Psychometric Properties of the PHQ-9, HADS, and CES-D Questionnaires and the Prevalence of Depression in Patients with Cancer Receiving Radiotherapy

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ABSTRACT

Objective: The primary aim was to compare the psychometric properties among the Patient Health Questionnaire (PHQ-9) (both including and excluding somatic symptom items), the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D), and the Center for Epidemiologic Studies Depression Scale (CES-D) in detecting depression in cancer patients receiving radiotherapy. The secondary aim was to investigate the prevalence of depression in this group of patients.

Materials and Methods: Overall, 198 participants with cancer diagnosis from a radiotherapy clinic took part in the study. They completed PHQ-9, HADS-D, and CES-D questionnaires and were interviewed in line with the Mini-International Neuropsychiatric Interview (M.I.N.I.) to confirm the diagnosis. The PHQ-9 was analyzed for three scoring methods: sum-score, inclusive (including all items), and exclusive (excluding 4 somatic symptom items) methods. The psychometric properties of each questionnaire were analyzed. The prevalence of depression measured by the M.I.N.I. was evaluated.

Results: The sum-score method of the PHQ-9 had an equal sensitivity (100%) to the HADS-D and CES-D, and had a slightly higher specificity (91.1%) than the HADS-D (87.4%) and CES-D (90.6%). When compared results within the PHQ-9, the sum-score method had greater sensitivity than the inclusive (71.4%) and exclusive (42.9%) methods, and had a slightly lower specificity than the inclusive (96.9%) and exclusive (97.4%) methods. The prevalence of depression assessed by the M.I.N.I was 3.5%.

Conclusion: The sum-score method of the PHQ-9 seemed to be the best tool to use for depression screening in cancer patients receiving radiotherapy due to its excellent sensitivity and specificity.

Keywords: PHQ-9; HADS; CES-D; Depression; Cancer; Radiotherapy (Siriraj Med J 2021; 73: 793-800)

INTRODUCTION

Depression is a common problem in patients with cancer. In one meta-analysis, the prevalence of depression among cancer patients was found to be 14.9%.[1] It has been reported that depression increases the mortality rate[2], decreases the quality of life[3], and decreases the will to live of patients with cancer.[4,5] So, effective screening for depression is required among patients with cancer.

The depression screening tools commonly used in patients with cancer include the Patient Health Questionnaire (PHQ-9)[6], Hospital Anxiety and Depression Scale (HADS)[7], and Center for Epidemiologic Studies Depression Scale

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(CES-D).[8] The PHQ-9 was developed based on the major depressive episode criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV-TR). It is a 9-item self-report questionnaire, which can be scored using a sum-score method or a DSM IV-TR-based algorithm. It has shown satisfactory concurrent and discriminant validity and also reliability when validated in patients with cancer.[9] The HADS is also a self-report questionnaire, consisting of 14 items divided into depression and anxiety subscales. It was developed for screening depression and anxiety in a general medical population. Validation studies of the HADS in cancer patients showed it had a stable factor structure, moderate to high discriminant validity, and adequate internal consistency.[9] The CES-D is a 20-item self-report questionnaire developed for screening depression in a general medical population and in patients with cancer.[10] Results from validation studies in cancer patients demonstrated its good sensitivity, specificity, and internal consistency.[9] Although all these three self-report questionnaires are easy to complete by patients with physical illnesses and have been validated in cancer populations, there is no consensus on which screening tool is preferred for screening depression in cancer patients.

Screening as well as diagnosing depression in patients with cancer is challenging as cancer can produce somatic symptoms that are similar to somatic symptoms of depression, such as a decreased appetite, weight loss, sleep problems, and fatigue.[11] Suggestions have been made to exclude these somatic symptoms when evaluating depression in cancer patients. Indeed, a previous study of the PHQ-9 tried to explore the effect of excluding somatic symptom items on detecting depression. In that study, 4 somatic symptom items, namely decreased appetite, sleep problems, fatigue, and psychomotor retardation, were excluded from the questionnaire and depression was diagnosed when 3 of the remaining 5 items were present. The results demonstrated that excluding those items when assessing somatic symptoms of depression had very little effect on detecting depression.[12] However, the limitation of that study was that the gold standard used for validity testing was not a structured diagnostic interview.

