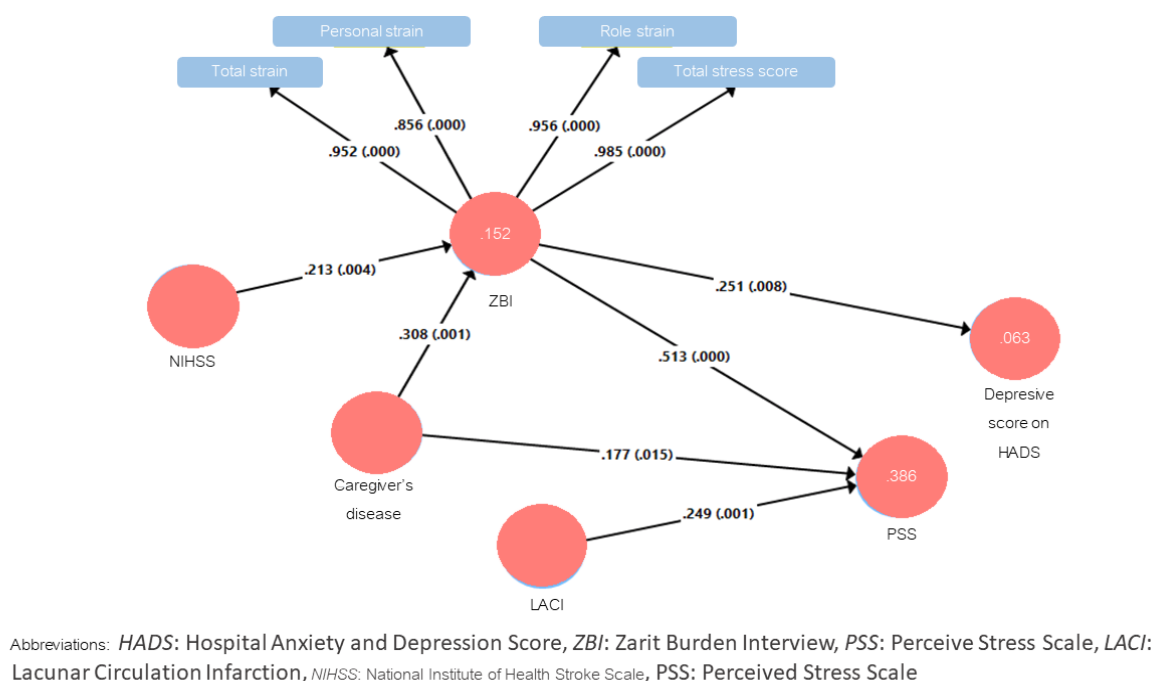


Figure 1. Results of PLS path analysis. PLS, partial least squares.

The PLS-SEM analysis results are shown in **Figure 1**. With AVE = 0.888, Cronbach = 0.954, rho A = 0.960, and composite reliability = 0.967, the construct reliabilities of the ZBI latent vector are good. The outer model loadings on the ZBI latent vector were >0.856 at $P < 0.0001$. The model fit was excellent with SRMR = 0.024. The confirmatory tetrad analysis demonstrated that the outer model was not an undefined reflective model, and the cross-validated redundancies of the latent vectors were more than sufficient. Full compositional invariance was acquired based on the outcomes of prediction-oriented segmentation analysis, measurement invariance assessment, and multigroup analysis. The ZBI latent vector accounted for 6.3% of the variation in the HADS score, whereas the ZBI factor, lacunar circulation infarcts, and caregivers' illness explained 38.6% of the variance in the PSS score. Finally, the NIHSS and caregivers' underlying medical conditions explained 15.2% of the variation in the ZBI factor. The NIHSS ($P = 0.041$) and the caregiver's underlying medical conditions ($P = 0.042$) both had significant specific indirect effects on the HADS score, which was mediated via the ZBI component. The NIHSS also exerted a substantial indirect influence on the PSS ($P = 0.007$), mediated by the ZBI latent vector. Furthermore, the caregiver's underlying medical conditions had a significant, specific, and indirect influence

($P = 0.003$) on the PSS score, revealing that it is a partial mediator. Shown are the path coefficients and exact P -values between brackets and the percentage of variance that is explained (white figures in the circles).

