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Anger, Hostility, and Cardiac Symptoms in Women with Suspected Coronary Artery Disease: The Women's Ischemia Syndrome Evaluation (WISE) Study

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ABSTRACT

Objective: To determine the relationship of anger and hostility to angiographic coronary artery disease (CAD), symptoms, and functional status among women with suspected CAD.

Methods: Data were collected from 636 women with suspected CAD referred for diagnostic angiography in the Women's Ischemia Syndrome Evaluation (WISE) Study. CAD was assessed as angiographic presence/absence of disease ($\geq 50\%$ stenosis in any epicardial coronary artery). Hostility/anger, angina, symptoms, and functional status were assessed by the Cook-Medley Hostility Inventory, Spielberger Anger Expression Scale, cardiovascular symptom history, and the Duke Activity Status Index.

Results: Logistic regression revealed that anger-out (i.e., aggressive behavior in response to angry feelings) was independently associated with the presence/absence of angiographic CAD (OR = 1.09, CI 1.01-1.17). Anger and hostility were higher among women reporting increased cardiovascular symptoms. In women without angiographic CAD, those with nonanginal car-

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diac symptoms had the highest anger-out, anger expression, hostile affect, and aggressive responding scores, and those with typical angina reported the lowest functional status. Among women with CAD, functional status was lowest in women with atypical angina.

Conclusions: Among women with suspected CAD, anger-out scores were associated with the presence of angiographic CAD. Anger/hostility traits were associated with increased symptoms, particularly with nonanginal chest pain in women without angiographic CAD. Relationships among psychosocial factors, cardiac symptoms, and angiographic CAD are potentially important in the management of women with suspected CAD.

INTRODUCTION

STUDIES OF PREDOMINANTLY MALE SAMPLES suggest that the psychosocial traits hostility and anger may be predictive of coronary artery disease (CAD),¹⁻⁵ particularly in younger men.⁶ CAD patients with high levels of hostility also show a faster rate of restenosis after coronary angioplasty⁷ and manifest more ischemia during mental stress testing than other CAD patients.⁸ However, some studies have failed to demonstrate a relationship between hostility and coronary atherosclerosis^{9,10} after adjusting for age and gender. Other studies indicate that the mode of expression of anger (anger-in/anger-out) is important.¹¹⁻¹³

Hostility as a risk factor for CAD in women has been less well studied than in men, as women have generally been underrepresented or absent from cardiovascular research samples.⁶ In healthy postmenopausal women, anger suppression and hostility predicted carotid intima-media thickness (IMT),¹⁴ and hostility was predictive of recurrent CAD events in postmenopausal women with coronary disease.¹⁵ Hostility also was related to ambulatory ischemia in a small sample of female subjects¹⁶ but was not predictive of myocardial infarction (MI) in a small sample of women with premature acute MI.¹⁷

Prior studies have demonstrated that hostility is moderately associated with other measures of negative emotion, such as anxiety and depression,¹⁸ and that measures of negative emotion can be associated with anginal symptom reports and poor quality of life.^{19,20} Indeed, because of their association with anginal symptoms and poor quality of life, prior studies of primarily female samples suggest that anxiety and negative emotions may be high in some patients with suspected CAD and negative angiographic findings.^{18,21} The associations of some measures of hostility and anger with cardiac symptoms have

not been previously explored among women with suspected CAD.

The Women's Ischemia Syndrome Evaluation (WISE) study provides an opportunity to determine possible relationships among hostility, angiographic CAD, and anginal symptoms in a large sample of women. A previous report from the WISE study showed that hostility and anger are positively related to CAD risk factors²² and that hostility was positively predictive of CAD events in this sample.²³ To determine the relationship of psychological characteristics to initial CAD diagnosis, the present study compared (1) anger and hostility in symptomatic women with and without angiographic CAD and (2) the relationship of measures of anger and hostility to anginal and cardiac-related symptom reports and functional status in the WISE sample.

