The Validity and Reliability of the Patient Health Questionnaire-9 in Screening for Post-stroke Depression

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Abstract

Depression affects about 30% of stroke survivors within five years. Timely diagnosis and management of post-stroke depression (PSD) facilitate motor recovery and improve independence. The original version of the Patient Health Questionnaire-9 (PHQ-9) is one of the good screening tools for post-stroke depression. As yet, no validation studies of depression in Thai stroke patients by the Thai PHQ-9. Methods: The objectives of the study were to determine the criterion validity and reliability of the Thai PHQ-9 in screening for post-stroke depression by comparing with a psychiatric interview as the gold standard. First-ever stroke patients aged ≥ 45 years with a stroke duration 2 weeks–2 years were administered the Thai PHQ-9. The gold standard was a psychiatric interview leading to a DSM-5 diagnosis of depressive disorder. The summed-scored based diagnosis of depressive disorder with the PHQ-9 was obtained. The validity and reliability analyses, and a receiver operating characteristic curve analysis, were performed. Results: 115 stroke patients (mean age, 64 ± 10 years) were enrolled. The mean PHQ-9 score was 5.2 ± 4.8 . Using DSM-5 criteria, 23 patients (20%) were diagnosed with depressive disorder. The Thai PHQ-9 had satisfactory internal consistency (Cronbach's alpha, 0.78). The algorithm-based diagnosis of the Thai PHQ-9 had low sensitivity (0.52) but very high specificity (0.94) and positive likelihood ratio (9.6). Used as a summed-scored based diagnosis, an optimal cut-off score of six revealed a sensitivity of 0.87, specificity of 0.75, positive predictive value of 0.46, negative predictive value of 0.95, and positive likelihood ratio of 3.5. The area under the curve was 0.87 (95% CI, 0.78–0.96). Conclusions: The PHQ-9 (Thai language version) has acceptable psychometric properties for screening for post-stroke depression, with a recommended cut-off score of 6 or greater in a Thai population. Keywords: depression, Patient Health Questionnaire-9, reliability, screening, stroke, Thai, validity

Background

Depression is the most common psychological problem experienced by survivors of a stroke.¹ The pool frequency is 31% of stroke survivors at any time up to five years after their stroke.² However, the review of prospective longitudinal research³ showed that there was a biphasic pattern in post-stroke depression rates. The depressive symptoms would rise in the first 6 months, drop slightly around 12 months, and rise again within the second year after stroke. Post-stroke depression (PSD) is associated with longer length of hospital stay, decreased participation in rehabilitation programs, resulting in less functional improvement.^{4,5} After patients are discharged, they tend to become physically inactive and socially isolated.⁶ Depressed patients had less daily activities, and a lower quality of life.⁷ This may lead to more cognitive impairment,⁸ and increased mortality during the 2–5 year period following a stroke.⁹

It is difficult to make a diagnosis of depression after stroke because the symptoms of depression can be confused with certain symptoms that are typical of stroke patients.¹⁰ For example, swallowing impairment after stroke can cause weight loss, yet a stroke patient might be suffering from loss of appetite resulting from depression. Clinicians would tend to pay more attention to a stroke as an etiology to a swallowing impairment than to ruling out other possibilities. Similarly, in solely considering weakness, reduction in physical movement, and fatigue as the consequence of the stroke, it omits the fact that such symptoms are found in the DSM-5 criteria for depressive disorder.