Discussion

We discovered that 7.2% and 17.5% of caregivers had at least moderate depression and anxiety symptoms, respectively. The caregiver's burden, as measured by the ZBI, influenced the depression HADS score, and the patient's impairment and caregiver's underlying medical conditions were indirectly related to the depression scores and were mediated by the burden load. Our findings support previous research indicating that the degree of reliance and caregiving strain is related to sadness and anxiety symptoms.^(10, 15) Furthermore, in our research, caregiver distress, as measured by the PSS, was positively associated with LACI, caregivers' underlying medical conditions, and caregiver burden, but not with the depressed scores.

Stroke of unknown etiology (SOD), as defined by the TOAST criteria, was linked to caregiver distress, sadness, and anxiety symptoms. This is most likely related to SOD's uncommon etiology and high mortality rate.^(28, 35) Specific cognitive assessments (e.g., anxiety about future care) may moderate this result.

We discovered that the NIHSS score of patients with stroke was substantially related to their caregivers' PSS and HADS ratings and that these effects were mediated by increases in burden as measured by the ZBI. Survivors of ischemic stroke have neurological sequelae of diverse impairments (e.g., visual, movement, tactile sensory, and linguistic impairments), and the degree of stroke, disability, and neurological symptoms (including aphasia) corresponds with the caregiver's burden. Caregiving tasks require verbal communication between the dyad. Failure to follow caregiver instructions and trouble conveying the patient's demands may explain why caregivers of patients with aphasia are more stressed. Furthermore, the duty of caregiving is time-consuming and may be perceived as negative life distress, which may result in the deterioration of the caregiver's mental health.^(10, 36, 37) The relationship between the survivor's physical health and the caregiver's mental health is most likely why caregivers with underlying medical conditions feel more burdened. Surprisingly, relative caregivers who get caregiving assistance exhibited a greater proportion of anxiety symptoms. Because caregiving entails stressful tasks (e.g., physically and emotionally supporting the patient), and anxiety is a response to perceived future threat, a familiar caregiver may respond more effectively to the patient's needs.⁽³⁸⁾ Because caregivers recruited in our study were required to have the most contact time with the patient, delegating care to those who are inexperienced may leave the primary caregivers fearful of what could potentially go wrong.

The comprehensive coverage of possible covariates (patient and caregiver) and the use of PLS-SEM to improve methodological validity are the study's strengths. However, our research has limitations. First, because this was cross-sectional research, no causal relationship between these variables and symptoms can be established. Second, the main tool we used (HADS) was established for the Western general population and has not been validated in Thai patients with illness or healthy Thai individuals. This raises the question of whether the claimed prevalence exceeds that of the overall population. Many factors might contribute to our study's reduced prevalence of depressed and anxiety symptoms when compared to the previous meta-analysis.⁽¹⁴⁾ The self and public stigma of mental illnesses persists, with 43.0% of people failing to report symptoms of depression to their primary care physician,⁽³⁹⁾ and this decreased occurrence might be attributed to cultural differences.

Furthermore, in our survey, the average household size was four people, which is larger than that in Western countries. There is some evidence that a close bond among family members might lower the risk of depression.⁽⁴⁰⁾ In addition, HADS is a screening tool that motivates physicians to conduct a fuller review. According to the DSM/ICD criteria, the prevalence of both symptoms based on the HADS cannot substitute for a clinical diagnosis of severe depression and anxiety disorders. Furthermore, the characteristics of our participants may not accurately reflect those of the Thai community (for example, the household income in our study was double that of the Thai average). As a result, extrapolation of our results may benefit the urban population solely. Moreover, although we identified successive dyads who visited the clinic, they may not accurately reflect all relative caregivers.

