ORIGINAL ARTICLE

Depressive Symptom Dimensions and Cardiovascular Prognosis Among Women With Suspected Myocardial Ischemia

A Report From the National Heart, Lung, and Blood Institute–Sponsored Women's Ischemia Syndrome Evaluation

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Context: Symptoms of depression and cardiovascular disease (CVD) overlap substantially. Differentiating between dimensions of depressive symptoms may improve our understanding of the relationship between depression and physical health.

Objective: To compare symptom dimensions of depression as predictors of cardiovascular-related death and events among women with suspected myocardial ischemia.

Design: Cohort study of women with suspected myocardial ischemia who underwent evaluation at baseline for a history of cardiovascular-related problems, depressive symptoms using the Beck Depression Inventory, and coronary artery disease severity via coronary angiography. Principal components analyses (PCAs) of the Beck Depression Inventory items were conducted to examine differential cardiovascular prognosis according to symptom dimensions of depression.

Setting: The Women's Ischemia Syndrome Evaluation (WISE), a multicenter study sponsored by the National Heart, Lung, and Blood Institute to assess cardiovascular function using state-of-the-art techniques in women referred for coronary angiography to evaluate chest pain or suspected myocardial ischemia.

Participants: Five hundred fifty women (mean [SD] age, 58.4 [11.2] years) enrolled in the WISE study and followed up for a median of 5.8 years.

Main Outcome Measures: Cardiovascular-related mortality and events (stroke, myocardial infarction, and congestive heart failure).

Results: When a 3-factor structure from PCA was used, somatic/affective (hazards ratio, 1.35; 95% confidence interval, 1.04-1.74) and appetitive (1.42; 1.21-1.68) but not cognitive/affective (0.89; 0.70-1.14) symptoms predicted cardiovascular prognosis in adjusted multivariate Cox regression analysis. When a 2-factor structure from PCA was used, adjusted results indicated that somatic (hazards ratio, 1.63; 95% confidence interval, 1.28-2.08) but not cognitive/affective (0.87; 0.68-1.11) symptoms predicted worse prognosis.

Conclusions: In a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with an increased risk of cardiovascular-related mortality and events. These results support the need to research dimensions of depression in CVD populations and have implications for understanding the connection between depression and CVD.

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THE COEXISTENCE OF DEPRESSION and cardiovascular disease (CVD) has been well established.[1] Although knowledge about the etiology, biology, and treatment of depression and CVD has increased in the past 2 decades,[2] the exact mechanisms linking these 2 illnesses have yet to be established. Research has demonstrated that depression and CVD may each precede the other, that they may develop concurrently, and that early signs of CVD may be mistaken for depressive symptoms.[2] Even in the absence of clearly delineated mechanisms for their relationship, the coexistence of depression and CVD is associated with worse CVD prognosis.[2,3] Treatment of depression in patients with CVD has not been demonstrated to reduce subsequent clinical events (eg, the Enhancing Recovery in Coronary Heart Disease Patients [ENRICHD] trial,[4] Sertraline Antidepressant Heart Attack Randomized Trial [SADHART],[5] and Myocardial Infarction and Depression–Intervention Trial

[MIND-IT][6]). However, because the treatments in these trials only partially alleviated depressive symptoms, we cannot definitively conclude that depression treatments do not improve CVD prognosis. Nevertheless, these unsuccessful studies underscore our incomplete understanding of the link between depression and CVD.[7]

The Beck Depression Inventory (BDI)[8] is a 21-item self-report measure of depressive symptoms that is frequently used within CVD populations.[9] The BDI assesses cognitive/affective and somatic depressive symptoms.[10] The BDI's somatic items (eg, difficulty sleeping and fatigue) frequently overlap with symptoms experienced by individuals with a variety of medical illnesses, making depression severity difficult to assess with this measure in medical populations.[11] Nevertheless, most researchers conducting depression studies on patients with CVD use the BDI rather than other self-report measures that contain primarily or exclusively cognitive/affective symptoms, such as the Hospital Anxiety and Depression Scale.[12]

Beck and colleagues[13] recognized the potential for misdiagnoses among patients with certain medical conditions and designed the BDI for Primary Care, a modified version of their original scale that assesses depressive symptoms within medical populations. This modified version includes only the cognitive/affective items from the original scale, thus circumventing the potential problem of overlapping depressive and CVD symptoms and reducing the potential for misdiagnoses of depression. However, to our knowledge, only 1 identified study[14] has used this modified scale (referred to as the BDI–Fast Scale) to examine the relationship between depressive symptoms and subsequent cardiovascular events in patients with CVD.

