

# Tension and Anxiety and the Prediction of the 10-Year Incidence of Coronary Heart Disease, Atrial Fibrillation, and Total Mortality: The Framingham Offspring Study

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**Objective:** Conflicting research findings regarding the ability of tension or anxiety to predict incident coronary heart disease (CHD) have created uncertainty in the literature. In addition, there are no prospective studies relating these characteristics to the development of atrial fibrillation (AF). **Methods:** From 1984 to 1987, 3682 participants (mean age  $48.5 \pm 10.1$  year; 52% women) of the Framingham Offspring Study were examined and followed for 10 years for the incidence of CHD, AF, and total mortality. Measures of tension, anxiety, and risk factors for CHD and AF were collected at the baseline examination. **Results:** After adjusting for age, systolic blood pressure, body mass index, current cigarette smoking, diabetes, and total cholesterol/high-density cholesterol in Cox proportional hazards models, increased tension was predictive of 10-year incidence of definite CHD (relative risk (RR) = 1.25 relative to a one SD difference; 95% confidence interval (CI), 1.05–1.49) and total mortality (RR = 1.23; 95% CI, 1.06–1.42) in men. After adjusting for AF risk factors, tension also predicted AF in men (RR = 1.24; 95% CI, 1.04–1.48). Anxiety in men (RR = 1.22; 95% CI, 1.08–1.38), and in women (RR = 1.27; 95% CI, 1.05–1.55) was significantly related to total mortality. **Conclusions:** Tension was observed to be an independent risk factor for incident CHD, AF, and mortality in men. Anxiety was a risk factor for total mortality in men and women. Our findings suggest that further research into the pathophysiology of the excess morbidity and mortality observed with tension and anxiety is merited. **Key words:** tension, anxiety, coronary heart disease, atrial fibrillation, mortality.

AF = atrial fibrillation; CHD = coronary heart disease; RR = relative risk; CI = confidence interval; BMI = body mass index.

## INTRODUCTION

Assessing the temporal relations between tension, anxiety, and coronary heart disease (CHD) is methodologically complex. Tension and anxiety are commonly the consequence of CHD but also have been noted to predispose subjects to CHD. Therefore it is important to design prospective longitudinal studies to examine the etiologic role of these psychological variables to the development of disease (1).

The literature on anxiety is uncertain. Winters and Schneiderman (2) have stated that "... unequivocal support for a causal role for anxiety in the pathogenesis of CHD has not been established." Some studies have found no associations between measures of anxiety and incident ischemic heart disease in men (3–5) and women (4,5) after adjustment for potential confounding variables. Other studies have found a positive association between phobic anxiety and sudden death (6) or fatal ischemic heart disease (7) in men. One study found a positive association between tension and anxiety and incident CHD in women, particularly women who self-identified as housewives (8). In addition, the Framingham Heart Study measure of tension has been found to be associated with the development of hypertension in middle-aged men (9).

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The role of tension and anxiety in the development of CHD and mortality is not clear, and the relations with incident atrial fibrillation (AF) are not known. The objective of the present study, therefore, is to test the hypotheses that tension and anxiety are related to the 10-year incidence of CHD, AF, and total mortality in men and women after adjusting for known risk factors. The study has critical advantages in that it includes both men and women, has the ability to adjust for confounding risk factors, and has the capacity to examine AF and CHD as outcomes.

## METHODS

The Framingham Offspring Study is a prospective longitudinal community-based study that began enrollment of the offspring (and their spouses) of the Original Framingham Heart Study cohort in 1971 (10). From 1984 through 1987 3873 Offspring participants returned for their third follow-up examination. A few weeks before the examination subjects were mailed psychosocial questionnaires, which were collected at the scheduled clinic visit; 95% were completed. Subjects were excluded from the present study for the following indications: incomplete questionnaire ( $n = 191$ ), prevalent CHD for the analyses of incident CHD ( $n = 107$ ), and prevalent AF ( $n = 25$ ) for the analyses of incident AF. In regard to attrition in the sample, >95% of participants attended subsequent examinations following the baseline exam.

