Original Article

Psychosocial Factors and Risk of Incident Heart Failure The Multi-Ethnic Study of Atherosclerosis

Rachel P. Ogilvie, MPH; Susan A. Everson-Rose, PhD, MPH; W.T. Longstreth, Jr, MD, MPH; Carlos J. Rodriguez, MD, MPH; Ana V. Diez-Roux, MD, PhD, MPH; Pamela L. Lutsey, PhD, MPH

Background—Heart failure (HF) is a major source of morbidity and mortality in the United States. Psychosocial factors have frequently been studied as risk factors for coronary heart disease but not for HF.

Methods and Results—We examined the relationship between psychological status and incident HF among 6782 individuals from the Multi-Ethnic Study of Atherosclerosis (MESA). Anger, anxiety, chronic stress, depressive symptoms, and hostility were measured using validated scales, and physician reviewers adjudicated incident HF events. Cox proportional hazards models were used to adjust for relevant demographic, behavioral, and physiological covariates. Interactions by age, race, sex, and self-reported health were examined in exploratory analyses. During a mean follow-up of 9.3 years, 242 participants developed incident HF. There was no association between psychosocial factors and HF hazard ratios (95% confidence interval) for the highest versus lowest quartile: anger=1.14 (0.81–1.60), anxiety=0.74 (0.51–1.07), chronic stress=1.25 (0.90–1.72), depressive symptoms=1.19 (0.76–1.85), and hostility=0.95 (0.62–1.42). In exploratory analysis, among the participants reporting fair/poor health at baseline, those reporting high versus low levels of anxiety, chronic stress, and depressive symptoms had 2-fold higher risk of incident HF, but there was no association for those with good/very good/excellent self-reported health.

Conclusions—Overall, these psychosocial factors were not significantly associated with incident HF. However, for participants reporting poor health at baseline, there was evidence that anxiety, chronic stress, and depressive symptoms were associated with increased risk of HF. Future research with greater statistical power is necessary to replicate these findings and seek explanations. (Circ Heart Fail. 2016;9:e002243. DOI: 10.1161/CIRCHEARTFAILURE.115.002243.)

Key Words: anger ■ anxiety ■ depression ■ epidemiology ■ heart failure

Heart failure (HF) affects 5.1 million Americans aged ≥20 years, and given the aging US population, its prevalence is projected to increase 25% by the year 2030. Because HF is a major source of morbidity and mortality, new potentially modifiable risk factors need to be identified.

See Clinical Perspective

Psychosocial risk factors have been frequently studied in relation to coronary heart disease. In observational studies, high levels of depression and anxiety have consistently been associated with incident coronary heart disease, whereas associations with hostility and social support have been mixed.² However, psychosocial factors have been examined less often in HF. Among patients with HF, depression is the most commonly researched psychosocial risk factor. Approximately 1 in 5 patients with HF meets the criteria for major depression, with a higher prevalence in patients with more severe HF.³ Depression is also a predictor of repeated hospitalization

in patients with HF and is an independent risk factor of cardiovascular and all-cause mortality in prevalent HF cases, although many early studies were cross-sectional or had short follow-up periods.⁴⁻⁶ Fewer studies have examined whether depression is associated with incidence of HF.^{3,7-12} Among those that have, the results have been mixed, although associations were stronger in populations at high-risk for HF.^{8,9}

Few other psychosocial factors have been examined in relation to risk of incident HF. Anxiety has also been examined in association with incident HF, with mixed results, and anger has been modestly associated with incident HF in 1 study. 10,11,113 Lack of social support has also been associated with greater incident HF risk, 3,14 although as noted in a recent meta-analysis, several studies had short follow-up periods and the majority were composed mostly of men. 4 Whether psychosocial factors, such as chronic stress and hostility, are associated with HF incidence is presently unknown.

Received April 10, 2015; accepted October 20, 2015.

From the Division of Epidemiology and Community Health, School of Public Health (R.P.O., P.L.L.) and Department of Medicine and Program in Health Disparities Research, University of Minnesota Medical School (S.A.E.-R.), Minneapolis; Departments of Neurology and Epidemiology, University of Washington, Seattle (W.T.L.); Section of Cardiology, Department of Medicine and Division of Public Health Sciences, Department of Epidemiology and Prevention, Wake Forest School of Medicine, Winston-Salem, NC (C.J.R.); and Department of Epidemiology and Biostatistics, Drexel University School of Public Health, Philadelphia, PA (A.V.D.-R.).