Since there is insufficient evidence for making a recommendation about which depression screening tool should be used in patients with cancer, this study aimed to compare the psychometric properties of the PHQ-9, HADS, and CES-D in detecting depression in cancer patients in a radiotherapy clinic. This study focused on cancer patients in a radiotherapy clinic because these patients represent variations in cancer type and stage. Furthermore, evidence regarding the effect of excluding somatic symptom items from the PHQ-9 remains inconclusive due to the lack of using a diagnostic interview as the gold standard in validity testing. Hence, this study also aimed to compare the psychometric properties of the PHQ-9 between including and excluding somatic symptom items by using a structured diagnostic interview as a gold standard. Finally, this study aimed to investigate the prevalence of depression in cancer patients receiving radiotherapy.

MATERIALS AND METHODS

Participants

Cancer patients with any type and any stage of cancer receiving treatment in a radiotherapy clinic of a tertiary care hospital were recruited from January to April 2020. The calculated sample size was 195. This sample size was calculated by using the Wayne formula and based on a prevalence of depression of 14.9% in cancer patients.[1]

Measures

The Thai version of the PHQ-9, the depression subscale of the HADS (HADS-D), and CES-D were used to assess depression. The Thai version of the Mini-International Neuropsychiatric Interview (M.I.N.I.) was used as the gold standard to confirm a diagnosis of major depressive episodes.

1) PHQ-9

The PHQ-9 is a 9-item self-report questionnaire which can be scored using two methods: a sum-score method with a cut-off score and an algorithm scoring method. In the sum-score method, each item can be rated from 0 to 3, with the total score ranging from 0 to 27. Patients are classified as having depression when the total score of the Thai version of the PHQ-9 is 9 or more.[13] However, the cut-off score used in this study was re-calculated to find the most appropriate cut-off score for cancer patients in this study. In the algorithm scoring method, each item of the PHQ-9 is counted as meeting a criterion if it is rated as 2 or 3. Patients are classified as having depression when 5 of 9 items meet the criteria, one of which must be item 1 (loss of pleasure in doing things) or 2 (depressed mood).[6,14] The algorithm scoring method in this study was split into two sub-methods for analysis: an inclusive and exclusive method. In the inclusive method, all 9 items of the PHQ-9 were included in the assessment. In the exclusive method, 4 items assessing somatic symptoms of depression were excluded in order to prevent false-positive results. These items

were item 3 (sleep problems), 4 (fatigue), 5 (appetite changed), and 8 (psychomotor retardation). Patients were classified as having depression when 3 of the remaining 5 items met the criteria, one of which must be item 1 or 2.[11,12,15]

2) HADS
The HADS is a 14-item self-report questionnaire, with 7 items for the anxiety subscale and 7 items for the depression subscale.[7] However, only the depression subscale of HADS (HADS-D) was used in this study. For each subscale, each item can be rated from 0 to 3, with the total score ranging from 0 to 21. A sum score of 11 or more in the Thai version of the HADS represents depression.[16] However, the cut-off score used in this study was re-calculated, as was also done with the PHQ-9.

3) CES-D
The CES-D is a 20-item self-report questionnaire. Each item can be rated from 0 to 3, with the total score ranging from 0 to 60.[8] A sum score of 19 or more in the Thai version of the CES-D represents depression.[17] However, the cut-off score used in this study was re-calculated, as was also done with the PHQ-9 and the HADS.

4) M.I.N.I.
The Thai version of the M.I.N.I. was translated from the M.I.N.I. 5.0.0/DSM-IV. It is a structured diagnostic interview comprising 16 modules for assessing common psychiatric disorders. In this study, the major depressive episode module was used as the diagnostic tool. This module had a sensitivity of 98% and specificity of 94%.[18]

Data collection

Ethics approval was obtained from the Siriraj Institutional Review Board. All the participants completed the demographic data, PHQ-9, HADS-D, and CES-D questionnaires. They were interviewed using the M.I.N.I. either by a psychiatric resident or a psychologist who had been trained and certified in M.I.N.I.. Both interviewers were blinded from the result of the self-rated questionnaires. If depression was confirmed by M.I.N.I., the interviewers would notify the attending physician to consider referring the participant to consult psychiatrist for evaluation and proper treatment. Data about cancer type, stage, treatment, pain score, and opioid use were obtained from the patients' medical records.

