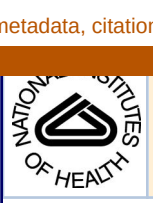

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Anger Proneness, Gender, and the Risk of Heart Failure

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Abstract

Background—Evidence concerning the association of anger-proneness with incidence of heart failure is lacking.

Methods—Anger proneness was ascertained among 13,171 black and white participants of the Atherosclerosis Risk in Communities (ARIC) Study cohort using the Spielberger Trait Anger Scale. Incident heart failure events, defined as occurrence of ICD-9-CM code 428.x, were ascertained from participants' medical records during follow-up 1990–2010. Relative hazard of heart failure across categories of trait anger was estimated from Cox proportional hazard models.

Results—Study participants (mean age 56.9 (SD 5.7) years) experienced 1,985 incident HF events during 18.5 (SD 4.9) years of follow-up. Incidence of HF was greater among those with high, as compared to those with low or moderate trait anger, with higher incidence observed for men as compared to women. The relative hazard of incident HF was modestly high among those with high trait anger, as compared to those with low or moderate trait anger (age-adjusted HR for men=1.44 (95% CI 1.23, 1.69). Adjustment for comorbidities and depressive symptoms attenuated the estimated age-adjusted relative hazard in men to 1.26 (95% CI 1.00, 1.60).

Conclusion—Assessment of anger proneness may be necessary in successful prevention and clinical management of heart failure, especially in men.

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BACKGROUND

Extensive evidence from existing studies underscores the role of emotional factors in the development of cardiovascular disease. The focus of the present study is trait anger, defined as sustained low threshold reactivity in which angry feelings, which can vary from mild irritation to extreme rage, are experienced in response to broadly defined triggers[1–3]. Trait anger as a construct shows considerable overlap with a hostile disposition[4] and may include anger-related affect, behavior, and cognition[5].

Multiple mechanisms have been proposed to explain the biological and behavioral aspects of the association of trait anger with cardiovascular disease. An anger-prone personality may lower a person's self-esteem and limit his or her ability to engage in constructive activities aimed at health improvement[6]. On the biological level, sustained anger can lead to chronically increased catecholamine levels [7], which in turn can trigger an inflammatory response, leading to the progression of atherosclerosis and eventually to clinically manifested heart disease [8].

Anger proneness confers significant risk for coronary heart disease (CHD)[9–14] and stroke[15] with effects that can be observed at the subclinical level[16–18]. Relatively little is known about the association of anger with the risk of heart failure[19] and with utilization of healthcare resources among those with heart failure[20]. Repeat hospitalizations are frequent among those with heart failure, and contribute significantly to costs of care[21]. With increasing prevalence of heart failure, more research is needed to identify modifiable factors, other than disease severity and presence of comorbidities, which may contribute to preventable hospital readmissions. In this study, we examined the association of anger-proneness with the incidence of heart failure and with subsequent healthcare utilization among 13,171 participants of the Atherosclerosis Risk in Communities (ARIC) Study cohort.

METHODS

Study population

The ARIC study cohort was established in 1987 as a probability sample of 15,792 men and women, aged 45 to 64 years, from the following four communities in the United States: suburbs of Minneapolis, Minnesota; Forsyth County, North Carolina; Washington County, Maryland; and Jackson, Mississippi. Extensive physical examinations were performed at baseline and at four subsequent clinic visits. Ongoing follow-up of the ARIC cohort is conducted through annual telephone interviews and surveillance of mortality and cardiovascular morbidity.

Participants of the ARIC cohort were selected for the present study if they completed the second physical examination (1990–1992) (n=14,348). Due to numbers that are too small to allow for adequate adjustment, excluded from analyses were study participants whose race was other than black or white (n=42) and black study participants from the Minnesota and Washington (n=49) ARIC study centers. Excluded from analyses were also study participants with prevalent HF at the second ARIC examination. Prevalent events were

ascertained from information obtained at the study baseline examination (1987–1989) and classified using Gothenburg HF classification criteria (n=753) and in follow-up of heart failure hospitalizations from the baseline examination to the second ARIC examination (n=86). Further excluded from analyses were study participants with missing outcome, exposure and key covariate information. The final study sample size was 13,171.