Correspondence to Rachel Ogilvie, MPH, Division of Epidemiology and Community Health, West Bank Office Bldg, 1300 S Second St, STE 300, Minneapolis, MN 55454. E-mail ogilv019@umn.edu

^{© 2015} American Heart Association, Inc.

Several plausible pathways could explain the relationship between psychosocial factors and HF. One pathway suggests that people with adverse levels of psychosocial factors may be more likely to experience a variety of poor physiological effects that may lead to HF. Potential biological pathways include inflammation, endothelial dysfunction, platelet activity, hormones, and brain-derived neurotrophic factor. 15 For example, depression causes heightened activation of the sympathetic nervous system,16,17 which is involved in the pathogenesis of HF,18 specifically left ventricular dysfunction and renal sodium retention. In addition, stress has been associated with impaired left ventricular function. 19 Also, depression and anxiety are associated with elevated inflammatory marker levels, which have been associated with HF.15 Another plausible pathway is that people with psychosocial problems are less likely to adhere to medical and behavioral guidelines, which makes them more likely to develop diseases, such as HF.²⁰

Because results from previous research have been mixed and mostly focused on depression, additional data are needed to elucidate the association between psychosocial factors and incident HF, especially in diverse samples of individuals who were healthy at baseline. Therefore, the aim of this study is to determine whether psychosocial factors, namely anger, anxiety, chronic stress, depressive symptoms, and hostility, are associated with incident HF. On the basis of previous research, we hypothesized that higher levels of these psychosocial factors would be associated with greater risk of incident HF.

Methods

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective cohort study designed to evaluate risk factors for clinical and subclinical cardiovascular diseases in several racial/ethnic groups.²¹ The study began in July 2000 and recruited 6814 adults free of clinical cardiovascular disease and aged 45 to 84 years from 6 field centers across the United States: Baltimore, MD; Chicago, IL; Los Angeles, CA; New York, NY; Saint Paul, MN; and Winston-Salem, NC. There have been 5 total examinations with similar protocols. MESA participants with data on psychosocial factors at baseline were included in the present analysis (n=6782). Local institutional review boards approved study protocols, and all participants gave written informed consent.

Exposures

Anger, anxiety,²² chronic stress,²³ and depressive symptoms²⁴ were measured via questionnaires administered at MESA examination 1, which occurred in 2000 to 2002. Hostility25 was measured at examination 2, which occurred in 2002 to 2004. Descriptions of these measures can be found in Table 1. For all of the psychosocial measures, individual questions were summed to create scores, and higher scores represent more severe symptoms. Some of these measures have been found valid and reliable in older populations.²⁶ For the primary analysis, the psychosocial measures were categorized according to their distribution, as shown in Table 1. For depression, we used the clinically relevant cut point of 16 as an additional separate category. Exposures were also modeled continuously per interquartile range. In addition, in exploratory analyses where we stratified according to self-reported health, dichotomous categorizations were used.

Outcome

New cases of HF were adjudicated by physician reviewers according to standard MESA procedures, as has been described elsewhere. 21,27 Three criteria were used to determine HF events: (1) physician-diagnosed HF and patient medical treatment, (2) pulmonary edema or congestion as indicated by chest x-ray, and (3) dilated ventricle, poor left ventricular function, or evidence of left ventricular diastolic dysfunction, as indicated by echocardiography, radionuclide ventriculogram/multigated acquisition, or other contrast ventriculography.

Covariates

For most analyses, all covariates came from examination 1. The exception was analyses where hostility, which was measured at examination 2, was the exposure of interest. When available, covariates for analyses of hostility came from examination 2. Sociodemographic characteristics include self-reported age, race/ethnicity (white, black, Hispanic, and Chinese American), sex, and field center. Behavioral factors included smoking status (current smoker, former smoker, and never smoker) and moderate-vigorous physical activity in Metminutes per week. HF risk factors included body mass index, systolic and diastolic blood pressures, high-density lipoprotein, low-density lipoprotein, triglycerides, diabetes mellitus status, C-reactive protein, fibrinogen, and albumin.