Tension and anxiety were assessed using the scales that were developed in the Original Framingham study. A complete description of these 2 scales including reliability coefficients, inter-scale correlations, male-female differences, and the questions and response sets were reported previously (11). It has been pointed out by Markovitz, et al. (9) that although these 2 scales have been shown to be highly correlated, they measure distinct psychological traits. The tension scale includes such items as "Are you often troubled by feelings of tenseness, tightness, restlessness, or inability to relax?" and "Have you often felt difficulties were piling up too much for you to handle?" The symptoms of anxiety scale is more reflective of physiological symptoms and includes such items as "Do you often have palpitations, or a pounding or racing heart?" and "Are you often bothered by breathlessness, sighing respiration, or difficulty in getting a deep breath?" and "Do you often have poor concentration or vagueness in thinking?" (see Appendix). Both the tension scale and symptoms of anxiety scale were thought to measure somatic strains resulting from symptoms of psychosocial stress. Previous reliability testing showed reliability (internal consistency) coefficients of 0.78 for the tension scale and 0.64 for the symptoms of anxiety scale (11).

For these 2 psychosocial scales, responses were scaled between 0 and 1

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with the higher score indicating more of the trait. Scale scores were obtained by taking the mean of the nonmissing values of variables determined to measure that trait.

The 3 outcomes of interest included the 10-year incidence of CHD, AF, and total mortality. The definition of CHD (12) and AF (13) have been published previously; the manifestations of interest for CHD in these analyses included myocardial infarction (recognized and unrecognized), coronary insufficiency, and coronary death (both sudden and not sudden). Angina pectoris was not included as an outcome for CHD. The diagnosis of AF was made if AF or atrial flutter was present on an electrocardiogram obtained from the Framingham clinic visit, hospital charts, or physician office record. Atrial fibrillation was diagnosed if P wave activity was not evident and if the ventricular response was irregularly irregular. Atrial flutter was diagnosed if typical flutter (saw-tooth) waves were seen on the electrocardiogram. AF electrocardiograms were reviewed and verified by 1 of 2 Framingham Study cardiologists. The assessment of endpoints included the following: a) physician administered history every 4 years blinded to psychosocial data, b) routine ascertainment of outside physician and hospitalization records, and c) detailed adjudication of all cardiovascular events by a panel of 3 experienced investigators using well accepted written criteria. For causes of death, 25% of men and 12% of women died from CHD. Stroke accounted for 2.8 and 4.4% of deaths in men and women, respectively. Cancer accounted for 35.4% of deaths in men and 55.4% of deaths in women.

Potential confounders were ascertained at the index examination. These confounders were selected for their known relations to the outcomes of interest. Multivariable models predicting the 10-year incidence of CHD and total mortality adjusted for age, systolic blood pressure, body mass index ( $\text{kg}/\text{m}^2$ ), current cigarette smoking, diabetes (defined as fasting blood glucose of at least 126 mg/dl or on treatment), and total cholesterol/high-density cholesterol. Multivariable analyses for AF included characteristics known to be related to its development: age, diabetes, hypertension, history of myocardial infarction or history of congestive heart failure, and valvular heart disease (defined as any diastolic murmur or  $\geq 3$  of 6 systolic murmur).

All analyses were sex-specific. We examined the relation of the psychosocial measures to education and CHD risk factors classified at baseline with Pearson correlations and analysis of variance for continuous and discrete variables, respectively. The 10-year age-adjusted rates and RRs of CHD, AF, and total mortality were estimated using Cox proportional hazards regression. For each psychosocial predictor variable that reached a significance level of  $p \leq .10$  in the age-adjusted analyses, we examined effects after adjustment using multivariable-adjusted Cox proportional hazards models. RRs for incident disease are presented relative to a one SD difference in each measure.

Because previous research has shown that the Framingham Heart Study measure of anxiety may have a differential effect by housewife/working woman status (8), for secondary analyses we analyzed the psychosocial

models above in this subset. Housewives were defined as those who responded positively to the question: "Would you consider yourself a housewife most of your adult years?"

The use of the psychosocial survey in the Framingham Offspring Study was approved by the Office of Management and Budget in 1983. All examinations and data collection were approved by the Boston University Medical Center Institutional Review Board. All participants signed informed consent.

### RESULTS

The study consisted of 3682 participants (48.1% men), who had a mean age of 48.5 (SD = 10.1; range, 18–77 years) at baseline. Women scored significantly higher on the tension scale compared with men (0.31 versus 0.24,  $p = .0001$ , respectively) and for anxiety (0.19 versus 0.12,  $p = .0001$ , respectively). Table 1 presents a description of the study sample and a comparison between men and women for selected demographic characteristics and risk factors. Except for total cholesterol and current cigarette smoking, men had a significantly less healthy risk profile compared with women. Table 2 presents the Pearson correlation coefficients for the measures of tension and anxiety to the CHD risk factors for men and women, respectively. The 2 psychosocial scales were positively associated with current cigarette smoking in both sexes. Tension was negatively associated with education in both sexes. Anxiety was negatively associated with education and positively associated with body mass index (BMI) in both men and women and positively associated with diabetes in women.