Event ascertainment

Incidence of hospitalized heart failure (HF) events was ascertained in follow-up from the date of the second ARIC examination (1990–1992) through December 31, 2010 on the basis of evidence of ICD-9-CM code 428.x in any position in the study participants' medical records. A HF hospitalization was defined as incident if no prevalent HF was recorded at the time of the baseline visit (ARIC Visit 2) and no HF-related hospitalizations (hospitalizations with ICD-9 code 428.x in any position) were observed in surveillance of all hospitalized events that the ARIC study conducts for all cohort participants. Prevalence of HF at the baseline visit was defined as (1) self-report of use of HF-related medications; (2) presence of HF classified according to Gothenburg criteria or missing information needed to define Gothenburg stage[22]; or (3) having had a hospitalization with ICD-9 428.x prior to the baseline (ARIC Visit 2) clinical examination. Death events were identified from linked National Death Index records and information provided by physicians and next of kin. All-cause hospital readmissions for study participants with incident HF events were identified from their hospital discharge records available through December 31, 2010.

Measurement of anger proneness

Information on anger proneness was obtained on the basis of the Speilberger Trait Anger Scale which was administered during an interview conducted as part of the second ARIC examination (1990–1992). This questionnaire, which consists of 10 items with responses graded on a Likert-type scale (range 10–40), shows high internal consistency (Cronbach's α=0.86)[23]. Factor analyses suggest that the scale consists of two components which assess anger temperament and anger reaction, with the final score representing the sum of responses for the these two subscales. In accordance with previous assessments of anger proneness with cardiovascular outcomes that has been conducted in the ARIC study[11, 12, 15, 17, 18], anger proneness was categorized as: (1) low anger (score: 10–14); (2) moderate anger (score: 15–21); and (3) high anger (score: 22–40).

Measurement of covariates

Physical examination of the cohort members and assessment of their risk factors, other than demographic, were conducted during the second ARIC examination. Gender and race were self-reported at the time of the first ARIC examination. Highest attained level of education was defined on the basis of a personal report at baseline of the highest grade completed in school and categorized as low (11th grade or less) or high (12th grade and above). At the first examination, ARIC study participants were asked to classify their total family income into one of the following eight categories: <$5000; $5000–$7999; $8000– $11 999; $12 000–$15 999; $16 000–24 999; $25 000–34 999; $35 000–$49 000; ≥$50 000. We collapsed these categories into three groups labeled as low (less than $15 999), medium ($16 000 to $34 999) and high (equal to or greater than $35 000). At the second ARIC examination

(considered baseline for the purposes of this study), members of the ARIC cohort had blood drawn from an antecubital vein into tubes containing EDTA (lipids), or a separating gel (glucose). Presence of a diagnosis of diabetes at the time of the clinical examination was based on any of the following: self-report of a physician's diagnosis of diabetes, self-report of use of hypoglycemic medication within two weeks of the ARIC examination, fasting (> 8 hours) blood glucose levels greater than 126 mg/dL, or non-fasting blood glucose levels greater than 200 mg/dL. Body mass index was calculated as the ratio of weight in kilograms to the square of height in meters. Sitting blood pressure was measured three times using a random zero sphygmomanometer. Blood pressure calculations were made as an average of the second and third measurement. Hypertension was defined as present based on self-reported use of antihypertensive medication within two weeks of baseline data collection or if systolic blood pressure measured at baseline was greater than or equal to 140 mm Hg, or diastolic blood pressure was greater than or equal to 90 mm Hg. Prevalence of coronary heart disease (CHD) at ARIC Visit 2 (baseline for the present study) was ascertained on the basis of a self-reported history of CHD and evidence of an adjudicated CHD hospitalization from ARIC Study baseline to Visit 2.

Plasma HDL-cholesterol levels were measured using the method of Warnick et al[24]. Total plasma cholesterol levels were determined enzymatically[25] using a Cobas-Bio analyzer with reagents purchased from Boehringer Mannheim Biochemicals. Plasma LDL–cholesterol levels were calculated using the method of Friedewald[26]. Self-reported vital exhaustion was assessed using a 21-item Maastricht Vital Exhaustion questionnaire developed by Appels et al.[27]. The continuous vital exhaustion scale (range: 0–42) was created on the basis of questions concerning participants' state of fatigue, lack of energy, feelings of hopelessness, loss of libido, and increased irritability. The Maastricht Vital Exhaustion questionnaire is highly correlated with validated depression scales (r=0.61–0.85)[28, 29], including the Beck Depression Inventory (r=0.62)[30]. To account for the non-normal distribution of the vital exhaustion scale in the ARIC Study population, we categorized responses to this questionnaire into quartiles based on the distribution and used the highest quartile, relative to quartiles 1–3, as the exposure category[31].