Analysis

Descriptive statistics were calculated for exposure variables at baseline. Cox proportional hazards models were used to model time to incident HF events. Person-time was calculated by using the time from the baseline examination until an HF event, death, loss to follow-up, or December 31, 2011. Examination 1 was baseline for chronic stress, depressive symptoms, anger, and anxiety, and examination 2 was for hostility. Exposures were categorized as indicated in Table 1 and also modeled continuously per interquartile range. The proportional hazards assumption was checked using interactions with time and graphs of the residuals, and no violations were detected.

We explored a series of models. The first model controlled for age, race/ethnicity, sex, and field center. Model 2 added smoking and physical activity. Model 3 additionally controlled for C-reactive protein, fibrinogen, and albumin, and model 4 further controlled for body mass index, diabetes mellitus, systolic and diastolic blood pressures, high-density lipoprotein, low-density lipoprotein, and triglycerides. C-reactive protein and triglycerides were log-transformed to account for skewness.

Multiplicative interactions by sex and self-reported health (categorized dichotomously as good [excellent/very good/good] or poor

Table 1. Psychosocial Exposures: The Multi-Ethnic Study of Atherosclerosis*

Construct	Measure	Range	Calculated	Modeled
Anger	Spielberger Trait Scale ²²	10-40	Summation, all responses on 4-point scale	Quartiles
Anxiety	Spielberger Trait Scale ²²	10-40	Summation, all responses on 4-point scale	Quartiles
Chronic stress	Chronic Burden Scale ²³	0-5	Summation of domains with an ongoing difficulty	Tertiles
Depressive symptoms	Center for Epidemiological Studies Depression Scale ²⁴	0–60	Summation, responses on 0–3 scale	5 categories: quartiles with the highest category split at >16†
Hostility	8 items from Cook–Medley Hostility Scale ²⁵	8–0	Summation	Quartiles

^{*}Measured at examination 1 (2000–2002) except for hostility, which was measured at examination 2 (2002–2004).

[†]A score of ≥16 on the Center for Epidemiological Studies Depression Scale is typically indicative of clinically significant symptomatology.

[fair/poor]) were tested by including cross-product terms in the models. Stratified analyses were performed for all significant or suggestive interactions. For stratified analyses, psychosocial exposures were dichotomized because power was low because of lower numbers of events occurring within strata. Anger, anxiety, and hostility were all dichotomized at their respective medians. For chronic stress, we combined the lower 2 tertiles, given the distribution of the data. Depressive symptoms were divided at the clinically relevant cut point of 16. Exposures were also modeled continuously per interquartile range. Models 1 and 2 were run again for each exposure in the stratified analysis.

Results

There were 242 new cases of HF through a total of 63 584 years of follow-up. On average, participants were followed up 9.3 years (SD=2.5), with a maximum follow-up time of 11.5 years. The incidence rate was 3.8 HF cases per 1000 person-years (95% confidence interval [CI], 3.4–4.3). Of those who did not develop HF, 638 were censored because of death by other causes, 367 were lost to follow-up, and 5535 were censored at the end of follow-up. The overall mean age at examination 1 was 62.2 years (SD=10.2), 52.9% of the sample were women, and 10.0% reported fair/poor health. At examination 1, the mean scores were 14.8 (SD=3.7) for anger, 15.9 (SD=4.5) for anxiety, 1.2 (SD=1.2) for chronic stress, and 7.6 (SD=7.6) for depressive symptoms. At examination 2, the mean score was 2.7 (SD=2.3) for hostility.

Characteristics of MESA participants by HF status are provided in Table 2. On average, those who developed HF during follow-up were, at baseline, older, had fewer Met-minutes per week of physical activity, had higher body mass index, and had higher systolic blood pressure compared with those who did not develop HF during follow-up. Those who developed HF during follow-up were also more likely at baseline to have less than a high school education, be current or former smokers, have diabetes mellitus, and be on hypertension medication compared with those who did not develop HF.

Tables 3 and 4 show hazard ratios (HRs) and 95% CIs for each psychosocial factor in relation to risk of incident HF. In model 1, which controlled for age, sex, race, and study site, we found no significant association between any of the psychosocial factors and risk of incident HF. Compared with participants in the lowest level, HRs for those categorized in the highest level of anger (HR, 1.14 [95% CI, 0.81-1.60]), anxiety (HR, 0.74 [95% CI, 0.51-1.07]), chronic stress (HR, 1.25 [95% CI, 0.90–1.72]), depressive symptoms (HR, 1.19 [95% CI, 0.76–1.85]), and hostility (HR, 0.95 [95% CI, 0.62–1.42]) revealed no association with incident HF. When modeled continuously, an interquartile range increase in chronic stress was associated with a 27% increase in risk of incident HF. The addition of smoking status and physical activity in the model slightly attenuated the estimates. Results were similar in models adjusted for inflammatory markers (model 3) and additionally for traditional cardiovascular disease risk factors (model 4; data not shown).

