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ABSTRACT

Title of Thesis: Hostility and Anger in Women with Suspected Coronary Artery Disease: The Women's Ischemia Syndrome Evaluation (WISE) Study

Carolyn Phan Kao, Master of Science, 2003

Thesis directed by: David S. Krantz, Ph.D., Professor and Chair, Department of Medical and Clinical Psychology

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Hostility and Anger in Women with Suspected Coronary Artery Disease:

The Women's Ischemia Syndrome Evaluation (WISE) Study

by

Carolyn Phan Kao

Master's Thesis submitted to the Faculty of the Department of Medical
and Clinical Psychology Graduate Program of the Uniformed
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Fulfillment of the requirements for the degree of
Master of Science, 2003

Dedication

For Gurudeva

hansa hansa parama-hansa, yogaananda gurave namah
yogi yogi mahaayogi, yogaananda gurave namah

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death in the U.S. for both women and men. However, more women than men have died from CAD annually since 1984, with CAD mortality among women increasing whereas CAD mortality among men is decreasing (Wenger, 2002). CAD is also a major cause of disability for women; among U.S. women aged 55-64 years with clinical manifestations of CAD, 36% are disabled by CAD symptoms, with disability rates increasing to 55% for women over 75 years of age (Pinsky, Jette, Branch, Kannel & Feinleib, 1990). Therefore, it is critical to establish a more thorough understanding of the CAD process in women.

Psychosocial variables such as anger and hostility are important risk factors for CAD in men (Barefoot, Dahlstrom, & Williams, 1983; Miller, Smith, Turner, Guijarro, & Hallet, 1996). Understanding the role of anger and hostility has led to the development of prevention and treatment programs (Friedman, Thoresen, Gill, et al, 1986). The role of these variables in CAD in women has not been as widely studied, leaving women at a distinct disadvantage regarding understanding of their condition as well as treatment and prevention options.

The purpose of the present study was to determine whether anger and hostility were associated with angiographic CAD in an exclusively female population with suspected CAD. We examined anger and hostility among women participating in a multi-center National Heart, Lung, and Blood Institute-sponsored study designed to investigate CAD manifestation and detection in women. In order to provide a framework for the question under study, gender differences regarding standard and psychosocial CAD risk factors, anger and hostility as CAD risk factors, and somatic symptoms will be discussed prior to the results of the present study.

Standard CAD Risk Factors for Women

There are significant gender differences in terms of CAD risk factors. In men, elevated total serum cholesterol (TSC) and low-density lipoprotein (LDL) levels confer the greatest risk, whereas elevated triglyceride levels and a low high-density lipoprotein (HDL) level are more predictive of CAD in women (Wenger, 1996). Diabetes mellitus is also a much more significant predictor of CAD and its prognosis in women than in men, providing more prognostic information about female patients than any of the other more traditional risk factors (Douglas & Ginsburg, 1996). DeSanctis (1993) reported that diabetes was the only risk factor in a sample of women who presented with chest pain that distinguished those with positive angiograms from those with negative angiograms. Furthermore, women in the Nurse's Health Study (Wenger, 1996) who had diabetes had up to a seven-fold increase in cardiovascular events. Diabetic women who have suffered a MI also have a doubled risk of reinfarction and fourfold greater likelihood of developing heart failure (Wenger, 2002).

Hypertension is also a potent risk factor in women, leading to as much as a ten-fold increase in CAD deaths among premenopausal women (Douglas & Ginsburg, 1996). Among the elderly, hypertension is a stronger predictor of CAD in women than in men, and is also more common in female than male CAD patients (Douglas & Ginsburg, 1996). With regard to smoking, however, the 2- to 6-fold relative risk of CAD for smokers versus nonsmokers is similar for men and women (Meilahn, Becker, & Corrao, 1995). Obesity also appears to be a risk factor for CAD in both women and men (Fetters, Peterson, Shaw, Newby, & Califf, 1996), but in women abdominal or central obesity (male fat pattern) appears to be a more powerful CAD risk factor than peripheral (female fat pattern) obesity (Bjorntorp, 1988; Lapidus, Bengtsson, Larsson, Pennert, Tybo, & Sjostrom, 1984).

A proposed risk factor unique to women is low estrogen levels. While prospective studies of endogenous estrogen levels and CAD risk in women have not been conducted, there is convincing evidence for such an association. Women who have undergone a bilateral oopherectomy prior to natural menopause, and without hormone therapy, have a significantly increased risk of CAD (Stampfer, Colditz, & Willett, 1990). Furthermore, postmenopausal women who report use of estrogen therapy have approximately one-half the risk of CAD as women not using therapy (Barrett-Connor, 1991). This decreased risk is even observed in elderly women, with estrogen-takers over 65 years of age having less carotid wall atherosclerosis than nontakers (Manolio et al., 1993). Women also typically develop CAD ten years later than men, usually after menopause, which results in lower endogenous estrogen levels (Wenger, 2000).

In light of several recent large-scale studies, however, hormone replacement therapy (HRT) is no longer recommended for the primary or secondary prevention of CAD. After 6.8 years of follow-up, the Heart and Estrogen/progestin Replacement Study (HERS), the first randomized trial of HRT for secondary prevention of heart disease, found no cardiovascular benefit of HRT therapy (Hulley, et al., 1998). HRT was associated with an increased risk of deep venous thrombosis and pulmonary embolism (HR = 2.89; CI = 1.50-5.58) and gallbladder disease (HR = 1.38; CI = 1.00-1.92). In the first randomized trial of HRT for the primary prevention of heart disease, the Women's Health Initiative, no overall cardiovascular benefit of HRT was found (Writing Group for WHI, 2002). The combination of estrogen and progestin resulted in an increased risk of CAD (HR = 1.29; CI = 1.02-1.63), increased risk of stroke (HR = 1.41; CI = 1.07-1.85), increased risk of pulmonary embolism (HR = 2.13; CI = 1.39-3.25), and an increased risk of breast cancer (HR = 1.26; CI = 1.00-1.59). The risk for thrombotic events was greatest in the first year, but the risk of breast cancer increased with the duration of HRTIn summary, women have different lipid risk profiles than men, and are also at greater risk for CAD from diabetes, hypertension, and possibly low estrogen levels. Smoking and obesity appear to confer similar risks for women and men. These standard medical CAD risk factors, however, have failed to fully explain the incidence of CAD in women as well as in men. Consequently, many researchers have investigated possible psychosocial risk factors over the past several decades.

Psychosocial Risk Factors for Women

Because cardiovascular research samples have generally excluded women or included very small numbers of women (Miller, Dahlstrohm, & Williams, 1996), cardiovascular risk factors, particularly psychosocial factors, have been understudied in women (Blumenthal & Matthews, 1993). Nonetheless, socioeconomic status, social support, and depression have emerged as significant psychosocial risk factors, clearly demonstrating that psychosocial variables can significantly affect health. Socioeconomic status (SES).

A study of over 2000 Finnish men revealed that those in the lower socioeconomic strata were almost 2.66 times more likely to die of cardiovascular disease than those in the highest strata (Lynch et al., 1996). This risk ratio was decreased to 1.71 when psychosocial risk factors (such as depression and social support) were controlled. This social gradient also exists among women. Feldman, Makuc, Kleinman, and Coroni-Huntley (1989) have reported that low educational attainment is associated with an increased risk of CAD in women, and that levels of known coronary risk factors and access to medical care can only partially explain this association. Matthews and colleagues (Matthews, Owens, Kuler, Sutton-Tyrell, & Jansen-McWilliams, 1989) have also found that lower educational attainment in women is related to a more atherogenic risk factor profile, including dyslipidemia, low level of physical exercise, and greater likelihood of cigarette smoking. SES is therefore a well-documented CAD risk factor for both men and women. Moreover, there is reason to believe that SES is associated with both hostility and depression. Analysis of cross-sectional data from the Dutch GLOBE study (1675 men and 1819 women) revealed that among both men and women, the likelihood of less than good health was higher in lower educational groups, and that a significant part of the educational gradient in health could be attributed to the intermediate effects of hostility (Schrijvers, Bosma, & Mackenbach, 2002). A meta-analysis by Lorant, Deliege, Eaton, Robert, Philippot, & Ansseau (2003) indicated that low-SES individuals had higher odds of being depressed than high-SES individuals, further highlighting the inter-relations among psychosocial variables.

Depression.

The impact of depression on CAD also has been examined in men and women. In a study by Carney, Rich, Freedland, and Saini (1988), male CAD patients who met criteria for major depression were 2.5 times more likely to develop a serious cardiac event over the next 12 months than non-depressed patients. Similarly, a secondary analysis of the Cardiac

Arrhythmia Pilot Study, involving 351 male post-MI patients, also showed a 1.6-fold increase in risk of mortality or cardiac arrest in those with, relative to those without, depressive symptoms, at 1 year (Ahern, gorkin, Anderson, Tierney, & Hallstrom, 1990). Depression in-hospital after MI has been reported as a significant predictor of 1-year cardiac mortality for women as well as for men, with its impact largely independent of other post-MI risk factors (Frasure-Smith, Lesperance, Juneau, Talajic, & Bourassa, 1999). Depressive symptoms have been shown to be related to fatal CAD in women and men, and depressive symptoms and hopelessness also have been shown to be associated with an increased risk of nonfatal CAD (Anda et al., 1993). Similarly, major depression, depressive symptoms, anxiety, and history of major depression all significantly predicted cardiac events in 222 male and female patients over the 12 months following a MI (Frasure-Smith, Lesperance, & Talajic, 1995). Therefore depression appears to confer a greater risk of cardiac events, as well as an increased CAD mortality risk, in both men and women. These findings have led some researchers to investigate the possibility that interventions targeting depression in CAD patients, such as social support interventions, may reduce the incidence of recurrent cardiac events.

Social support.

