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Association of Physical versus Affective Depressive Symptoms with Cardiac Event-Free Survival in Patients with Heart Failure

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Abstract

Objective—To determine whether physical depressive symptoms inflate the association between depressive symptoms as measured with the Patient Health Questionnaire (PHQ-9) and cardiac event-free survival in patients with heart failure (HF).

Methods—A total of 210 patients with HF were recruited from HF clinics affiliated with two academic medical centers. The PHQ-9 was used to assess levels of depressive symptoms. Cardiac event-free survival data (cardiac death, cardiac hospitalization, or cardiac emergency department visit) were collected for a median follow-up of 360 days. Cox proportional hazards regression analyses were performed separately for physical and affective depressive symptom dimensions of the PHQ-9 to examine predictive ability for time to first cardiac event.

Results—Scores of both physical and affective depressive symptom dimensions of the PHQ-9 predicted time to first cardiac event in separate unadjusted models. However, scores of the physical depressive symptom dimension did not predict time to first cardiac events while scores of the affective depressive symptom dimension remained as an independent predictor (hazard ratio = 1.12, 95% confidence interval = 1.03 – 1.22) after controlling for health status (comorbidities and New York Heart Association functional class) and clinical and socio-demographic factors.

Conclusions—Affective depressive symptoms, but not physical depressive symptoms, predicted time to first cardiac event independent of health status and clinical and socio-demographic characteristics. The use of the full PHQ-9 does not inflate the relationship of depressive symptoms to cardiac event-free survival. Thus, clinicians can use the PHQ-9 to assess depressive symptoms in their patients with HF without concern that the instrument over-estimates the relationship between depressive symptoms and outcomes.

Keywords

depressive symptoms; heart failure; prognosis

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Heart failure (HF) is a growing health care concern associated with adverse outcomes and staggering health care expenditures (1). In addition to traditional risk factors (e.g., age and comorbidities) (2, 3), psychological status is recognized as a significant predictor of outcomes (3–6). Depressive symptoms are related to poor prognosis and quality of life in patients with HF (3–8). Thus, it is important for health care providers to recognize and manage depressive symptoms appropriately in the HF population.

Depressive symptoms are common in patients with HF, with a prevalence from 30% to 51% (6–11). This large variability might be related to the selection of instruments to measure depressive symptoms and their cut points for defining varying levels of depressive symptoms (12). Instruments used to measure the levels of depressive symptoms often include physical depressive symptoms, such as changes in appetite, sleep disturbances, or fatigue. However, these symptoms are frequently reported by patients with HF (9, 13). This poses a challenge for health care providers to accurately screen and monitor depressive symptoms because these physical depressive symptoms may reflect the severity of HF rather than depressive symptom status (14).

Patients in more advanced stages of HF have greater physical symptom prevalence and burden than those in less advanced stage of HF (15). Patients with depressive symptoms experience more physical symptoms of HF (dyspnea, fatigue, sleep disturbance, and loss of appetite) than patients without depressive symptoms (9). Thus, the inclusion of physical symptoms might reflect HF severity, inflate the severity of depressive symptoms, and in turn, artificially increase their impact on outcomes in HF.

Researchers have expressed concern about measuring depressive symptoms in patients with HF using instruments that include physical symptoms (16, 17). One way to address this concern is to use an established depressive symptom instrument such as the Patient Health Questionnaire (PHQ-9) that includes physical and affective depressive symptoms to compare the predictive ability between versions of the instrument with and without physical depressive symptoms. The purpose of this study was to determine whether the presence of physical depressive symptoms on the PHQ-9 over-estimates the relationship of depressive symptoms to cardiac event-free survival. The specific aim was to compare the predictive ability for cardiac event-free survival of the full PHQ-9 with versions that contain just the physical and just the affective depressive symptoms after adjusting for health status and clinical and socio-demographic variables.

Methods

Design, Setting, and Procedure

This study was a prospective, longitudinal investigation. Patients with HF were recruited from outpatient clinics associated with two academic medical centers in Georgia and Kentucky from August 2004 to March 2009. This study was approved by the Institutional Review Boards at each study site. Patients with HF were identified by referral from their nurses and physicians, and their eligibility was confirmed by trained research nurses. Signed, informed consent was obtained from patients who agreed to participate in the study during a visit to the General Clinical Research Center (GCRC). Patients were interviewed to collect demographic and clinical data and completed questionnaire packets during the visit to the GCRC. Patients were followed up over a median of 360 days (2 – 1826 days) to determine cardiac events.