This study was conducted in Thailand, where family caregiving is rooted in cultural norms and expectations. In Thailand, caregiving is deeply embedded in cultural and familial expectations, with most caregivers being female relatives who often juggle employment and caregiving responsibilities without receiving formal support. Despite strong family ties, these caregivers face substantial emotional strain, which is compounded by limited access to mental health resources and persistent stigma surrounding psychological distress. Caregivers of patients with stroke are particularly vulnerable, yet their psychological needs are frequently overlooked in clinical practice. This neglect places them at risk of becoming "the next patient." Our findings highlight the urgent need for culturally sensitive psychosocial rehabilitation models tailored to Southeast Asian caregiving structures, where early screening and support could prevent long-term mental health consequences.

This study contributes new evidence by applying PLS-SEM to clarify how stroke severity and caregiver health indirectly influence depression and stress through the caregiver burden, which is an underexplored area in Thai caregiver populations. Our findings address a key knowledge gap by demonstrating that clinical factors translate into psychological symptoms via identifiable mediated pathways. Clinically, these results support the early risk-based screening of caregivers, prioritizing patients with higher NIHSS scores, comorbid medical conditions, or elevated ZBI burden. These identified predictors can guide targeted psychosocial interventions, such as stress management, caregiver

education, and support services, to reduce the downstream depression and anxiety. Integrating brief burden and mood assessments into the routine follow up of patients with stroke may enhance caregiver well being and prevent escalation of their psychological distress.

This study has several limitations. Its cross-sectional design precludes causal interpretation of the identified associations. The reliance on self reported measures such as the HADS, ZBI, and PSS 10 may introduce underreporting or social desirability bias, especially in cultures where mental health stigma persists. The participants were included from a single tertiary hospital in urban Bangkok with relatively high socioeconomic status, thereby limiting the generalizability of our findings to more diverse or rural caregiver populations. Clinic based consecutive sampling may also exclude highly burdened caregivers who do not attend follow up visits. In addition, the study did not assess potentially important factors, such as coping styles, family dynamics, or access to community support, that may influence caregivers' levels of distress. Finally, although PLS-SEM allowed exploration of indirect pathways, unmeasured confounders may still influence the observed mediation relationships.

Conclusion

The patients' disabilities, dependency, cognition, and stroke phenotypes, and the caregivers' health status and burden, all contribute significantly to the variation in stress and depression scores in caregivers of patients with ischemic stroke. Therefore, screening caregivers of patients with ischemic stroke for the aforementioned variables is crucial.

Author contributions

CT contributed substantially to data curation, statistical support, drafting the initial manuscript, and participating in statistical analysis and interpretation. SW contributed substantially to data presentation and visualization. AC contributed substantially to data curation. CT contributed to drafting the manuscript. MM provided conceptual supervision and contributed substantially to statistical calculations and interpretation. TS secured funding and APC, supervised the research process, and edited the final manuscript critically for important intellectual content. All authors approved the final version submitted for publication and take responsibility for statements made in the published article.

Acknowledgements

The authors would like to express their sincere gratitude to all the stroke survivors and their caregivers who participated in this study. We are especially thankful to the staff at King Chulalongkorn Memorial Hospital for their support during data collection. Special thanks to the Faculty of Medicine, Chulalongkorn University, for providing ethical oversight and guidance throughout the research process. This study would not have been possible without the dedication and cooperation of everyone involved. This study was supported by the Ratchadapiseksompoj Fund, Faculty of Medicine, Chulalongkorn University (grant: RA66/007). This manuscript is a revised version of the first draft previously posted as a preprint at www.preprint.org: DOI:10.20944/preprints202110.0214.v1.

Conflict of interest statement

All authors declare that they have no potential or actual conflicts of interest to disclose regarding the content of this article.

Data sharing statement

All data generated or analyzed in the present study are included in this published article. Further details are available for non-commercial purposes from the corresponding author upon reasonable request.