Screening for mood disorders after stroke is recommended by many stroke and stroke-rehabilitation guidelines.^{11,12} Given that the availability of psychiatrists is limited in Thailand, there is a need for a screening tool to assist primary care physicians and other specialists to assess for depression. Currently, several depression screening tools have been translated into Thai and are used for the general population.¹³ The tool selected for this study was the Patient Health Questionnaire-9 (PHQ-9). The original version was studied in primary care patients.¹⁴ It has been validated

with the structured diagnostic interview for the diagnostic and statistical manual of the mental disorders fourth edition (DSM-IV) for major depressive disorder in stroke patients.¹⁵ Extensively studied in the non-Thai population and post-stroke patients, it has been reported to be one of the good PSD screening tools with the highest sensitivity.^{16, 17} The PHQ-9 has been translated into Thai and validated in primary care patients.¹⁸ The cut-off score of the Thai PHQ-9 for major depression in primary care patients is 9 and greater, which differs from the original version of the PHQ-9.¹⁴ As to PSD, Williams et al¹⁹ reported a cut-off score for the original version of 10 for diagnosis of major depression, with a sensitivity of 91% and a specificity of 89%. However, the PHQ-9 has not been validated for PSD among Thais. Because Thailand and western countries have different health care systems, cultures, attitudes, mindsets, and family support systems, this study investigated the validity and reliability of the PHQ-9 in screening for PSD among Thais.

Methods

Subjects and procedures

Ethics approval was obtained from the Medical Ethics Committee of the Human research protection unit, Faculty of Medicine Siriraj hospital which is a medical ethical committee of Faculty of Medicine Siriraj Hospital (COA no.623/2017). The patients were recruited between November 2017 to December 2018 from the Department of Rehabilitation Medicine, Faculty of Medicine Siriraj Hospital which served as a tertiary hospital in Thailand and gave written consent to participate. All participants were informed that their emotional status would be assessed with a questionnaire and a psychiatric interview. The patient inclusion criteria were age ≥ 45 years; having first-time stroke as per WHO criteria,²⁰ with a stroke duration 2 weeks - 2 years; stable of vital signs, neurological signs and symptoms of stroke defined by a neurologist; and the ability to communicate in Thai. Excluded were patients with cognitive impairment score of < 24 , as measured by the Thai Mental State Examination,²¹ or a previous diagnosis of dementia, a psychiatric disorder, or another neurological disease.

Demographic characteristics were gathered from interviews with the enrolled patients, and information related to their stroke (such as any comorbid illnesses, and the types of stroke diagnosed from imaging studies) were obtained from medical records. The Modified Rankin Scales (MRS) were also obtained to determine the level of disability of the participants. The Thai PHQ-9¹⁸ was administered by one of the researchers (PD) at either inpatient rehabilitation ward or outpatient rehabilitation clinic depending on the patients' visit. On the same day, a psychiatrist interviewed each patient in a private area and gave a diagnosis according to the DSM-5 criteria. The researcher and a psychiatrist were blind to each other's assessment.

Measures

Thai Mental State Examination (TMSE)²¹

TMSE is the first neuropsychiatric test for the standard mental status examination for Thai people. The maximum score of TMSE was 30 points. The cut-off point for the diagnosis of normal healthy Thai elderly was 24 points.

Modified Rankin Scale (MRS)

The Modified Rankin Scale (MRS) is a clinician-reported measure of global disability and has been widely applied for evaluating recovery from stroke.^{22, 23} It is an ordinal scale with 7 categories ranging from zero (no symptoms) to six

(death). The MRS assesses ability to ambulate and complete activities of daily living. MRS scores greater than 3 are defined as disability.²⁴

Thai Patient Health Questionnaire-9 (PHQ-9)¹⁸

The PHQ-9 consists of 9 questions based on the 9 DSM-IV criteria for major depressive disorder. It refers to symptoms experienced by the patients during the two weeks prior to answering the questionnaires. Scores for each item in the PHQ-9 range from 0 (not at

all), to 1 (several days), 2 (more than half of the days) and 3 (nearly every day). The PHQ-9 also provides a preliminary diagnosis of “major depressive disorder” using an algorithm based diagnosis (≥ 5 items, including Items 1 and/or 2, are rated ≥ 2) and the score rated would be 10 or greater. It can be used as a screening tool for diagnosis of depression with summed-score based algorithm. The summed-score ranges from 0 to 27. Various cut-off scores allow for determination of different degrees of depression. The study of Thai PHQ-9 among general Thai population reported summed score of 9 or greater for detecting major depressive disorder with a sensitivity of 0.84 and specificity of 0.77.