Statistical analyses

Cox proportional hazard regression of the association of trait anger and incidence of HF was performed with evaluation of the following covariates for inclusion into the model: age, race/center, body mass index, gender, cigarette years of smoking, cigarette smoking status, diabetes status, hypertension status, and depression. Inclusion of variables into the model was based on the 10% change-in-estimate criterion[32]. The Jackson, MS component of the ARIC cohort is exclusively African American. The only other ARIC field center with a sizeable proportion of African Americans is Forsyth County, NC (27%). A categorical race/center variable encompassing 5 categories of race and ARIC field center was created to account for these demographic distributions.

We used partial likelihood ratio tests based on nested models that included multiplicative interaction terms to examine whether the risk of HF in association with trait anger differed by race, gender, and other selected covariates. All continuous variables were evaluated for

linearity of association with the main outcome using regression analyses with log hazard ratios plotted as a function of the exposure categorized into quintiles of distribution. Cox proportional hazard assumptions were examined for all variables individually and for the final model using the Cox test, the ln-ln plots, and plots of scaled Schoenfeld residuals. All time-to-event analyses were performed with consideration of competing risk of death performed according to the method of Allison[33]. Age-adjusted multinomial regression models were used to evaluate the relative risk of heart failure in addition to the relative risk of coronary heart disease, stroke among ARIC cohort participants. All analyses were conducted using STATA 12.0 (College Station, TX) and SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Study participants in the three categories of trait anger (low, moderate, and high) did not differ significantly by hypertension status, diastolic blood pressure levels and by cholesterol measures (Table 1). Small, although statistically significant differences were observed across trait anger categories with respect to gender, race, education level, hypertension and diabetes. Proportion of men and of those with less than high school education was highest among those with high trait anger as compared to those with moderate and low trait anger. Proportion of blacks was lowest among those with moderate anger. Proportion of study participants with diabetes was likewise the lowest among those with moderate trait anger. Systolic blood pressure levels were lowest among those with moderate trait anger, whereas participants' mean BMI levels increased across trait anger categories.

For purposes of this study, the second ARIC examination was considered as the baseline. There were 1,985 incident heart failure events identified in this cohort during mean 18.5 (SD 4.9) years of follow-up from baseline through December 31, 2010. Cumulative hazard of HF was greater in those with high trait anger as compared to those with moderate or low trait anger (Figure 1). This observation was independent of whether analyses were performed with or without consideration of the competing risk of death (presented data reflect analyses performed with consideration of competing risk of death).

Age-adjusted incidence of HF increased in the highest category of trait anger from 9.8 (95% CI 9.2, 10.4) per 1,000 person-years among those with low trait anger and 9.5 (95% CI 8.9, 10.2) per 1,000 person-years among those with moderate trait anger, to 13.3 (95% CI 11.4, 15.2) per 1,000 person-years among those with high trait anger (Figure 2). HF incidence rates were very similar in the low and moderate trait anger categories across levels of covariates of interest. Incidence of HF increased for those with high trait anger as compared to those with low or moderate trait anger in all gender and race categories, with the exception of black women. The highest rate of HF was observed among black men with high trait anger.

The relative hazard of incident HF was modestly high among those with high trait anger, as compared to those with low or moderate trait anger (age-adjusted HR=1.44 (95% CI 1.23, 1.69) (Table 2). We observed effect measure modification of this association by gender and accordingly stratified all analyses by gender. In analyses adjusted for race, education and income, the greatest hazard ratio of incident HF was observed among men (HR=1.52 (95%

CI 1.23, 1.88)). Additional adjustment for baseline diagnosis of diabetes, hypertension, and prevalent CHD attenuated the observed hazard ratio in men to 1.37 (95% CI 1.11, 1.70). Adjustment for vital exhaustion further attenuated the overall hazard ratio to 1.16 (95% CI 0.98, 1.39) and in men to 1.26 (95% CI 1.00, 1.60).