Participants

Patients who met the following criteria were eligible for this study: (1) diagnosis of HF by a cardiologist using the Framingham criteria (18); (2) no myocardial infarction within the

previous three months; (3) taking consistent doses of HF medications at the time of study participation; and (4) able to read and speak English. Patients who had valvular heart disease as an etiology of their HF, were referred for heart transplantation, had obvious cognitive impairments, or had major life-threatening comorbidities (e.g., end-stage renal or liver disease or cancer other than skin cancer) were excluded.

Measurement

Depressive symptoms. Depressive symptoms were assessed using the PHQ-9, which consists of nine items (Table 1) (19). Each item corresponds to one of the nine symptoms of the major depressive disorder criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV). Patients rate items based on how often they experience these symptoms over two weeks on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The scores were summed and ranged from 0 to 27, with scores of 5, 10, 15, and 20, representing mild, moderate, moderately severe, and severe levels of depression symptoms, respectively. The validity of the PHQ-9 has been demonstrated to screen for depression in patients with cardiac disease with high specificity and predictive value (20). Its brevity makes its use in clinical settings or research desirable (21).

Three items related to sleep disturbance, fatigue, and appetite change were classified as comprising the PHQ-9 physical depressive symptom dimension in this study because these are often experienced by patients with HF (13, 22). The remaining six items of anhedonia, depressed mood, negative feelings about oneself, concentration problems, psychomotor agitation/retardation, and suicidal ideation were classified as comprising the PHQ-9 affective depressive symptom dimension. The reliability of the scores for the two dimensions of depressive symptoms in this study was measured using Cronbach's α : 0.764 for physical depressive symptom and 0.814 for affective depressive symptom dimensions.

Health status and Clinical, socio-demographic characteristics—Health status in this study was operationally defined as comorbidity burden measured with the Charlson Comorbidity Index and functional status measured with New York Heart Association (NYHA) functional classification. The Charlson Comorbidity Index was used to measure comorbidity burden which is weighted by taking into account comorbid illnesses (i.e., the number and seriousness) (23). New York Heart Association functional classification was determined to assess limitations of physical activities resulting from symptoms by in-depth structured interviews by a trained research nurse. Clinical and socio-demographic characteristics (e.g., medication and marital status) were collected via patient interviews and medical record reviews.

Cardiac events—Cardiac events were defined as the composite end point of cardiac-related death, cardiac-related hospitalization, or emergency department (ED) visit attributable to cardiac reasons (e.g., worsening HF symptoms). The data were obtained by monthly follow-up calls to patients and their families and confirmed by reviewing medical records and public death records.

Statistical Analyses

Data were analyzed using SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina). Unadjusted Cox proportional hazards regressions were performed separately for physical and affective depressive symptom dimensions of the PHQ-9 in order to examine predictive ability for time to first cardiac event. Two series of multivariable analyses were done. Health status (the Charlson Comorbidity Index and NYHA class) was entered as covariates in the first model and health status and clinical, socio-demographic variables (age, gender, etiology of HF, body mass index [BMI], and anti-depressant medication

therapy) were entered together in the second model. Covariates included in the models were selected *a priori* based on previous studies (2, 8, 16, 17, 24).

The seven covariates included in our survival analysis models resulted in a ratio of seven events per predictors, which is lower than the recommended 10 events per predictor for survival analysis. To determine whether models with seven covariates provided reliable prediction, we ran progressive models in which the least significant predictors were removed one by one and compared information criteria values (e.g., Akaike's information criterion) among the models. The information criteria values in the reduced models were similar to the full model with seven covariates. Therefore, given that all covariates were identified as important in prior research we included all seven covariates in the analyses.

The proportional hazards assumptions were evaluated with graphical displays of deviations between the observed cumulative martingale residuals and the values of each explanatory variable from 20 random simulations. The Kolmogorov-type supremum tests from 1000 simulated patterns also were used. Both methods indicated that there was not a gross violation of the model assumption.

Results

Sample Characteristics

A total of 210 patients with HF participated in the study (Table 2). The majority of patients were male, Caucasian, and married or cohabitating. Ischemia was the most common HF etiology. The median score of the PHQ-9 was 4 (the first and third quartiles: 1 and 9, respectively). Patients having moderate to severe depressive symptoms (PHQ-9 scores ≥ 10) were 23% (49/210) of total participants. Of these patients having moderate to severe depressive symptoms, 41% (20/49) were prescribed anti-depressants.

