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Original Article

Evaluating Screening Tests for Depression in Post-Stroke Older Adults

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Abstract

Background: Uncertainty surrounds which screening test to use in older patients with poststroke depression, in whom symptoms of depression are more complex and often occur in conjunction with other comorbidities. We evaluated screening tests for depression among a cohort of older ambulatory individuals with comorbid ischemic heart disease and prior stroke. **Methods:** We administered 4 depression screening instruments to 148 participants with ischemic heart disease and self-reported stroke from The Heart and Soul Study. Instruments included the 10-item Center for Epidemiologic Studies Depression Scale (CES-D), 9-item and 2-item versions of the Patient Health Questionnaire (PHQ-9 and PHQ-2), and the Whooley questions, a 2-item yes/no questionnaire. We administered the computerized version of the National Institute of Mental Health Diagnostic Interview Schedule as a gold standard. **Results:** Of the 148 participants, 35 (24%) had major depression. The Whooley questions demonstrated the highest sensitivity for detection (89%), followed by the CES-D (80%), PHQ-2 with cut point $\geq$2 (79%), PHQ-9 (51%), and PHQ-2 with cut point $\geq$3 (32%). The Whooley questions had a specificity of 0.66, a positive likelihood ratio of 2.61, and a negative likelihood ratio of 0.82. We observed no significant difference in the area under the receiver operating characteristic curve across the 4 instruments. **Conclusion:** In a cohort of ambulatory older adults with coronary heart disease and prior stroke, depression occurred in a fourth of the participants. The simple Whooley questions screening instrument can efficiently detect depression with a high sensitivity in this population, one representative of older patients commonly encountered within a primary care setting.

Keywords

stroke, depression screening, geriatric populations

Introduction

Depression occurs in nearly one-third of stroke survivors at any given time after their stroke.[1] The high rate of depression is due both to areas of impaired brain function following a stroke, which may cause changes in affect, behavior, and cognition, and to psychological factors related to functional disability after the stroke.[2] Poststroke depression negatively influences recovery and quality of life, results in caregiver stress, and is associated with higher mortality.[3-5] Underdiagnosis occurs in part because markers of psychiatric disease may be confused with neurological symptoms, and also because of limited data regarding the validity of depression screening tools in this specific population.[2,6]

In addition, older patients may experience poststroke depression differently than younger individuals. Estimates of the incidence of poststroke depression in the elderly population are higher than those in younger populations.[7] Risk factors for depression in the elderly patients include lack of health-care access, inadequacy of social support, and perceived poorer functional status.[8] Depression in these patients is underdiagnosed in part due to atypical symptoms including somatization, attribution of depressive symptoms to dementia or normal aging, and lack of access to health care.[7,9] Furthermore, depression in older patients exhibits strong associations with coexisting comorbidities.[9]

Cerebrovascular disease is often comorbid with ischemic heart disease, which in itself is associated with mood disorders, including major depression.[10] In this study, we sought to evaluate screening tests for depression among a population of ambulatory older adults with ischemic heart disease and previous history of stroke, whose mood may be affected by both psychological and neurobiological factors.[2] Our aim was to evaluate and compare 4 commonly used screening tools: (1) the 10-item Center for Epidemiological Studies Depression

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Scale (CES-D), (2) the 9-item Patient Health Questionnaire (PHQ-9), (3) the 2-item PHQ (PHQ-2), and (4) the Whooley questions, a 2-item yes/no questionnaire that is sometimes referred to as the yes/no PHQ-2.