Social support, broadly meaning any process through which social relationships might promote health and well being (Cohen, Gottleib, & Underwood, 2000), has emerged as a significant psychosocial risk factor in men and a questionable one for women. In a prospective study of 13,301 men and women, men with few social connections were at increased risk of cardiac death after adjustment for standard risk factors (Kaplan, Salonen, Cohen, Brand, Syme, & Puska, 1988). Another study of 736 men revealed that social integration and social attachment were significant predictors of new CAD events after adjustment for other risk factors (Orth-Gomer, Rosengren, & Wilhelmsen, 1993). However, social support has been inconsistently associated with risk of CAD in women (Luten & Powell, 2000). A study of older women who suffered MI revealed 43% mortality among those who had previously reported no sources of emotional support, compared with a 22% mortality rate among the women with two or more sources of emotional support (Berkman, Leo-Summers, & Horwitz, 1992). Results from the Stockholm Female Coronary Risk Study show an association between social support and severity of CAD (Orth-Gomer, et al., 1998). After adjustment for age, lack of social support was associated with presence of stenosis greater than 50% in at least one coronary artery and the number of stenoses greater than 20% within the coronary tree. A review by Shumaker and Hill (1991), however, indicates that while some studies show the expected protective association with higher levels of social support, others only show racial and age differences, as well as increased CAD risk at only the very lowest levels of social support. This brief review shows that there is not a consistent association between social support and CAD in women. The reason for these conflicting results in women is unclear, but it is possible that the discrepancy is due to differences in assessing social support, restriction of range when using high-risk groups, and inconsistency in scoring methods to evaluate disease.

Hostility as a CAD Risk Factor

Studies using predominantly male samples have suggested that hostility and trait anger are independent risk factors for CAD. Barefoot, Dahlstrom, and Williams (1983) found that high levels of hostility, as assessed by the Cook-Medley Hostility Scale (Ho;

Cook & Medley, 1954) were predictive of both clinical coronary disease incidence and total mortality in a 25-year follow-up of 255 medical students. Similarly, in a study of patients who underwent diagnostic coronary arteriography for suspected coronary heart disease, only 48% of those patients with very low scores (less than or equal to 10) on the Ho scale exhibited a significant occlusion. Patients in all groups scoring higher than 10 on the Ho scale showed a 70% rate of significant disease (Williams, Haney, Lee, Kong, Blumenthal, & Whalen, 1980). Ho scale scores also were positively associated with crude 20-year mortality from CAD in a prospective study of 1877 men (Shekelle, Gale, Ostfeld, & Paul, 1983). Coronary artery disease patients with high levels of hostility also show a faster rate of restenosis after coronary angioplasty (Goodman, Quigley, Moran, Meilman, & Sherman, 1996), and manifest more ischemia during mental stress testing than other CAD patients (Burg, Jain, Soufer, Kerns, & Zaret, 1993). In 1996, Miller, Smith, Turner, Guijarro, and Hallet (1996) concluded that hostility is an independent risk factor for CAD, with an increased risk among younger males, based on a meta-analysis of research on hostility and physical health. Together, these findings indicate that high hostility may be of prognostic value for men. However, there are also null findings that have challenged the association of hostility and CAD.

Helmer, Ragland, and Syme (1991) found no significant positive association between hostility and angiographic disease, and Hearn, Murray, and Luepker (1989) found that higher Ho scores did not predict CAD mortality, CAD morbidity, or total mortality either before or after adjustment for baseline risk factors in a 33-year follow-up of 1,399 men. Similarly, while Maruta and colleagues (1993) found that hostility significantly predicted CAD, CAD-related mortality, and total mortality, hostility was not predictive after adjusting for age and sex. Furthermore, a review by Hemingway and Marmot (1999) and a meta-analysis by Miller et al. (1996) conclude that as many as half of the hostility and cardiovascular disease studies yield null findings. A recent meta-analysis by Myrtek (2001) of prospective population studies observed a very small population effect size ($R=0.022$, $p=0.003$) for associations of hostility and CAD, thus calling into question the clinical significance of a true association.

In trying to reconcile these contradictory results, many researchers have suggested that because studies of hostility and CAD often use different measures of hostility, they thereby tap into different dimensions of hostility, and differing results are therefore to be expected. It is important to note that hostility is a multi-dimensional construct, with attitudinal, emotional, and behavioral aspects (Barefoot, Dodge, Peterson, Dahlstrohm, Williams, 1989; Dembroski & Costa, 1987). The attitudinal component reflects a negative view of others that can be described as an attitude of resentment, distrust, cynicism, and suspicion, and is often assessed by the Cook-Medley Hostility (Ho) Scale, which has been described as a measure of cynical hostility (Smith & Frohm, 1985). The emotional component of hostility, which has been referred to as neurotic hostility (Dembroski & Costa, 1987), focuses on hostility-related emotions such as anger, irritability, and resentment (Dujovne & Houston, 1991). The behavioral component of hostility, also referred to as expressive or reactive hostility, is indicative of aggressive, antagonistic behavior (Dembroski & Costa, 1987). Until a comprehensive study examines the existing literature on hostility and CAD according to the specific measures of hostility, the exact nature of the hostility-CAD association in men will remain unclear. The relatively few studies examining predominantly or exclusively female samples also have inconsistent findings.

A positive relationship between self-reported hostility and angiographic results in women has been reported, with a stronger relationship in younger individuals (Williams et al, 1980). Matthews and colleagues (1998) also found that anger suppression and hostility predicted carotid intima-media thickness, indicating atherosclerosis, in a sample of 200 postmenopausal women, and in a post-MI sample, an interview-based measure of hostility discriminated post-MI women from controls (Low, Thoresen, Pattillo, King, & Jenkins, 1994). Hostility was also a significant predictor of coronary stenosis in a female sample after controlling for traditional CAD risk factors (Low et al., 1998). Recently Chaput and colleagues (2002) reported that hostility is a risk factor for recurrent CAD events in post-menopausal women. However, hostility was not predictive of mortality in a sample of 83 women with premature acute myocardial infarction (Powell, Shaker, Jones, Vaccarino, Thoresen, & Patillo, 1993), nor did hostility predict nonfatal myocardial infarction in 670 women participating in the Edinburgh Artery Study (Whiteman, Deary, Lee, & Fawkes, 1997). Furthermore, Helmer, Ragland, and Syme found no association between hostility and degree of stenosis in a sample of women, although a trend between occlusion and hostility was noted in younger women. While these studies may be inconclusive, they do indicate that hostility may have some association with CAD in women. Further research may lead to effective CAD prevention programs for women, similar to existing programs for men.

Psychosocial Variables and Cardiac Symptoms

In addition to their role as possible risk factors for the development and/or progression of CAD, psychosocial factors are also important in cardiac symptom perception. When CAD descriptors are compared between women and men, women have a higher frequency of chest pain than men, but men have a higher prevalence of CAD (Lerner, 1986). The mechanisms for chest pain in the absence of epicardial coronary disease is not well understood. Abnormalities of the small arteries of the coronary vascular bed have been hypothesized, but psychological characteristics, including anxiety, depression, and somatization have been found to influence the expression of symptoms in a number of studies (Barsky, Hochstraser, Coles, Zisfein, O'Donnell, & Eagle, 1990; Kellner, 1985; Lipowski, 1989; Mayou, 1989).

In a 12-year follow-up study of middle-aged women, neuroticism and experience of strain, psychiatric disorders, and the severity of depression were predictive of angina. These associations remained significant after adjustments for age, social class, marital status, and standard CAD risk factors, although none of these psychosocial factors were associated with the mortality rate (Hallstrom, Lapidus, Bengtsson, & Edstrom, 1986). A study of patients with stable angina found that while women were more likely to have disturbed sleep and psychosomatic symptoms, they reported less Type A behavior and hostility than men (Billing, Hjemdahl, & Rehnquist, 1997). Beitman and colleagues have also reported that 30% of atypical or nonanginal chest pain patients presenting in a cardiology clinic had a history of CAD, whereas 60% fulfilled the criteria for panic disorder. Nearly 20% of the patients with panic disorder also had CAD.The panic disorder patients without CAD were primarily women with predominantly nonanginal chest pain, whereas patients with both CAD and panic disorder were primarily men with predominantly atypical angina.

However, it is important to note that women with chronic stable angina are also more likely to experience symptoms in locations other than the substernum, such as in the lower jaw and teeth, both arms, shoulders, back, and epigastrium (Sullivan, Holdright, Wright, Sparrow, Cunningham, & Fox, 1994; Goldberg, O'Donnell, Yarzebski, Bigelow, Savageau, & Gore, 1998; Penque et al., 1998). Furthermore, rather than chest pain, women's symptoms may include dyspnea, palpitations, syncope, fatigue, sweating, or nausea (Eaker, Packard, Wenger, Clarkson, & Tyroler, 1988; Maynard & Weaver, 1992; Willich, Lowell, Lewis, Arntz, Schubert, & Schroder, 1993; Lusiani, Perrone, Pesavento, & Conte, 1994).

Summary of Psychosocial Risk Factors in Men Versus Women

This brief summary of the influence of SES, depression, social support, and hostility on CAD indicate that all of these psychosocial variables increase the risk of CAD to varying degrees. Low SES increases the risk of CAD for both men and women, and is associated with a more atherogenic risk factor profile in women. Depression also imparts an increased risk of cardiac events and CAD-mortality in men as well as women. Men with low social support are more likely to suffer from new CAD events, as well as CAD mortality, while low social support in women has been associated with CAD severity and increased mortality post-MI. There is some indication, however, that the protective effect of social support in women can be explained by race and age, or very low levels of support. Furthermore, marital status is not protective in women, whereas men benefit from being married (Kallan, 1997). There are mixed results for both genders regarding the association of hostility and CAD, but positive studies indicate that hostility is related to CAD, ischemia, restonisis, MI, and recurrent cardiac events. Based on these results, however, many cardiac rehabilitation centers have incorporated hostility and anger management into their programs. Because research on hostility and CAD in women represents a small fraction of the corresponding research in men, the appropriateness and significance of hostility as a target for treatment and prevention in women is not as clear. The role of hostility among women with or at-risk for CAD should be further studied.

