Depression Is Associated With Cardiac Symptoms, Mortality Risk, and Hospitalization Among Women With Suspected Coronary Disease: The NHLBI-Sponsored WISE Study

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Objective: Depression is a robust predictor of cardiovascular risk. In this study, we examined the association between depression measured in terms of symptom severity and treatment history, cardiac symptom presentation, and clinical outcomes among a sample of women with suspected myocardial ischemia. **Methods:** Seven hundred fifty women with chest pain, mean age 53.4, completed a diagnostic protocol including depression measures, coronary angiogram, ischemia testing, and coronary disease risk factor assessment. Five hundred five participants also completed the Beck Depression Inventory. We further tracked participants over a mean 2.3-year period to evaluate subsequent cardiac events, hospitalization, and mortality. **Results:** Depression treatment history and current symptom severity were differentially associated with cardiac symptoms and outcomes. Both measures were reliably associated with coronary artery disease (CAD) risk factors and more severe cardiac symptoms. Depression symptom severity was linked to an increased mortality risk over follow-up (RR = 1.05; 95% CI, 1.01–1.09), whereas depression treatment history predicted an increased risk of hospitalization (RR = 1.3; 95% CI, 1.02–1.6), less severe CAD from angiogram, and a reduced likelihood of a positive ischemia test. **Conclusion:** Among a sample of women with suspected myocardial ischemia, depression was associated with cardiac symptoms and health outcomes over follow-up. The findings extend the range of depression effects by demonstrating relationships within a sample of women experiencing symptoms of myocardial ischemia but showing a relative absence of flow limiting coronary stenoses. Depression measurements can assist the clinician in evaluating cardiac symptom presentation and cardiovascular risk status in women. **Key words:** women, CAD, depression, mortality, ischemia.

CAD = coronary artery disease; **WISE** = Women's Ischemia Syndrome Evaluation; **BDI** = Beck Depression Inventory.

INTRODUCTION

Depression is a robust predictor of coronary artery disease (CAD) development and prognosis (1), but the etiology underlying this relationship remains unclear. Despite the lack of survival benefits shown for post-MI patients receiving a cognitive-behavioral treatment for depression in the recently completed ENRICHD trial (2), evidence for an association between depression and cardiovascular events continues to grow (3–6). Results from this literature favor the conclusion that the presence of depression increases the risk of cardiovascular events and mortality; predicts poor treatment adherence and more frequent and earlier hospital readmissions; is linked with higher rates of major CAD risk factors such as smoking, obesity, and sedentary lifestyle; and contributes to a lower quality of life (6–8). Further, even subclinical levels of depression severity are associated with changes in sympathetic and parasympathetic nervous system activity and alterations in platelet responsiveness (1,9,10), providing support for plausible biological pathways. To date, much of this evidence is based on samples of patients with advanced CAD, leaving depression relationships among patients without severe atherosclerosis comparatively understudied. Given the still-limited understanding of depression effects on the cardiovascular system, it is important that new research address depression effects among healthy and diseased individuals, as well as study populations most susceptible to depression.

Women have traditionally received less focus in heart disease research relative to men, despite well-known gender differences indicating comparatively less aggressive treatments, less accurate diagnostic tests, and higher post-MI mortality among women (11,12). More recent research is beginning to change these trends, however, with an abundance of new data available addressing risk factors, treatments, and diagnostic issues affecting CAD among women (13–15). Because depression rates among women exceed those for men by a factor of more than 2 to 1 (16) and may be associated with clinical symptoms that affect cardiac diagnosis and treatment (11), the study of the quality and severity of depression symptoms of women with subclinical or clinically evident ischemic heart disease can stimulate improved understanding of the pathophysiology and impact of central nervous system symptoms on cardiovascular-related health.