Statistical analysis

The analysis was done with SPSS version 24. By using the M.I.N.I. as the gold standard, the cut-off scores of the PHQ-9, HADS-D, and CES-D were determined by plotting their receiver operating characteristic (ROC) curves. The psychometric properties of each questionnaire were analyzed and demonstrated in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratio. Convergent validity between the PHQ-9 and HADS-D, between PHQ-9 and CED-D, and between HADS-D and CES-D were analyzed by Spearman's rho correlation. The internal consistency of each questionnaire was analyzed by Cronbach's alpha. The prevalence of depression measured by each questionnaire and the M.I.N.I. were evaluated.

RESULTS

In total, 198 participants were enrolled on the study, and their demographic data are shown in Table 1. There was nearly an equal number of female (53.3%) and male (46.5%) participants. Half the participants were more than 60 years old. The majority of participants (86.9%) were recruited from an outpatient clinic. The most common cancer types were breast (27.3%), prostate (13.6%), oro-pharyngo-laryngeal (12.1%), and gastrointestinal cancer (10.1%). The most common stage was the non-metastatic stage (83.8%). Most of the participants did not have pain (62.6%) and did not receive opioids (91.9%).

The most appropriate cut-off scores were 11 for the PHQ-9, 7 for the HADS-D, and 20 for the CES-D. The ROC curves for these cut-off values are displayed in Fig 1. The area under the curve values for each were 0.97 (SD = 0.01; 95% CI 0.94 to 0.99) for the PHQ-9, 0.95 (SD = 0.02; 95% CI 0.91 to 0.98) for the HADS-D, and 0.98 (SD = 0.01; 95% CI 0.95 to 1.00) for the CES-D. All of these values show high accuracy.[19]

The psychometric properties of the PHQ-9, HADS-D, and CES-D are listed in Table 2. The sum-score method used for the PHQ-9, the HADS-D, and the CES-D demonstrated good sensitivity (100%) and good specificity (91.1%, 87.4%, and 90.6%, respectively). Although the inclusive and exclusive methods of the PHQ-9 demonstrated slightly higher specificity than the sum-score method (96.9% for the inclusive method and 97.4% for the exclusive method), their sensitivities were much lower (71.4% for the inclusive method and 42.9% for the exclusive method). Comparing the inclusive and exclusive method, the inclusive method demonstrated greater sensitivity with similar specificity. Convergent validity testing showed good correlations between the PHQ-9 and HADS-D ($r = 0.67$, $p < 0.01$), between the

TABLE 1. Demographic data.

Characteristics (n = 198)	n (%)
Gender	
Female	106 (53.5)
Male	92 (46.5)
Age (mean 59.4, SD 13.3)	
Education	
High school or less	119 (60.1)
Undergraduate degree or more	79 (39.9)
Setting	
Outpatient	172 (86.9)
Inpatient	26 (13.1)
Cancer type	
Breast	54 (27.3)
Prostate	27 (13.6)
Oro-pharyngo-laryngeal	24 (12.1)
Gastrointestinal	20 (10.1)
Gynecologic	19 (9.6)
Lung	16 (8.1)
Brain	14 (7.1)
Others*	24 (12.0)
Disease stage	
Non-metastasis	166 (83.8)
Metastasis	32 (16.2)
Treatment	
Radiotherapy	16 (8.1)
Radiotherapy + Surgery	59 (29.8)
Radiotherapy + Chemotherapy	42 (21.2)
Radiotherapy + Surgery + Chemotherapy	81 (40.9)
Pain (mean 1.76, SD 2.8)	
No pain	124 (62.6)
Mild (Pain score 1-3)	30 (15.2)
Moderate (Pain score 4-6)	23 (11.6)
Severe (Pain score 7-10)	21 (10.6)
Opioids use	
No	182 (91.9)
Yes	16 (8.1)

*Thyroid 7, Hematologic 7, Liver 2, Urinary tract 3, Anus 1, Cholangiocarcinoma 1, Nasal cavity 1, Epithelioid tumor 1, Multiple primary 1.