The WISE Study

The Women's Ischemia Syndrome Evaluation (WISE) study, conducted to optimize symptom evaluation and diagnostic testing for ischemic heart disease in women (Bairey Merz, et al., 1999), provides an opportunity to determine possible relationships between hostility and angiographic CAD in a large sample of women. The study consists of three specific phases. Phase I (1996-1997) was a pilot phase and enrolled 256 women. Phase II (1997-1999) included an additional 680 women, for a total WISE enrollment of 936 women. Phase III (2000-present) is dedicated to patient follow-up and data analysis. Women are followed for at least one year to assess clinical events and symptom status (Bairey Merz, et al., 1999).

A previous report from the WISE study has shown that hostility and anger are positively related to CAD risk factors (Rutledge, et al., 2001). Lower high-density lipoprotein cholesterol (HDL-C) levels were associated with higher Anger Out and Cynical Hostility scores, while higher low density lipoprotein cholesterol (LDL-C) levels were associated with higher Anger Out scores. A history of hypertension was associated with elevated cynical hostility, and larger BMI scores were associated with higher Anger Out scores. Current smokers also showed higher Anger In and Cynical Hostility scores.

Study rationale and hypotheses

The present study is an attempt to assess the association between hostility and anger with angiographic CAD in women with suspected heart disease. The primary study hypothesis is that: (1) Hostility and Anger, as measured by the Cook-Medley Hostility subscales and the Anger Expression Scale, will be significantly higher in women with angiographic CAD, compared to women without angiographic CAD. (2) It is further hypothesized that Hostility and Anger scores will be higher among women with suspected CAD than a Reference Group of women. (3) A third hypothesis is that Hostility and Anger scores will be significant independent predictors of angiographic CAD. (3) A fourth hypothesis is that Hostility and Anger scores will be associated with a higher number of general cardiac symptoms, and also with typical angina.

METHODS

Participants

The study sample consisted of 636 WISE women who completed the angiogram procedures, core diagnosis protocol, and hostility questionnairesAll 936 women enrolled in WISE were not eligible for this study because the hostility questionnaires were not administered at all of the study sites, and the questionnaires were added to the protocol after the study had begun. Exact participation rates are not available. Eligibility requirements for enrollment in the WISE study were age over 18 years and undergoing a clinically indicated coronary angiogram for suspected myocardial ischemia. Enrollment occurred after an angiogram had been ordered and performed by referring physicians caring for the women (Sharaf et al., 2001). Therefore these were not protocol-driven angiograms. Participants underwent testing at four clinical sites: Allegheny General Hospital (Pittsburgh), University of Alabama at Birmingham, University of Florida (Gainesville), or the University of Pittsburgh Medical Center.

Major exclusion criteria included: comorbidity which could compromise one-year follow-up, pregnancy, contraindications to provocative diagnostic testing cardiomyopathy, New York Heart Association class IV congestive heart failure, recent myocardial infarction, significant valvular or congenital heart disease, and a language barrier to questionnaire testing. Women who underwent coronary angioplasty or coronary bypass surgery after angiography but before their WISE testing were also excluded (Merz et al., 1999).

A convenience sample of 44 staff members from the participating sites was recruited to participate as a reference control group. These women were in the age range of 35- to 64-years old.

Procedure

Coronary angiography was performed and reviewed at the clinical sites according to usual methods. All angiograms were evaluated for extent of atherosclerosis in the central core laboratory at the University of Pittsburgh, by personnel blinded to all clinical data. All coronary segments identified visually as abnormal were then measured quantitatively. Angiograms received on cine film were analyzed using an electronic cine projector based "cross-hair" caliper technique. Interobserver variability with this technique was 0.196 mm with 6.3% coefficient of variation. Anigograms received in Digital Communications in Medicine format on CD-ROM were analyzed using a computer-based edge detection algorithm. The system required minimal user interaction (Sharaf, 2001). For the purposes of this study, the quantitative assessment as to 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 (Sharaf, 2001).

Measures

Hostility was measured using the sum of three subscales of the Cook-Medley Hostility Inventory, a subscale of the Minnesota Multiphasic Personality Inventory, with high scores indicating bitterness, mistrust, and cynicism (Cook & Medley, 1954). The three subscales, cynicism, aggression, and hostile affect, were derived through factor analysis

(Barefoot, Dodge, Peterson, Dahlstrom, & Williams, 1989). The sum of the three subscales (χ^2 of 9.45,p = 0.002), was a better predictor CAD incidence than the full hostility scale. There are 13 items that assess Cynicism (range: 0-13), 9 items measuring Aggression (range: 0-9), and 5 items that assess Hostile Affect (range: 0-5).

We also administered the Spielberger Anger Expression Scale, which assesses the degree to which individuals inhibit/suppress angry feelings (Anger In), as well as their likelihood of expressing anger toward other persons or objects (Anger Out; Spielberger, Krasner, & Soloman, 1988). The scale's reliability has been reported to range from .73 to .85 (Spielberger, Krasner, & Soloman, 1988). Anger In and Anger Out were assessed using eight separate items, with each set having a range of 8-32. A composite Anger Expression score was derived as a function of the Anger In and Anger Out scores, with a range of 0-72.

The Duke Activity Status Index (DASI; Hlatky, Boineau, & Higgenbotham 1989), a 12-item measure of functional capacity, was also used. The DASI has a range of 12-48, and reliability has been reported between 0.81 and 0.89 (Alonso, Permanyer-Miralda, Cascant, Brotons, Prieto, & Soler-Soler, 1997).

Chest pain was evaluated according to three criteria: (1) whether the discomfort is substernal; (2) whether the discomfort is precipitated by physical exertion; and (3) whether the discomfort is relieved within 10 minutes by rest or nitroglycerin (Diamond, Staniloff, Forrester, & Pollock, 1983). Typical angina was defined as the presence of all three symptom characteristics; atypical angina was defined as the presence of any two of these; nonanginal discomfort was defined as the presence of only one; and asymptomatic referred to patients without any of these symptom characteristics. Prior to the development of this classification system, The Coronary Artery Surgery Study (CASS) found that among women, 72% with definite angina had CAD; 36% with probable angina had CAD, and only 6% with nonanginal pain had CAD. These rates were higher among men, with 93% of patients with definite angina, 66% of patients with probable angina, and 14% of patients with nonanginal pain having CAD (Chaitman et al., 1981).

A cardiovascular symptom history form was used to collect information on anginal symptoms that led to cardiac catheterization and evaluation. These included areas of pain (abdomen, shoulder, back, chest, neck, jaw), symptom descriptors (pressure, tightness, discomfort) and 23 general symptoms such as coughing, dizziness, headache, heartburn, fainting, nausea, weakness and fatigue.

The majority of the participants, 85%, completed these questionnaires after having undergone angiography. Of these women, 83% knew the results of their angiography.

Data Analysis

Data are presented as means and standard deviations for continuous variables and percentages for categorical variables. Comparisons of hostility and anger measures between the WISE Group and Reference Group of non-CAD women were performed using a general linear model to adjust for age and educational level. Cardiovascular symptom data, angina status (atypical, typical, no angina), and disease status were also analyzed using a general linear model. Age adjustments were made where age was significantly related to angiographic CAD. Discrete variables such as education were analyzed using Chi square analysis. Two-tailed probability values ≤ 0.05 were considered significant.

Logistic regression was used to model the probability of significant CAD as a function of age, risk factors, current HRT use, social support, and hostility and anger scores.

After examination of goodness of fit statistics, the variable showing the strongest association was entered into a forward step regression model (level for entry, $p=0.05$). Additional variables were entered and the effect was examined at each step. The Hosmer-Lemshow test was used to examine the lack of fit in the final model.

Analyses were done using SAS software, version 6.12 (Cary, NC).

RESULTS

WISE Demographics and Risk Factors

When WISE women with angiographic CAD (N = 218, 34%) were compared to women without angiographic CAD (N = 418, 66%), the former were older ($p<.01$) and less likely to have completed education beyond high school ($p=.05$). Furthermore, these women were more likely to have a history of dyslipidemia ($p<.01$), diabetes ($p<.01$), and hypertension ($p<.01$), and were less likely to be currently using hormone replacement therapy than women without angiographic CAD ($p<.01$; Table 1). There were no significant group differences regarding BMI and current smoking status.

Hostility/Anger and Angiographic Presence/Absence of CAD

WISE women with angiographic CAD did not differ from those without angiographic CAD on any univariate analysis of the Anger or Hostility measures, both with and without adjustment for all significant variables (Table 2).

Reference Group Demographics

When the WISE women were compared to the Reference Group, the former were older ($p<.01$) and less likely to have completed education beyond high school ($p<.01$). The WISE women were also more likely to be current smokers ($p<.01$), and to have a history of hypertension ($p<.01$). The two groups did not differ in terms of BMI (Table 3)

Hostility and Anger in WISE Women vs. Reference Group

When compared to the Reference Group, the WISE women had higher Anger Expression scores ($p<.01$), and a trend towards higher Anger Out scores ($p=.08$), after adjusting for all significant variables (Table 4). No other hostility or anger measure showed a significant group difference. When the WISE women were separated into CAD and no CAD groups, and then compared to the Reference Group, the only significant difference was observed in the Anger Expression scores, with both the CAD and no CAD groups showing higher scores than the Reference group, but not differing from each other (Table 5).

Hostility and Anger as Related to Extend of CAD

Given the lack of differences between the CAD and no CAD groups, we decided to examine hostility and anger scores according to the number of diseased vessels, as opposed to defining CAD as >50% occlusion in any one vessel. Subjects were categorized as having 0-20% occlusion in any/all vessels (0 diseased vessels), 20-49% occlusion in any/all vessels (Minimal diseased vessels), or 50% occlusion in one, two, or three vessels (1, 2, or 3 diseased vessels). No differences were found on any of the hostility or anger measures (Table 6).

Hostility and Anger as Predictors of Angiographic CAD

Logistic regression was used to examine the association of the Hostility and Anger measures with CAD, with the WISE non-CAD women serving as the reference group. When the six anger and hostility measures were entered into individual models, none were significant. Separate multivariable modeling for risk factors and each of the anger and hostility measures revealed that Anger Out was the only anger/hostility measure that was significantly associated with CAD, with an OR of 1.08 (CI: 1.00-1.16), when age (OR: 1.05, CI: 1.02-1.07), history of diabetes (OR: 1.83, CI: 1.03-3.26), and history of dyslipidemia (OR: 3.05, CI: 1.77-5.28) were included in the model. Models with each of the anger and hostility scores in the model with age, history of diabetes, history of dyslipidemia, and Anger Out revealed that Anger Out was always a significant predictor. Cynicism, Hostile Affect, Aggression, and Anger In were never significantly associated with CAD, nor did their inclusion significantly strengthen the Anger Out-CAD association.