In the current study, we describe depression relationships among a sample of women with suspected CAD as part of the Women's Ischemia Syndrome Evaluation (WISE). Participants provided information on current depression symptom severity, as well as depression treatment history, as part of a protocol that included questionnaires, physical examination, coronary angiography, and ischemic testing. We further followed WISE participants for more than 2 years in order to track the incidence of hospitalization and mortality. Our de-

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scription includes data concerning depression prevalence in the WISE sample; associations among depression, cardiac symptoms, and primary CAD risk factors; and relationships among depression, hospitalization, and mortality. Based on previous studies, we projected that depression symptom severity would be associated with coronary symptoms and mortality outcomes for women. The comparative predictive power of depression treatment history was assessed as an exploratory measure.

METHODS

Participant Recruitment and Entrance Criteria

The WISE is a National Heart, Lung, and Blood Institute–sponsored multicenter study assessing cardiovascular function using state-of-the-art techniques in women referred for coronary angiography to evaluate chest pain or suspected CAD. An extensive description of the WISE protocol and methodology has been previously published (17). Participants completed a battery of symptom and psychological questionnaires at baseline, along with quantitative coronary angiography, exercise stress testing, and other diagnostic procedures. Presented results are based on a total of 750 women with complete depression treatment history and follow-up survival data. A total of 505 women also completed the Beck Depression Inventory (BDI), all of which also have complete survival outcome data. Most of the missing psychosocial data are accounted for by early changes to the WISE questionnaire battery.

Women were eligible for participation in WISE if they were older than 18 years of age and were referred for a coronary angiogram. Exclusion criteria included current pregnancy, cardiomyopathy, recent myocardial infarction or revascularization procedure (PTCA, CABG), language barrier preventing questionnaire completion, and a history of congenital heart disease, among other criteria. Recruitment for WISE preceded psychological questionnaire development by approximately 3 months, accounting for the absence of questionnaire data among early participants. The WISE study received institutional review board approval from each participating site, and all participating women provided informed consent.

Measurement of CAD, CAD Risk Factors, and Mortality

We derived estimates of coronary disease severity based on two criteria. First, using the quantitative angiogram results, we assigned each participant to a "no CAD" (<20% maximum stenosis), "nonobstructive CAD" (20% to 49% maximum stenosis), or "obstructive CAD" (≥50% maximum stenosis). Second, we used the raw maximum stenosis score from the participant's angiogram. In addition, a total of 343 participants completed one or more noninvasive tests for myocardial ischemia, including exercise and pharmacologic stress testing with or without echocardiographic or radionuclide imaging. Finally, WISE participants responded to questionnaires assessing the presence of angina and querying the types of symptoms they experienced.

Women were followed for the tracking of new cardiovascular events, hospitalizations, and death over a mean 2.3 years of follow-up. For the purpose of the current paper, cause of death was not differentiated in primary analyses due to insufficient numbers. Follow-up was conducted by telephone interview at 6 weeks and then yearly thereafter. Follow-up consisted of a scripted interview by an experienced nurse or physician. Each patient was queried for the occurrence of hospitalizations and the reason for hospitalizations. Among the total of 988 enrolled participants, only 34 were lost to follow-up (3%). No participants with valid depression data were lost. Events were defined as hospitalization for unstable angina, myocardial infarction, congestive heart failure, stroke, other vascular events, and death. When a major cardiovascular event was identified, the referring physician was contacted for confirmation, dates, and documentation of the occurrence. In the event of death, a death certificate was obtained.

Major CAD risk factors in the WISE protocol included body mass index, smoking, cholesterol, diabetes history, hypertension, and education history. The assessment of smoking, diabetes, and hypertension status was based on participants' self-report of diagnosis and treatment history. Cholesterol was assessed with a standard blood serum test, and BMI was calculated using results from a physical examination, including height and weight. All testing was performed in accordance with institutional guidelines. Participants responded to categorical questions concerning their education history. Participants also completed the Social Network Index (18), a validated instrument assessing the size of participant's social circles. A 3-item study-designed quality-of-life scale was also included in the protocol. These items evaluated the patient's perceived health, quality of life, and life satisfaction on a Likert scale.