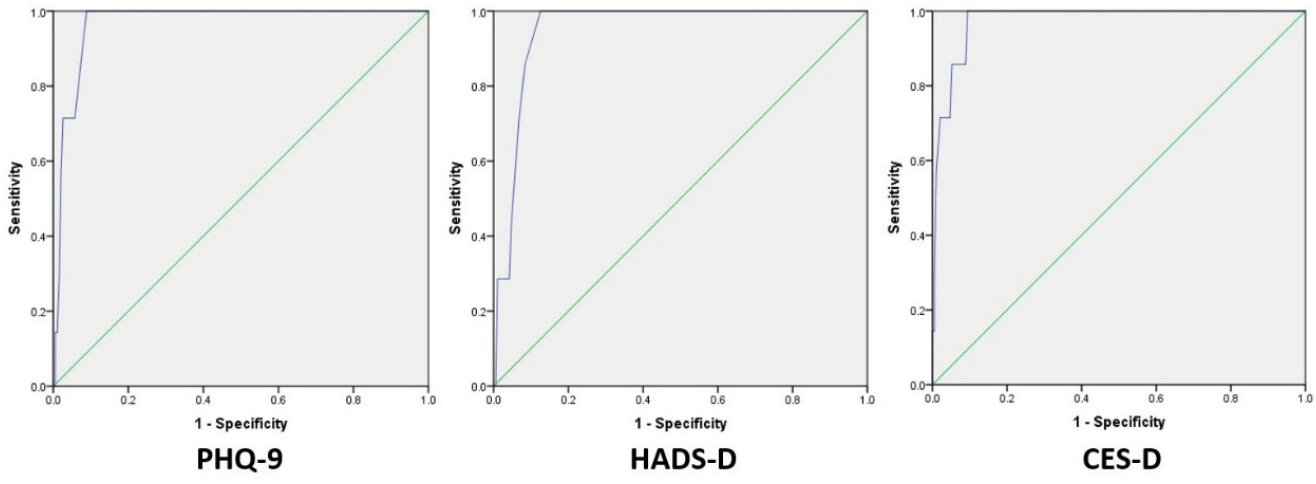

Fig 1. ROC curve

TABLE 2. Psychometric properties.

	Sensitivity	Specificity	PPV	NPV	+ likelihood	- likelihood	Internal consistency (Cronbach's alpha)
PHQ-9							
Sum-score (cut-off 11)	100	91.1	29.2	100	11.2	0	0.804
Algorithm scoring							
Inclusive	71.4	96.9	45.5	98.9	22.7	0.3	-
Exclusive	42.9	97.4	37.5	97.9	16.4	0.6	-
HADS-D (cut-off 7)	100	87.4	22.6	100	8	0	0.772
CES-D (cut-off 20)	100	90.6	28	100	10.6	0	0.815

PHQ-9 and CES-D ($r = 0.68$, $p < 0.01$), and between HADS-D and CES-D ($r = 0.74$, $p < 0.01$). The internal consistencies of the PHQ-9 and CES-D were good (Cronbach's alpha = 0.80 and 0.82, respectively), while the internal consistency of the HADS-D was acceptable (Cronbach's alpha = 0.77).[20]

The prevalence of depression measured by each questionnaire and the M.I.N.I. are presented in Table 3. The prevalence measured by the inclusive method (5.6%) and exclusive method (4.0%) of the PHQ-9 were close to the prevalence measured by the M.I.N.I. (3.5%), which represents the gold standard. However, the prevalence measured by the sum-score methods of the PHQ-9 (12.1%), HADS-D (15.7%), and CES-D (12.6%) were much higher than the prevalence measured by the M.I.N.I..

DISCUSSION

The study aimed to test the psychometric properties of the three self-rating questionnaires PHQ-9, HADS-D, and CES-D for screening depression in cancer patients receiving radiotherapy. The results showed that the psychometric properties, both validity and reliability, of all questionnaires were nearly equivalent. Comparing the sum-score methods of the PHQ-9, HASD-D, and CES-D, the sum-score method of PHQ-9 is recommended for depression screening in cancer patients receiving radiotherapy because it showed high sensitivity and the highest specificity and all of its items are similar to the major depressive disorder criteria of the DSM-5.[14] In addition, because the PHQ-9 consists of 9 items that can be completed within a few minutes, it is convenient

TABLE 3. Prevalence.

	%
M.I.N.I.	3.5
PHQ-9	
Sum-score method	12.1
Algorithm scoring methods	
Inclusive method	5.6
Exclusive method	4.0
HADS-D	15.7
CES-D	12.6

for patients with physical illness. Although the CES-D showed a similar specificity to the sum-score method of the PHQ-9, the major limitation of the CES-D is it is time consuming to complete because it consists of 20 items.