Patients were grouped by the median split of PHQ-9 scores for physical depressive symptom and affective depressive symptom dimensions (Table 2). The high PHQ-9 physical depressive symptom group (scores > 3) had a greater proportion in NYHA functional classes III and IV, higher comorbidity burden scores, and a greater number of prescribed anti-depressants than the low PHQ-9 physical depressive symptom group (scores ≤ 3). The high PHQ-9 affective depressive symptom group (scores > 1) were younger and had a greater proportion in NYHA functional classes III and IV, higher comorbidity burden scores, and a greater number of prescribed anti-depressants compared to the low PHQ-9 affective depressive symptom group (scores ≤ 1).

Cardiac Events

During the follow-up period, 59 cardiac events occurred: 2% (4/210) were cardiac death, 23% (48/210) were cardiac-related hospitalizations, and 3% (7/210) were ED visits due to cardiac causes.

Prediction of Cardiac Event-free Survival

Full version of the PHQ-9—The total scores of the PHQ-9 predicted cardiac event-free survival in the unadjusted and adjusted analyses (Table 3). The association between total scores of the PHQ-9 and time to first cardiac event remained significant after adjusting for the covariates (unadjusted hazard ratio [HR] = 1.08, 95% confidence interval [CI] = 1.03 – 1.13; adjusted HR for health status [the Charlson Comorbidity Index and NYHA functional class] = 1.07, 95% CI = 1.03 – 1.13). Every one point increase in total PHQ-9 score was associated with a 6% increase in the risk for a cardiac event after controlling for all covariates (adjusted HR for all covariates = 1.06, 95% CI = 1.01 – 1.12).

PHQ-9 physical depressive symptom dimension—In the unadjusted Cox regression analysis scores of the PHQ-9 physical depressive symptom dimension were a predictor for cardiac event (unadjusted HR = 1.11, 95% CI = 1.02 – 1.21). Scores of the PHQ-9 physical depressive symptom dimension did not predict cardiac event-free survival after adjusting for health status. Neither the Charlson Comorbidity Index nor NYHA functional class predicted cardiac event-free survival.

After entering all covariates, the association between scores of the PHQ-9 physical depressive symptom dimension and cardiac event-free survival was not significant (Table 4). Only anti-depressant medication therapy was an independent predictor of cardiac event-free survival (adjusted HR = 1.98, 95% CI = 1.06 – 3.71). Patients prescribed anti-depressants had nearly double the risk for a cardiac event than patients not prescribed anti-depressants.

PHQ-9 affective depressive symptom dimension—The scores of the PHQ-9 affective depressive symptom dimension predicted cardiac event-free survival in both unadjusted and adjusted models (unadjusted HR = 1.14, 95% CI = 1.06 – 1.22). In the two series of multivariable analyses the association between scores of the PHQ-9 affective depressive symptom dimension and cardiac event-free survival remained significant. In the first model adjusting for health status, scores of the PHQ-9 affective depressive symptom dimension was the only predictor of cardiac event-free survival (adjusted HR for health status = 1.13, 95% CI = 1.05 – 1.21). In the second model adjusting for all covariates, scores of the PHQ-9 affective depressive symptom dimension independently predicted cardiac event-free survival (Table 5). Every one point increase in the scores of the PHQ-9 affective depressive symptom dimension was associated with a 12% increase in the risk for a cardiac event (adjusted HR for all covariates = 1.12, 95% CI = 1.03 – 1.22).

Discussion

We found different predictive outcomes for the PHQ-9 physical and affective depressive symptom dimensions in patients with HF. Both affective and physical depressive symptom dimensions were predictive of a cardiac event in unadjusted models. However, affective depressive symptoms, but not physical depressive symptoms, persistently predicted time to cardiac event in adjusted models controlling for health status (the Charlson Comorbidity Index and NYHA functional class) and clinical, socio-demographic factors. These results suggest that physical depressive symptoms may largely reflect health status, and the relationship between depressive symptoms and risk for a cardiac event is limited to affective depressive symptoms.