We constructed age-adjusted multinomial models to simultaneously evaluate the relative risk of HF, coronary heart disease and stroke in relation to levels of anger proneness (data not shown). Results of this analysis suggest that while high, as compared to low, anger proneness was associated with greatest risk of stroke (73% excess risk), high anger proneness conferred a comparable increase in the risk of coronary heart disease (60% excess risk) and heart failure (43 % excess risk). The differences in the relative risk estimates for these three different clinical manifestations of cardiovascular disease were not significant.

During follow-up from the time of incident HF hospitalization (mean follow-up time: 4.3 years (SD 4.0)) 1,596 ARIC cohort participants (80.4%) experienced a re-hospitalization event (all-cause). The proportion of participants with at least one hospital readmission increased from 79.9% among those with low trait anger to 82.0% among those with high trait anger (Table 3). The average number of hospital readmissions during the follow-up period was 4 (interquartile range (IQR): 2, 7). Number of readmissions did not vary across categories of trait anger. Proportion of those with a first readmission occurring within 30 days of index HF hospitalization was 31.2% overall. This proportion increased across trait anger categories from 30.1% among those with low trait anger to 33% among those with high trait anger. The median time to first readmission was 133.5 days (IQR: 30,530), with 138 (IQR: 33, 535) observed for those with low trait anger and 124 (IQR: 28, 510) observed for those with high trait anger. No differences were observed across categories of trait anger in age-adjusted length of stay (results not shown). In multivariable analyses, with adjustment for age, race, gender, diabetes, and education (Table 4), the relative risk of all-cause readmission was marginally increased among those with high anger as compared to those with low and moderate anger (HR= 1.19 (95% CI 1.00, 1.22)). Similar estimates for the associations of trait anger with the risk of readmission were obtained from analyses limited to HF-related re-hospitalizations (ICD-9 code 428.x in any position, as well as ICD-9 code 428.x in the first position on the medical record; data not shown). All analyses were adjusted for competing risk of death.

DISCUSSION

Despite efforts to reduce the prevalence of cardiovascular disease risk factors, incidence of heart failure remains high[34] and healthcare utilization among those with heart failure constitutes the single largest healthcare expenditure among those 65 years of age and older[35]. In an attempt to look beyond the obvious in identifying factors that may reduce heart failure incidence and improve outcomes for those with heart failure, we examined the effect of anger proneness on heart failure incidence and on hospital readmissions following incident HF diagnosis.

Anger management styles can be broadly categorized as (1) trait anger characterized by a sustained inclination towards an angry response; (2) anger-out manifested by a direct

expression of anger at others; and (3) anger-in, a suppression of angry emotions[3]. The focus of this study was trait anger. We observed a modest positive association of high trait anger with the incidence of heart failure. The observed risk was independent of the level of attained education, income and comorbidity status. We observed gender and race differences in the association of trait anger with the incidence of heart failure hospitalization, with a persistent association noted among black men. No increased risk of the incidence of heart failure was observed among women with high, as compared to low, trait anger. This observation is consistent with the results of the few existing studies which have examined gender-specific effects of anger on the risk of cardiovascular disease[10, 17, 36, 37]. Results of those studies suggest a stronger harmful effect of anger on coronary heart disease events among men, as compared to women, perhaps reflecting the predominance of outward expression of anger among men (anger-out) and the extent to which this anger coping style may be associated with greater risk of cardiovascular disease. To our knowledge the present study is the first to examine gender differences in the association of anger with the risk of heart failure.

Previous studies have demonstrated an association of depressive states with heart failure hospitalization[38]. We found that although presence of depressive symptoms, approximated on the basis of responses to the Maastricht Vital Exhaustion questionnaire, attenuated the association of trait anger with heart failure incidence, it explained only a portion of the variance. Contrary to the expectation that depression, a dominant factor in patients' coping with cardiovascular disease[37], would be significant in the association of anger with healthcare utilization among those with heart failure, we found no effect of the presence of depressive symptoms on the association of trait anger with the risk of all-cause hospital readmission. However, it is possible that the observed overall effect of anger on the risk of hospital readmission was too small for a meaningful assessment of potential covariates. Further, fatigue, feelings of demoralization, and irritability which were measured by the vital exhaustion questionnaire may not have provided a full ascertainment of study participants' depressive status.