The age-adjusted relations between tension and anxiety to the 10-year incidence of CHD, AF, and total mortality in men and women were examined, and all RR were expressed per one SD of the scale. Increased tension was significantly related to CHD (RR = 1.28; 95% confidence interval (CI), 1.08–1.51), AF (RR = 1.28; 95% CI, 1.08–1.52), and total mortality (RR = 1.25; 95% CI, 1.09–1.44) in men. Increased symptoms of anxiety were associated with an increased risk of incident AF in men (RR = 1.16; 95% CI, 1.01–1.33) and total mortality in men (RR = 1.23; 95% CI, 1.09–1.39) and women (RR = 1.24; 95% CI, 1.04–1.48).

TABLE 1. Description of Study Sample

Characteristic	Total Sample ( <i>n</i> = 3682)	Men ( <i>n</i> = 1769)	Women ( <i>n</i> = 1913)	<i>P</i> value
Mean (SD) age	48.5 (10.1)	48.8 (10.2)	48.2 (10)	0.0383
Mean (SD) years of education	13.7 (2.3)	13.9 (2.4)	13.5 (2.1)	<0.0001
Marital status				<0.0001
Married	82%	85.3%	79%	
Never married	6%	5.4%	6.6%	
Div/sep/widowed	12%	9.3%	14.4%	
Mean (SD) SBP	124.0 (17)	126.4 (15.7)	121.7 (17.9)	<0.0001
Mean (SD) total Cholesterol	212.1 (41.6)	212.4 (39.4)	211.9 (43.6)	0.7142
Mean (SD) total/HDL cholesterol	4.5 (1.7)	5.1 (1.7)	4.0 (1.5)	<0.0001
Mean (SD) body mass index	26.3 (4.7)	27.2 (3.8)	25.4 (5.3)	<0.0001
% Menopause	—	—	49.5%	—
Hypertension	20%	22.1%	18%	0.0022
Diabetes	3.8%	5%	2.6%	0.0002
Current smoker	28.8%	28.2%	29.4%	0.3945

HDL = high density lipoprotein; SBP = systolic blood pressure.

**TABLE 2.**  
Association Between Tension and Anxiety to Risk Factors for CHD, Atrial Fibrillation, and Total Mortality

	Pearson Correlation Coefficients					Mean Scores			
	Age	Education	SBP	BMI	Total-C/HDL-C	Cigarette Smoker		Diabetes	
						No	Yes	No	Yes
<b>Men</b>									
Tension	-0.127	-0.060	-0.041	0.032	0.017	0.23	0.28	0.24	0.25
<i>p</i> value	<b>0.0001<sup>a</sup></b>	<b>0.0132</b>	0.0882	0.1843	0.4952	<b>0.0005</b>		0.7801	
Anxiety	0.038	-0.157	0.017	0.096	0.045	0.12	0.14	0.12	0.17
<i>p</i> value	0.1138	<b>0.0001</b>	0.4789	<b>0.0001</b>	0.0656	<b>0.0147</b>		0.0738	
<b>Women</b>									
Tension	-0.009	-0.12	-0.011	0.013	0.031	0.28	0.37	0.31	0.3
<i>p</i> value	0.6881	<b>0.0001</b>	0.6374	0.5722	0.2009	<b>0.0001</b>		0.8949	
Anxiety	-0.016	-0.169	0.024	0.093	0.028	0.18	0.22	0.19	0.27
<i>p</i> value	0.4882	<b>0.0001</b>	0.2967	<b>0.0001</b>	0.2404	<b>0.0031</b>		<b>0.0213</b>	

C/HDL-C = total cholesterol/high density lipoprotein cholesterol; SBP = systolic blood pressure.

<sup>a</sup> *P* values < 0.05 are shown in bold.

The multivariable analyses for the 10-year incidence of CHD, AF, and total mortality in men and women per 1SD of the tension and anxiety scales are presented in Table 3. Men with increased tension were at significantly higher risk of developing CHD (RR = 1.25; 95% CI, 1.05–1.49) and AF (RR = 1.24; 95% CI, 1.04–1.48). For total mortality, men with increased tension had a RR of death of 1.23 (95% CI, 1.06–1.42). In multivariable analyses, anxiety in men (RR = 1.22; 95% CI, 1.08–1.38) and women (RR = 1.27; 95% CI, 1.05–1.55) was significantly related to total mortality. Among women the RR estimates between tension and all 3 outcomes and anxiety and CHD and AF were all close to zero.