There is evidence that affective depressive symptoms may be a useful indicator to detect levels of depressive symptoms. In the study of Holzapfel and colleagues affective depressive symptoms (e.g., depressed mood and worthless/guilty) were more often reported by depressed patients with HF than those without HF, while the frequency of physical depressive symptom experience did not differ (14). In a study in which depressive symptoms were measured with the Beck Depression Inventory (BDI)-II, somatic depressive symptom scores were not different between patients with post acute myocardial infarction and psychiatric outpatients matched on age, gender, and cognitive/affective depressive symptom scores (25). Simon and Von Korff demonstrated that the overall pattern of physical symptoms, such as weight and appetite changes, fatigue, and sleep disturbances, was similar to depressed patients with and without chronic illness (26). The removal of overlapping physical symptoms from self-report depressive symptom instruments does not improve the discriminating ability for the presence of depression using diagnostic interview

based on the DSM-IV criteria for major depressive episode in patients with chronic pain (27, 28).

In the study of Azevedo and colleagues in which the association between depressive symptoms, which were measured with the BDI, and HF stages, which were defined by the American College of Cardiology and American Heart Association, patients with a higher stage (more advanced HF) had higher levels of depressive symptoms. This relationship between HF stages and depressive symptom levels remained significant after deleting physical symptom items (i.e., fatigue, sleep disturbance, and changes in appetite) from the BDI (16).

We found that the unique contribution of the physical depressive symptoms to risks for a cardiac event disappeared with the inclusion of health status (comorbidities and NYHA functional class) in regression models. This might indicate the significant association between health status and physical depressive symptoms. There are several studies in which the relationship between health status and physical depressive symptoms was demonstrated. In a previous study in which the BDI was used to measure depressive symptoms in patients with HF scores of the BDI somatic/affective depressive symptom dimension (e.g., irritability, crying, fatigue, and sleep disturbances), but not scores of the BDI cognitive/affective symptom dimension (e.g., sense of failure, self-accusation, and suicidal ideas), were different by NYHA classes (29). Significant differences in depressive symptom levels between patients with and without HF were observed only when using a depressive symptom measure incorporating physical symptoms (the Centers for the Epidemiological Studies of Depression Questionnaire), but not measures free of physical symptoms (Profile of Mood States-Short form dejection-depression and the Hospital Anxiety and Depression Scale-depression) (30).

Similarly, the BDI somatic/affective symptoms, but not the BDI cognitive/affective symptoms, were significantly related to the Charlson Comorbidity Index in patients with myocardial infarction (31). Watkins and colleagues also showed a stronger relationship of comorbidities, which were measured by the Charlson Comorbidity Index, with the BDI physical depressive symptoms ($r=0.24$) than the BDI cognitive symptoms ($r=0.06$) in patients after acute myocardial infarction (32).

Barefoot and colleagues demonstrated the important role of affective depressive symptoms in predicting cardiac death among patients with coronary artery disease (33). Hazard ratios of four depressive symptom dimensions, which were measured with the Zung Self-rating Depression Scale (SDS), were compared between unadjusted models and an adjusted model in which all depressive symptom dimensions were entered simultaneously. The hazard ratio of the SDS affective symptoms (e.g., sadness, irritability, restlessness, and suicidal ideas) remained similarly while the hazard ratios of the others including somatic (e.g., tiredness and sleep difficulties) and well-being (e.g., satisfaction and optimism) dimensions substantially reduced. Similarly, affective depressive symptoms were associated with cardiac mortality in patients after coronary artery bypass surgery while physical depressive symptoms were not (34). This result suggests that the relationship between depressive symptom levels and cardiac mortality is not altered by physical symptoms due to disease conditions (34).

Conflicting findings that physical depressive symptoms, not affective depressive symptoms, predict cardiac outcomes (e.g., mortality or hospitalizations) are observed in previous studies in patients with coronary heart diseases, such as acute myocardial infarction (35–37). The significant relationship between physical depressive symptoms and all-cause mortality was also reported in the HF population (29). Schiffer and colleagues reported that the BDI

somatic/affective symptom dimension (e.g., irritability, crying, fatigue, and sleep disturbances) was an independent predictor of all-cause mortality while the BDI cognitive/affective symptom dimension (e.g., sense of failure, self-accusation, and suicidal ideas) was not in patients with HF (29). This conflicting finding with the current study may be related to different outcome variables. The outcome of their study was all-cause mortality while ours was the combined end point of mortality, hospitalization, and ED visit related to cardiac reasons. The majority of cardiac events in this study were hospitalizations. It is possible that factors related to death are different from factors related to hospitalizations. For instance, left ventricular ejection fraction or NYHA functional class was an independent predictor of mortality, but not hospitalization (38, 39).