Methods

Study Participants

We studied participants from the Heart and Soul Study with self-reported history of stroke. The Heart and Soul Study is a prospective cohort study of 1024 participants with stable (CHD) who have been followed for 15 years to assess the association between psychosocial factors and cardiovascular health outcomes. Methods regarding recruitment methods and study design have been previously described.[11] In brief, participants were recruited from 2 Veterans Affairs Medical Centers (San Francisco and Palo Alto), 1 university medical center (University of California, San Francisco), and 9 public health clinics in the Community Health Network of San Francisco. Participants were eligible if they met one or more of the following criteria: (1) history of myocardial infarction, (2) evidence of at least 50% stenosis in one or more coronary vessels on cardiac catheterization, (3) evidence of exercise-induced ischemia by treadmill or nuclear testing, or (4) a history of coronary revascularization or a diagnosis of coronary artery disease by an internist or cardiologist. We excluded participants with a history of myocardial infarction in the previous 6 months, inability to walk 1 block, or plans to move out of the local area within 3 years. A total of 1024 participants were enrolled between September 2000 and December 2002. Of these, 148 reported a history of stroke. One participant was removed due to missing data and the remaining 147 are the participants of this analysis. All study participants completed a baseline study appointment that included a medical interview, physical examination, an exercise treadmill test with a stress echocardiogram, and a comprehensive questionnaire that included 4 depression screening instruments followed by a diagnostic interview for depression. Demographic data and medical history were obtained via self-report questionnaire. The Heart and Soul Study was approved by the Committee on Human Research at the University of California, San Francisco, and all participants provided written, informed consent.

Depression Screening Instruments

We compared 4 screening instruments for depression: the 10-item form of the CES-D, the 9-item and 2-item versions of the PHQ (PHQ-9 and PHQ-2), and the Whooley questions, a simplified screening with 2 yes/no items derived from the Primary Care Evaluation of Mental Disorders Procedure.[2,12-14] Each test was administered as part of a self-report questionnaire at the beginning of the Heart and Soul study.

The CES-D is a well-validated screening tool to assess the number and duration of depressive symptoms.[15] The 10-item version consists of 30 total possible points with a standard cut point of $\geq$10.[16] The PHQ-9 is a widely used depression screening instrument that evaluates symptoms of depression according to the *Diagnostic and Statistical Manual of Mental Disorders*. Participants rate frequency of each symptom over the past 2 weeks with 4 answer choices: not at all, several days, more than half the days, or nearly every day. We used the standard cut point of $\geq$10 to identify depression.[17]

The PHQ-2 is a shortened version of the PHQ-9 that has been shown to perform well in a primary care setting, as well as among patients with cancer.[18-20] The recommended cut point for the PHQ-2 in the general population is $\geq$3; however, a cutoff of $\geq$2 points is more effective in some populations.[18,21] Therefore, we evaluated test characteristics for this instrument using cut points of $\geq$2 and $\geq$3.[21] We also administered the Whooley questions, a 2-item yes/no questionnaire asking, "during the past month, have you often been bothered by feeling down, depressed, or hopeless?" and "During the past month, have you often been bothered by little interest or pleasure in doing things?" An answer of "yes" to 1 or both questions was considered a positive result.[22] This screening test has been validated in several populations and is the recommended screening test for general practitioners in the United Kingdom.[12]

Criterion Standard

We determined the presence or absence of depression during the past month using the computerized version of the National Institute of Mental Health Diagnostic Interview Schedule (C-DIS). The DIS is an accurate and reliable test that has been well validated in diagnosing depression according to the *Diagnostic and Statistical Manual of Mental Disorders* and has been used in older adults as a criterion standard.[23-25] The C-DIS has previously demonstrated acceptable validity and reliability. The C-DIS was administered on the same day as the screening tests, and the administrator was blinded to the results of all tests. Participants with a major depressive episode in the past month were informed of this diagnosis, instructed to discuss their symptoms with their primary care provider, and provided a list of local resources.