In age-adjusted analyses tension and anxiety were not related to incident CHD, AF, or total mortality in self-identified housewives in the Framingham Offspring Study.

## DISCUSSION

To our knowledge this study is the first to systematically examine the predictive relations between tension and anxiety and incident AF in a large prospective community sample. Previously we documented that anger and hostility predicted

incident AF in men after adjusting for baseline and interim risk factors (14). In the current study tension was shown to be a significant independent risk factor for AF in men. It is important to place our AF findings in context. The peak prevalence of AF occurs between the ages of 70 and 84 years (15). The cases we observed in this particular study could be characterized as “early onset” or “premature” AF, largely occurring without preexisting heart disease. Thus, risk factors for the early development of AF in men seem to be associated with psychosocial risk factors such as tension, anger, and hostility. The Framingham Heart Study measure of tension was also significantly related to the development of CHD and total mortality in men.

Measures of anxiety in both sexes, and tension in men, were significantly related to death after adjusting for CHD risk factors in the present study. Our findings are consistent with other studies that have shown anxiety to be related to fatal heart disease or sudden and fatal ischemic heart disease but not related to nonfatal heart disease (3,7). We are unaware of other studies that have examined anxiety or tension as predictors of total mortality. It should be noted that even though we

**TABLE 3.** Multivariable Adjusted Relative Risks for the 10-Year Occurrence of Atrial Fibrillation and Total Mortality in Men and Women

	Coronary Heart Disease <sup>a</sup>		Atrial Fibrillation <sup>b</sup>		Total Mortality <sup>a</sup>	
	Men	Women	Men	Women	Men	Women
Event numbers/persons at risk	126/1680	47/1895	132/1750	62/1908	175/1769	92/1913
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Tension	<b>1.25 (1.05–1.49)</b>	0.99 (0.72–1.36)	<b>1.24 (1.04–1.48)</b>	0.83 (0.63–1.11)	<b>1.23 (1.06–1.42)</b>	1.14 (0.92–1.43)
Anxiety	1.12 (0.95–1.32)	0.99 (0.74–1.32)	1.10 (0.95–1.27)	1.03 (0.81–1.31)	<b>1.22 (1.08–1.38)</b>	<b>1.27 (1.05–1.55)</b>

RR are expressed relative to a (sex-specific) 1SD change in scale scores; statistically significant relations are in bold.

<sup>a</sup> Adjusted for age, systolic blood pressure, body mass index, current cigarette smoking, diabetes (defined as fasting blood glucose of at least 126 mg/dl or on treatment), total cholesterol/high-density cholesterol.

<sup>b</sup> Adjusted for age, diabetes, hypertension, history of myocardial infarction or history of congestive heart failure, and valvular heart disease (defined as any diastolic murmur or ≥3 out of 6 systolic murmur).

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adjusted known risk factors for the disease endpoints at baseline, we cannot exclude the possibility that anxiety or tension may be related to the development of interim or intermediate risk factors, such as hypertension, that are in turn related to CHD, AF, and total mortality.

Previous research in the Original Framingham cohort found that higher levels of tension were associated with later incidence of hypertension among middle-aged men (9). Markovitz et al. (9) have maintained that the Framingham scale called "tension" is actually a measure of the frequency of feelings of anxiety, including somatic symptoms potentially related to anxiety. This may or may not be the case; without validation studies Markovitz's observation cannot be refuted or supported. We contend that the Framingham Heart Study measure of anxiety reflects what has been described as anxiety in the literature: apprehensiveness, sweats, nervousness, palpitations, faintness, rapid breathing, tachycardia, and labile blood pressure (16). It has been noted that studies of cardiovascular disease and anxiety have used measures of anxiety that reflect sympathetic arousal and are characterized by somatic symptoms such as increases in heart rate (17). As can be seen in the Appendix, the Framingham Heart Study measure of anxiety symptoms reflects a sympathetic arousal construct. Whereas the tension and anxiety scales were correlated with each other (Pearson correlation coefficients of 0.52 for men and 0.53 for women), the current study found feelings of tension to be a consistent risk factor in men for all 3 outcomes after adjusting for known risk factors, including baseline hypertension or systolic blood pressure. Tension in women did not convey the same predictive value as anxiety with regard to total mortality. This may reflect the lack of physical arousal measured by tension as compared with anxiety. Because of its predictive value in men, it may be advisable to take the tension scale at face value until validation studies are undertaken.