MATERIALS AND METHODS

Participants

The study sample was enrolled between 1996 and 2000 and consisted of 636 women who completed the angiogram procedures, core diagnosis protocol, and hostility and symptom questionnaires. Eligibility requirements for enrollment in the WISE study were age >18 years and recently or currently undergoing a clinically indicated coronary angiogram for suspected myocardial ischemia.²⁴ Major exclusion criteria included comorbidity that could compromise 1-year follow-up, pregnancy, contraindications to provocative diagnostic testing, cardiomyopathy, New York Heart Association class IV congestive heart failure (CHF), recent MI, significant valvular or congenital heart disease, and inability to complete questionnaires. Women who underwent coronary angioplasty ($n = 8$) or coronary bypass surgery ($n = 5$) or who had other serious condi-

tions ($n = 5$) occurring after angiography but before WISE testing were excluded. (For a full report of WISE methods, see ref. 24.)

Procedure

Angiograms were evaluated for extent of atherosclerosis by a core laboratory. For the purposes of this study, the quantitative assessment of the presence and complexity of epicardial coronary artery stenoses was the principal cardiovascular measure. Women with $\geq 50\%$ stenosis in any one major epicardial coronary artery were categorized as having CAD. Women with stenoses $< 50\%$ in at least one vessel were categorized as not having CAD.

Measures

Psychosocial measures. Hostility was assessed using the 27-item Cook Medley Hostility Inventory (Ho), which has demonstrated significantly better prediction of CHD than the 50-item scale.²⁵ The Ho comprises three subscales, cynicism, aggressive responding, and hostile affect, which are thought to reflect the cognitive, behavioral, and mood components of hostility.

The State Trait Anger Expression Inventory (STAXI) is a 24-item scale that assesses the frequency of how angry feelings are expressed.²⁶ The STAXI scale contains three factors: anger-out (i.e., how anger is expressed toward others or the environment), anger-in (suppression of angry feelings), and anger control (control of angry feelings). The total STAXI score (i.e., anger expression) and the anger-in and anger-out subscales were used for these analyses.

Functioning. Functional capacity was assessed using the 12-item Duke Activity Status Index (DASI), which was designed to assess self-reported functional ability on a variety of common tasks.²⁷ Higher scores are indicative of greater functional capacity. The DASI demonstrated previous associations with cardiac symptoms in the WISE study.²⁰

Symptoms. The angina symptom history classification developed by Diamond²⁸ was used to collect information on anginal symptoms that led to cardiac catheterization and evaluation. Anginal classification was based on subject response to three questions concerning pain in center of chest, onset with exercise, and relief with rest. Typical

angina was classified as endorsement of all three anginal symptoms, atypical angina as endorsement of two of three symptoms, and nonanginal classification as endorsement of one or less of the three symptoms.

An additional questionnaire was used to assess²² general patient symptomatic complaints (see Appendix). A median split was used to categorize women into high (> 10) and low (≤ 10) symptom reporters. In a previous WISE report, endorsement of a higher number of symptoms was related to reduced quality of life.²⁰

The majority of study participants (85%) completed these questionnaires after having undergone angiography. Of these women, 83% knew the results of their angiography at the time of questionnaire completion.

Data analysis

Data are presented as means and standard deviations (SD) for continuous variables and percentages for categorical variables. For continuous measures, comparisons between women with vs. without CAD were done using two-sample *t* tests or Wilcoxon two-sample tests, depending on sample distributions. Chi-square tests were used to compare categorical variables. Functional scores by anginal status (typical, atypical, and nonangina) were evaluated using analysis of variance (ANOVA). *Post hoc* comparisons were done using Tukey-Kramer tests for those models that were significant. Cardiovascular symptom data were analyzed as dichotomous variables using two-sample tests.

Logistic regression was used to model the probability of CAD as a function of age, education, risk factors, current hormone replacement therapy (HRT), hostility and anger scores, and social support. Variables were chosen for entry into the model based on significant univariate associations and prior relevant literature. Stepwise forward regression techniques were used to evaluate models with relevant risk factors and hostility/anger measures as covariates. The final model is the one with the best predictive value (C index). The issue of collinearity among variables was examined, and the tolerance and variance factors (vif) were well within acceptable ranges and indicated no multicollinearity. All statistical tests were two-sided, and a *p* value < 0.05 was considered statistically significant. Analyses were completed using SAS software version 8.2 (SAS Institute Inc., Cary, NC).