Cardiac Symptom Assessment

As part of the baseline protocol, participants completed a study-designed comprehensive symptom history questionnaire. This measure assessed the presence of a wide variety of body symptoms, including pain, weakness, breathing difficulties, chest symptoms such as tightness and pressure, dizziness, and heart rate changes, among others. The measure also queried the frequency and duration of reported symptoms, circumstances producing them, and the effects of intervention efforts such as rest or taking nitroglycerin.

Depression Measures

As part of the baseline self-report battery, participants completed the BDI (19). The BDI is a widely used, 21-item instrument for assessing a variety of depression symptoms and has been shown to predict cardiovascular disease outcomes among cardiovascular patient populations in several studies (8). Although completion of the BDI provides continuous scores ranging from 0 to 48, previous research suggests that scores of 17 or more indicate the presence of moderate to severe depression. Because psychosocial distress levels were high in WISE (17), we felt this high cutoff score for marking elevated depression symptoms was appropriate. WISE participants also reported whether they had ever received treatment for depression as part of their baseline examination. Some elements of the psychosocial test battery were delayed in implementation during the beginning of WISE, accounting for some of the incomplete questionnaire data.

Statistical Analyses

We explored depression relationships using both continuous and categorized scores (less than 17 or greater on the BDI). Depression treatment history was a simple dichotomous predictor in all analyses. Comparisons among cardiac symptoms were completed using *t* tests. The latter tests compared the high and low Beck Depression scorers in one series and those with a positive and negative depression treatment history in a separate series of analyses. For the analysis of hospitalization and mortality events, we used Cox regression models to evaluate age and CAD severity-adjusted depression relationships and effects after controlling for the previously described CAD risk factors (diabetes, hypertension, cholesterol, BMI, smoking, and education). For comparison purposes, we also performed models that included both depression predictors in the same equation. Because these models did not change the interpretation, we do not include them. Statistical power for the survival analyses exceeded 0.80 based on a sample size of 505, an α of 0.05, and a projected 30% increase in mortality for depressed versus nondepressed participants but was reduced to approximately 0.60 after adjusting for covariates. We completed all statistical tests using SPSS 10.0 software.

RESULTS

Table 1 provides a description of WISE participants separated by depression status on measured CAD risk factors. Approximately 18% of WISE participants reported depression scores consistent with the presence of at least moderate depression (i.e., BDI scores of 17 or more) at the time of baseline assessment, and 39% of respondents reported a history of treatment for depression symptoms. Based on self-reported BDI scores, participants with more severe depression showed

TABLE 1. A Description of Major Coronary Artery Disease Risk Factors Across Measures of Depression Among WISE Participants

	Total Sample (n = 988)	Low BDI Scores (n = 413)	High BDI Scores[a] (n = 92)	−Depression History (n = 558)	+Depression History (n = 192)
Age	53.4 (10.9)	54.6 (11.2)	48.5 (8.2)**	60.4 (11.8)	50.3 (10.7)**
Maximum stenosis	35.8 (35.1)	35.1 (34.9)	39.9 (36.1)	41.4 (37.2)	34.6 (32.8)*
Married (%)	63.1	64.5	55.7	64.5	56.8
HDL	54.2 (12.1)	54.3 (12.1)	53.7 (12.5)	52.9 (12.2)	54.0 (13.8)
LDL	113.8 (39)	112.8 (37.7)	118.9 (45.3)	116.2 (40)	110.8 (39.6)
BMI	29.6 (6.5)	29.6 (6.5)	29.8 (6.1)	30.3 (6.6)	29.9 (6.9)
Hypertensive (%)	55.6	55.5	55.7	57.2	60.9
Diabetic (%)	21.5	21.4	20.3	24.4	23.4
High school ED (%)	81.6	84.2	68.4**	79.7	80.0
Smoking (%)	18.6	15.4	35.4**	16.3	29.7**
Social network	6.4 (1.8)	6.6 (1.8)	5.6 (1.7)**	6.5 (1.8)	6.2 (1.7)
+Ischemia test (%)	46.3	41	43.2	50	35.6**