Hostility/Anger and Symptoms

WISE women reporting $\geq$ 10 symptoms in their cardiovascular symptom history had significantly higher scores on all six measures of anger and hostility than WISE women reporting <10 symptoms (Figure 1). Women with $\geq$ 10 symptoms also reported lower functioning status (p<.01), measured by the Duke Activity Status Index. Within the group of WISE women with angiographic CAD, there was no difference in anger and hostility based on their angina classification (typical angina, atypical angina, and non-anginal chest pain). Among WISE women without angiographic evidence of CAD, however, those with non-anginal chest pain had significantly higher Anger Out ($p<.01$) and Anger Expression ($p=.02$) scores than women with either atypical or typical angina, as well as a trend towards higher Aggression ($p=.06$) scores. Women without angiographic CAD and with atypical angina also had higher Hostile Affect ($p=.05$) and Anger Out ($p<.01$) scores than women with no angiographic CAD and typical angina (Figure 2). Women with no angiographic CAD and either atypical angina or non-anginal chest pain reported significantly lower functioning status than those with typical angina ($p<.01$), but did not differ from each other.

Inter-Correlations of Anger/Hostility Measures

Inter-correlations among the various anger and hostility measures were all statistically significant. However, the correlation coefficients were relatively low to moderate, indicating that these measures assess much, but not all of the same aspects of anger and hostility (Table 7).

DISCUSSION

The major findings of this study are that: 1) while angiographic presence of CAD was not distinguished from angiographic absence of disease in univariate analyses, logistic regression analyses indicate that in combination with risk factors, Anger Out is significantly correlated with angiographic CAD; and 2) that atypical symptoms and quantity of symptoms are both associated with elevated hostility and anger.

Hostility/Anger and Angiographic Presence/Absence of CAD

Given that a behavioral measure of hostility (Anger Out) was significantly associated with CAD, and measures of the cognitive aspect of hostility (Cook-Medley subscales) were not, it appears that in women the overt expression of anger toward other persons or objects is more "toxic" than the cognitive aspect of hostility. Several studies have revealed an association between behavioral hostility and elevated plasma lipids, suggesting that plasma lipids may mediate this relationship between behavioral hostility and CAD.

Dujovne and Houston (1991) found that in both women and men, expressive hostility was associated with elevated TSC and LDL. However, cynical (cognitive) hostility was related to elevated levels of LDL in men, but not in women. Suarez, Bates, and Harralson (1998) also have reported that antagonistic hostility, characterized by the outward expression of anger in a verbal or physical manner and an antagonistic interpersonal style, was positively associated with TSC, LDL cholesterol, triglycerides, and the TSC to HDL ratio. However, while WISE women with CAD were significantly more likely to have a history of dyslipidemia than women without CAD, the two groups did not differ in terms of current LDL levels or TSC. It is possible that in the women with CAD, a past history of dylipidemia may be responsible for atherosclerosis, but that lipid levels are currently controlled through medication or lifestyle changes. If lipid levels were systematically reduced in the CAD population and not in the non-CAD WISE participants, then one potential mechanism accounting for elevated Anger Out among women with CAD versus without CAD could be related to the psychological correlates of lipid reduction. A number of studies have found that low cholesterol levels are associated with depressive symptoms, anxiety, aggression, hostility, and impulsivity (Steegmans, Hoes, Bak, van der Does, &

Grobbee, 2000; Suarez, 1999; Aijenseppa, et al., 2002). Such an interpretation would also support the present observation that the relationship between Anger Out and CAD-status is only observed when history of dyslipidemia is statistically adjusted for, whereas univariate analyses do not show an overall relationship between Anger Out and CAD.

Costa, McCrae, and Dembroski (1988) also have asserted that the behavioral component of hostility, represented in expressive hostility, is the important hostility-related risk factor for CAD. If this is true, then a measure assessing the cognitive aspect of hostility, such as the Cook-Medley hostility scale, will be a less direct and sensitive predictor of what may be the important hostility-related risk factor for CAD, particularly in women (Dujovne & Houston, 1991). Measures that assess the outward manifestations of hostility, such as the Anger Expression Scale, therefore may be more appropriate.

Assuming an association between composite hostility and CAD, hostile individuals may be more vulnerable to heart disease than non-hostile persons because they have a substantially greater sympathetic nervous system response to stressful or demanding circumstances. Because hostile persons may be reactive in a greater number of circumstances, they are likely to experience these heightened physiological responses for longer periods of time each day. The increases in heart rate and blood pressure, as well as the frequent surges of epinephrine and other adrenal hormones that accompany the stress response, may injure the endothelium of the coronary artery walls, making them more susceptible to atherosclerosis (Esch, Stefano, Fricchione, & Benson, 2002). The pernicious effects of stress hormones on the heart and the arteries would therefore be greater in hostile individuals than non-hostile individuals, resulting in a higher incidence of CAD and cardiac events.

Hostility/Anger and Symptoms

Our results also demonstrated that atypical cardiac symptoms without a plausible cardiac cause were correlated with higher levels of anger and hostility. Not having a definitive diagnosis or treatment for their symptoms may be frustrating and thus manifest as increased aggression and anger in these women. Nonetheless, the role of other variables such as neuroticism cannot be discounted, as women high in neuroticism may be hypersensitive to bodily symptoms (Williams & Wiebe, 2000), perhaps becoming angry or hostile when no medical explanation is provided. Unfortunately, no measure of neuroticism was included in the WISE protocol.

All WISE women reported chest pain or other cardiac symptoms for entry into the study, compared to the relatively asymptomatic Reference Control Group, where only three women reported any symptoms. Compared to the Reference Group, coping with discomforting symptoms such as frequent chest pain, may be increasing the WISE women's hostility and anger. The finding that among the WISE women, those with 10 or more symptoms express significantly more anger than those with fewer than 10 symptoms supports this. Another possibility is that the highly symptomatic WISE women have a heightened awareness of their emotions, which then enhances symptom perception, as patients who are unaware of or deny negative emotions such as anger seem to have diminished perception of ischemia (Linden, 1991; Reynaert, 1991).

Study Limitations

The cross-sectional design of this study prohibits any causal inferences, making it unclear whether hostility and anger lead to the manifestation of CAD, or whether patients with CAD become more hostile and angry following their diagnosis. Furthermore, because the majority of the participants completed the psychological measures after having undergone and received the results of their angiography, we cannot ignore the fact that their responses may have been influenced by the knowledge of their disease state. Psychological measures would ideally be administered prior to any testing and reporting of test results.

It is also important to note that the present study examined only a small portion of the information collected in WISE. Numerous diagnostic tests were employed at the clinical sites, including echocardiography, exercise stress testing, magnetic resonance imaging, nuclear scintigraphy, and positron emission tomography. Examining hostility across the diverse diagnostic methodologies employed may provide a clearer picture of the association between hostility and CAD in women.

Another significant limitation of the study is the Reference Control Group, which is substantially smaller in number than the overall WISE population. The Reference Control Group is also less than ideal in that these women were not matched to the WISE women in terms of age and level of education. Furthermore, these women were alarmingly obese, with 40.9% having a BMI of >30. When the Reference Control Group was first proposed, the intent was to recruit women with a low probability of CAD (<1% or <5%), based on the sequential Bayesian analysis of age, sex, symptoms, coronary risk factors, and noninvasive test results. However, in the face of recruitment difficulties, the decision was made to utilize a convenience sample consisting of staff at the various clinical sites. Future studies should clearly strive for a more appropriate control group in order to make meaningful comparisons between women with suspected CAD and women who are healthy.

Insufficient statistical power was also a limitation for some of the psychosocial measures. Post-hoc power analyses revealed that substantially larger sample sizes would be necessary to make the effect sizes obtained in this study statistically significant. Despite this shortcoming, however, our sample is larger than that of prior studies conducted on exclusively female samples. Nevertheless, the fact that only one of six anger and hostility measures was significantly associated with angiographic disease, and only after adjusting for several risk factors, suggests that a hostility-CAD association in women may be small and of questionable clinical significance.

The use of stepwise regression may also be viewed as a study limitation. Cohen and Cohen (1983) have argued that stepwise regression is inappropriate for explanatory research because it is not based on the a priori hierarchical ordering of variables. Furthermore, the order produced from a set of variables in one sample is unlikely to be found in other samples from the same population. Cohen's and Cohen's most serious objection to stepwise regression, however, is that it capitalizes in chance due to the fact that the significance test of a variable's contribution to the overall variance does not account for the other numerous tests being performed simultaneously for competing variables.

Another possible source of bias is that coronary angiographic populations, such as the WISE population, are not appropriate for the evaluation of the role of hostility as a risk factor for CAD. Pickering (1985) has argued that using a coronary angiography sample can lead to a biased selection of subjects, as individuals undergoing catherization are more likely to have CAD than not. Furthermore, anatomic CAD may not be the right end point for the expression of CAD risk factors, as mortality from CAD is also related to factors in addition to anatomical extent of atherosclerosis (Pickering, 1985). While the WISE study is an important first-step in that it examines CAD in a large cohort of exclusively female patients, prospective studies are necessary to better understand the relationship between hostility and CAD in women.

Conclusions

The present study indicates that only a behavioral component of hostility, assessed by the Anger Out scale, is associated with angiographic CAD in a large sample of women undergoing coronary angiography. These results appear to differ from the literature on males, in which Cook-Medley hostility scores are found to be associated with CAD, particularly in younger men (Miller et al., 1996), independent of adjustment for confounding variables. Combined with previous WISE analyses (Rutledge et al., 2001), however, it appears that anger and hostility in women do tend to cluster with adverse risk factors, similar to men, and that anger and hostility are elevated in highly symptomatic women.