The findings here differ from an earlier study done in the Original Framingham cohort; Original cohort members were the parents of the present study's participants (8). In the Original cohort study it was found that tension and anxiety were both significantly related to the incident definite CHD in women, particularly in housewives. We did not find tension or anxiety to be related to definite CHD in housewives or all women combined in Framingham Offspring. The discrepancy may be a function of the younger sample in the Offspring study (mean age was 48.2 years in women). The age range in the cohort analyses was 45 to 64 years of age at baseline (8). The differences in findings may also reflect the change in psychosocial risk factors for incident CHD among women over time. Women's lifestyles, responsibilities, and expectations have changed over the last 25 years, and it is not unreasonable to speculate that the psychosocial variables may have a different impact on their health (18)

The strengths of the Framingham Offspring Study include a prospective community-based design, inclusion of both men and women, a stable cohort, carefully assessed endpoints, and routinely ascertained information on standard risk factors. However, the study cohort was predominantly Caucasian and

middle-aged; the findings may not be generalizable to other ethnicities/races and the elderly.

Our community-based sample was middle-aged and had typically low event rates in women (47 CHD and 62 AF). However, because the nonsignificant RR estimates between tension and anxiety and the 3 outcomes in women were very close to 0, we suspect that the lack of significance was not likely because of an underpowered study. When the data were pooled for men and women and tests for sex by risk factor interactions were examined, no significant interactions were observed. This may be attributed to the relatively low event rate in women. The a priori power estimates, for example, for men and women for a hazard ratio of 1.5 for total mortality if the predictor variable is dichotomized was 67% for men and 37% for women. Despite the low event rates, our sample in the Framingham Offspring Study constitutes one of the larger datasets with prospective psychosocial data in women. The sex-specific models seem to be more informative and biologically appropriate than the pooled data, however, these results should be considered tentative and interpreted with caution. It should also be noted that correction was not made for multiple comparisons.

We recognize the difficulty in measuring psychosocial variables, such as tension and symptoms of anxiety, in a population. Scales used in epidemiological studies are not necessarily the same scales used to make diagnoses in individuals. Scales used in epidemiological research are usually shorter, easier to administer and score, and emphasize population means and deviations from these means rather than the diagnosis of an individual. The scales used here have demonstrated predictive validity in their association with CHD (8) and hypertension (9) and have known reliability (11) in population research.

In summary, we found that after adjusting for known risk factors, increased tension in men was significantly related to the development of CHD, AF, and total mortality; furthermore, anxiety in both sexes was significantly related to total mortality. Our findings are similar to a recent study in which we reported anger related to mortality and anger and hostility related to the development of AF in this community sample of men. Among women, increased anxiety was significantly related to total mortality. To put these findings in perspective, it might be helpful to view the hazard ratios (HR) for tension and anxiety in relation to the hazard ratios for some of the standard risk factors. For total mortality the HR in men for tension is 1.23 for a 1SD change. For systolic blood pressure the HR was also 1.23 for a 1SD change. For BMI the HR was 1.08, and for smoking (yes/no) the HR was 2.18. In women, the HR for anxiety in relation to total mortality was 1.27. The HR for systolic blood pressure was 1.09, and for smoking it was 1.54.

There are several implications from this study. First, our data would suggest that further investigation of the pathophysiology of the observed relations between tension, anxiety, and mortality are merited. In addition, the findings that these personality and psychosocial variables are very important to

the health of both men and women have implications for the medical setting. Clinicians should consider querying patients' psychological well-being with regard to these characteristics, and the possibility of referral for counseling could be explored with the patient.

### Appendix

Items in the Tension and Symptoms of Anxiety Scales (responses were Yes or No)

#### 1. Tension (response yes or no):

Often troubled by feelings of tenseness, tightness, restlessness, or inability to relax?

Often bothered by nervousness or shaking?

Often have trouble sleeping or falling asleep?

Feel under a great deal of tension?

Have trouble relaxing?

Often have periods of restlessness so that you cannot sit for long?

Often felt difficulties were piling up too much for you to handle?

#### 2. Symptoms of Anxiety (response yes or no):

Often become tired easily or feel continuously fatigued?

Often have giddiness or dizziness or a feeling of unsteadiness?

Often have palpitations, or a pounding or racing heart?

Often bothered by breathlessness, sighing respiration or difficulty in getting a deep breath?

Often have poor concentration or vagueness in thinking?

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