[a] Defined by a score of 17 or more on the BDI. * $p < .05$ (Group differs from reference group), ** $p < .01$ (Group differs from reference group).

several markers of elevated CAD risk, including lower SES and a greater than twice the rate of smoking compared with participants with lower depression scores (p values $<.01$). Our assessment of participants with a positive versus negative depression treatment history suggested a similar pattern of CAD risk, with the positive-history group also evidencing significantly higher rates of smoking. Although participants' depression treatment history correlated only moderately with current BDI symptom severity ($r = 0.24$, $p < .001$), the groups in Table 1 overlap in constituency (e.g., a participant could be in both the low-BDI-depression and positive-treatment-history groups), permitting comparisons only among the Beck Depression less than 17/greater than or equal to 17 depression groups and between the positive and negative depression treatment history groups. Participants with either higher baseline BDI scores or positive depression treatment histories tended to be younger, and higher BDI scorers reported greater social isolation. Table 1 includes the complete WISE sample for comparison purposes. The depression subgroups did not differ from the WISE sample on any of the listed variables.

Table 1 also highlights two important differences in the risk factor results of WISE participants based on their depression symptoms. We observed no differences among the quantitative angiogram results or ischemia test findings using the BDI; however, depression treatment history proved a discriminating factor for both outcomes. Relative to those with no reported history of depression treatment, participants with a positive treatment history showed evidence of less severe CAD ($t = 2.2$, $p = .02$) and a reduced likelihood of a positive ischemia test ($t = 2.9$, $p = .004$). This relationship remained reliable after adjusting for participants' age and history of smoking, diabetes, and hypertension ($t = 1.95$, $p = .05$). Women with a history of depression treatment were 29% less likely to have a positive ischemia test (35.6% versus 50% for those with no depression treatment history) and 22% less likely to show clinically significant CAD (defined as a 50% or greater stenosis in a coronary artery) on angiogram testing (32% versus 41% rates of clinically significant CAD for those with a positive versus negative depression-treatment history).

Depression and Cardiac Symptom Patterns

In the next phase of analyses, we examined whether our depression markers would be associated with chest pain symptom patterns among WISE participants. The results are summarized in Table 2.

Participants reporting higher baseline BDI scores or a positive history of depression treatment showed a consistent pattern of heightened cardiac and somatic symptoms, as defined by the presence of chest tightness, left arm pain, angina during sleep hours, experience of sharp, knife-like pain in the left chest, and the use of nitroglycerin (all p values $<.05$). Participants with higher BDI scores also reported a greater frequency of back pain, suggesting that somatic symptom differences in these groups generalized beyond angina and cardiac presentation factors. Finally, more depressed participants indicated a lower quality of life ($p < .01$) based on a single-item assessment of overall satisfaction. Although the significance test patterns differed slightly using the two different markers of depression, the chest pain symptom profiles were generally very similar.

Depression, Hospitalization, and Mortality Risk

Following baseline, WISE participants were tracked for a variety of events, including hospitalization and death. Among participants with valid BDI measures, there were a total of 34 deaths (6.9% of sample). Further, 233 participants (roughly 48% of sample) were hospitalized over follow-up. The parallel statistics for those with valid depression treatment histories were 8% mortality rate ($n = 60$ events) and a 49.6% hospitalization rate ($n = 372$ events).