On the other hand, Simon and von Korff[15] concluded in a meta-analysis that somatic depression symptoms do not constitute a significantly greater proportion of overall depressive symptoms among medically ill patients than among generally physically healthy individuals, a finding that argues against the necessity of using depression measures that de-emphasize somatic symptoms when assessing CVD populations. Taken together, the literature on this topic remains inconclusive, and whether measures such as the BDI are biased by somatic symptom overlap remains unclear because this possibility has not been tested empirically.

Recently, de Jonge and colleagues[16] used factor analysis to examine the differential abilities of cognitive/affective and somatic depressive symptoms as assessed by the BDI to predict CVD prognosis within a mixed-sex population who had experienced myocardial infarction (MI) (post-MI population). Their analysis revealed 3 factors, which they labeled cognitive/affective, somatic/affective, and appetitive, based on a combination of the labels used by Beck and Steer[10] in the BDI manual and Morley et al[17] in a factor analysis of the BDI items in a population with chronic pain. Neither of the factor structures from these 2 prior reports[10,17] aligned precisely with those discovered in the 2 post-MI population samples (which were subjected to cross-validation through multisample structural equation modeling) examined by de Jonge and colleagues.[16] Results revealed a significant bivariate association between the somatic/affective symptom scale score and CVD prognosis, such that somatic/affective symptoms predicted a higher risk of events. The relationship between cognitive/affective symptoms and CVD prognosis was not statistically significant. Neither of the 2 factors remained significant in multivariate analyses with combined cardiovascular-related events and mortality as the end point. However, the somatic/affective factor's hazard score was only slightly reduced after covariate adjustment (from 1.39 to 1.30), and it continued to predict cardiovascular-related mortality. Appetitive symptoms, a factor consisting of only 2 BDI items (loss of appetite and weight loss) did not significantly predict CVD prognosis in any of the models. Moreover, at baseline, 4 indicators of poor physical health were significantly correlated with somatic/affective and appetitive symptoms, whereas only 1 was related to cognitive/affective symptoms.[16] Of note, the reporting of these analyses[16] has been called into question,[18] particularly with regard to the failure of de Jonge et al[16] to address issues that may affect the results' interpretability, such as multicollinearity and high interfactor correlations.

Watkins et al[19] examined cognitive and somatic symptoms of depression as assessed by the BDI in relation to medical comorbidities after acute MI among patients enrolled in the ENRICHD trial. The researchers separated the items according to their face content, creating cognitive and somatic factors. Results showed that, although both factors were positively and statistically significantly correlated with medical comorbidity, the relationship was stronger for somatic ($r=0.24$) than for cognitive ($r=0.06$) symptoms.[19]

The purpose of the present study is 2-fold: (1) to create composite factors (eg, somatic and cognitive/affective) from the 21 BDI items via data reduction techniques in a sample consisting of women with suspected myocardial ischemia; and (2) to subsequently examine and compare the differential associations of these identified depressive symptom types with cardiovascular-related events, including congestive heart failure, MI, stroke, and cardiovascular-related death, for a median of 5.8 years. In light of the previously summarized research conducted on this topic in similar cardiac populations, we hypothesized that somatic but not cognitive depressive symptoms would predict cardiovascular-related events in this sample.

METHODS

STUDY DESIGN

Women undergoing angiography for suspected myocardial ischemia at 1 of 4 sites (University of Alabama at Birmingham; University of Florida, Gainesville; University of Pittsburgh; and Allegheny General Hospital, Pittsburgh, Pennsylvania) were enrolled in the Women's Ischemia Syndrome Evaluation (WISE) study. The WISE study was designed to improve the understanding and diagnosis of ischemic heart disease in women. Exclusion criteria included current pregnancy, cardiomyopathy, a recent MI or revascularization procedure (percutaneous coronary intervention or coronary artery bypass graft), a history of congenital heart disease, a language barrier preventing questionnaire completion, and an inability to provide consent, among