Clinical Implications

A primary objective of the WISE study is to optimize symptom evaluation and diagnostic testing for CAD in women. The inclusion of psychosocial measures of anger and hostility may help to accomplish this, particularly measures that assess the behavioral expression of anger and hostility. Furthermore, women with atypical cardiac symptoms may also need assistance in coping with their symptoms as well as the psychological effects 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 clinical management of heart disease.

TABLES

Table 1

Demographics and Risk Factors of Women With Vs. Without CAD

Variable	CAD[a] (N=218)	No CAD[a] (N=418)	p
Demographics			
Age	61.2 (12.0)	56.0 (10.6)	0.001
Education > high school	36.0	45.0	0.05
Standard Risk Factors			
Cholesterol			
Total	195.5 (45.9)	196.4 (44.8)	0.80
LDL	110.0 (41.1)	113.0 (38.4)	0.32
BMI			
> 30	36.0	40.0	0.33
Smoking	22.0	18.0	0.25
History of Hypertension	65.0	54.0	0.006
History of Diabetes	37.0	15.0	0.001
History of Dyslipidemia	71.0	44.0	0.001
Current HRT use	39.0	54.0	0.002

[a]Values represent % or mean (standard deviation) as appropriate

Table 2

*Hostility Scores of Women With vs. Without CAD**

	CAD (N=218)	No CAD (N=418)	p
Hostility/Anger Measure			
Cynicism	5.3 (3.6)	4.9 (3.4)	0.53
Aggression	2.8 (1.7)	2.8 (1.7)	0.95
Hostile Affect	1.8 (1.3)	2.0 (1.3)	0.15
Anger In	14.8 (4.0)	15.2 (4.3)	0.61
Anger Out	13.4 (3.3)	13.1 (3.5)	0.18
Anger Expression	19.5 (9.5)	19.2 (9.6)	0.38

*Adjusted for age, education, history of hypertension, current smoking status, and BMI>30

Table 3
Demographics and Risk Factors of WISE Vs. Reference Group

Variable	WISE[a] (N=44)	Reference Group[a] (N=636)	p
Demographics			
Age	57.8 (11.4)	48.6 (7.2)	0.0001
Education > high school	41.7	90.9	0.001
Standard Risk Factors			
Cholesterol			
LDL	13.1	3.6	0.92
BMI			
Kg	76.8 (16.4)	76.8 (15.5)	-----
> 30	38.6	40.9	0.76
Smoking			
Current	19.1	0	0.001
Hypertension	57.7	2.3	0.001

[a]Values represent % or mean (standard deviation) as appropriate

Table 4
*Hostility Scores of WISE vs. Reference Group**

	WISE (N=636)	Reference (N=44)	p
Hostility/Anger Measure			
Cynicism	5.0 (3.4)	3.9 (3.3)	0.99
Aggression	2.8 (1.7)	2.5 (1.7)	0.86
Hostile Affect	1.9 (1.3)	1.5 (1.1)	0.23
Anger In	15.1 (4.2)	13.8 (3.4)	0.51
Anger Out	13.2 (3.4)	12.1 (2.5)	0.08
Anger Expression	19.3 (9.4)	14.0 (7.1)	0.009

*Adjusted for age, education, history of hypertension, current smoking status, and BMI>30

Table 5
*Hostility Scores of Women With CAD vs. Without CAD vs. Reference Sample**

	CAD (N=218)	No CAD (N=418)	Reference (N=44)	p
Hostility/Anger Measure				
Cynicism	5.2 (3.5)	4.9 (3.4)	3.9 (3.3)	0.10
Aggression	2.8 (1.6)	2.8 (1.7)	2.5 (1.7)	0.68
Hostile Affect	1.7 (1.3)	2.0 (1.3)	1.5 (1.1)	0.16
Anger In	14.7 (4.0)	15.2 (4.3)	13.8 (3.4)	0.16
Anger Out	13.3 (3.4)	13.1 (3.5)	12.1 (2.5)	0.10
Anger Expression	19.0 (9.6)	19.2 (9.6)	14.0 (7.1)	<.01

*Adjusted for age and education

Table 6
*Hostility and Anger Scores as Related to Extent of CAD**

	Vessel Disease**					
	0 (N=250)	Min (N=168)	1 (N=99)	2 (N=60)	3(N=50)	p
Hostility/Anger Measure						
Cynicism	4.7 (3.3)	5.2 (3.4)	5.6 (3.7)	4.8 (3.2)	5.0 (3.5)	0.07
Aggression	2.8 (1.8)	2.8 (1.7)	2.9 (1.8)	2.9 (1.8)	2.6 (1..2)	0.79
Hostile Affect	2.0 (1.3)	2.0 (1.3)	1.8 (1.3)	1.8 (1.2)	1.6 (1.3)	0.39
Anger In	15.1 (3.9)	15.3 (4.8)	15.0 (3.8)	14.8 (4.0)	13.9 (4.3)	0.68
Anger Out	12.9 (3.3)	13.4 (3.7)	13.3 (3.6)	13.4 (3.5)	13.1 (2.9)	0.19
Anger Expression	19.0 (8.9)	19.4 (10.6)	19.9 (8.9)	19.0 (9.9)	17.2 (10.5)	0.38

*Adjusted for age and education
**0=0-20% occlusion in any/all vessels; Min=20-49% occlusion in any/all vessels; 1,2,3=>50% occlusion in one, two, or three vessels

Table 7
*Correlations of Anger/Hostility Measures**

Variable	1	2	3	4	5	6
1. Cynicism		.39	.51	.44	.23	.37
2. Aggression			.39	.27	.40	.41
3. Hostile Affect				.47	.38	.52
4. Anger In					.31	.68
5. Anger Out						.75
6. Anger Expression						

*All correlations are significant, p=.0001

FIGURES

Figure 1. Anger and hostility scores (mean ± sd) among women with <10 symptoms compared to women with ≥10 symptoms. *p<0.05; ** p<0.01

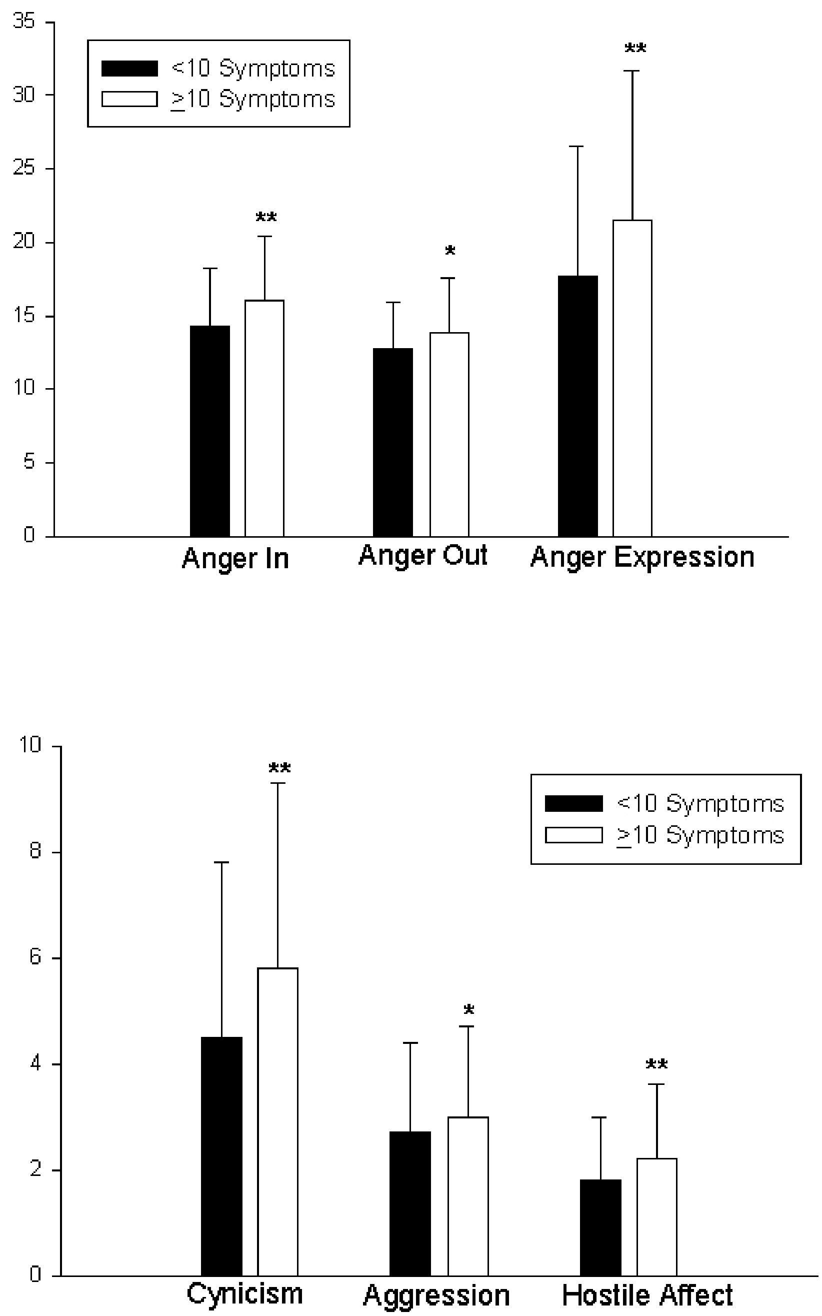
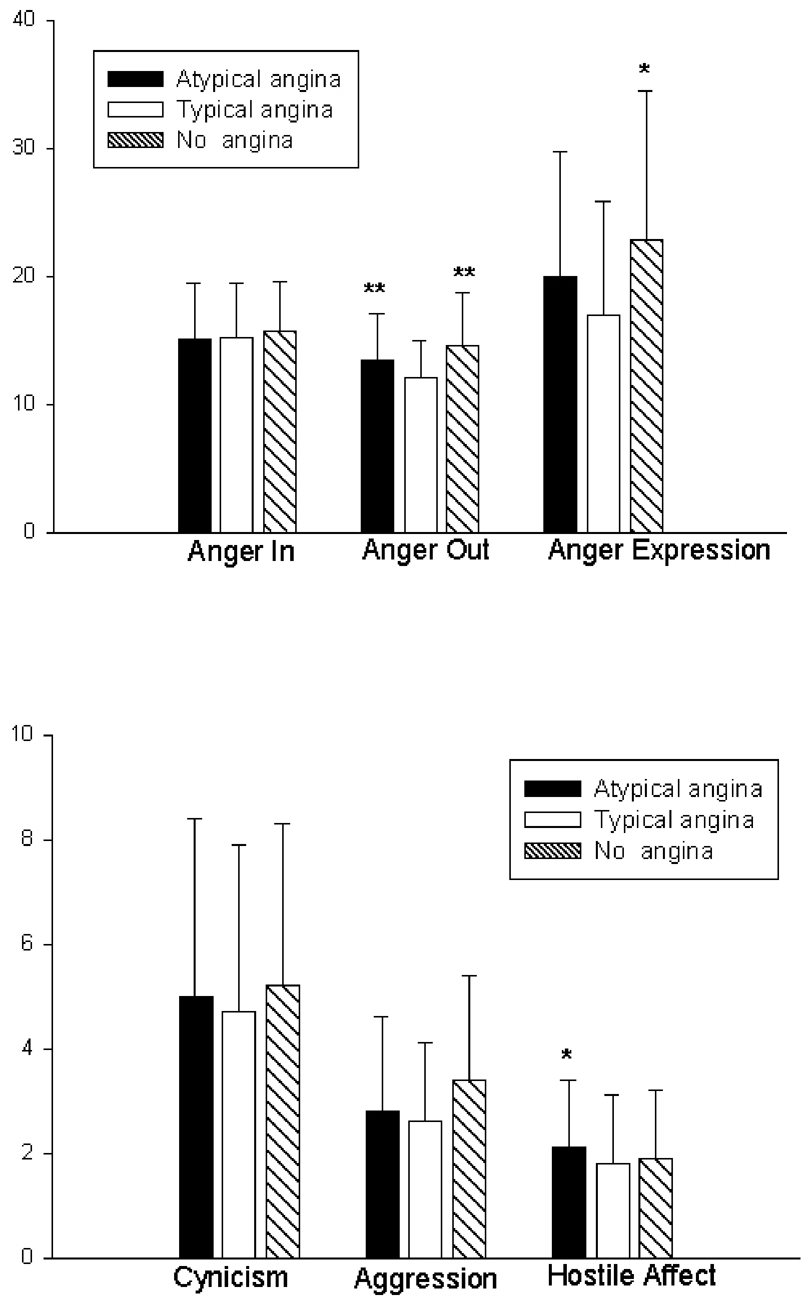