Depression measures were associated with each category of events. For hospitalization occurrence, a positive depression treatment history was a more reliable predictor compared with

TABLE 2. Relationships Between Cardiac Symptom Presentation, Depression Symptom Severity, and Depression Treatment History in WISE (n = 505)

Symptom	Low BDI Scores	High BDI Scores[a]	−Depression History	+Depression History
% Daily angina	38.4	39.3	40.1	39.8
% Using nitroglycerin	42.5	58.6*	40.5	53.3*
% Angina from exertion	55.8	48.1	55.5	55.7
% Report sharp, knifelike pain	22.4	44.0*	24.1	31.2
% Report chest tightness	64.9	83.3*	66.3	70.4
% Angina relieved by rest	65.2	72.0	67	63.2
% Angina awakes at night	40.6	53.8*	41.7	51.1*
% Left arm pain	35.5	43.3	34.3	45.2*
% Shortness of breath	61.6	70.1*	70	64.6
% Back pain	39.8	55.1*	40.2	48.0
Quality of life[b]	7.4 (2.0)	5.7 (2.1)*	7.1 (2.1)	6.4 (2.1)*

* $p < .05$ (Group differs from comparison depression group participants).
[a] Defined by a score of 17 or more on the BDI.
[b] Quality of life rated on a 10-point scale.

BDI scores. Women with a history of depression were hospitalized over follow-up at a significantly greater rate (55% versus 47%, respectively, $t = 2.3$, $p = .02$ after adjustment for age and CAD severity) compared with participants with no history of depression treatment. The Cox regression model describing the relationship between depression history and risk of hospitalization is described at the top of Table 3, suggesting an approximate 30% increase in adjusted risk over 2.3 years of follow-up. Depression predictors derived from BDI scores were not reliable predictors of hospitalization (RR = 1.01; 95% CI, 0.99–1.03; $p = .25$ for continuous BDI scores).

Mortality events, in contrast, proved to be more strongly related to depression symptom severity as measured by BDI scores relative to depression treatment history. As illustrated in Table 3, each point increase on participant's Beck Depression Scores was associated with an approximate 3% increase in mortality risk after adjustment for age, disease severity, and CAD risk factors. Mortality risk increased in a generally linear fashion with increasing depression severity, with an approximate death risk of 6.5% (9/137 cases) among the lowest quartile scorers on the BDI (5 or below) versus a death rate of 10% (11/112 cases) among the highest quartile participants (14 or above). Depression treatment history was not linked to mortality over follow-up after age and CAD severity adjustment (RR = 1.04; 95% CI, 0.55–1.9; $p = .86$), or the inclusion of additional CAD risk factors (RR = 0.86; 95% CI, 0.44–1.7; $p = .66$). Although we did not examine specific categories of death due to insufficient numbers, the relationship between depression symptom severity and CAD risk was further supported by an age and maximum stenosis severity adjusted association between BDI scores and heart attack risk over follow-up (RR = 1.1; 95% CI, 1.01–1.2; $p = .01$).

DISCUSSION

Among a sample of women with suspected coronary disease, depression was associated with a number of important indicators of CAD risk and prognosis. For the purposes of this investigation, we included two related but temporally distinct measures of depression in the form of baseline symptom severity and self-reported depression treatment history in order to clarify the nature of depression associations with different diagnostic and risk factor variables.

Not surprisingly, both treatment history and current depression symptom measures were associated with participant's CAD risk factor profiles, with the most consistent differences appearing in smoking rates, as well as differences in social isolation and socioeconomic status. Similarly, we observed consistent relationships between both depression measures and cardiac symptom patterns among WISE participants, with depression in either form disposing an increase in the presence and severity of physical symptoms.

Depression treatment history and current symptoms also differed in several important ways in their associations with

TABLE 3. Relationship Between Beck Depression Scores, Hospitalization, and Mortality Among WISE Participants After Covariate Adjustment

	RR	95% CI	*p* Value
Regression 1. Age and CAD severity-adjusted relationship between depression history and hospitalization[a]	1.3	1.02–1.6	.04
Regression 2. Age and CAD severity-adjusted relationship between BDI depression scores and mortality	1.05	1.01–1.09	.02
Regression 3. Age, CAD severity, and CAD risk factors–adjusted relationships between BDI scores and mortality	1.03	1.00–1.05	.05

[a] CAD risk factors included smoking, BMI, cholesterol, diabetes status, education, and hypertension history. The No History of Depression Treatment group served as the reference category for this analysis.