DSM-5 criteria for depressive disorder

The DSM-5 criteria for depressive disorder was used as a reference standard.²⁵ The psychiatric interview was performed to an individual patient. Three psychiatrists had a process of standardization on their interviews to one another. The depressive disorder could occur in major depressive disorder, persistent depressive disorder (dysthymia), depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder.

Data Analysis

PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, Ill., USA)²⁶ and MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium)²⁷ were used for the statistical analyses. The demographic data, MRS, and PHQ-9 scores were analyzed by descriptive statistics. The quantitative data (age) was analyzed by an independent-sample t-test, while the stroke durations and PHQ-9 scores were analyzed with the Mann–Whitney U test. The qualitative data (gender, education levels, risk factors, pathology of stroke, side of weakness, and MRS scale) were analyzed by Chi-square.

The stroke patients were divided into normal and depression groups according to psychiatric diagnosis. The psychiatrist determined types of depressive disorders according to the DSM-5 criteria for depressive disorder. The depression scores of the normal and depression groups were analyzed by the independent-sample t-test. All analyses were significant at a p-value of < 0.05 . Internal consistency was analyzed by Cronbach's alpha. As a bivariate response, the psychiatric diagnosis of depression was used as the reference standard to calculate the sensitivities and specificities of all possible PHQ-9 cutoff scores. The positive and negative predictive values as well as the positive and negative likelihood ratios were calculated for each PHQ-9 cut-off score. The ROC analyses combined instrument sensitivity and specificity into one measure (referred to as the area under the curve, or AUC) for all possible cut-off scores.

Results

In all, 190 stroke patients were approached for participation. Seventy-five of these were excluded: 21 had recurrent stroke, 17 had cognitive impairment, 17 had aphasia, 10 were < 45 years, and 10 had a stroke duration > 2 years (Fig 1). After applying an exclusion criteria, 115 stroke patients were enrolled, there were 63 males (54.8%) and 52 females (45.2%), with a mean age of 64 ± 10 years (min, max: 45,88). The majority had graduated primary school, followed by lower-secondary school and upper-secondary school. The comorbid illnesses found were, in descending order of frequency, hypertension, dyslipidemia, diabetes mellitus, and heart disease. The median duration of stroke was 59 days. Most patients (81.7%) suffered from ischemic stroke, and left-side weakness was dominant (61%). Most patients (65.2%) were recruited from inpatient rehabilitation.

All patients were administered the PHQ- 9 as the index test. The reference standard was a psychiatric interview with diagnoses based on the DSM-5 criteria on the same day. This was administered blind to, and regardless of, scores on the index test. The mean PHQ-9 score was 5.2 ± 4.8 . According to the DSM-5 criteria, 23 patients (20%) had PSD, while 92 (80%) were normal. In the PSD group, 8 (6.9%) were diagnosed with MDD, 2 (1.7%) had depressive disorder not otherwise specified, and 1 (0.9%) had other specified depressive disorder and 12 patients (10.5%) had adjustment disorder with depressed mood.

The demographic characteristics of the normal and depression groups revealed no statistically significant (age, gender, education level, risk factors, median duration after stroke, pathology of stroke, side of weakness, and settings of the patients). However, the MRS and the median PHQ-9 scores of the groups differed. MRS scores of 0–3 were defined as no disability, while an MRS score > 3 was defined as disability; more stroke patients were disabled in the depression group (78%) than in the normal group (55.4%).

Reliability and item analysis

As shown in Table 1, the highest mean score of the nine PHQ-9 items was found for item 3 (“trouble falling or staying asleep, or sleeping too much”). Item 9 (“thoughts that you would be better off dead or of hurting yourself”) had the lowest score. As to the internal consistency of the PHQ-9, Cronbach’s alpha was 0.78. All items, if deleted, would consistently decrease the total scale alpha. The least item-total correlation was item 5 poor appetite or overeating.