others. The complete design and methods of the WISE study are described elsewhere.[20] In short, each woman's demographic characteristics, cardiovascular risk profile, and history of other known risk factors were gathered in an extensive baseline evaluation. Race was determined via participants' self-reported selection from a list of options created by the research team, including an "other" option, to assess whether cardiovascular-related health differences exist among women from various racial backgrounds. To enable the assessment of psychosocial characteristics that may be related to cardiovascular outcomes, the women completed a battery of psychosocial questionnaires, including the BDI,[8] to assess depressive symptoms. All participants were queried about their history of certain cardiovascular-related events and conditions, including congestive heart failure, percutaneous coronary intervention, coronary artery bypass graft, MI, cerebrovascular disease (eg, stroke and transient ischemic attack), peripheral vascular disease (eg, claudication and peripheral vascular surgery), and cardiovascular risk factors (eg, diabetes mellitus, hypertension, and dyslipidemia). The WISE angiographic core laboratory, which was blinded to all other subject data, analyzed coronary angiograms using a quantitative method described in detail elsewhere.[21] The angiogram results were used to assign each participant a continuous coronary artery disease (CAD) severity score based on a modified Gensini index.[22]

All participants provided written informed consent that was approved by the institutional review board at their local WISE clinical site. Although 936 women were enrolled in WISE, this study examined a subsample of 550 women for whom data were available on all variables included in the analyses. Two hundred sixty-nine (28.7%) data points were missing because the psychosocial questionnaires, including the BDI, were not added to the WISE protocol until the study's second year. The remaining missing data points (117 [12.5%]) are attributed to missing follow-up or covariate data and/or incomplete BDI scores (ie, skipping BDI items).

CLINICAL EVENT TRACKING

Women were contacted via telephone and/or mail 6 weeks after baseline and annually thereafter for a median of 5.8 years to track their subsequent adverse cardiovascular events (congestive heart failure, stroke, and MI) and mortality, together referred to as *clinical events* or *cardiovascular prognosis*. The names of treating physicians, clinical centers, and hospitals were collected and subsequently contacted for relevant documentation and test results of reported clinical events. Death certificates were obtained to confirm deaths reported by significant others and were reviewed by an independent study physician blinded to the patient's CVD status or other study data. For purposes of the current study, deaths were counted as clinical events if they were classified as definitely or probably due to cardiovascular reasons.

STATISTICAL ANALYSIS

Principal components analysis (PCA) was conducted using the WISE sample (n = 550) to reduce the 21 individual BDI items into fewer factors/components while retaining the original item information. We selected PCA rather than factor analysis for 2 primary reasons: (1) its ultimate goal is to reduce data into components useful for other purposes (in this case to predict cardiovascular prognosis according to aggregate types of depressive symptoms rather than individual depressive symptoms), as opposed to the primary goal of factor analysis, which is to reveal underlying variables that cause manifest variables to covary[23]; and (2) its superior ability to remedy multicollinearity among factors, should they exist.[23,24]

Promax rotation was selected because it is an oblique method, which allows factors to correlate with each other (as BDI factors are expected to do), as opposed to an orthogonal method, which artificially forces factors to be uncorrelated.[23,25] Factor scores were calculated on the basis of unstandardized item factor loadings and transformed into standardized z scores (using the Anderson-Rubin method) to increase their interpretability.

We first conducted PCA to examine a solution including all factors with eigenvalues greater than 1. A scree plot of eigen values and the number of complex items were used as additional criteria for selecting the best overall solution.[26] Although 3 factors emerged in this initial analysis, a combination of the aforementioned criteria indicated that 2 or 3 factors may form the optimal solution of the analysis. Subsequently, a PCA specified to extract only 2 factors was completed for 2 purposes: (1) to permit a comparison between 2 data-driven solutions because the original PCA's results were inconclusive in terms of whether a 2- or a 3-factor solution was optimal; and (2) to examine a solution comparable to the traditional 2-factor structure of the BDI (ie, cognitive vs somatic symptoms).