CAD severity and health outcomes over follow-up. Specifically, we observed that depression treatment history was uniquely linked to a reduced rate of clinically significant atherosclerosis and myocardial ischemia, as well as to an increased risk of hospitalization. Depression symptoms measured via the BDI were not reliable statistical predictors of these variables but were prospectively related to an increased mortality risk.

Although it may be tempting to interpret depression history as having a protective effect on atherosclerosis in WISE—possibly through improved treatment-seeking behavior, greater psychological hardiness from previous mood difficulties, or differences in pathopysiological mechanisms—this association may also represent a bias resulting from the sample characteristics in WISE. Anxiety history showed a similar effect in WISE (20), suggesting that, among women experiencing symptoms indicative of myocardial ischemia serious enough to warrant angiography, those reporting a mental health history of anxiety or depression are more likely to be "false-positive" cases, with chest pain symptoms of a noncardiac origin. We have speculated that the mental health histories of WISE participants may have served as a flag for identifying patients who are generally more somatic (20), a theory that is partly supported by the consistently higher rates of reported psychological, chest pain, and bodily sensations reported by those with a history of depression treatment. In light of the somewhat different pattern of results from our measures of depression, an issue of potential future research interest concerns the stability or recurrence of depression symptoms. More stable or recurrent depression symptoms may represent the subgroup of greatest risk (21), for which baseline symptom or treatment history assessments alone are poor estimates.

Depression and Cardiac Symptom Presentation

A distinguishing feature of the WISE sample is that participating women were selected based on clinical criteria indicating a likelihood of underlying CAD. As a result, the characteristics of the WISE cohort are very similar to women undergoing cardiology examinations in standard clinical settings. These similarities underlie the primary purpose of WISE, which is to better understand contributing mechanisms among women with abnormal diagnostic tests for myocardial ischemia in the absence of coronary atherosclerosis (17,20).

Gender differences in the sensitivity and specificity of ischemia tests are well documented but not well understood (22–24). Although there remain a number of plausible theories based on potential cardiovascular factors, such as differences in microvascular function (25), it is also plausible that psychosocial variables play an important role. Recent population studies confirm a strong link between depression and somatic symptoms (26), as well as reporting sizable gender differences in the reporting of both psychological and somatic symptoms (27,28). Combined with the greater tendency among women to pursue treatment for their symptoms, these characteristics can dramatically increase the rate of false-positive medical examinations in which angina symptoms are found to lack any identifiable cardiovascular cause. Experienced physicians are likely to be aware of these gender patterns from their interactions with patients and may be susceptible to downplaying the seriousness of women's cardiovascular symptoms as a result (29).

In this and previous psychosocial reports on WISE participants (20), we have presented evidence to suggest that a brief assessment of a woman's past and present mental health can provide useful information for cardiologists considering the need for invasive testing. Among a large group of women with symptom patterns indicative of CAD, knowledge of a woman's depression treatment history helped to predict those who were likely to show positive results on an ischemia tests or to have clinically significant CAD on angiogram. Therefore, even brief, 1-item questions concerning mental health history may be useful to the cardiologist by helping reduce the rates of false-positive cases referred for unnecessary angiogram tests.

Depression and Mortality

The results of our hospitalization and mortality assessments were consistent with the now large literature suggesting poorer health outcomes among those with depression (2–5). Because of the clinical characteristics of the WISE sample, however, namely, the presence of acute clinical symptoms with a low rate of underlying atherosclerosis on angiogram, these results can be distinguished somewhat from many of the previous papers demonstrating depression effects among post–myocardial infarction or otherwise-documented CAD populations.