Table 1 Mean score, standard deviation and internal reliability score for the PHQ-9 score

PHQ-9 items	mean	Standard Deviation	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
1. Little interest or pleasure in doing things	0.72	0.881	0.612	0.708
2. Feeling down, depressed, or hopeless	0.64	0.926	0.516	0.723
3. Trouble falling or staying asleep, or sleeping too much	1.11	1.256	0.404	0.749
4. Feeling tired or having little energy	0.68	0.984	0.321	0.755
5. Poor appetite or overeating	0.47	0.955	0.199	0.773
6. Feeling bad about yourself – or that you are a failure	0.71	1.015	0.612	0.704
7. Trouble concentrating on things	0.27	0.641	0.345	0.749
8. Moving or speaking so slowly that other people have noticed	0.35	0.731	0.555	0.722
9. Thoughts that you would be better off dead or of hurting yourself	0.25	0.662	0.525	0.729

Validity analysis

The performance of the PHQ-9 against the diagnosis of depressive disorder by the DSM-5 criteria for depressive disorder as a criterion standard was examined. According to the DSM-5 criteria, 23 patients (20%) met the diagnosis of post-stroke depression. The median PHQ-9 score for the depression group was 10 (IQR_{25,75}: 7,15) whereas the median score of the normal group was 4 (IQR_{25,75}: 0.5,5.75). These median PHQ-9 score showed statistically different between 2 groups.

Table 2 The performance of different PHQ-9 cut-off scores in detecting depression

Score	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)	Positive predictive value (%) (95%CI)	Negative predictive value (%) (95%CI)	Positive likelihood ratio (95%CI)	Negative likelihood ratio (95%CI)	Accuracy (95%CI)	Youden's index
The algorithm-based diagnosis								
≥10	34.8 (16.4, 57.3)	97.8 (92.4, 99.7)	80.0 (47.6, 94.6)	85.7 (81.6, 89.0)	16.0 (3.6, 70.3)	85.7 (81.6, 89.0)	85.2 (77.4, 91.2)	-----
The summed item based diagnosis								
≥5	91.3 (71.9, 98.9)	65.2 (54.6, 74.8)	39.6 (32.6, 47.2)	96.8 (88.8, 99.1)	2.62 (1.9, 3.6)	0.13 (0.04, 0.5)	70.4 (61.2, 78.6)	0.565
≥6	87.0 (66.4, 97.2)	75.0 (64.9, 83.4)	46.5 (37.1, 56.2)	95.8 (88.8, 98.5)	3.5 (2.4, 5.1)	0.2 (0.1, 0.5)	77.4 (68.6, 84.7)	0.620
≥7	78.3 (56.3, 92.5)	81.5 (72.1, 88.8)	51.4 (39.6, 63.1)	93.8 (87.3, 97.0)	4.2 (2.6, 6.8)	0.3 (0.1, 0.6)	80.9 (72.5, 87.6)	0.598
≥8	65.2 (42.7, 83.6)	83.7 (74.5, 90.6)	50.0 (36.6, 63.4)	90.6 (84.5, 94.4)	4.0 (2.3, 6.9)	0.42 (0.2, 0.7)	80.0 (71.5, 86.9)	0.489
≥9	56.5 (34.5, 76.8)	90.2 (82.2, 95.4)	59.1 (41.4, 74.7)	89.3 (83.8, 93.0)	5.8 (2.8, 11.8)	0.5 (0.3, 0.8)	83.5 (75.4, 89.7)	0.467
≥10	52.2 (30.59, 73.2)	94.6 (87.7, 98.2)	70.6 (48.4, 85.9)	88.8 (83.7, 92.4)	9.6 (3.7, 24.5)	0.5 (0.3, 0.8)	86.1 (78.4, 91.8)	0.467