Other Participant Characteristics

Age, gender, race, education, income, smoking status, and medical history were determined by self-report questionnaire. We calculated body mass index by measuring height and weight at baseline visit. Participants were instructed to bring their medications to their study appointment. Study personnel recorded medication names and dosing. Alcohol use was measured using the Alcohol Use Disorders Identification Test of Alcohol Consumption (AUDIT-C) score.[26] Significant alcohol use was defined as an AUDIT-C score of 4 or greater. Physical inactivity was self-reported using the following categories: not at all active, a little active (1-2 times per month), fairly active (3-4 times per month), quite active (1-2 times per week), very active (3-4 times per week), or extremely active (4 or more times per week). Participants who reported that they were not at

all or a little active were considered physically inactive. Medication adherence was assessed via the question, "In the past month, how often did you take your medications as the doctor prescribed?" Medication nonadherence was defined as taking prescribed medications $\leq$75% of the time.[27]

Statistical Analysis

Baseline characteristics among participants with and without depression were compared using *t* tests for normally distributed continuous variables, χ^2 for binary or categorical variables, and Fisher exact test for sample sizes $\leq$5. Sensitivity, specificity, and likelihood ratios were determined using standard formulas, with the C-DIS results as the reference standard. Receiver operating characteristic (ROC) curves were generated using logistic regression to predict depression for ordinal values of each screening instrument. Areas under the ROC curves (AUC) were generated using the trapezoidal rule and 95% confidence intervals (CIs) were calculated using the DeLong method.[28] Analyses were performed using R version 3.4.0.[29,30]

Results

Of the 147 individuals with a history of stroke, the mean age was 69.6 (10.2) years. Thirty-five (24%) individuals had major depression, as determined by the CDIS questionnaire. As compared to those who were not depressed, participants with depression were more likely to be female, to be significant alcohol drinkers, and to be taking an antidepressant medication (Table 1).

The PHQ-2 screening instrument had the lowest sensitivity (0.32), while the Whooley questions instrument had the highest (0.89; Table 2). The CES-D instrument had the second highest sensitivity for detecting depression (0.80). The PHQ-9 had a relatively high specificity (0.87) and positive likelihood ratio (3.84), while the Whooley questions had the lowest specificity (0.66) and lowest negative likelihood ratio (0.17). The CES-D had the highest AUC of 0.82 (95% CI: 0.75-0.89), followed by the PHQ-9 (AUC: 0.82, 95% CI: 0.74-0.90), PHQ-2 (AUC: 0.79, 95% CI: 0.71-0.87), and the Whooley questions (AUC: 0.79, 95% CI: 0.71-0.87). We compared the AUCs of all screening tools via the DeLong method[28] and found no significant differences (Figure 1).

The Whooley questions had a specificity of 0.66, a positive likelihood ratio of 2.61, and a negative likelihood ratio of 0.82 (Table 2). We tested for significant differences in discriminatory ability by age, sex, and race. We found a significant interaction between the Whooley questions and sex, with the screening instrument being more sensitive (and less specific) in women versus men (Table 3). Specifically, the Whooley questions accurately detected depression in 100% of the 24 women in the cohort (sensitivity = 1.00), with a specificity of 0.77, whereas in men, the test performed with a sensitivity of 0.83 and a specificity of 0.65.

Table 1. Baseline Characteristics of 147 Patients With a History of Stroke.

Characteristic	n (%) or Mean (SD)		*P* Value
	Depressed (n = 35)	Not Depressed (n = 112)	
Age, years	66.3 (10.6)	70.4 (9.6)	.05
Men	24 (69%)	99 (88%)	.01
Race			
White	19 (54%)	62 (55%)	1.0
Hispanic	4 (11%)	12 (11%)	1.0
African American	7 (20%)	18 (16%)	.78
Asian	3 (9%)	17 (15%)	.40
Other	2 (6%)	3 (3%)	1.0
High school graduate	30 (86%)	98 (88%)	1.0
Body mass index, kg/m^2	27.4 (4.5)	28.4 (4.6)	.3
Income <US$20 000	20 (57%)	62 (55%)	1.0
Comorbid conditions			
Hypertension	29 (83%)	88 (79%)	.76
Myocardial infarction	20 (57%)	77 (69%)	.29
Coronary revascularization	23 (66%)	71 (63%)	.96
Congestive heart failure	9 (26%)	33 (29%)	.83
Chronic obstructive lung disease	9 (26%)	26 (23%)	.94
Diabetes	10 (29%)	34 (30%)	1.0
Kidney disease	17 (49%)	64 (57%)	.49
Medication use			
Aspirin	25 (71%)	68 (61%)	.34
Beta-blocker	17 (49%)	66 (59%)	.38
Renin-angiotensin inhibitor	16 (80%)	63 (56%)	.37
Antidepressant	15 (43%)	17 (15%)	.001
Health-related behaviors			
Medication nonadherence	4 (11%)	11 (10%)	.76
Regular alcohol use	15 (43%)	21 (19%)	.008
Current smoking	10 (29%)	19 (17%)	.21
Physical inactivity	17 (49%)	51 (46%)	.9