In WISE, depression symptom severity was associated with an increased mortality risk despite a lack of differences on objective indicators of atherosclerosis or ischemia. However, depression was related to a number of important behavioral mechanisms that could translate to increased risk of mortality and secondary events, including higher smoking rates, social isolation, and lower SES standing. The latter are each established independent predictors of cardiovascular health and are important not only for highlighting possible pathways for depression effects but also because they represent opportunities for intervention. With the negative findings from ENRICHD now widely known (1), it is clear that broadly applied depression treatments among patients with heart disease are not a cost-effective means of achieving mortality reductions. Instead, it is likely a more fruitful effort to direct our research efforts toward better understanding the behavioral and biological mechanisms that explain the heightened heart risk associated with depression, which may themselves serve as more effective treatment targets.

It should be noted that despite our inclusion of established CAD risk factors, we did not incorporate any of a number of potentially important pathophysiological mechanisms often linked to depression symptoms. Measures of immune system function, platelet activity, sleep, and heart rate variability,

among others (9), could each compose an important key to understanding depression effects on cardiovascular health.

In the relationship between depression and mortality among WISE participants, current symptom severity measured at baseline proved to be a more reliable predictor relative to depression history. Several previous papers have also shown that baseline-assessed depression symptom severity was more important to predicting clinical outcomes than depression history (30,31). The failure to account for the BDI-mortality relationship based on standard CAD risk factors suggests that other, unaccounted for, risk factors associated with depression symptom severity were important factors in determining participant's mortality risk. Further, it is important to stress that, irrespective of the measure of depression used, our results reinforce the high prevalence of depression symptoms in clinical samples of women, with roughly 40% reporting a history of depression treatment and 20% showing depression symptom severity at baseline consistent with at least moderate depression.

Study Limitations

Although WISE participants were rated as high risk for CAD based on clinical symptoms, rates of clinically significant atherosclerosis were low based on angiogram testing. As a result, the incidence of mortality and revascularization events (and resulting statistical power for survival analyses) were low, preventing us from assessing questions such as depression relationships with differential causes of mortality. The time lag in implementing the psychosocial testing among WISE participants was a further constraint, as we have BDI data for only about half of the WISE sample.

With regard to the assessment of participant's depression treatment history, we did not collect information regarding the severity of past depression, benefits or types of treatment, or the duration of the symptoms, all of which could be useful in attempts to link historical mental health data to current or prospective cardiovascular variables. Reported depression relationships are based on questionnaires and a single-item self-reported treatment history. We did not include diagnostic interviews by which to subdivide participants who met criteria for major depression. Given the high levels of psychological distress expressed by WISE participants, we must further consider the possibility of a referral bias in study recruitment, such that patients who appeared or vocalized more distress were more likely to be referred. Arguably, the same biases may exist under everyday cardiology referrals, yet it is necessary to recognize that WISE included women based on clinical symptoms rather than objective indicators of disease, which may limit generalizability.

Summary

Using a two-pronged measurement approach to depression in a sample of women with suspected myocardial ischemia, we documented associations between current depression symptom severity and depression treatment history with a pattern of increased heart disease risk, including elevated CAD risk factor standing, and higher prospective rates of hospitalization and death. Depression was also related to women's cardiac symptom presentation. The latter findings suggest that assessments of mental health factors like depression can be helpful in the context of a cardiology examination by identifying characteristics associated with symptom presentation, which can be useful in evaluating the need for invasive procedures such as the coronary angiogram.

Although the depression measures showed many similarities in predicting cardiovascular symptoms and outcomes, there were also several important differences, particularly in regard to the relationship between depression treatment history and lower rates of ischemia and clinically significant atherosclerosis. We observed a relatively high prevalence of depression among WISE participants, with nearly 40% reporting a history of depression treatment. Relationships between depression and outcome events were robust to adjustments for atherosclerosis severity and CAD risk factors, indicating that depression scores were not simply a marker of participants with more advanced physical risk factors. Even in the time-intensive environments of cardiology testing, the evidence reported here indicates that brief assessments of depression can offer information that is valuable in evaluating cardiac symptoms and predicting disease course.

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