Our findings of the association of trait anger with heart failure are consistent with previous research indicating a positive association of anger with clinical CVD risk factors[39, 40] and with clinical CVD outcomes other than heart failure[10]. Mechanisms involved in this association are complex and the present study was not designed to elucidate those. Nevertheless, our results are consistent with research such as that of Ironson et al.[41] which points to an association of psychological stressors, including that of anger, with low left ventricular ejection fraction. This research makes plausible the theory that autonomic dysfunction observed as part of the anger response[42] affects downstream arterial remodeling and subsequent myocardial ischemia which can in turn lead to cardiac insufficiency and heart failure.

Our results suggest that the risk of heart failure among those with high, as compared to low, anger proneness is similar to their risk of stroke or coronary heart disease and emphasizes the need for the evaluation of psychosocial risk factors in overall primary and secondary prevention of cardiovascular disease.

The present study suggests that the effect of trait anger extends beyond the initial hospitalization for heart failure. We observed a 19% greater risk of all-cause hospital readmission following incident HF hospitalization among those with high trait anger as compared to those with low trait anger. This increased risk was independent of the metabolic and sociodemographic cardiovascular disease risk factors. To our knowledge, only one other study examined the association of anger with the use of healthcare services among heart failure patients[20]. In that small prospective clinical study of heart failure patients, the authors concluded that high trait anger was predictive of increased length of stay during hospital readmissions. Results of our study, however, do not support that observation – we did not observe differences across categories of trait anger in length of stay during the first hospital readmission. Healthcare organizations are under increasing pressure to decrease the number of hospital readmissions and associated length of stay in an effort to reduce costs and improve clinical outcomes. Readmission rates following a HF hospitalization discharge approach 24% and have remained stable[21, 43], despite multiple hospital and practice-based efforts to improve quality of care for patients with HF. A multifaceted approach to the identification of factors associated with hospital readmission among those with HF is therefore necessary for implementation of targeted prevention. We chose to examine all-cause re-hospitalization among those with HF as recurrent HF and cardiovascular disease hospitalizations account for only approximately half of all hospital readmissions among those with HF, with comorbid conditions accounting for the remaining large proportion of re-hospitalizations[44, 45].

Several strengths and limitations of this study should be noted. This is the largest biracial study to date to examine the association of anger with the incidence of HF. Research concerning the effect of anger on HF incidence and outcomes is rare. The majority of existing studies were conducted using small patient populations. The prospective nature of the ARIC study has allowed for an extended follow-up period from the measurement of anger proneness. We ascertained anger proneness using a questionnaire known to have a high internal consistency (0.86) and high test-retest reliability (0.77)[46] and which has been validated in multiple other populations. Evaluation of risk factors at study baseline, performed using established protocols, was thorough and allowed for detailed assessment of comorbidity status of study participants. An important limitation of this study was that ascertainment of HF events was limited to HF-related hospitalizations. Although a significant proportion of HF events is diagnosed and treated in the outpatient setting, comprehensive assessment of HF events occurring in the outpatient setting is beyond the scope of current ARIC study protocols. We were not able to ascertain medication use at the time of the HF hospitalization, therefore we could not provide potentially explanatory information on the role of hypertension in the association of trait anger with the risk of HF, beyond that available from baseline data. The potential social response desirability bias of the self-report of anger proneness could have resulted in an underestimation of trait anger.

In conclusion, we observed a modest association of trait anger with heart failure incidence, and with the risk of subsequent re-hospitalization. Results of this study suggest that inclusion of anger management may be necessary in successful prevention and clinical management of heart failure. This intervention may be more significant for men as compared to women.