Figure 2. Anger and hostility scores of women without CAD (mean $\pm$ sd) according to angina classification. *p<0.05; ** p<0.01



APPENDICES

Appendix A: Cook-Medley Cynicism Subscale

	True 1	False 0
I have often had to take orders from someone who did not know as much as I did.	( )	( )
I think a great many people make a lot of their bad luck in order to gain the sympathy and help of others.	( )	( )
It takes a lot of argument to convince most people of the truth.	( )	( )
Most people are hones mainly through fear of being caught.	( )	( )
Most people will use somewhat unfair means to gain profit or an advantage rather than to lose it.	( )	( )
No one cares much what happens to you.	( )	( )
It is safer to trust no one.	( )	( )
Most people make friends because friends are likely to be useful to them.	( )	( )
Most people inwardly do not like putting themselves out to help other people.	( )	( )
I have often met people who were supposed to be experts who were no better than I.	( )	( )
People often demand more respect for their own rights than they are willing to allow for others.	( )	( )
A large number of people are guilty of bad sexual behavior.	( )	( )
I think most people would lie to get ahead.	( )	( )

Appendix B: Cook-Medley Aggression Subscale

	True 1	False 0
When someone does me wrong I feel I should pay him back if I can, just for the principle of the thing.	( )	( )
I can be friendly with people who do things which I consider wrong.	( )	( )
I don't blame anyone for trying to grab everything he can get in this world.	( )	( )
I do not blame a person for taking advantage of someone who lays himself open to it.	( )	( )
I would certainly enjoy beating a crook at his own game.	( )	( )
I have at times had to be rough with people who were rude or annoying.	( )	( )
I am often inclined to go out of my way to win a point with someone who has opposed me.	( )	( )
I do not try to cover up my poor opinion or pity of a person so that he won't know how I feel.	( )	( )
I strongly defend my own opinions as a rule	( )	( )

Appendix C: Cook-Medley Hostile Affect Subscale

	True 1	False 0
It makes me impatient to have people ask my advice or otherwise interrupt me when I am working on something important.	( )	( )
Some of my family have habits that bother and annoy me very much.	( )	( )
People often disappoint me.	( )	( )
I am not easily angered.	( )	( )
There are certain people whom I dislike so much that I am inwardly pleased when they are catching it for something they have done.	( )	( )

Appendix D: Spielberger Anger Expression Scale

Everyone feels angry or furious from time to time, but people differ in the ways they react when they are angry. A number of statements are listed below which people use to describe their reactions when they feel angry or *furious*. Read each statement and then fill in the circle with the number which indicates how *often* you *generally* react or behave in the manner described when you are feeling angry or furious. Remember that there are no right or wrong answers. Do not spend too much time on any one statement.

When Angry or Furious…

	Almost Never	Sometimes	Often	Almost Always
I control my temper	( )	( )	( )	( )
I express my anger	( )	( )	( )	( )
I keep things in	( )	( )	( )	( )
I am patient with others	( )	( )	( )	( )
I pout or sulk	( )	( )	( )	( )
I withdraw from people	( )	( )	( )	( )
I make sarcastic remarks to others	( )	( )	( )	( )
I keep my cool	( )	( )	( )	( )
I do things like slam doors	( )	( )	( )	( )
I boil inside, but I don't show it	( )	( )	( )	( )
I control my behavior	( )	( )	( )	( )
I argue with others	( )	( )	( )	( )
I tend to harbor grudges that I don't tell anyone about.	( )	( )	( )	( )
I strike out at whatever infuriates me	( )	( )	( )	( )
I can stop myself from losing my temper	( )	( )	( )	( )
I am secretly quite critical of others.	( )	( )	( )	( )
I am angrier than I am willing to admit	( )	( )	( )	( )
I calm down faster than most people	( )	( )	( )	( )
I say nasty things	( )	( )	( )	( )
I try to be tolerant and understanding	( )	( )	( )	( )

Appendix E: When Angry or Furious…

	Almost Never	Sometimes	Often	Almost Always
I'm irritated a great deal more than people are aware of	( )	( )	( )	( )
I lose my temper	( )	( )	( )	( )
If someone annoys me, I'm apt to tell him or her how I feel.	( )	( )	( )	( )
I control my angry feelings.	( )	( )	( )	( )

Appendix F: Duke Activity Status Index

Can you……	**Yes, with no difficulty. (1)**	**Yes, with some difficulty. (2)**	**No, I can't do this. (3)**	**Don't do this for other reasons. (4)**
1. Take care or yourself, that is, eating, dressing, bathing, and using the toilet?	O	O	O	O
2. Walk indoors, such as around your house?	O	O	O	O
3. Walk a block or tow on level ground?	O	O	O	O
4. Climb a flight of stairs or walk up a hill?	O	O	O	O
5. Run a short distance?	O	O	O	O
6. Do light work around the house like dusting or washing dishes?	O	O	O	O
7. Do moderate work around the house like vacuuming, sweeping floors, carrying in groceries?	O	O	O	O
8. Do heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?	O	O	O	O
9. Do yard work like raking leaves, weeding or pushing a power mower?	O	O	O	O
10. Have sexual relations?	O	O	O	O
11. Participate in moderate recreational activities, like golf, bowling, dancing, double tennis, or throwing baseball or football?	O	O	O	O
12. Participate in strenuous sports like swimming, singles tennis, football, and basketball or skiing?	O	O	O	O

Total Score ______

Appendix G: WISE Symptom History Questionnaire
Part I: General Symptoms

What problems or complaints did you experience that eventually led to your having this evaluation?

	Yes 1	No 0
Abdominal pain		
Arm pain or should pain		
Back pain		
Chest pain		
Chest pressure		
Chest tightness		
Chest discomfort (heaviness, burning, tenderness)		
Cough		
Dizziness, lightheadedness		
Feel louse/general blahness		
Headache		
Heartburn/indigestion/stomach problem		
Impending doom		
Jaw pain		
Loss of consciousness/fainting		
Nausea/vomiting		
Neck pain		
Numbness/tingling in arm or hand		
Palpitations/rapid heart rate		
Shortness of breath/difficulty breathing		
Sweating		
Weakness/fatigue/faintness		
Other		

Specify:____

REFERENCES

Ahern, D. K., Gorkin, L., Anderson, J. L., Tierney, C., & Hallstrom, A. (1996). Cardiac Arrhythmia Pilot Study (CAPS) investigators: Biobehavioral variables and mortality or cardiac arrest in the Cardiac Arrhythmia Pilot Study (CAPS). *American Journal of Cardiology*, 66, 59-62.

Aijanseppa, S., Kivinen, P., Helkala, E. L., Kivela, S. L., Tuomilehto, J., & Nissinen, A. (2002). Serum cholesterol and depressive symptoms in elderly Finnish men. *International Journal of Geriatric Psychiatry*, 17, 269-234.

Alonso J, Permanyer-Miralda G., Cascant, P., Brotons, C., Prieto, L., & Soler-Soler, J. (1997). Measuring functional status of chronic coronary patients. Reliability, validity and responsiveness to clinical change of the reduced version of the Duke Activity Status Index (DASI). *European Heart Journal*, 19, 414-419.

And, R. Williamson, D., Jones, D., Macera, C., Eaker, E., Glassman, A., & Marks, J. (1993). Depressed affect, hopelessness, and the risk of ischemic heart disease in a cohort of U. S. adults. *Epidemiology*, 4, 285-294.

Bairey Merz, C. N. , Kelsey, S. F., Pepine, C. J., Reichek, N., Reis, S. E., Rogers, W. J., Sharaf, B. L., & Sopko, G. (1999). The Women's Ischemia Syndrome Evaluation (WISE) study: Protocol, design, methodology, and feasibility report. *Journal of the American College of Cardiology*, 33, 1453-1461.