TABLE 1. BASELINE CHARACTERISTICS OF WOMEN WITH AND WITHOUT CAD

Variable	CAD (n = 218)	No CAD (n = 418)	p value
Demographics			
Age (M, SD)	61.2 (12.0)	56.0 (10.6)	<0.001
Education > high school (%)	36	45	<0.05
Standard Risk Factor			
Social Diversity Index (M, SD)	5.4 (1.8)	6.1 (1.9)	<0.001
Cholesterol (mg/dL)			
Total (M, SD)	195.5 (45.9)	196.4 (44.8)	NS
LDL ^a (M, SD)	110.0 (41.1)	113.0 (38.4)	NS
BMI ≥ 30 (%)	36	40	NS
Smoking (%)	22	18	NS
History of hypertension (%)	65	54	<0.01
History of diabetes (%)	37	15	<0.001
History of dyslipidemia (%)	71	44	<0.001
Current HRT use (%)	39	54	<0.01

^aLDL, low-density lipoprotein; BMI, body mass index; HRT, hormone replacement therapy.

RESULTS

Demographics and risk factors

Table 1 presents the demographic and baseline clinical characteristics of the women with and without angiographic CAD. Women with angiographic disease were more likely to be older, have less education, and have CAD risk factors, including history of hypertension, diabetes, and dyslipidemia. Furthermore, women with CAD were less likely to be using HRT and had smaller socially diverse networks. These variables were used as covariates in the logistic regression models.

Age and education were related to hostility and anger (data not shown). Younger women had higher scores on four of the six measures: Cook-Medley aggression, Cook-Medley hostile affect, anger-out, and anger Expression ($p < 0.05$). Women with a high school education or less had sig-

nificantly higher scores on five of the six measures: Cook-Medley cynicism, Cook-Medley aggression, Cook-Medley hostile affect, anger-out, and anger expression ($p < 0.05$).

Anger, hostility, and CAD status

Table 2 presents the means and SD of the three Cook-Medley subscales and the STAXI scores by CAD status. There were few differences in anger or hostility between women with and without angiographic CAD, although women without angiographic evidence of CAD had higher hostile affect scores than those with CAD ($p < 0.05$).

Associations with CAD

To further investigate associations of risk factors and hostility/anger scores with CAD status, both univariate and multivariable logistic regression models were developed. Each risk factor and

TABLE 2. BASELINE HOSTILITY/ANGER SCORES^a BETWEEN WOMEN WITH AND WITHOUT CAD

Hostility/anger measures	No CAD	CAD	p value
Cook-Medley			
Cynicism	4.9 (3.4)	5.3 (3.6)	NS
Aggressive responding	2.8 (1.7)	2.8 (1.7)	NS
Hostile affect	2.0 (1.3)	1.8 (1.3)	<0.05
STAXI			
Anger-in	15.2 (4.3)	14.8 (4.0)	NS
Anger-out	13.1 (3.5)	13.4 (3.3)	NS
Anger expression	19.2 (9.6)	19.5 (9.5)	NS

^aMean (SD).

TABLE 3. LOGISTIC REGRESSION MODEL: SIGNIFICANT INDEPENDENT PREDICTORS OF CAD^a, C INDEX = 0.742

Variable	Odds ratio	95% CI	p value
Age	1.05	1.03–1.08	<0.001
History of dyslipidemia (1 = yes, 0 = no)	3.52	2.06–6.02	<0.001
Current HRT (1 = yes, 0 = no)	0.58	0.35–0.97	<0.05
Anger-out score	1.09	1.01–1.17	<0.05

^aVariables entered into the model that were not significant independent predictors were education, history of diabetes, history of hypertension, and the Social Diversity Index.

hostility score was entered separately into models. The final logistic regression model adjusted for significant covariates indicated that anger-out scores were associated with the presence of CAD ($p < 0.05$) (Table 3).