Abbreviation: SD, standard deviation.

Discussion

We evaluated the test characteristics of 4 screening instruments for depression in 147 older adults with postacute stroke and comorbid ischemic heart disease, including 35 (24%) who met criteria for major depressive disorder during the past month. In this sample, the Whooley questions demonstrated the highest sensitivity (89%), followed by the 10-item CES-D (80%), PHQ-2 cut point $\geq$2 (79%), PHQ-9 (51%), and PHQ-2 cut point $\geq$3 (32%). However, because sensitivity always comes at the cost of lower specificity, the Whooley questions also demonstrated the lowest specificity (66%), followed by the CES-D (71%), PHQ-2 $\geq$ 2 (75%), PHQ-9 (87%), and PHQ-2 $\geq$ 3 (88%). The Whooley questions appeared to perform particularly well in women, although the sample size was small. Overall, we observed no difference in ROCs across the 4 instruments. These findings suggest that the Whooley questions

Table 2. Test Characteristics of 4 Depression Screening Instruments in 147 Participants With History of Stroke.

Screening Instrument	Cut Point	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Area Under the ROC[a] Curve (95% CI)[b]
CES-D	≥10 vs <10	0.80 (0.63-0.91)	0.71 (0.62-0.79)	2.80 (2.00-3.91)	0.28 (0.61 -1.25)	0.82 (0.75-0.89)
PHQ-9	≥10 vs <10	0.51 (0.34-0.68)	0.87 (0.79-0.92)	3.84 (2.17-6.79)	0.56 (0.39-0.79)	0.82 (0.74-0.90)
PHQ-2	≥3 vs <3	0.32 (0.18-0.50)	0.88 (0.79-0.93)	2.59 (1.29-5.16)	0.77 (0.61-0.98)	0.79 (0.71-0.87)
PHQ-2	≥2 vs <2	0.79 (0.62-0.91)	0.75 (0.66-0.82)	3.18 (2.21-4.57)	0.27 (0.14-0.53)	0.79 (0.71-0.87)
Whooley questions	≥1 vs 0	0.89 (0.72-0.96)	0.66 (0.56-0.75)	2.61 (1.96-3.47)	0.17 (0.07-0.44)	0.79 (0.71-0.87)

Abbreviations: CES-D, Center for Epidemiological Studies Depression Scale; 95% CI, exact binomial 95% confidence intervals; PHQ, Patient Health Questionnaire; ROC, receiver operating characteristic.
[a]Determined by the trapezoidal rule, a nonparametric estimate of the area under the curve.
[b]The 95% CI for area under the curve was calculated as area ± (1.96 × SE [standard error]) using DeLong's formula for SE.