Barefoot, J. C., Dahlstrom, W. G., & Williams, R. B., Jr. (1983). Hostility, CAD incidence, and total mortality: A 25-year follow-up study of 255 physicians. *Psychosomatic Medicine*, 45, 59-63.

Barefoot, J. C., Dodge, K. A., Peterson, B. L., Dahlstrom, W. G., & Williams, R. B. (1989). The Cook-Medley hostility scale: Item content and ability to predict survival. *Psychosomatic Medicine*, 451, 46-57.

Barrett-Connor, E. (1991). Estrogen and coronary heart disease in women. *Journal of the American Medical Association*, 265, 1861-1867.

Barsky, A. J., Hochstraser, B., Coles, N. A., Zisfein, J., O'Donnell, C., & Eagle, K. A. (1990). Silent myocardial ischemia: Is the person or the event silent? *Journal of the American Medical Association*, 264, 1132-1135.

Beitman, B. D., Basha, I., Flaker, G., DeRosear, L., Mukerji, v., Trombka, L. Katon, W. (1987). Atypical or nonanginal chest pain? Panic disorder or coronary artery disease? *Archives of Internal Medicine*, 147, 1548-1552.

Berkman, L. F., Leo-Summers, L. L., & Horwitz, R. I. (1992). Emotional support and survival after myocardial infarction. *Annals of Internal Medicine*, 117, 1003-1009.

Billing, E., Hjemdahl, P., & Rehnquist, N. (1997). Psychosocial variables in female vs male patients with stable angina pectoris and matched healthy controls. *European Heart Journal*, 18, 911-918.

Bjorntorp, P. (1988). The associations between obesity, adipose tissue distribution and disease. *Acta Medica Scandinavica*, 723, 121-134.

Blumenthal, S. J & Matthews, K. A. (1993). Psychosocial aspects of cardiovascular disease in women: Introduction and overview. *Annals of Behavioral Medicine*, 15, 109-112.

Burg, M. M., Jain, D., Soufer, R., Kerns, R. D., & Zaret, B. L. (1993). Role of behavioral and psychological factors in mental stress-induced silent left ventricular dysfunction in coronary artery disease. *Journal of the American College of Cardiology*, 22, 440-448.

Carney, R. M., Rich, M. W., Freedland, K. E., & Saini, J. (1988). Major depressive disorder predicts cardiac events in patients with coronary artery disease. *Psychosomatic Medicine*, 50, 627-633.

Chaitman, B. R., Bourassa, M. G., Davis, K., Rogers, W. J., Tyras, D. H., Berger, R., Kennedy, J. W., Fisher, L., Judkins, M. P., Mock, M. B., & Killip, T. (1981). Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). *Circulation*, 64, 360-367.

Chaput, L. A., Adams, S. H., Simon, J. A., et al. (2002). Hostility predicts recurrent events among postmenopausal women with coronary heart disease. American Journal of Epidemiology, 156, 1092-1099.

Cohen, J. & Cohen, P. (1983). *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*. (2nd Ed.). New Jersey: Lawrence Erlbaum Associates.

Cohen, S., Gottlieb, B. H., & Underwood, L. G. Social relationships and health. In Cohen, S., Gottlieb, B. H., & Underwood, L. G. (eds.) *In Social Support Measurement and Intervention*. Pp. 3-25. New York, NY: Oxford University Press.

Collins, A. & Frankenhauseur, M. (1978). Stress responses in male and female engineering students. *Journal of Human Stress*, 4, 43-48.

Cook, W. W. & Medley, D. M. (1954). Proposed hostility and pharisaic-virtue scales for the MMPI. *Journal of Applied Psychology*, 38, 414-418.

Cost, P. T., Jr., McCrae, R. R., & Dembroski, T. M. (1988). Antagonism: Explication of a potential risk factor for CAD. In Siegman, A. W. & Dembroski, T. M. (eds). *In*

Search of Coronary-Prone Behavior: Beyond Type A. pp. 41-63. Hillsdale, NJ: Erlbaum.

Dembroski, T. M., MacDougall, J. M., Williams, R. B., Haney, T. L., & Blumenthal, J. A. (1985). Components of Type A, hostility, and anger-in: Relationship to angiographic findings. *Psychosomatic Medicine*, 47, 219-233.

Dembroski, T. M., & Costa, P. T. (1987). Coronary-prone behavior: Components of the Type A pattern and hostility. *Journal of Personality*, 55, 211-235.

Diamond, G. A., Staniloff, H. M., Forrester, J. S., & Pollock, B. H. (1983). Computer-assisted diagnosis in the noninvasive evaluation of patients with suspected coronary artery disease. *Journal of the American College of Cardiology*, 1, 444-455.

Dujovne, V. F. & Houston, B. K. (1991). Hostility-related variables and plasma lipid levels. *Journal of Behavioral Medicine*, 14, 555-565.

Eaker, E. D., Packard, B., Wenger, N. K., Clarkson, R. B., & Tyroler, H. A. (1988). Coronary artery disease in women. *American Journal of Cardiology*, 61, 641-644.

Earle, T.L., Linden, W., & Weinberg, J. (1999). Differential effects of harassment on cardiovascular and salivary cortisol stress reactivity and recovery in women and men. *Journal of Psychosomatic Research*, 46, 125-141.

Esch, T., Stefano, G. B., Fricchione, G. L., & Benson, H. (2002). Stress in cardiovascular diseases. *Medical Sciences Monitor*, 8, RA93-RA101.

Feldman, J. J., Makuc, D. M., Kleinman, J. C., & Coroni-Huntley, J. (1989). National trends in educational differentials in mortality. *American Journal of Epidemiology*, 129, 919-933.

Fetters, J. K., Peterson, E. D., Shaw, L. J., Newby, L. K., & Califf, R. M. (1996). Sex-specific differences in coronary artery disease risk factors, evaluation, and treatment: Have they been adequately evaluated. *American Heart Journal*, 131, 796-813.

Frasure-Smith, N., Lesperance, F., Talajic, M. (1995). The impact of negative emotions on prognosis following myocardial infarction: is it more than depression? *Health Psychology*, 14, 5, 388-398.

Frasure-Smith, N., Lesperance, F., Juneau, M., Talajic, M., & Bourassa, M. G. (1999). Gender, depression, and one-year prognosis after myocardial infarction. *Psychosomatic Medicine*, 61, 1, 26-37.

Friedman, M., Thoresen, C. E., & Gill, J. J. (1986). Alteration of type A behavior and its effect on cardiac recurrences in post-myocardial infarction patients: Summary results of the Recurrent Coronary Prevention Project. *American Heart Journal*, 112, 653-662.

Goldberg, R. J., O'Donnell, C., Yarzebski, J., Bigelow, C., Savageau, J., & Gore, J. M. (1998). Sex differences in symptom presentation associated with acute myocardial infarction: A population-based perspective. *American Heart Journal*, 136, 189-195.

Goodman, M., Quigley, J., Moran, G., Meilman, H., & Sherman, M. (1996). Hostility predicts restenosis after percutaneous transluminal coronary angioplasty. *Mayo Clinic Proceedings*, 71, 729-734.

Hallstrom, T., Lapidus, L., Bengtsson, C., & Edstrom, K. (1986). Psychosocial factors and risk of ischaemic heart disease and death in women: A twelve-year follow-up of participants in the population study of women in Gothenburg, Sweden. *Journal of Psychosomatic Research*, 30, 451-459.

Haney, T. O., Maynard, K. E., Hoseworth, S. J., Scherwitz, L. W., Williams, R. B., & Barefoot, J. C. (2000). Antagonistic behavior, dominance, hostility, and coronary heart disease. *Psychosomatic Medicine*, 62, 248-257.

Hearn, M. D., Murray, D. M., & Luepker, R.V. (1989). Hostility, coronary heart disease, and total mortality: a 33-year follow-up study of university students. *Journal of Behavioral Medicine*, 12, 105-121.

Helmer, D. C., Ragland, D. R., & Syme, S. L. (1991). Hostility and coronary artery disease. *American Journal of Epidemiology,* 133, 112-122.

Helmers, K. F., Krantz, D. S., Howell, R. H., Klein, J., Bairey, C. N., & Rozanski, A. (1993). Hostility and myocardial ischemia in coronary artery disease patients: Evaluation by Gender and Ischemic Index. *Psychosomatic Medicine*, 55, 29-36.

Hemingway, H. & Marmot, M. (1999). Evidence based cardiology: Psychosocial factors in the aetiology and prognosis of coronary heart disease: systematic review of prospective cohort studies. *British Medical Journal*, 318, 7196, 1460-1467.

Hlatky, M., Boineau, R., & Higgenbotham, M. (1989). A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *American Journal of Cardiology*, 64, 651-654.

Hulley, S., Grady, D., Bush, T., Furberg, C., Herrington, D., Riggs, B., & Vittinghoff, E. (1998). Randomized Trial of Estrogen Plus Progestin for Secondary Prevention of Coronary Heart Disease in Postmenopausal Women. *JAMA*, 280, 605-613.

Julkunen, J., Salonen, R., Kaplan, G. A., Chesney, M. A., & Salonen, J. T. (1994). Hostility and progression of carotid atherosclerosis. *Psychosomatic Medicine*, 56, 519-525.

Kallan, J. (1997). Effects of sociodemographic variables on adult mortality in the United States: comparisons by sex, age, and cause of death. *Social Biology*, 44, 136-147.

Kaplan, G. A., Salonene, J. T., Cohen, R. D., Brand, R. J., Syme, S. L., & Puska, P. (1988). Social connections and mortality from all causes and from cardiovascular disease: Prospective evidence from eastern Finland. *American Journal of Epidemiology*, 128, 370-380.

Kellner, R. (1985). Functional somatic symptoms and hypochondriasis: A survey of empirical studies. *Archives of General Psychiatry*, 42, 821-833.

Lai, J.Y. & Linden, W. (1992). Gender, anger expression style, and opportunity for anger release determine cardiovascular reaction to and recovery from anger provocation. *Psychosomatic Medicine*, 54, 297-310.