Anger, hostility, and symptoms

Anger and hostility were examined in the context of anginal symptom status (i.e. typical, atypical, or nonanginal) and low (≤ 10) and high (> 10) symptom groups. There was no difference in anger and hostility across anginal status in the total sample or among women with angiographic CAD. However, in women without CAD, those

with non-anginal symptoms had significantly higher anger-out ($p < 0.001$), anger expression ($p < 0.01$), aggressive responding, and hostile affect scores (both $p < 0.05$) (Fig. 1).

A median split was used to divide the total sample of women into low (≤ 10) and high (> 10) symptom groups based on their responses to the 22-item physical symptom checklist. Women who reported a high number of symptoms, regardless of CAD status, had significantly greater anger and hostility scores on all six subscales compared with women who reported a low number of symptoms (Fig. 2). Interestingly, there was no difference in the mean number of symptoms reported by women with CAD ($\bar{X} = 9.4 \pm 4.9$) com-

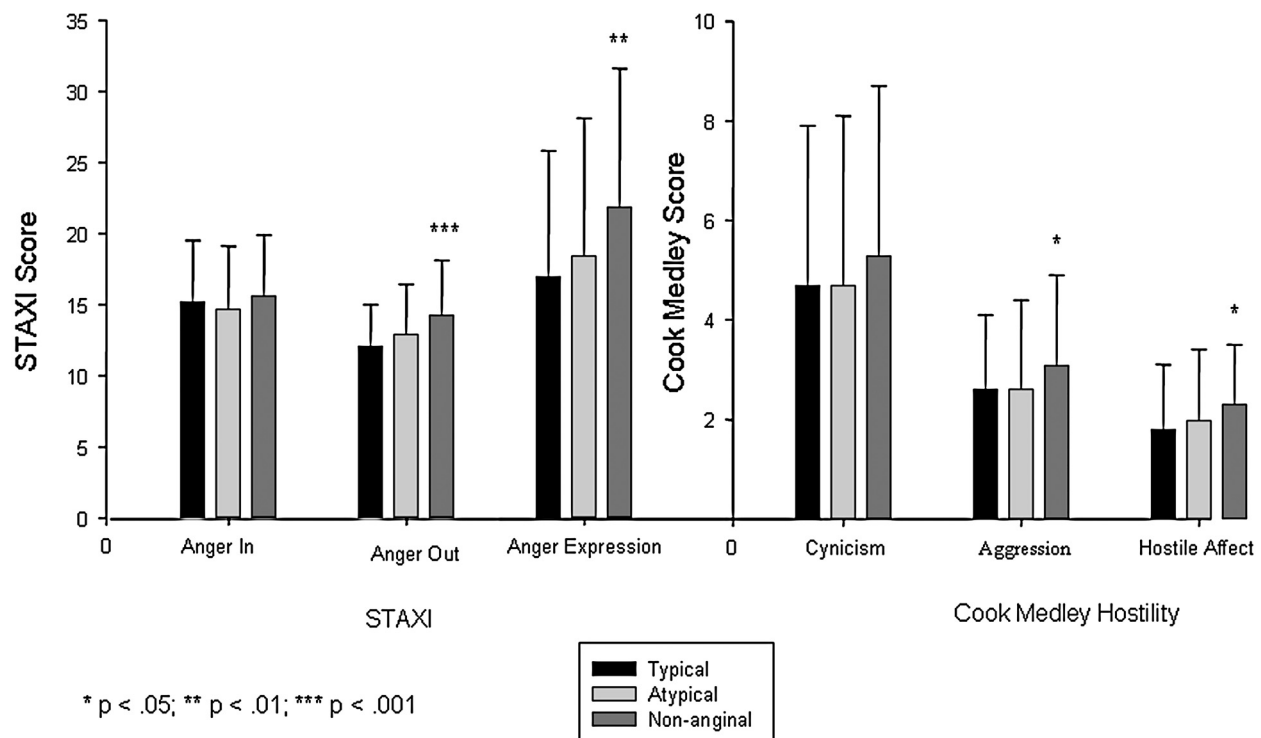


FIG. 1. Anger and hostility scores in women without CAD by anginal status.