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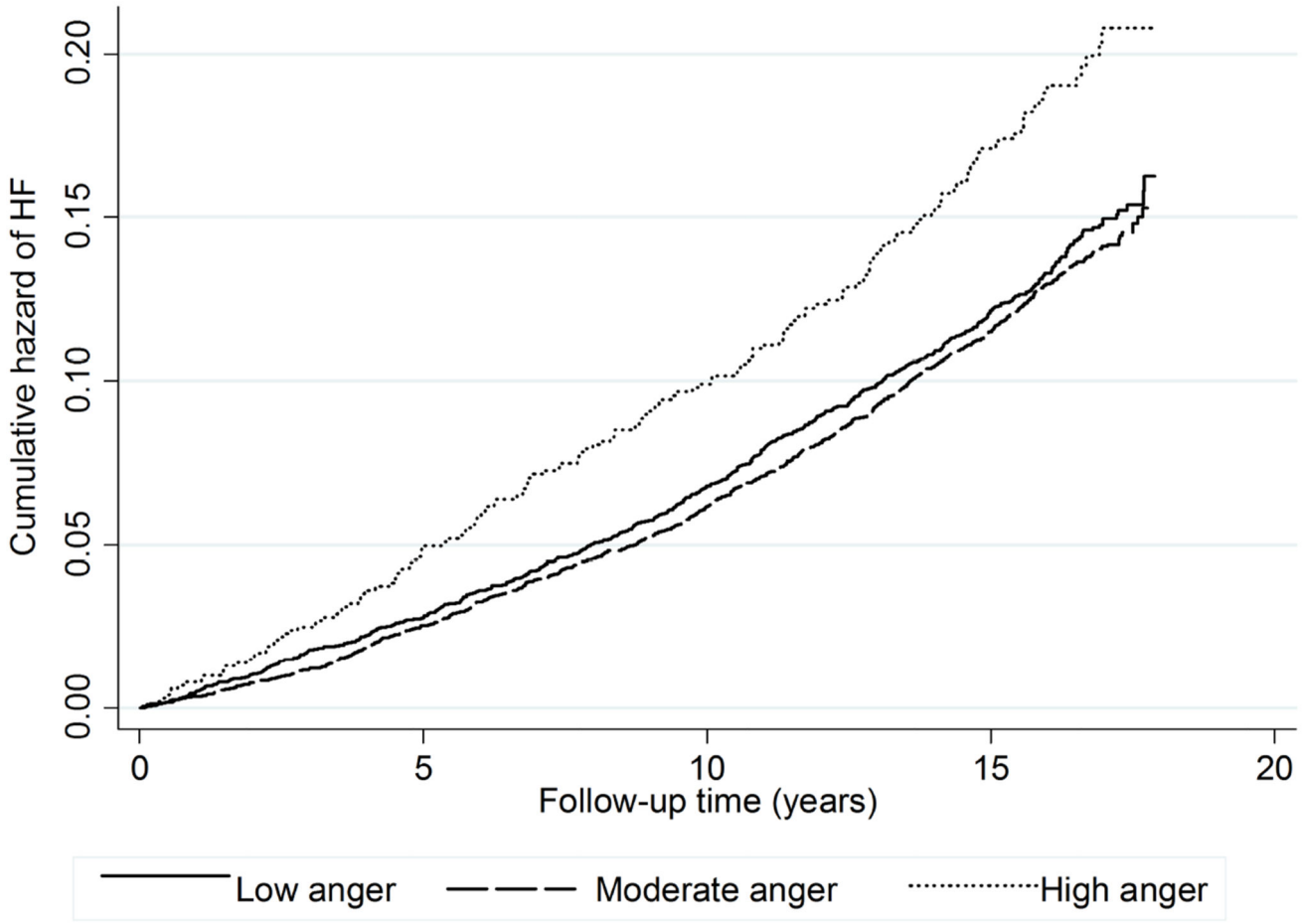

Figure 1.
Cumulative hazard of heart failure (HF) according to categories of trait anger. The ARIC cohort Study 1990–2010.