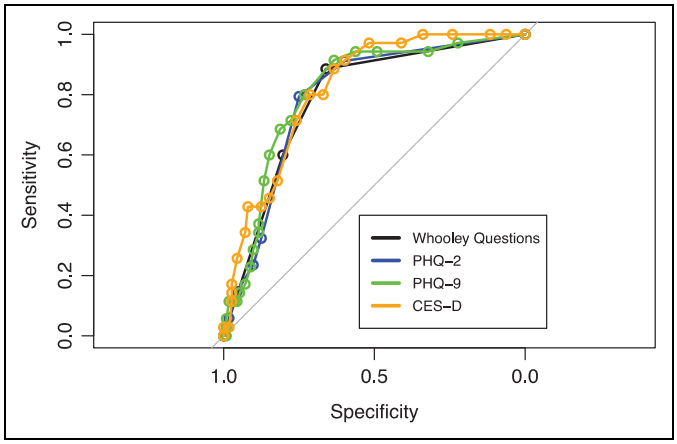

Figure 1. No significant difference in area under the receiver operating characteristic curves for the PHQ-2, PHQ-9, CES-D, and Whooley questions screening instruments. CES-D denotes Center for Epidemiologic Studies Depression Scale; PHQ, Patient Health Questionnaire.

instrument is an effective screening tool in this population because it has a negative predictive value of 95% and, therefore, effectively rules out depression in the ≥50% of patients who screen negative. However, its low specificity means that patients who screen positive must undergo a clinical interview to confirm the diagnosis of depression. In contrast, the PHQ-9 has high specificity but its low sensitivity fails to identify depression in almost half of depressed patients.

The 24% prevalence of depression that we observed in our cohort was slightly higher than that among the general population of participants with CHD in the Heart and Soul Study (22%).[10,11] However, it was slightly lower than previous pooled estimates of prevalence up to 5 years after stroke.[1] In a meta-analysis on depression screening methods in individuals with a history of stroke, Meader et al found that the tests with the highest utility (ruling out a diagnosis with minimal false negatives) in a postacute stroke population were the CES-D and the Hamilton Rating Scale for Depression.[19] They were unable to evaluate the Whooley questions due to limited data, but as in our study, they found that the PHQ-2 had lower sensitivity than had been reported in other populations. Studies that have specifically focused on elderly stroke survivors have suggested adequate validity of the Brief Assessment Schedule Depression Cards and the Geriatric Depression Scale.[7] We previously found that the Whooley questions have a high sensitivity for detecting depression in individuals with CHD, and our current findings further expand this literature by providing similar data on test characteristics of the Whooley screening instrument in a poststroke population.

Both the Whooley questions and the PHQ-9 can be used for depression screening purposes because they reduce the number of individuals who require a follow-up interview. If an instrument cannot rule in or rule out depression in any patients, then screening would be useless because all patients will require a diagnostic interview. The high sensitivity of the Whooley questions eliminates the need for a follow-up interview in the approximately 50% of individuals who screen negative. However, the approximately 50% of patients who screen positive must have a follow-up diagnostic interview to determine the presence or absence of major depressive disorder. In contrast, the high specificity of the PHQ-9 eliminates the need for a follow-up interview in approximately 20% of patients who have a score of ≥10, but the PHQ-9 misses depression in about half of depressed patients.

As an example, adopting the Whooley questions for routine screening in an ambulatory poststroke population of 100 individuals with a prevalence of depression similar to that in our study (24%) would correctly identify depression in 21 patients (true positives) and miss depression in 3 patients (false negatives). However, it also would result in 26 false positives. This low positive predictive value means that more than half of the patients who test positive for depression would need to undergo a diagnostic interview that ultimately would determine they were not depressed. In contrast, administering the PHQ-9 would result in only 10 false positives and 66 true negatives. However, it would fail to identify depression in half of the affected patients (12 false negatives). Thus, if the goal is sensitivity, it is best to use the Whooley questions, but if the goal is specificity, it is better to use the PHQ-9. Since both the CES-D and the PHQ-2 have mediocre sensitivity and specificity, neither eliminates the need for a follow-up evaluation in any patients, and therefore, neither are useful for screening purposes.

Table 3. Test Characteristics of Whooley Questions, Stratified by Sex.