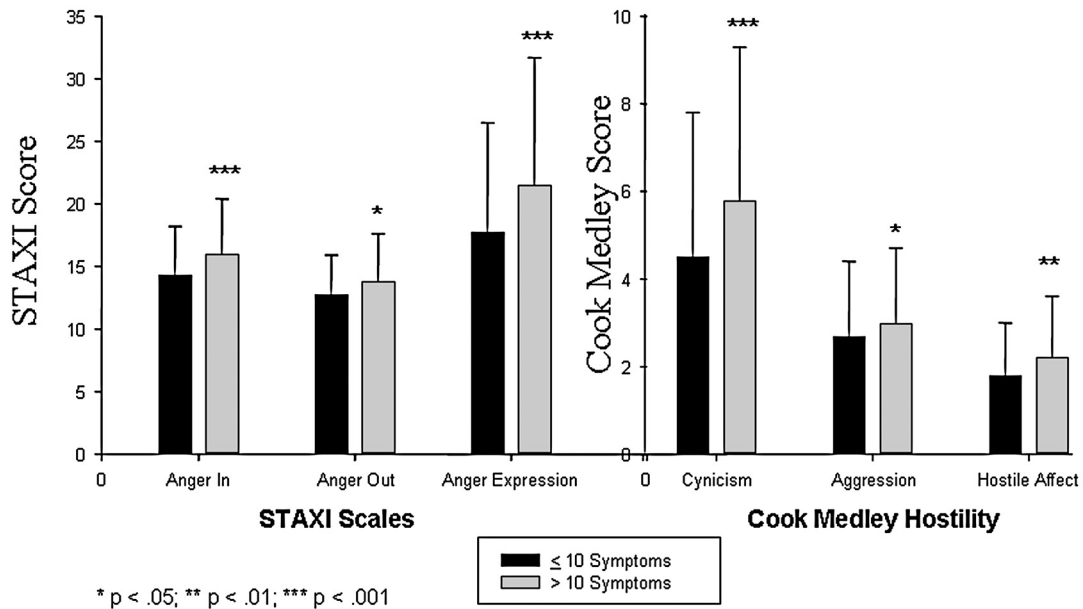


FIG. 2. Anger and hostility scores among women referred for angiography according to number of symptoms reported.

pared with those without CAD ($\bar{X} = 10.0 \pm 4.7$). Women with CAD who reported a high number of symptoms had higher hostility/anger across all scales (all $p < 0.05$). The pattern was not as consistent in women without CAD. Those who had a high number of symptoms reported significantly higher cynicism ($p < 0.01$) and higher anger-in ($p < 0.01$) compared with women with a lower number of symptoms.

Functioning and symptoms

Similar to anger and hostility, functional status (i.e., DASI score) was assessed across anginal categories and symptom frequency groups. In general, functioning was lower in the women with CAD across both symptom categories (Table 4). Examination of DASI scores within each anginal

and CAD group revealed differential patterns of functioning. Among the women with CAD, functional status was significantly lower in those with atypical angina compared with those with nonanginal symptoms ($p < 0.05$). Among those without CAD, functioning was significantly lower in those with typical angina compared with women with nonanginal ($p < 0.01$) and atypical angina ($p < 0.01$) symptoms. There were significantly lower levels of functioning in women who reported > 10 symptoms for the CAD ($p < 0.05$) and non-CAD ($p < 0.001$).

DISCUSSION

The present study indicates that in women with suspected CAD, relationships among trait

TABLE 4. DUKE ACTIVITY STATUS INDEX (DASI) FUNCTIONAL STATUS SCORES^a ACCORDING TO SYMPTOM STATUS IN WOMEN WITH AND WITHOUT ANGIOGRAPHIC CAD

CAD status	Anginal symptom status			Symptom status	
	Typical	Atypical	Nonanginal	Low (≤10)	High (>10)
No CAD	18.7 (13.8) ^b	24.9 (16.9) ^c	25.3 (15.5) ^c	26.7 (15.2) ^f	18.6 (15.2) ^g
CAD	17.5 (14.2)	15.2 (12.7) ^d	20.5 (13.6) ^e	19.4 (14.0) ^h	15.1 (12.6) ⁱ