Bivariate correlations between all pairs of factors in each solution were conducted to assess interfactor correlations. Three diagnostic tests for multicollinearity—variance inflation factor, tolerance, and condition number or index (κ)[24]—were examined within linear regression analyses in which raw factor scores predicted time to first event after baseline. Subsequently, multivariate hazard ratios and 95% confidence intervals (CI) were computed using Cox regression to examine differences in time to first event among the women according to standardized factor scores. Angiographic severity scores were included as a covariate in adjusted multivariate models to control for baseline CAD severity. An additional covariate included in the adjusted multivariate models—history of CVD—was determined by adding the total number of cardiovascular-related events or conditions (percutaneous coronary intervention, coronary artery bypass graft, congestive heart failure, MI, cerebrovascular disease, and peripheral vascular disease) each woman had reportedly experienced previously. Four additional covariates (education, race, history of diabetes mellitus, and history of smoking) were included in ancillary adjusted multivariate models that were conducted to further scrutinize the relationship between depression symptom types and cardiovascular outcomes. These 4 covariates were selected from a larger pool of CVD risk factors based on their sustained individual prediction of cardiovascular outcomes after depression dimension factor scores, angiographic severity scores, and history of CVD were included in the model. Analyses were conducted using SPSS version 11.5 (SPSS Inc, Chicago, Illinois), and the significance criterion was set at $P < .05$.

RESULTS

Baseline characteristics of the women are listed in **Table 1**. Of note, 39.3% of the women reported a history of at least 1 cardiovascular-related event or condition before the baseline evaluation, including 17.3% who had previously experienced multiple events or conditions. Coronary angiography severity scores were positively skewed, indicating a low amount of coronary obstruction within this population. Approximately half of the women reported that they were current or former smokers. Most of the women (83.6%) identified themselves as white, and 40.9% reported that they had obtained at least some higher education after achieving a high school diploma or equivalent.

Table 1. Baseline Characteristics of the WISE Subsample

Baseline Characteristic	No. (%) of Total (N=550)
Age, mean (SD), y	58.4 (11.2)
CAD severity score, mean (SD)	13.3 (12.7)
≤High school education	325 (59.1)
White	460 (83.6)
Cigarette smoking, current or former	288 (52.4)
Medical history	
Diabetes mellitus	119 (21.6)
Hypertension (n=549)	314 (57.2)
Dyslipidemia (n=519)	269 (51.8)
Cardiovascular-related events or conditions	
No. of events or conditions	
Any	216 (39.3)
1	121 (22.0)
2	70 (12.7)
3	15 (2.7)
4 or 5	10 (1.8)
Types of events or conditions	
Congestive heart failure	44 (8.0)
Myocardial infarction	103 (18.7)
Coronary artery bypass graft surgery	26 (4.7)
Percutaneous coronary intervention	81 (14.7)
Cerebrovascular disease	50 (9.1)
Peripheral vascular disease	44 (8.0)

Abbreviations: CAD, coronary artery disease; WISE, Women's Ischemia Syndrome Evaluation.

PRINCIPAL COMPONENTS ANALYSIS

The Kaiser-Meyer-Olkin measure of sampling adequacy (0.93) and the Bartlett test of sphericity ($P < .001$) indicated that the factor matrix was adequate for data reduction. Both models contained some items that loaded greater than 0.32 on more than 1 factor (ie, crossloading), making the classification of these items uncertain.[23] Similarly, the irritability item did not attain this minimum loading of greater than 0.32 on any factor in either model, indicating that it may not contribute to and/or belong with any of the identified factors.[23]

The 3-factor solution's aptness was questionable because the third factor consisted of only 2 items, which may render it unstable and weak because at least 3 items are generally advised to constitute each factor.[23] The item loadings for these 3 factors are presented in **Table 2**. Based on the face content of the items that loaded on each of them, the 3 factors were conceptualized as (1) cognitive/affective, (2) somatic/affective, and (3) appetitive.

The second PCA, constrained to 2 factors, appeared to produce an adequate solution. Both factors had eigenvalues greater than 1, the scree plot supported a 2-factor solution, and both factors consisted of multiple, strongly loading items. Based on the face content of the items that loaded on these factors, they were conceptualized as (1) cognitive/affective and (2) somatic. All of the affective items that had higher loading values on the somatic/affective component of the 3-factor solution loaded more strongly on the cognitive/affective component of the 2-factor solution, except for the irritability item, which loaded weakly (0.31) on the somatic factor. In addition, the 2 appetitive items (loss of appetite and weight loss) from the 3-factor solution loaded on the somatic component of the 2-factor solution.