The validity of the index test PHQ-9, using algorithm-based diagnosis, had a sensitivity of 34.8%, specificity of 97.8%, positive predictive value (PPV) of 80%, and negative predictive value (NPV) of 85.7%, and positive likelihood ratio of

16.0 (table 2). When using the summed-score based diagnosis, a sensitivity, specificity, PPV, NPV, and likelihood ratio of different PHQ-9 thresholds in diagnosing PSD showed in table 2. At the cutoff score of 6 showed the highest Youden's index. This cutoff score had a sensitivity of 87.0 % (95% CI=66.4, 97.2), specificity of 75.0% (95% CI=64.9, 83.4), positive predictive value of 46.5% (95% CI=37.1, 56.2), negative predictive value of 95.8% (95% CI=88.8, 98.5), positive likelihood ratio of 3.5 (95% CI=2.4, 5.1), and negative likelihood ratio of 0.2 (95%CI=0.1, 0.5). The ROC curve illustrates that the PHQ-9 performed well in identifying patients with PSD (figure 2). The area under the curve (AUC) in our study was 0.87 (95%CI=0.78,0.96) which demonstrated good discrimination.

Discussion

This study was the first in Thailand to determine the validity of a depression screening questionnaire with stroke patients. The questionnaire investigated was the PHQ-9, one of the good screening tools for PSD.¹⁶ The reference standard was a psychiatric interview according to the DSM-5 criteria for depressive disorder. In this study, the validity of the PHQ-9 in screening post-stroke depression was good in term of its discriminatory power (AUC=0.87) relative to the gold standard, DSM-5 criteria. In addition, its internal consistency was acceptable (Cronbach's alpha=0.78).

Based on the DSM-5 criteria, PSD was found in 23 patients (20%) which was less than the previous studies. A meta-analysis conducted by Hackett and Pickles²⁸ found that 31% of stroke patients developed depression diagnosis or depressive symptom in any setting at any time up to 5 years following their stroke. Robinson²⁹ undertook a pool analysis and reported mean incidence for major and minor depression of 19.3% and 18.5% respectively, among hospitalized patients in acute or rehabilitation hospitals. By comparison, the low incidence in the present study probably stemmed from having the inclusion criterion that only stroke patients be aged ≥ 45 years. Previous research found that younger stroke survivors were more likely to become depressed than older survivors.^{30,31} Nevertheless, the incidence established by the current study was in line with that of research by Fuentes et al., which recruited stroke patients of the same age group and found a low depression incidence of 9.9%.³²

Moving on to the demographic characteristics of stroke patients with and without PSD, our study revealed no significantly different of demographic-related variables between groups.

For the disability-related variable, the Modified Rankin Scale (MRS) is used to determine the level of disability after stroke. The patients with MRS score >3 who were classified as having disability appeared more frequently in the depression group. PSD has been found to be associated with more severe neurological deficit and physical disability in the acute and chronic phases.³³ Consistent with a meta-analysis of longitudinal studies, Blöchl et al³⁴ found that depressed stroke patients were generally more disabled.

The internal consistency of the PHQ-9 administered among stroke patients in this study was 0.78 which is considered acceptable. However, the level of internal consistency differed from the original version of the PHQ-9. The original studies, performed in primary care and obstetrics and gynecology, showed internal consistency of 0.89 and 0.86 respectively.¹⁴ In addition, Turner et al, who employed PHQ-9 to screen for PSD, found an internal consistency of 0.82.¹⁵ In the case of the Thai version of the PHQ-9, a validity study on the Thai population reported an internal consistency of 0.79.¹⁸ Later Lee and Dajpratham, who employed the Thai version on elderly Thais, reported an internal consistency of 0.76.³⁵ In the present study, the internal consistency was 0.78, which is highly congruent with those two previous studies using the Thai version of the PHQ-9.