Lapidus, L, Bengtsson, C., Larsson, B., Pennert, K., Tybo, E., & Sjostrom, L. (1984). Distribution of adipose tissue and risk of cardiovascular disease and death: 12-year follow-up of participants in the population study of women in Gothenburg, Sweden. *British Medical Journal*, 289, 1257-1261.

Linden, W., Earle, T. L., Gerin, W., & Christenfeld, N. (1997). Physiological stress reactivity and recovery: Conceptual siblings separated at birth? *Journal of Psychosomatic Research*, 42, 117-135.

Lipowski, A. J. (1988). Somatization: The concept and its clinical applications. *American Journal of Psychiatry*, 145, 1358-1368.

Lorant, V., Deliege, D., Eaton, W., Robert, A., Philippot, P., Ansseau, M. (2003). Socioeconomic inequalities in depression: A meta-analysis. *American Journal of Epidemiology*, 157-98-112.

Low, K. G., Fleisher, C., Colman, R., Dionne, A, Casey, G., & Legendre, S. (1998). Psychosocial variables, age, and angiographically-determined coronary artery disease in women. *Annals of Behavioral Medicine*, 20, 221-226.

Low, K. G., Thoresen, C. E., Pattillo, J., King, A. C., & Jenkins, C. (1985). Anxiety, depression and heart disease in women. *International Journal of Behavioral Medicine*, 1, 305-319.

Lusiani, L, Perrone, A. Pesavento, R., & Conte, G. (1994). Prevalence, clinical features, and acute course of atypical myocardial infarction. *Angiology*, 45, 49-55.

Luten, A. G., & Powell, L. H. (2000) Psychosocial Factors. In Wong, N. D., Black, H. R., & Gardin, J. M., Preventive Cardiology. New York: McGraw-Hill.

Lynch, J. W., Kaplan, G. A., Cohen, R. D., Tuomilehto, J., & Salonen, J. T. (1996). Do cardiovascular risk factors explain the relation between socioeconomic status, risk of all-cause mortality, cardiovascular mortality, and acute myocardial infarction? *American Journal of Epidemiology*, 144, 934-942.

Manolio, T. A., Furberg, C. D., Shemanski, L., Psaty, B. M., O'Leary, D. H., Tracy, R. P., & Bush, T. L. (1993). Associations of postmenopausal estrogen use with cardiovascular disease and its risk factors in older women. *Circulation*, 88, 2163-2174.

Maruta, T., Hamburgen, M. E., Jennings, C. A., Offord, K. P., Colligan, R. C., Frye, R. L., & Malinchoc, M. (1993). Keeping hostility in perspective: Coronary heart disease and the hostility scale on the Minnesota Multiphasic Personality Inventory *Mayo Clinic Proceedings,* 68, 109-114.

Matthews, K. A., Owens, J. F., Kuller, L. H., Sutton-Tyrrell, K., & Jansen-McWilliams, L. (1998). Are hostility and anxiety associated with carotid atherosclerosis in healthy postmenopausal women? *Psychosomatic Medicine*, 60, 633-638.

Maynard, C. & Weaver, W. D. (1992). Treatment of women with acute MI: New findings from the MITI registry. *Journal of Myocardial Ischemia*, 4, 27-33.

Mayo, R. (1989). Atypical chest pain. *Journal of Psychosomatic Research*, 22, 393-406.

Meilahn, E. N., Becker, R. C., & Corrao, J. M. (1995). Primary prevention of coronary heart disease in women. *Cardiology*, 86, 286-298.

Miller, T. Q., Smith, T. W., Turner, C. W., Guijarro, M. L., & Hallet, A. J. (1996). A meta-analytic review of research on hostility and physical health. *Psychological Bulletin*, 119, 322-348.

Myrtek, M. (2001). Meta-analyses of prospective studies on coronary heart disease, type A personality, and hostility. *International Journal of Cardiology,* 79, 245-251.

Orth-Gomer, K., Horsten, M., Wamala, S. P., Mittleman, M. A., Kirkeeide, R., Svane, B., Ryden, L., Schenck-Gustafsson, K. (1998). Social relations and extent and severity of coronary artery disease. The Stockholm Female Coronary Risk Study. *European Heart Journal*, 19, 11, 1603-1605.

Orth-Gomer, K., Rosengren, A., & Wilhelmsen, L. (1993). Lack of social support and incidence of coronary heart disease in middle-aged Swedish men. *Psychosomatic Medicine*, 55, 37-43.

Orth-Gomer, K., Wamala, S. P., Horsten, M., Schenck-Gustafsson, K., Schneiderman, N., & Mittleman, M. A. (2001). Marital stress worsens prognosis in women with coronary heart disease: The Stockholm Female Coronary Risk Study. *Journal of the American Medical Association*, 285, 10, 1289-1290.

Penque, S., Halm, M., Smith, M., Deutsch, J., Van Roekel, M., McLaughlin, L, Dzubay, S., Doll, N., & Beahrs, M. (1998). Women and coronary disease: Relationship between descriptors and signs and symptoms and diagnostic and treatment course. *American Journal of Critical Care*, 7, 175-182.

Pickering, T. G. (1985). Should studies of patients undergoing coronary angiography be used to evaluate the role of behavioral risk factors for coronary artery disease? *Journal of Behavioral Medicine,* 8, 203-213.

Porter, L. S., Stone, A. A., & Schwartz, J. E. (1999). Anger expression and ambulatory blood pressure: A comparison of state and trait measures. *Psychosomatic Medicine*, 61, 454-463.

Powell, L. H., Shaker, L. A., Jones, B. A., Vaccarino, L. V., Thoresen, C. E., & Patillo, J. R. (1993). Psychosocial predictors of mortality in 83 women with premature acute myocardial infarction. *Psychosomatic Medicine*, 55, 426-433.

Rutledge, T., Reis, S.E., Olson, M., Owens, J., Kelsey, S.F., Pepine, C.J., Reichek, N., Roger, W.J., Bairey Merz, C.N., Sopko, G., Cornell, C.E., & Matthews, K.A. (2001). Psychosocial variables are associated with atherosclerosis risk factors among women with chest pain: The WISE study. *Psychosomatic Medicine*, 63, 282-288.

Shekelle, R. B., Gale, M., Ostfeld, A. M., & Paul, O. (1983). Hostility, risk of coronary heart disease, and mortality. *Psychosomatic Medicine*, 45,109-114.

Shumaker, S. A. & Hill, D. R. (1991). Gender differences in social support and physical health. *Health Psychology*, 10, 102-111.

Sharaf, B. L., Pepine, C. J., Kerensky, R. A., Reis, S. E., Reichek, N., Rogers, W. J., Sopko, G., Kelsey, S. F., Holubkov, R., Olson, M., Miele, N. J., Williams, D. O., & Bairey Merz, C. N. (2001). Detailed angiographic analysis of women with suspected ischemic chest pain. *The American Journal of Cardiology*, 87, 937-941.

Schrijvers, C. T., Bosma, H., & Mackenbach, J. P. (2002). Hostility and the educational gradient in health. The mediating role of health-related behaviours. *European Journal of Public Health*, 12, 110-116.

Siegman, A. W., Dembroski, T. M., & Ringel, N. (1987). Components of hostility and the severity of coronary artery disease. *Psychosomatic Medicine*, 49, 127-135.

Smith, T. W. & Frohm, K. D. (1985). What's so unhealthy about hostility? Construct validity and psychosocial correlates of the Cook and Medley Ho Scale. *Healthy Psychology*, 4, 503-520.

Spielberger, CD, Krasner, SS, & Soloman, EP. (1988). *The experience, expression, and control of anger*. In Chesney, MA, Rosenman, RH, (Eds.), Anger and hostility in cardiovascular and behavioral disorders. New York: Hemisphere/McGraw- Hill.

Steegmans, P. H., Hoes, A. W., Bak, A. A., van der Does, E., & Grobbee, D. E. (2000). Higher prevalence of depressive symptoms in middle-aged men with low serum cholesterol levels. *Psychosomatic Medicine*, 62, 205-211.

Suarez, E. C. (1986). The relationship among components of the type A behavior pattern, Cook-Medley hostility scores, and atherosclerosis. *Dissertation Abstracts International*, 47, 2635.

Suarez, E. C. (1999). Relations of trait depression and anxiety to low lipid and lipoprotein concentrations in healthy young adult women. *Psychosomatic Medicine*, 61, 273-279. Sullivan, A. K., Holdright, D. R., Wright, C. A., Sparrow, J. L., Cunningham, D., & Fox, K. M. (1994). Chest pain in women: Clinical, investigative, and prognostic features. *Behavioral Medicine Journal*, 308, 883-886.

Wenger, N. K. (2002). Clinical characteristics of coronary heart disease in women: Emphasis on gender differences. *CardiovascularResearch*, 53, 558-567.

Whiteman, M. C., Deary, I. J., Lee, A. J., & Fawkes, F. G. R. (1997). Submissiveness and protection from coronary heart disease in the general population: Edinburgh Artery Study. *Lancet*, 350, 541-545.

Williams, R. B. (1989). Biological mechanisms mediating the relationship between behavior and coronary heart disease. In Siegman, A. W., and Dembroski, T. M. (Eds.), *In Search of Coronary-Prone Behavior: Beyond Type A*. pp. 195-205. Hillsdale, N. J.: Erlbaum.

Williams, P. G. & Wiebe, D. (2000). Individual differences in self-assessed health: Gender, neuroticism and physical symptom reports. *Personality & Individual Differences*, 28, 823-835.

Williams, R. B., Jr., Haney, J. T. L., Lee, K. L., Kong, Y. H., Blumenthal, J. A., & Whalen, R. E. (1980). Type A behavior, hostility, and coronary atherosclerosis. *Psychosomatic Medicine*, 42, 539-549.

Willich, S. N., Lowell, H., Lewis, M. Arntz, R. Schubert, F. & Schroder, R. (1993). *Journal of Myocardial Ischemia*, 4, 27-33.

Writing Group for the Women's Health Initiative Investigators. (2002). Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial. *JAMA*, 288, 321-333.