ANALYSIS OF INDIVIDUAL BDI ITEMS AND SUBSCALE SCORES

Mean total BDI and subscale scores for each of the factor structures are listed in **Table 3**. Also listed in Table 3 are the percentages of the total BDI score attributable to each factor and the mean score on each item (possible range, 0-3) within each factor. Somatic/affective symptoms constituted nearly three-fourths of the total BDI score in the 3-factor structure, and somatic symptoms constituted more than two-thirds of the total score in the 2-factor structure. All items were positively skewed, with all but 2 item means greater than 1.

As expected, correlations among subscale scores (ie, interfactor correlations) were large and significant. The strong correlation between the somatic/affective and cognitive/affective subscale scores in the 3-factor solution ($r=0.66$) was reduced in the 2-factor solution ($r=0.61$) but remained large nonetheless. The correlations between appetitive and somatic/affective symptoms ($r=0.26$) and between appetitive and cognitive/affective symptoms ($r=0.23$) in the 3-factor solution were much lower but still statistically significant. Despite these large interfactor correlations, multicollinearity did not appear to pose a problem because the diagnostic test values were all well within acceptable limits[24] (variance inflation factor, 1.08-1.82; tolerance, 0.55-0.93; κ, 2.24-5.30).

RELATIONSHIP BETWEEN FACTOR STRUCTURE AND CARDIOVASCULAR PROGNOSIS

Altogether, 91 of the women (16.5%) experienced at least 1 adverse cardiovascular-related outcome during the mean 5.8-year follow-up, for a total of 107 independent events, including those experienced by women who had multiple events. Among these events were 31 cases of congestive heart failure, 19 cases of MI, 28 cases of stroke, and 29 cardiovascular-related deaths. An additional 19 women died of causes not determined to be cardiovascular related. Results from unadjusted and adjusted multivariate Cox regression analyses in which the 3 factors from the initial PCA or the 2 from the second PCA were included as the independent variables predicting cardiovascular events are presented in **Table 4**. None of the cognitive/affective factors was significant in any of the models. However, the somatic/affective and appetitive components of the 3-factor model were significant predictors of events in the unadjusted and adjusted multivariate analyses. Similarly, the somatic factor of the 2-factor structure remained significant in the unadjusted and adjusted multivariate models. In identical models with only cardiovascular-related death or non–cardiovascular-related death as the outcome of interest, none of the factor components remained significant after adjustments (data not shown).

ANCILLARY ANALYSES

Results from the ancillary adjusted multivariate Cox regression analyses in which 4 additional variables were

Table 2. Individual Item Factor Loadings of BDI Depressive Symptom Dimensions and Relationships With Previous Dimensional Constructs[a]

	Factor Loading					Corresponding Dimensions in Previous Studies' Constructs	
	3-Factor PCA			2-Factor PCA			
	Cognitive/ Affective	Somatic/ Affective	Appetitive	Cognitive/ Affective	Somatic/ Affective	de Jonge et al[16]	Beck and Steer[10]
Sadness	0.57			0.58		Somatic/affective	Cognitive
Pessimism	0.62			0.64		Cognitive/affective	Cognitive
Sense of failure	0.87			0.85		Cognitive/affective	Cognitive
Dissatisfaction	*0.37*	0.48		0.45	0.39	Somatic/affective	Cognitive
Guilt	0.76			0.76		Cognitive/affective	Cognitive
Punishment	0.77			0.76		Cognitive/affective	Cognitive
Self-dislike	0.74			0.82		Cognitive/affective	Cognitive
Self-accusations	0.81			0.85		Cognitive/affective	Cognitive
Suicidal thoughts	0.46			0.51		Cognitive/affective	Cognitive
Crying	0.45			0.44		Somatic/affective	Cognitive
Irritability		0.30			0.31	Somatic/affective	Cognitive
Social withdrawal	0.41	*0.34*		0.47		Cognitive/affective	Cognitive
Indecisiveness	*0.36*	0.43		0.45	*0.31*	Somatic/affective	Cognitive
Negative body image		0.52		0.31	*0.30*	Cognitive/affective	Somatic
Work difficulty		0.81			0.74	Somatic/affective	Somatic
Insomnia		0.66			0.69	Somatic/affective	Somatic
Fatigability		0.88			0.80	Somatic/affective	Somatic
Loss of appetite			0.65		0.47	Appetitive	Somatic
Weight loss			0.76		0.41	Appetitive	Somatic
Somatic preoccupation		0.49			0.39	Somatic/affective	Somatic
Decreased libido		0.41			0.50	Somatic/affective	Somatic

Abbreviations: BDI, Beck Depression Inventory; PCA, principal components analysis.
[a]Factor loadings less than 0.30 are not reported for easier readability. Italics indicate loadings greater than 0.30 but less than those of the same item on another factor in the same analysis.