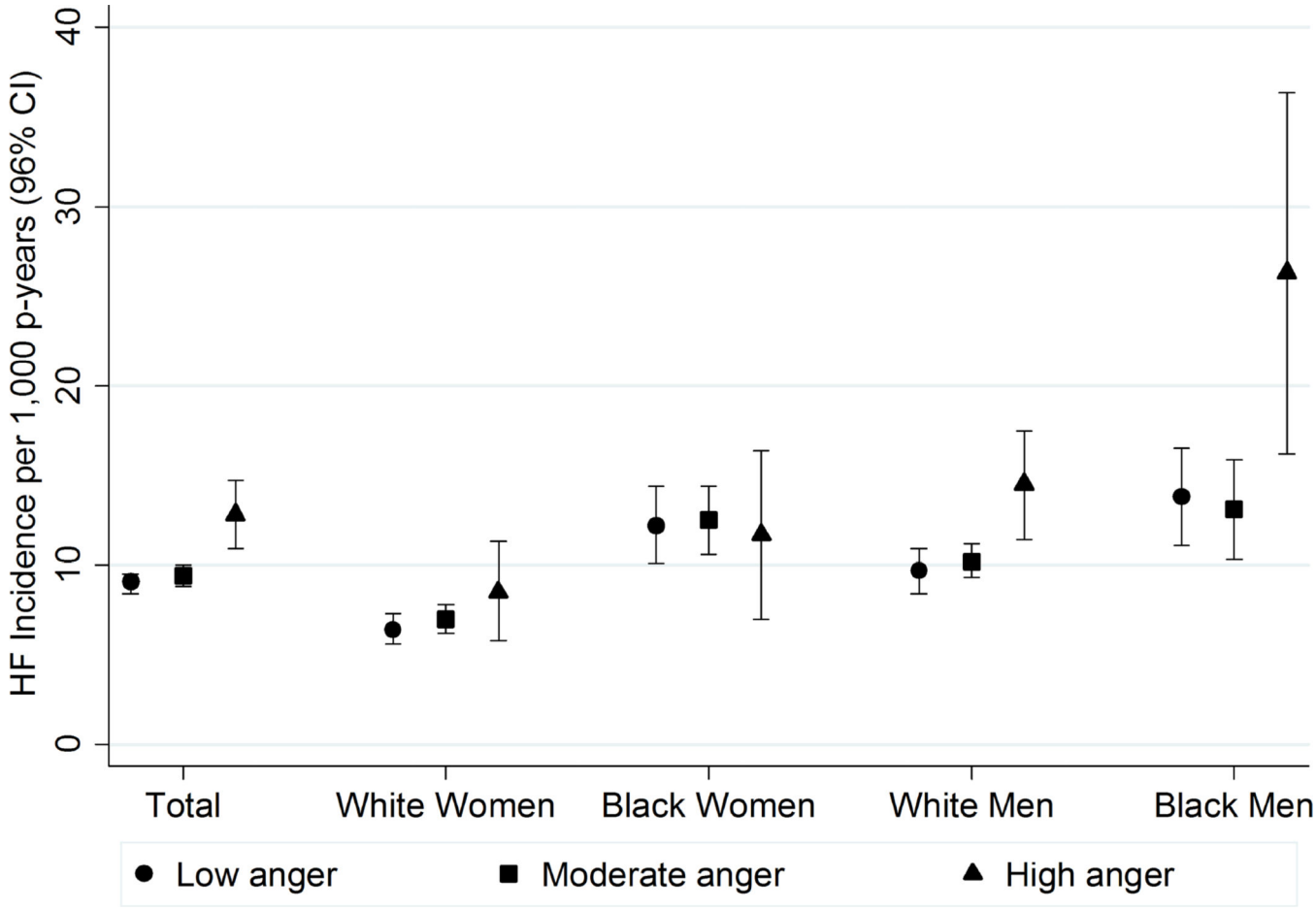

Figure 2.
Age adjusted incidence of heart failure (HF) across categories of trait anger. The ARIC cohort study 1990–2010.

Table 1

Baseline characteristics of study participants across categories of trait anger. The ARIC Study cohort.

Characteristic	Low anger n=4,880	Moderate anger n=7,263	High anger n=1,028	p
Age, years, mean (SD)	57.4 (5.8)	56.7 (5.7)	56.5 (5.8)	<0.01
Gender, % men	43.8	45.1	51.0	<0.01
Race, % Black	27.2	21.5	24.8	<0.01
Education, <HS, %	22.1	18.9	29.9	<0.01
Income				
Low, %	20.6	16.2	22.4	
Medium, %	31.2	31.4	33.9	
High, %	48.3	52.0	43.7	<0.01
Hypertension, %	34.9	33.1	35.5	0.07
Diabetes, %	14.3	13.6	17.5	<0.01
Vital exhaustion, %	42.6	54.2	76.8	<0.01
Prevalent CHD, %	4.3	4.8	8.8	<0.01
Systolic BP, mmHg (SD)	122 (19)	120.7 (18)	121.8 (18.8)	0.03
Diastolic BP, mm Hg (SD)	72.3 (10.3)	72 (10.1)	72.2 (10.5)	0.27
Total cholesterol, mg/dL (SD)	5.42 (1.03)	5.43 (1.00)	5.40 (1.05)	0.81
LDL cholesterol, mg/dL (SD)	3.45 (0.96)	3.45 (0.94)	3.44 (0.95)	0.86
HDL-cholesterol, mg/dL (SD)	1.30 (0.43)	1.28 (0.43)	1.25 (0.44)	0.03
Triglycerides, mg/dL (SD)	1.49 (1.00)	1.53 (0.98)	1.58 (1.05)	0.01
BMI, kg/m^2 (SD)	27.7 (5.3)	27.8 (5.3)	28.3 (5.3)	<0.01