	Depressed (%)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Area Under the ROC Curve[a] (95% CI)[b]
Men (n = 123)	24 (20%)	0.83 (0.62-0.95)	0.65 (0.54-0.74)	2.36 (1.71-3.25)	0.26 (0.10-0.64)	0.77 (0.67-0.87)
Women (n = 24)	11 (46%)	1.00 (0.68-1.00)	0.77 (0.46-0.94)	4.33 (1.61-11.69)	0[c]	0.87 (0.72-1.0)

Abbreviations: 95% CI, exact binomial 95% confidence intervals; ROC, receiver operating characteristic.
[a]Determined by the trapezoidal rule, a nonparametric estimate of the area under the curve.
[b]The 95% CI for area under the curve was calculated as area $\pm$ (1.96 $\times$ SE [standard error]) using DeLong's formula for SE.
[c]Confidence interval cannot be calculated.

The National Institute of Health and Care Excellence recommends the Whooley questions for use by general practitioners in the United Kingdom.[31,32] In a meta-analysis, this screening test was found to have a pooled sensitivity of 0.95 (95% CI: 0.88-0.97) with a pooled specificity of 0.65 (95% CI: 0.56-0.74) in a combination of primary care, community, and inpatient settings.[12] Our findings demonstrate the potential for its use in a poststroke older ambulatory population. The high sensitivity effectively identifies individuals with possible depression, and the low negative likelihood ratio indicates that a negative test result adequately rules out depression. As there has yet to be a test developed to adequately rule in depression in this population with few false positives, a positive screening result should be followed up with a diagnostic interview or clinical assessment.[19]

Although the US Preventive Services Task Force recommends screening for depression in older adults, the impact of screening on outcomes in poststroke depression in this population requires more extensive study.[33] It has been shown that a multidisciplinary approach to management of depression, including active follow-up, monitoring of adherence to treatment, structured psychotherapy as needed, and interprofessional communication improves outcomes in a population of patients with chronic illnesses and depression.[14,34] To our knowledge, this collaborative approach has only been studied in 1 randomized control trial in a population of patients specifically with poststroke depression.[35] The screening plus collaborative care arm was found to result in a reduction of depression symptoms in comparison with screening and usual care coordinated by a primary care provider. It is important to point out that unless such a collaborative care model is in place, screening for depression has questionable benefit on patient outcomes.

Several limitations must be kept in mind while interpreting our results. First, this subgroup of the Heart and Soul Study cohort represents stroke survivors in an ambulatory care setting, with a history of stroke ascertained by self-report without subsequent confirmation of stroke diagnosis. Although self-reported stroke has been found to be consistent with data from medical records among veterans, we acknowledge that self-reported medical conditions are not always accurate.[36] Second, we did not collect information on date of stroke, severity of stroke, residual symptoms, or related physical or cognitive disability, which have been found to be consistent predictors of poststroke depression.[2,37] Therefore, the study cohort was not a uniform population, and we cannot relate severity of functional impairment after stroke to depression. In addition, the Heart and Soul Study excluded participants who were unable to walk 1 block, and therefore, the poststroke individuals in this population had a baseline level of physical function. Neurologic sequelae affecting cognition and expression would likely affect participation in screening tests. A comparison of screening tests for depression among poststroke patients with more than mild language, cognitive, and physical deficits would require a more targeted study. In addition, we did not exclude people with prior depression. This issue has been recognized in other studies of depression screening tests and it is possible that a prior diagnosis of depression may bias test results.[12] We did not include longer depression scoring instruments that are sometimes used as screening tools in older populations, including the aforementioned Geriatric Depression Scale and Beck Depression Inventory Fast Screen.[38] Finally, although our results suggest gender-specific findings, our study participants were mostly white men and the proportion of women in the cohort was small. Further studies are required to address generalizability of our findings to women or to other populations.

In summary, we found that in a cohort of ambulatory older adults with ischemic heart disease and postacute self-reported stroke, depression as determined via a standardized interview occurred in about 24% of participants. The Whooley questions provide a simple and effective screening tool that can be easily and quickly administered in this population. As compared with the PHQ-9, the 2-item questionnaire was much more sensitive, although less specific.

Declaration of Conflicting Interests

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