Table 3. BDI Total Score and Factor Components

Variable	Total Scale Score, Mean (SD)	Mean (SD) Response to All Items on Scale	Mean (SD) % of Total BDI Scale Score
Total BDI score	10.4 (8.0)	0.50 (0.38)	100.0 (. . .)
3-Factor PCA			
Cognitive/affective symptoms	3.0 (4.1)	0.30 (0.41)	19.7 (20.0)
Somatic/affective symptoms	6.7 (4.3)	0.75 (0.48)	72.5 (22.0)
Appetitive symptoms	0.7 (1.2)	0.37 (0.59)	7.8 (14.0)
2-Factor PCA			
Cognitive/affective symptoms	4.5 (5.4)	0.35 (0.41)	32.3 (24.0)
Somatic/affective symptoms	5.9 (3.6)	0.74 (0.45)	67.7 (24.0)

Abbreviations: BDI, Beck Depression Inventory; PCA, principal components analysis; ellipses, not applicable.

included as covariates are also presented in Table 4. The previously significant relationship between the somatic/affective component of the 3-factor model and cardiovascular prognosis failed to remain statistically significant after controlling for the 4 additional covariates. None of the predictive values of the other factors from either of the models decreased appreciably in these ancillary analyses.

COMMENT

In a sample of 550 women with suspected myocardial ischemia, symptom dimensions of depression measured by the BDI and determined through PCA were examined in relation to cardiovascular prognosis during 5.8 years of follow-up. Results indicated that somatic/affective and appetitive but not cognitive/affective symptoms of depression significantly predicted cardiovascular events in a 3-factor model. Similarly, somatic but not cognitive/affective symptoms significantly predicted cardiovascular events in a 2-factor model. These findings persisted in models adjusted for a history of CVD events and conditions as well as for CAD severity at baseline. Thus, the predictive ability of somatic symptoms was not entirely attributable to increased somatic symptoms due to more severe physical disease at baseline, although an overlap of somatic symptoms between depression and physical illness cannot be dismissed.

MECHANISMS

Results from this study have implications for the mechanisms by which depression may affect cardiovascular prog-

Table 4. Results From Cox Regression Analyses Demonstrating the Relationships Among Depressive Symptom Dimensions From the 3-Factor and 2-Factor Models and Cardiovascular Prognosis

	Symptom Dimension					
	Cognitive/Affective		Somatic/Affective		Appetitive	
Measure of Cardiovascular Prognosis	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
3-Factor Model						
Unadjusted multivariate analysis	0.84 (0.66-1.08)	.18	1.36 (1.06-1.74)	.02	1.47 (1.25-1.74)	<.001
Adjusted multivariate analysis[a]	0.89 (0.70-1.14)	.36	1.35 (1.04-1.74)	.02	1.42 (1.21-1.68)	<.001
Ancillary adjusted multivariate analysis[b]	0.85 (0.66-1.09)	.21	1.19 (0.91-1.55)	.21	1.30 (1.10-1.55)	.003
2-Factor Model						
Unadjusted multivariate analysis	0.79 (0.62-1.02)	.07	1.71 (1.36-2.14)	<.001	...	...
Adjusted multivariate analysis[a]	0.87 (0.68-1.11)	.26	1.63 (1.28-2.08)	<.001	...	...
Ancillary adjusted multivariate analysis[b]	0.81 (0.64-1.03)	.09	1.39 (1.08-1.79)	.01	...	...