Regarding the PHQ-9, its sum-score method demonstrated a much higher sensitivity but with a similar specificity when compared to the algorithm scoring methods. This finding suggested that the sum-score method is better than the algorithm scoring methods for screening depression in patients with cancer. Comparing the methods within the algorithm scoring methods, the exclusive method had a much lower sensitivity than the inclusive method. This result reflected that the items concerning the somatic symptoms of depression should not be excluded from the PHQ-9 when screening for depression in cancer patients. This finding is supported by evidence from another study which demonstrated that the somatic symptoms of depression were more likely to be present in depressed than in non-depressed cancer patients.[21]

The cut-off scores of the screening tools were different from the recommendation from the previous study. According to our findings, the cut-off scores of the PHQ-9, HADS-D, and CES-D were 11, 7 and 20, respectively, while the cut-off scores of the Thai version recommended in previous studies were 9, 11, and 19, respectively.[13,16,17] One of the reasons for this disparity may be the difference in somatic symptoms in the population between the studies. Previous studies of the Thai version of the PHQ-9 was conducted in family medicine clinic and the CES-D was conducted in general populations which tend to have less somatic symptoms. While the Thai HADS-D study was conducted in in-patients with cancer which tend to have more somatic symptoms. To the best of our knowledge, the present study is the first one to investigate the cut-off score in this specific population.

The prevalence of depression assessed by the structured interview (M.I.N.I.) was nearly equal to the prevalence assessed by the algorithm scoring methods of the PHQ-9. This may be explained by the high specificity of the algorithm scoring methods. Comparing the methods within the algorithm scoring methods, the inclusive method is preferred for assessing the prevalence or diagnostic purpose due to its high specificity and higher sensitivity than the exclusive method. However, inspection of the raw data showed that some patients had a diagnostic mismatch between the M.I.N.I. assessment and the PHQ-9 algorithm scoring methods. Thus, evaluation of the psychometric properties through a diagnostic interview conducted by a psychiatrist as the gold standard should be conducted in a further study in order to confirm whether the PHQ-9 algorithm scoring methods are appropriate for assessing the prevalence of depression in patients with cancer.

In contrast, the prevalence as assessed by the PHQ-9 sum-score method, HADS-D, and CES-D was relatively high when compared with the M.I.N.I. due to the false-positive cases. Since these three questionnaires are scored using a sum-score method, the severity ratings of the somatic symptoms that overlap with cancer symptoms need to be taken into account. As a consequence, cancer symptoms may have an influence on increasing the somatic symptoms scores, leading to false-positive results.[12] We suggest that these three questionnaires may not be appropriate for assessing the prevalence of depression in patients with cancer.

The prevalence of depression assessed by the M.I.N.I. in our study was lower than the average prevalence in a meta-analysis in the literature (3.5% vs. 14.9%).[1] This discrepancy may be due to the difference in cancer stage of participants among the studies. Our study and the studies with a similar prevalence were conducted in patients with cancer of any type and stage, mostly the non-metastatic stage.[22-25] In contrast, the studies with a prevalence of around 14.9% were conducted in cancer patients within 12 months of diagnosis[26], post-treatment cancer patients[27], and patients with recurrent or metastatic cancer.[28] This may imply that patients are more likely to develop depression when initially facing cancer diagnosis and when facing advanced cancer. Therefore, depression screening should be performed within the first year of cancer diagnosis and upon progressing to an advanced stage. Moreover, a systematic review reported that the rate of depression is higher in adolescents and young adults with cancer because of the disruptions in their school life, career path, or early marital life.[29] It can be implied that if we include more young age patients in the study, we will gain more prevalence of depression. Further study should be designed to include patients in all age groups to improve the precision of the results.

Study limitations

Several limitations in the present study should be considered. We use the M.I.N.I. as the gold standard for depression diagnosis instead of using the standard interview by psychiatrists because it consumed much less time when must deal with the high volume of participants. Therefore, it could have some false positive and false negative cases. The sensitivity and specificity in this study may be different from a previous study conducted in a population with a higher prevalence of depression.[30] Hence, further studies should be investigated in cancer patients with a higher prevalence of depression, such as newly diagnosed cancer patients, post-treatment cancer patients, and patients with more advanced-stage cancer. Furthermore, patients in a surgery and chemotherapy clinic should be recruited to apply the results more broadly.

CONCLUSION

The sum-score method of the PHQ-9 seemed to be the best tool to use for depression screening among cancer patients receiving radiotherapy. The inclusive method of the PHQ-9 may be useful for prevalence studies or could serve a diagnostic purpose due to its high specificity and acceptable sensitivity. The prevalence of depression assessed by the M.I.N.I. was 3.5%, nearly equal to the prevalence assessed by the inclusive method of the PHQ-9, which was 5.6%.

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