The use of different measures to assess depressive symptoms may contribute to the inconsistent findings. The items in the BDI and the PHQ-9 are different although there are some items that are overlapped between the two measures including anhedonia, suicidal ideation, psychomotor agitation/retardation, and fatigue. Physical and affective depressive symptom dimensions were defined with different items between the study of Schiffer et al. and ours. An item indicating psychomotor agitation/retardation was categorized as the BDI somatic/affective symptom dimension in the study of Schiffer et al. while the item was categorized as the PHQ-9 affective depressive symptoms in our study.

One interesting finding in this study is the association between being prescribed anti-depressants and higher risk for cardiac events. The prescription of anti-depressants was a significant predictor of a cardiac event in the multivariable model which included the PHQ-9 physical symptom dimension. However, this relationship was not significant in the adjusted models using total PHQ-9 scores or PHQ-9 affective symptom dimension scores. We extrapolate that the impact of taking anti-depressants differs by dimensions of depressive symptoms. However, we cannot determine from our data whether patients prescribed anti-depressants actually took the medication or that the dose prescribed was adequate to treat depressive symptoms. Therefore, our results should be interpreted as demonstrating that prescribing anti-depressants was associated with an increased risk for a cardiac event. Our results do, however, suggest that simply prescribing anti-depressants is not sufficient and without proper follow-up to assure adequate treatment, it may increase the risk for a cardiac event.

It is important to acknowledge the differential influence of physical and affective depressive symptoms on cardiac event-free survival in patients with HF. The use of the measures including physical depressive symptoms does not inflate the association between depressive symptoms and cardiac event-free survival.

There are limitations that should be noted in this study. The sample may not be representative of the HF population because men and Caucasians predominated. Because this was an observation study, no definitive inferences can be drawn regarding causal relationships. The number of covariates included in our multivariable models exceeded the recommended number of covariates per event. However, our model testing demonstrated that the full model provided as reliable prediction as models with fewer covariates without causing an overfitting issue. Therefore, the full model, which had empirical support, was the optimal model to include in the analyses.

Conclusion

The accurate assessment of depressive symptoms in patients with HF has been a critical issue because of their adverse effects on outcomes. However, shared physical symptoms between HF and depressive symptoms are barriers to prevent evaluating the severity of

depressive symptoms in HF. In this study we demonstrated a distinctive prognostic ability between physical and affective depressive symptoms to outcomes in patients with HF. Affective depressive symptoms were associated with cardiac event-free survival independent of health status, but not physical depressive symptoms. The use of depressive symptom measures including physical symptoms does not inflate the relationship of depressive symptoms to cardiac event-free survival. Thus, clinicians can use instruments that contain physical depressive symptoms to assess depressive symptoms in their patients with HF without concern that the instruments overestimate the relationship between depressive symptoms and outcomes.

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Glossary

HF	heart failure
PHQ-9	the Patient Health Questionnaire

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Figure 1.
Depressive symptom levels ($N=210$).

TABLE 1

Items of the Nine-Item Patient Health Questionnaire

Physical depressive symptom dimension	
1	Trouble falling/staying asleep, sleeping too much
2	Feeling tired or having little energy
3	Poor appetite or overeating
Affective depressive symptom dimension	
1	Little interest or pleasure in doing things
2	Feeling down, depressed, or hopeless
3	Feeling bad about yourself—or that you are a failure or have let yourself or your family down
4	Trouble concentrating on things, such as reading the newspaper or watching television
5	Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual
6	Thoughts that you would be better off dead or of hurting yourself in some way

TABLE 2

Sample Characteristics (*N* = 210)