Interactions between sex and each psychosocial factor were tested but were only significant for hostility (*P*=0.03). In sex-specific analyses, compared with the lowest quartile, the HR for incident HF in the highest quartile was 0.71 (0.40–1.26) among men and 1.39 (0.76–2.54) among women.

Interactions between race/ethnicity and each psychosocial factor were also tested, but none was statistically significant (all *P*>0.20).

Interactions were also tested between psychosocial factors (modeled dichotomously) and self-reported health (modeled dichotomously). Only hostility was significant at the 0.05 level, although anxiety and chronic stress were significant at the 0.10 level. Table 4 presents results stratified by dichotomous self-reported health categories. For anxiety, chronic stress, and depressive symptoms, those in the highest versus lowest categorization, and also self-reporting poor health at baseline, were at 2-fold greater risk of incident HF. For those with good self-reported health at baseline, there was no evidence of an association between these psychosocial characteristics and HF risk. The opposite was true for hostility, where HRs for the highest versus lowest categorization were larger among those with good self-reported health. For anger, associations were similar regardless of self-reported health status. Estimates were modestly attenuated when smoking status and physical activity were entered into the model.

Discussion

There was no association between several psychosocial factors (ie, anger, anxiety, chronic stress, depressive symptoms, and hostility) and risk of incident HF in this multiethnic population-based study. When modeled continuously, more chronic stress was associated with a slight increase in risk of incident HF. Although not statistically significant, there were some suggestions that the association between certain psychosocial factors and incident HF may differ by baseline self-reported health status. However, these results must be interpreted cautiously because of low power.

Relatively few previous studies have examined associations between psychosocial factors and incident HF, and most have only examined depression or depressive symptoms. Williams et al⁷ found that high levels of depressive symptoms, as defined by Center for Epidemiological Studies Depression Scale scores ≥21, were associated with greater risk of incident HF in an elderly population (mean age, 74 years) from Connecticut, but this effect was only found in women, not men. Abramson et al⁸ also found an independent association between depression and incident HF in an older sample of people (mean age, 72 years) with isolated systolic hypertension. More recently, a study examined anxiety and depression in a large U.S. Department of Veteran's Affairs population (mean age, 63 years) using International Classification of Diseases, Ninth Revision, codes and found a small but statistically significant relationship between these factors and incident HF.10 Another recent European study found a positive association between depression and incident HF but found no association between anxiety and incident HF.11 Although previous research has frequently reported associations between adverse levels of psychosocial factors and the development of stroke and coronary heart disease, 28,29 it is worthwhile to note that the onset of stroke and coronary heart disease is typically acute, whereas HF is a chronic condition that develops gradually. It is possible that pathways between psychosocial exposures and acute versus chronic cardiovascular outcomes may be different.

Table 2. Baseline Participant Characteristics Stratified by Those Who Developed Heart Failure During Follow-Up vs Those Who Did Not: The Multi-Ethnic Study of Atherosclerosis (2000-2012)