^aMean (SD); higher scores indicate higher functioning.
^{b,c} $p < 0.01$; ^{d,e} $p < 0.05$; ^{f,g} $p < 0.001$; ^{h,i} $p < 0.05$.

measures of anger and hostility, angiographic CAD, and presenting chest pain symptoms are complex. Among women referred for angiography because of suspected CAD, outward expression of anger (i.e., anger-out) was associated with angiographic evidence of CAD after controlling for other risk factors. Additionally, in this sample referred for angiography, women who endorsed a high number of chest pain symptoms (i.e., >10) had increased levels of anger/hostility traits and lower levels of functioning compared with women who reported a low number of chest pain symptoms (i.e., <10). Although there was no difference in anger and hostility scores across anginal status categories in women with documented evidence of CAD, these traits were higher in women who reported nonanginal chest pain and had no angiographic evidence of CAD. These data suggest that anger-related traits in women with suspected CAD should be evaluated in the context of type and number of presenting cardiac symptoms.

In the present sample, the expression of anger toward other persons or objects is the most toxic aspect of anger and was associated with the presence of angiographic CAD. The present findings differ from the few studies conducted in female samples in which anger suppression was related to outcome. In the Framingham Heart Study,²⁹ women who reported suppression of anger were more likely to develop CHD (particularly angina) over an 8-year period. Among healthy postmenopausal women, suppression of anger was related to increased carotid IMT at follow-up 10 years later.¹⁴ Results of this study also appear to differ from male samples, in which Cook-Medley hostility scores are found in some, but not all, studies to be associated with CAD, independent of confounding variables.⁶ These inconsistent results across studies may reflect gender differences or differences between healthy women and those seeking medical evaluation for suspected CAD.

The reason for such inconsistent results across the literature is unclear, but one issue may be the mediating role of CAD risk factors.³⁰ For example, previous WISE analysis found that anger-out was related to dyslipidemia and BMI.²² In our sample, history of dyslipidemia, but not BMI, was significantly different between women with and without angiographic CAD. Furthermore, both anger-out and dyslipidemia were significant independent predictors of angiographic CAD in this sample. If adverse risk factors are the mech-

anism by which hostility and anger impact cardiovascular disease, comparisons across different populations (i.e., healthy, at risk) or controlling for them in analyses may diminish associations, making interpretation of results difficult.³⁰

The present data and previous reports from the WISE study³¹ indicate that women with angiographic CAD have less diverse social networks than women without CAD. These findings resemble those obtained in a primarily male sample indicating that low social support is related to angiographic severity of CAD in patients with type A behavior.³² Particularly notable in conjunction with the present results for anger-out is prior evidence indicating that the combination of anger-out and low social support is associated with progression of angiographic CAD in a predominantly male sample of CAD patients.³³

Anger/hostility, cardiac symptoms, and functional status

Examination of general cardiac symptoms indicated that regardless of CAD status, women who reported a high number of cardiac symptoms (i.e., > 10) had higher anger and hostility scores than those who reported a low number of symptoms (i.e., < 10). Furthermore, the highest levels of anger and hostility were reported in women who had no evidence of CAD and reported nonanginal chest pain. These results suggest that anger and hostility are associated with cardiac symptoms regardless of CAD status and that there are differential patterns within each group.

The relationship between symptoms and emotion in the WISE sample may reflect frustration and anger resulting from not having a definitive diagnosis or treatment for chest pain symptoms.³⁴ Furthermore, greater symptom report associated with anger and hostility may also reflect overlap with other psychological variables, such as neuroticism,^{25,35} and women high in neuroticism may be hypersensitive to bodily symptoms.^{18,19} Anger and hostility may be independently related to increased pain sensitivity. Evidence from the general pain literature reveals relationships between increased pain sensitivity and anger, hostility in acute (e.g., headache) and chronic (e.g., back) pain populations.^{36,37} Both anger-out and anger-in are related to poor adjustment to chronic pain,^{27,38,39} and anger-out is related to increased pain intensity and to increased sensitivity in the labo-

ratory setting.⁴⁰ Thus, it is possible that the relation between high symptom report and anger/hostility scores is related to decreased pain tolerance. This has not been specifically addressed within a female chest pain population and may be an area of further research, as anger and hostility can have significant impact on treatment compliance and patient-provider relationships, in turn leading to reduced treatment satisfaction and efficacy.⁴¹