Abbreviations: CI, confidence interval; HR, hazard ratio; ellipses, not applicable.
[a] Adjusted for coronary artery disease severity scores at baseline and self-reported history of cardiovascular-related events and conditions.
[b] Adjusted additionally for education, race, history of diabetes mellitus, and history of smoking.

nosis. Individuals reporting depressive symptoms at baseline, when their CVD symptoms were acute, may have subsequently engaged in negative health behaviors often associated with depressed mood and the progression of CVD, such as smoking and physical inactivity. Alternatively, perhaps certain physiological correlates of depression (eg, inflammation and autonomic nervous system activity) contributed to the worse prognosis.[27] Likewise, somatic symptoms may be more closely related to the physiological alterations associated with depression; indeed, somatic symptoms are reminiscent of the vital exhaustion concept.[28] These hypotheses differ from the idea that somatic depressive symptoms may simply be physical manifestations of more severe CVD but do not negate the somatic-CVD link. Indeed, the relationship between somatic/affective depressive symptoms and cardiovascular prognosis remained after controlling for the CAD severity score and a history of CVD. However, because many factors play prognostic roles in CVD outcomes, our ability to characterize baseline disease severity was limited. Moreover, the greater prevalence of somatic than cognitive/affective symptoms in this population should also be noted because somatic symptoms had greater potential for statistical relationships with cardiovascular prognosis.

TREATMENT IMPLICATIONS

Differentiating between cognitive and somatic symptoms of depression may also have important treatment implications. A question that has been posed many times but continues to emerge is whether treating depression within the context of CVD can improve future physical health outcomes in addition to allaying depressive symptoms. Although treatment trials have been largely discouraging,[4-6] hope still remains that treating depression will increase event-free survival. Indeed, a secondary analysis of patients in the ENRICHD trial who were treated with antidepressants in addition to cognitive behavioral therapy indicated that this combination treatment was associated with increased event-free survival, despite a lack of relatively greater improvement in BDI scores over time.[29] Similarly, results from the SADHART study[5] showed a trend toward increased event-free survival among patients who were depressed after MI and were treated with sertraline hydrochloride. Moreover, nonresponders to mirtazapine in the MIND-IT study experienced worse prognosis compared with treatment responders and untreated control subjects.[30] However, the fact that these 3 studies' primary results showed no effect of depression treatment on cardiovascular prognosis[4-6] must be emphasized.

The precise mechanisms underlying the effectiveness of antidepressants are unknown. As suggested by the ENRICHD writing group,[4] these results may indicate that antidepressants improve CVD prognosis through mechanisms not mediated by decreased depressive symptoms. Previous observational research also demonstrated a reduced risk for MI associated with antidepressants, particularly selective serotonin reuptake inhibitors.[31] These results may reflect the inhibitory effects of selective serotonin reuptake inhibitors on platelets[32] or combinations of other effects. Perhaps other types of depression treatments should be examined more thoroughly in this context. For example, recent evidence demonstrates that exercise is as efficacious at alleviating depressive symptoms as antidepressants[33] and also improves clinical outcomes in patients with coronary heart disease.[34]

One potential criticism on this topic is that the small effects of minimal reductions in depressive symptoms seen in treatment studies (1%-4% of variance) could not realistically be expected to translate into end results related to cardiovascular prognosis. However, minimal to modest improvements in other risk factors for worse cardiovascular prognosis (eg, overweight/obesity, inactivity, hyperlipidemia, and hypertension) are often associated with improved prognosis.[35,36] The null primary findings of studies on the effect of depression treatment on cardiovascular prognosis[4-6] underscore our currently incomplete understanding of the depression-CVD link.

COMPARISON WITH PREVIOUS RESEARCH

We attempted to closely duplicate the methods of de Jonge and colleagues[16] to facilitate an accurate comparison of

the 2 studies' results. Our ability to generally support the previous findings strengthens the literature on this topic. However, in the process of reproducing their methods, we sacrificed a certain degree of quality control, particularly with regard to omitting certain covariates in the primary multivariate models. Therefore, we conducted ancillary adjusted multivariate analyses, controlling for 4 additional variables that appeared to statistically influence the relationship between depression dimensions and cardiovascular outcomes. The inclusion of these covariates resulted in a diminished relationship between somatic/affective symptoms of depression (from the 3-factor model) and cardiovascular risk that was no longer statistically significant. However, the relationships between cardiovascular risk and both appetitive (from the 3-factor model) and somatic (from the 2-factor model) symptoms of depression remained significant after adjusting for these 4 additional covariates.