ORCID

Chanatip Tongyonk  <https://orcid.org/0000-0003-4631-1835>,

Sorawit Wainipitapong  <https://orcid.org/0000-0001-6306-0930>

Chavit Tunvirachaisakul  <https://orcid.org/0000-0001-9356-1461>

Aurauma Chutinet  <https://orcid.org/0000-0002-9762-5562>

Michael Maes  <https://orcid.org/0000-0002-2012-871X>

Thitiporn Supasitthumrong  <https://orcid.org/0000-0001-6555-0781>

References

1. Ovbiagele B, Goldstein LB, Higashida RT, Howard VJ, Johnston SC, Khavjou OA, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. *Stroke* 2013;44:2361–75.

2. GBD 2017 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1859–922.
3. Greenwood N, Mackenzie A. Informal caring for stroke survivors: meta-ethnographic review of qualitative literature. *Maturitas* 2010;66:268–76.
4. Visser-Meily A, Post M, van de Port I, Maas C, Forstberg-Wärleby G, Lindeman E. Psychosocial functioning of spouses of patients with stroke from initial inpatient rehabilitation to 3 years poststroke: course and relations with coping strategies. *Stroke* 2009;40:1399–404.
5. Malhotra R, Chei CL, Menon EB, Chow WL, Quah S, Chan A, et al. Trajectories of positive aspects of caregiving among family caregivers of stroke-survivors: the differential impact of stroke-survivor disability. *Top Stroke Rehabil* 2018;25:261–8.
6. Patten SB, Williams JV, Lavorato DH, Wang JL, McDonald K, Bulloch AG. Descriptive epidemiology of major depressive disorder in Canada in 2012. *Can J Psychiatry* 2015;60:23–30.
7. Graf R, LeLaurin J, Schmitzberger M, Freytes IM, Orozco T, Dang S, et al. The stroke caregiving trajectory in relation to caregiver depressive symptoms, burden, and intervention outcomes. *Top Stroke Rehabil* 2017;24:488–95.
8. Em S, Bozkurt M, Caglayan M, Ceylan Cevik F, Kaya C, Oktayoglu P, et al. Psychological health of caregivers and association with functional status of stroke patients. *Top Stroke Rehabil* 2017;24:323–9.
9. Tsai YC, Pai HC. Burden and cognitive appraisal of stroke survivors' informal caregivers: An assessment of depression model with mediating and moderating effects. *Arch Psychiatr Nurs* 2016;30:237–43.
10. Jessup NM, Bakas T, McLennon SM, Weaver MT. Are there gender, racial or relationship differences in caregiver task difficulty, depressive symptoms and life changes among stroke family caregivers? *Brain Inj* 2015;29:17–24.
11. Hu P, Yang Q, Kong L, Hu L, Zeng L. Relationship between the anxiety/depression and care burden of the major caregiver of stroke patients. *Medicine (Baltimore)* 2018;97:e12638.
12. Denno MS, Gillard PJ, Graham GD, DiBonaventura MD, Goren A, Varon SF, et al. Anxiety and depression associated with caregiver burden in caregivers of stroke survivors with spasticity. *Arch Phys Med Rehabil* 2013;94:1731–6.
13. Hultman MT, Everson-Rose SA, Tracy MF, Lindquist R, Hadidi NN. Associations between characteristics of stroke survivors and caregiver depressive symptoms: a critical review. *Top Stroke Rehabil* 2019;26:528–37.
14. Loh AZ, Tan JS, Zhang MW, Ho RC. The Global prevalence of anxiety and depressive symptoms among caregivers of stroke survivors. *J Am Med Dir Assoc* 2017;18:111–6.
15. McCurley JL, Funes CJ, Zale EL, Lin A, Jacobo M, Jacobs JM, et al. Preventing chronic emotional distress in stroke survivors and their informal caregivers. *Neurocrit Care* 2019;30:581–9.
16. Maggio MG, Corallo F, De Francesco M, De Cola MC, De Luca R, Manuli A, et al. Understanding the family burden and caregiver role in stroke rehabilitation: insights from a retrospective study. *Neurol Sci* 2024;45:5347–53.
17. Oosterveer DM, Mishre RR, van Oort A, Bodde K, Aerden LA. Anxiety and low life satisfaction associate with high caregiver strain early after stroke. *J Rehabil Med* 2014;46:139–43.
18. Boerboom W, Jacobs EA, Khajeh L, van Kooten F, Ribbers GM, Heijenbrok-Kal MH. The relationship of coping style with depression, burden, and life dissatisfaction in caregivers of patients with subarachnoid haemorrhage. *J Rehabil Med* 2014;46:321–6.
19. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;24:385–96.
20. Wongpakaran N, Wongpakaran T. The Thai version of the PSS-10: An investigation of its psychometric properties. *Biopsychosoc Med* 2010;4:6.
21. Bédard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. *Gerontologist* 2001;41:652–7.
22. Cheah WK, Han HC, Chong MS, Anthony PV, Lim WS. Multidimensionality of the Zarit Burden Interview across the severity spectrum of cognitive impairment: an Asian perspective. *Int Psychogeriatr* 2012;24:1846–54.
23. Silpakit O, Silpakit C, Chomchuen R. Psychometric study of the Thai version of Zarit Burden Interview in psychiatric caregivers. *J Ment Health Thai* 2015;23:12–24. (in Thai)
24. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
25. 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;52:69–77.
26. Nilchaikovit T, Lotrakul M, Phisansuthideth U. Development of Thai version of hospital anxiety and depression scale in cancer patients. *J Psychiatr Assoc Thai* 1996;41:18–30. (in Thai)
27. Yang Y, Wang A, Zhao X, Wang C, Liu L, Zheng H, et al. The Oxfordshire Community Stroke Project classification system predicts clinical outcomes following intravenous thrombolysis: a prospective cohort study. *Ther Clin Risk Manag* 2016;12:1049–56.

28. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35–41.
29. Harrison JK, McArthur KS, Quinn TJ. Assessment scales in stroke: clinimetric and clinical considerations. *Clin Interv Aging* 2013;8:201–11.
30. Balu S. Differences in psychometric properties, cut-off scores, and outcomes between the Barthel Index and Modified Rankin Scale in pharmacotherapy-based stroke trials: systematic literature review. *Curr Med Res Opin* 2009;25:1329–41.
31. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
32. Train The Brain Forum Committee. Thai mental state examination (TMSE). *Siriraj Hospital Gazette* 1993;45:359–74. (in Thai)
33. Hemrungronj S, Tangwongchai S, Charoenboon T, Panasawat M, Supasitthumrong T, Chaipresertsud P, Maleevach P, Likitjaroen Y, Phanthumchinda K, Maes M. Use of the Montreal Cognitive Assessment Thai Version to discriminate amnesic mild cognitive impairment from alzheimer's disease and healthy controls: machine learning results. *Dement Geriatr Cogn Disord* 2021;50:183–94.
34. Shmueli G, Sarstedt M, Hair JF, Cheah J, Ting H, Vaithilingam S, et al. Predictive model assessment in PLS-SEM: Guidelines for Using PLSpredict. *Eur J Mark* 2019;53:2322–47.
35. Wei W, Li S, San F, Zhang S, Shen Q, Guo J, et al. Retrospective analysis of prognosis and risk factors of patients with stroke by TOAST. *Medicine (Baltimore)* 2018;97:e0412.
36. Tooth L, McKenna K, Barnett A, Prescott C, Murphy S. Caregiver burden, time spent caring and health status in the first 12 months following stroke. *Brain Inj* 2005;19:963–74.
37. Haley WE, Allen JY, Grant JS, Clay OJ, Perkins M, Roth DL. Problems and benefits reported by stroke family caregivers: results from a prospective epidemiological study. *Stroke* 2009;40:2129–33.
38. Robertson JJ, Long B. Suffering in silence: Medical error and its impact on health care providers. *J Emerg Med* 2018;54:402–9.
39. Corrigan PW, Watson AC. Understanding the impact of stigma on people with mental illness. *World Psychiatry* 2002;1:16–20.
40. Werner Seidler A, Afzali MH, Chapman C, Sunderland M, Slade T. The link between social support networks and depression in the 2007 National Survey of Mental Health and Well Being. *Soc Psychiatry Psychiatr Epidemiol* 2017;52:1463–73.