The Thai PHQ-9 can be used as a screening tool since the AUC showed a good level of discriminatory power (AUC, 0.87). The result of this study was in line with other studies that reported a good discriminatory power of the PHQ-9,

with AUC > 0.8.^{15, 19, 36-38} As to its validity, PHQ-9 score can be used in 2 ways to diagnose depression. The first way is an algorithm-based diagnosis with cut-off score of 10 to diagnose major depression. In 2015, Manea et al.³⁹ conducted a diagnosis meta-analysis of the PHQ-9 algorithm-based scoring method as a screening for depression. They found that the sensitivity was as low as 53% (95%CI, 42-65) whereas the specificity was as high as 94% (95%CI, 91-96). Our study applied the algorithm-based diagnosis of PSD in the setting of tertiary hospital. The diagnostic accuracy revealed low sensitivity and high specificity (table 2) as of the result from the study of Manea et al.³⁹ The low sensitivity is not a good property of a screening tool. Therefore, all the previous validation studies of PHQ-9 in detecting PSD used summed-scored based diagnosis to compare with various structured interviews as their reference standard.^{15, 19, 36, 38, 40} Pettersson et al.⁴¹ performed a systematic review to explore the diagnostic accuracy of the structured interviews as index tests. The structured interviews which had sufficient accuracy for depression diagnosis were only the Structured Clinical Interview for DSM-IV (SCID) and the Mini International Neuropsychiatric Interview (MINI). The summed-scored based diagnosis of PHQ-9 in this study was validated with the DSM-5 criteria interviewed by the psychiatrist and revealed the optimum cutoff score of 6 to diagnose depression. This finding was different from the previous studies.^{15, 19} Turner et al.¹⁵ validated the PHQ-9 with the DSM-IV criteria in detecting PSD and reported the summed score greater than 8 as the cut-off score for diagnosis. Meanwhile, Williams et al.¹⁹ validated the PHQ-9 with the DSM-IV criteria in detecting PSD and reported the summed score of 10 and greater as the cut-off score for diagnosis.

There were some limitations of this study. Firstly, the mean age of the participants was 64 years old meant that the findings cannot be generalized to the younger stroke patients. However, the incidence of stroke in the younger age was lower and made up of small number in clinical practice. Secondly, only participants who could communicate were recruited. The stroke patients who cannot communicate would probably be very depressed. Moreover, the mood assessment scale for patients who cannot communicate is different. Thirdly, this study did not perform test-re-test reliability. It remains that temporal stability of the measure in Thai people with a stroke is unknown.

Conclusion

The Thai version of the PHQ-9 had good validity and acceptable reliability for screening PSD. The summed-scored based depression diagnosis should be employed for screening and the cutoff score of 6 were positive for post-stroke depression.

Abbreviations

he Patient Health Questionnaire 9: PHQ-9; positive predictive value: PPV; negative predictive value: NPV; area under the curve: AUC; receiver operating characteristic curve: ROC; the Structured Clinical Interview for DSM-IV (SCID) and the Mini International Neuropsychiatric Interview (MINI).

Declarations

Ethics approval and consent to participate

Ethics approval was obtained from the Medical Ethics Committee of the Human Research Protection Unit, Faculty of Medicine Siriraj hospital which is a medical ethical committee of Faculty of Medicine Siriraj Hospital (COA no.623/2017). All the participants gave written consents to participate.

Consent for publication

Consent for publication was "Not applicable".

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Competing Interests

The authors declare that they have no competing interests.

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No funding was obtained for this study.

Authors' contribution

PD conceived the study, design protocol, analyzed the data, and prepared the manuscript. PP participated in the study design, designed protocol, assisted in data collection, and gave comment on the manuscript. WA participated in the study design, assisted in data collection, and gave comment on the manuscript. KW participated in the study design, assisted in data collection, and gave comment on the manuscript. JB designed protocol and gave comment on the manuscript. KP designed protocol and gave comment on the manuscript. All authors have read and approve the final version of the manuscript.

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Figures

Figure 1

Flow diagram of participants

Figure 2

The receiver operating characteristic curve of the PHQ-9 in screening depression among stroke patients.