Many items loaded strongly or nearly equally well on more than 1 dimension in this study and that of de Jonge et al,[16] suggesting that some symptoms measure more than 1 construct in cardiovascular populations. However, we should note a few key differences between the two studies. Although both samples initially produced a 3-factor structure, 3 of the BDI items that loaded on the somatic/affective or cognitive/affective component in one sample loaded on the opposite component in the other sample (Table 1). No obvious explanations for these specific items' variability are apparent. However, the populations from which the samples were drawn are different in some noteworthy respects. For instance, the WISE population consists solely of women who presented with signs and symptoms of myocardial ischemia at baseline, whereas the 2 populations from which de Jonge et al[16] drew their samples included both sexes, and all had recently experienced an MI, a major event that may have affected responses to the BDI in a much different way than symptoms of myocardial ischemia would have. The varying degrees of disease severity among the samples may also help to explain the differential results.

Barefoot and colleagues[37] reached quite different conclusions in their examination of the relationship between depressive symptoms and prognosis. This group reported that negative affective symptoms of depression (including sadness, crying, suicidal ideas, irritability, and restlessness) but not well-being, somatic, or appetitive symptoms predicted mortality in CAD patients. Although Barefoot et al[37] also used factor analytic techniques in their study, they assessed depressive symptoms using the Zung Self-rating Depression Scale[38] rather than the BDI, so differences between their results and ours should be interpreted with caution. Nevertheless, because these 2 particular scales contain relatively equal representations of cognitive/affective and somatic symptoms of depression, other potential explanations for the differing study results may be more plausible.

Another noteworthy point is that all of the aforementioned studies that have used factor analysis to examine the differential effects of cognitive/affective and somatic symptoms of depression on CVD prognosis have included both sexes in their CVD patient populations, unlike the WISE population. Although no significant differences have been found between the sexes on cognitive symptoms of depression, women tend to report more somatic depression symptoms than men.[39] Perhaps the somewhat differing results obtained between this and similar studies can be attributed to the greater elevation and representation of somatic symptoms within this exclusively female sample.

Although relatively few factor-analytic studies of depressive symptoms have been conducted within CVD populations, many other populations, including those with various medical diseases or complications, have been examined using similar analyses.[40,41] Results have varied widely across specific types of populations, suggesting that they probably cannot be extrapolated accurately to other populations or even to other samples that vary on secondary characteristics, as is evident by the results presented herein.

LIMITATIONS

As we have noted, the results of this study cannot necessarily be extrapolated to populations other than women with symptoms of myocardial ischemia. Also, the subsample of subjects included in these analyses (550 of 936) may not have been completely representative of the entire WISE sample, and power was lowered by the missing data. Self-reported cardiovascular-related events and conditions that occurred before baseline were not verified by medical records and hence may not have been entirely accurate. Furthermore, depressive symptom severity was assessed at baseline, when some of the depressive symptoms women were experiencing may have been temporary, attributable to their acute cardiovascular concerns. Hence, their baseline depressive symptom levels were likely transitory, increasing or decreasing in response to their subsequent health status. Similarly, some women may have altered their lifestyles or modified their risk factor profiles via medications and/or psychotherapy during follow-up, thus increasing or decreasing their risk of events over time. Future studies would serve the literature if they incorporated repeated assessments of depressive symptoms and other risk factors, gathered at various points during follow-up. Future studies investigating the mechanisms underlying the differential association between cognitive/affective vs somatic depressive symptoms and subsequent event rates are also warranted.

A few statistics-related limitations are noteworthy. Principal components analysis is influenced by sample-specific characteristics, making the stability of its factors rather precarious. We elected to use PCA (an exploratory method) rather than confirmatory factor analysis, despite its deviation from standard best-practice methods for replication attempts, because of inconsistencies in the results obtained across previous samples exploring the BDI's factor structure. Finally, we conducted PCA using the standard matrix of Pearson correlations rather than that of polychoric interitem correlations, as is recommended by some researchers when analyzing ordinal variables.[42]

In conclusion, in a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with an

increased risk of cardiovascular-related mortality and events. These results support the need to research the dimensions of depression in CVD populations and have implications for understanding the connection between depression and CVD.

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