	Total	PHQ-9 Physical Symptom Dimension		PHQ-9 Affective Symptom Dimension	
		Low Scores (<i>n</i> = 115)	High Scores (<i>n</i> = 95)	Low Scores (<i>n</i> = 126)	High Scores (<i>n</i> = 84)
Age, ^a M (SD), y	61 (11)	63 (12)	60 (10)	64 (11)	58 (11)
Female, <i>n</i> (%)	55 (26.2)	26 (22.6)	29 (30.5)	29 (23.0)	26 (31.0)
Ethnicity, <i>n</i> (%)					
White	169 (80.5)	91 (79.1)	78 (82.1)	100 (79.4)	69 (82.1)
Others	41 (19.5)	24 (20.9)	17 (17.9)	26 (20.6)	15 (17.9)
Marital status, <i>n</i> (%)					
Married/cohabitate	117 (55.7)	65 (56.5)	52 (54.7)	72 (57.1)	45 (53.6)
Single/divorced/widowed	93 (44.3)	50 (43.5)	43 (45.3)	54 (42.9)	39 (46.4)
Body mass index, M (SD), kg/m ²	31.6 (7.4)	31.1 (7.8)	32.2 (7.0)	31.4 (7.8)	31.9 (6.8)
Charlson Comorbidity Index, ^{a,b} M (SD)	3.4 (2.1)	3.1 (2.0)	3.7 (2.1)	3.2 (2.0)	3.6 (2.3)
Ischemic etiology of HF, <i>n</i> (%)	158 (75.2)	83 (72.2)	75 (79.0)	94 (74.6)	64 (76.2)
NYHA class, ^{a,b} <i>n</i> (%)					
I/II	105 (50.0)	70 (60.9)	35 (36.8)	74 (58.7)	31 (36.9)
III/IV	105 (50.0)	45 (39.1)	60 (63.2)	52 (41.3)	53 (63.1)
Medications, <i>n</i> (%)					
Antidepressant ^{a,b}	43 (20.5)	12 (10.4)	31 (32.6)	15 (11.9)	28 (33.3)
ACE I or ARB (<i>n</i> = 209)	172 (81.9)	97 (85.1)	75 (79.0)	107 (84.9)	65 (78.3)
β-Blocker (<i>n</i> = 209)	184 (87.6)	104 (91.2)	80 (84.2)	110 (88.0)	74 (88.1)

PHQ-9 = nine-item Patient Health Questionnaire; M = mean; SD = standard deviation; HF = heart failure; NYHA = New York Heart Association; ACE I = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blocking agents.

^aSignificant differences between groups with low and high scores of the PHQ-9 affective symptom dimension (median split), *p* < .05.

^bSignificant differences between groups with low and high scores of the PHQ-9 physical symptom dimension (median split), *p* < .05.

TABLE 3
Multivariable Cox Regression Analysis Using the Total Scores of the PHQ-9 ($N = 210$)

	Hazard Ratio	<i>p</i>	95% Confidence Interval
Age	0.99	.41	0.97–1.01
Female	0.85	.61	0.46–1.59
Charlson Comorbidity Index	1.05	.53	0.91–1.20
Ischemic etiology	2.14	.07	0.95–4.82
NYHA class (I/II versus III/IV)	0.91	.76	0.51–1.64
Body mass index (kg/m^2)	0.96	.07	0.92–1.00
Antidepressant use	1.80	.07	0.96–3.36
Total scores of the PHQ-9	1.06	.019	1.01–1.12

PHQ-9 = nine-item Patient Health Questionnaire; NYHA = New York Heart Association. Total model $p = .001$.

TABLE 4
Multivariable Cox Regression Analysis Using Scores of PHQ-9 Physical Depressive Symptoms ($N = 210$)

	Hazard Ratio	<i>p</i>	95% Confidence Interval
Age	0.99	.21	0.96–1.01
Female	0.80	.48	0.42–1.50
Charlson Comorbidity Index	1.06	.49	0.93–1.22
Ischemic etiology	2.09	.08	0.93–4.71
NYHA class (I/II versus III/IV)	0.96	.88	0.53–1.72
Body mass index (kg/m^2)	0.96	.06	0.92–1.00
Antidepressant use	1.98	.033	1.06–3.71
PHQ-9 physical scores	1.07	.18	0.97–1.19

PHQ-9 = nine-item Patient Health Questionnaire; NYHA = New York Heart Association. Total model $p = .007$.

Multivariable Cox Regression Analysis Using Scores of PHQ-9 Affective Depressive Symptoms (*N* = 210)

TABLE 5

	Hazard Ratio	<i>p</i>	95% Confidence Interval
Age	0.99	.62	0.97–1.02
Female	0.94	.83	0.50–1.75
Charlson Comorbidity Index	1.04	.57	0.91–1.20
Ischemic etiology	2.22	.06	0.98–5.02
NYHA class (I/II versus III/IV)	0.94	.82	0.52–1.67
Body mass index (kg/m ²)	0.96	.08	0.92–1.00
Antidepressant use	1.83	.06	0.99–3.38
PHQ-9 affective scores	1.12	.006	1.03–1.22

PHQ-9 = nine-item Patient Health Questionnaire; NYHA = New York Heart Association. Total model *p* < .001.