Table 2

Association of trait anger with incident heart failure*. The ARIC Study cohort, 1990–2010.

	Low anger n=4,880	Moderate anger n=7,263	High anger n=1,028
Model 1			
Total (n=13,171)	1	0.97 (0.88, 1.06)	1.32 (1.13, 1.54)
Women (n=7,234)	1	0.98 (0.86, 1.12)	1.07 (0.83, 1.39)
Men (n=5,937)	1	0.94 (0.82,1.08)	1.46 (1.19, 1.79)
Model 2			
Total	1	1.03 (0.94, 1.13)	1.44 (1.23, 1.69)
Women	1	1.06 (0.93, 1.22)	1.21 (0.94, 1.56)
Men	1	0.98 (0.86, 1.13)	1.55 (1.26, 1.90)
Model 3			
Total	1	1.06 (0.96, 1.17)	1.37 (1.16, 1.61)
Women	1	1.06 (0.93, 1.232)	1.06 (0.82, 1.33)
Men	1	1.05 (0.91, 1.21)	1.52 (1.23, 1.88)
Model 4			
Total	1	1.04 (0.94, 1.14)	1.23 (1.04, 1.45)
Women	1	1.07 (0.93, 1.23)	1.00 (0.76, 1.30)
Men	1	1.00 (0.87, 1.15)	1.37 (1.11, 1.70)
Model 5			
Total	1	0.97 (0.86, 1.08)	1.16 (0.98, 1.39)
Women	1	0.96 (0.83, 1.12)	1.02 (0.78, 1.33)
Men	1	0.96 (0.82, 1.14)	1.26 (1.00, 1.60)

* Estimates adjusted for competing risk of death.

Model 1: unadjusted
Model 2: adjustment for age
Model 3: adjustment for age, race, education, income
Model 4: adjustment for age, race, education, income, diabetes, hypertension, prevalent CHD
Model 5: adjustment for age, race, education, income, diabetes, hypertension, prevalent CHD, vital exhaustion

Table 3

All- cause re-hospitalization following incident HF according to categories of trait anger. The ARIC Study cohort 1999–2010.

	Number of readmissions (IQR)	Median (IQR) time to first readmission (days)	Proportion with at least one readmission	Proportion with first readmission within 30 days
Overall (n=1,985)	4 (2,7)	133.5 (30, 530)	80.4	31.2
Low anger (n=735)	4 (2,7)	138 (33, 535)	79.9	30.1
Moderate anger (n=1,056)	3 (2,7)	128.5 (29, 530)	80.5	31.7
High anger (n=194)	4 (2,7)	124 (28, 510)	82.0	33.0

Table 4

Multivariable estimates of the association of trait anger with the risk of all-cause re-hospitalization following incident HF. The ARIC Study cohort 1990–2010

	Low anger n=735	Moderate anger n=1,056	High anger n=194
Model 1	1	1.12 (1.00, 1.24)	1.17 (0.99, 1.40)
Model 2	1	1.12 (1.01, 1.25)	1.19 (1.00, 1.42)
Model 3	1	1.13 (1.01, 1.25)	1.20 (1.01, 1.43)
Model 4	1	1.14 (1.02, 1.27)	1.19 (1.01, 1.42)

* Estimates adjusted for competing risk of death.

Model 1: unadjusted
Model 2: adjusted for age
Model 3: adjusted for age race gender
Model 4: adjusted for age race gender diabetes, hypertension, education