Thus, these data reinforce the notion that various emotional and psychological factors are associated with referral for diagnostic coronary angiography, especially among women with anomalous chest pain and suspected coronary disease. Furthermore, the differential pattern in emotions and symptoms in the CAD and non-CAD groups suggests different relationships between underlying pathophysiology and symptom patterns in these two groups.

Study limitations

The majority of the participants in this study were informed of the results of their angiography prior to completing the psychological measures. Consequently, their responses to symptom assessment may have been influenced by knowledge of their disease status. However, the univariate analyses in our sample suggest that there were few differences in hostility or anger scores between women with and without CAD. Without a baseline measure of anger or hostility, it is difficult to draw conclusions from this similarity between the two groups. However, a recent qualitative study investigating women's CHD diagnostic experiences before and after MI indicated that the most common emotional experience of women who experienced atypical chest pain was anger and frustration.³⁴ Women reported frustration and anger with physician treatment prior to diagnosis and following their MI. The women explicitly stated that these emotions occurred because no one had believed their symptoms. It is possible that women in the WISE study could experience increased levels of anger and frustration at the time of diagnosis if there was no explanation for their symptoms (i.e., no CAD) and if they received a positive diagnosis. A prospective study investigating emotion and symptoms prior to angiography would allow for better understanding of the complex relations among emotion, symptoms, and diagnostic status.

It is also possible that coronary angiographic populations, such as the WISE population, are not appropriate for evaluation of the role of hostility as a risk factor for CAD. It has been argued that using a coronary angiography sample can lead to a biased selection of subjects, as individuals undergoing catheterization are more likely to have CAD than not, therefore misestimating the risk of psychological factors.⁴² The lack of a normal control group increases the difficulty of interpreting the anger and hostility results. For example, the association of anger-out with CAD may reflect that the absence of anger-out makes women more likely to develop psychosomatic chest pain. The fact that only one of the anger and hostility measures was a significant predictor of angiographic disease also suggests that an anger-atherosclerosis association in women may be of small magnitude, and anger expression could be both a cause of such referral and a consequence of undiagnosed cardiovascular symptoms.

Anatomic CAD may not be the ideal end point for the assessing the impact of CAD risk factors, as CAD mortality and future clinical events are related to pathophysiological or behavioral factors in addition to anatomical extent of atherosclerosis.⁴² These conclusions are reinforced by a recently reported prospective follow-up of this WISE cohort²³ that demonstrated that higher Cook-Medley scores reflecting cynicism, hostile affect, and aggressive responding are associated with poorer event-free survival and a higher risk of adverse CAD events.

Clinical implications

A primary objective of the WISE study is to optimize symptom evaluation and diagnostic testing for CHD in women. The inclusion of psychosocial measures of anger may help to accomplish this, particularly measures that assess the behavioral expression of anger and hostility. Women with cardiac symptoms may also need assistance in coping with their symptoms, as well as the psychological effects—including anger—that accompany their unexplained symptoms. Identification of the relationship of psychosocial factors to angiographic CAD and to cardiac symptoms in women is, therefore, of potential importance in the management of heart disease, as well as the psychological sequelae of suspected CAD in women.

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APPENDIX: SYMPTOMS FROM WISE SYMPTOM HISTORY FORM

Abdominal pain	Arm pain, shoulder pain	Back pain	Chest pain
Heartburn/indigestion/ stomach problems	Jaw pain	Impending doom	Chest pressure
Chest tightness	Nausea/vomiting	Neck pain	Chest discomfort (heaviness, burning, tenderness)
Numbness/tingling in arm or hand	Palpitations/rapid heart rate	Cough	Dizziness, lightheadedness
Feel lousy	Headache	Shortness of breath/ difficulty breathing	Sweating
Weakness/fatigue/ faintness	Loss of consciousness/fainting		