	HF Cases (n=242)	No HF (n=6567)	P Value*	
Demographics				
Age, mean±SD, y	68.7±8.8	61.9±10.2	< 0.001	
Race/ethnicity, n (%)†				
White	97 (40.1)	2522 (38.4)	0.76	
Chinese American	14 (5.8)	789 (12.0)		
Black	79 (32.6)	1813 (27.6)		
Hispanic	52 (21.5)	1443 (22.0)		
Education, n (%)†				
<high school<="" td=""><td>55 (28.5)</td><td>1170 (21.8)</td><td>0.05</td></high>	55 (28.5)	1170 (21.8)	0.05	
High school	36 (18.7)	1072 (20.0)		
>high school	102 (52.8)	3115 (58.2)		
Psychosocial exposures, mean±SD				
Anger	14.2±3.5	14.8±3.7	0.030	
Anxiety	15.1±4.2	15.9±4.5	0.007	
Chronic stress	1.2±1.2	1.2±1.2	0.83	
Depressive symptoms	7.3±6.9	7.6±7.6	0.50	
Hostility	3.0±2.3	2.7±2.3	0.08	
Self-reported health	3.3±0.9	3.6±0.9	< 0.001	
Behavioral characteristics				
Moderate-vigorous physical activity, Met-min/wk‡	4804.4±5116.1	5785.9±5922.2	0.001	
Smoking, n (%)†				
Current	37 (15.4)	850 (13.0)	0.013	
Former	104 (43.2)	2380 (36.4)		
Never	100 (41.5)	3316 (50.7)		
Physiological characteristics				
BMI (±SD), kg/m ²	29.9±6.0	28.3±5.4	< 0.0001	
Prevalent diabetes mellitus, n (%)†	75 (31.0)	781 (11.9)	< 0.0001	
Systolic BP (±SD), mm Hg	139.0±23.3	126.1±21.3	< 0.0001	
Hypertension medication use, n (%)†	148 (61.2)	2385 (36.3)	< 0.0001	
Total cholesterol (±SD), mg/dL	189.7±35.4	194.3±35.7	0.048	
HDL cholesterol (±SD), mg/dL	48.6±13.9	51.1±14.9	0.012	
LDL cholesterol (±SD), mg/dL	114.71±32.0	117.3±31.4	0.126	
Triglycerides(±SD), mg/dL‡	140.9±118.1	131.1±87.4	0.242	
C-reactive protein (±SD), mg/dL‡	5.0±6.5	3.7±5.9	< 0.0001	
Albumin (±SD), mg/dL‡	15.3±71.3	2.4±12.6	< 0.0001	
Fibrinogen (±SD), mg/dL	370.5±78.3	345.9±73.6	< 0.0001	

BMI indicates body mass index; BP, blood pressure; HDL, high-density lipoprotein; HF, heart failure; and LDL, low-density lipoprotein.

Although our study did not find significant overall results between psychosocial factors and HF, among those with poor self-reported health, there was some evidence suggesting that those scoring higher on the anxiety, chronic stress, and depressive symptoms scales were at greater risk of incident HF. The idea that psychosocial factors may play a greater role in HF development among those with poor self-reported healthwho likely have prevalent comorbidities—is supported by the existing literature. Like depression,⁵ poor self-rated health has been associated with increased risk of emergency department visits, hospitalization, and mortality among patients with HF.^{30,31} As noted above, in previous publications, associations between depression, anxiety, and incident HF were observed in study populations who were older^{7,8} and hypertensive⁸ and therefore may also have been more prone to comorbidities and poor self-reported health. In addition, those with lower

^{*}t tests were used for linear variables that were normally distributed; for categorical variables (designated with an \uparrow), χ^2 tests were used and for non-normally distributed linear variables (designated with an \uparrow), the Wilcoxon–Mann– Whitney test was used.

Table 3. Adjusted Hazard Ratios (95% Confidence Intervals) for Psychosocial Factors and Risk of Incident Heart Failure: The Multi-Ethnic Study of Atherosclerosis (2000–2012)

						<i>P</i> -Trend Categories	Continuous per IQR	<i>P</i> -Trend Continuous
Anger quartile (range)	1 (10–12)	2 (13–14)	3 (15–16)	4 (17–40)				
No. of incident HF events	88	55	41	57			241	
Total no. of participants	2007	1703	1313	1754			6777	
Model 1	1.00 (referent)	0.90 (0.64-1.26)	0.94 (0.65-1.37)	1.14 (0.81-1.60)		0.80	1.02 (0.85-1.23)	0.80
Model 2	1.00 (referent)	0.89 (0.64-1.26)	0.92 (0.63-1.35)	1.11 (0.78-1.56)		0.97	1.00 (0.83-1.20)	0.99
Anxiety quartile (range)	1 (10–12)	2 (>12–15)	3 (>15–18.75)	4 (>18.75–37)		•••		•••
No. of incident HF events	84	57	53	47			241	
Total no. of participants	1766	1803	1406	1795			6770	
Model 1	1.00 (referent)	0.78 (0.56-1.10)	1.04 (0.73-1.48)	0.74 (0.51-1.07)		0.49	0.93 (0.75–1.15)	0.49
Model 2	1.00 (referent)	0.78 (0.55-1.09)	1.04 (0.73-1.47)	0.72 (0.50-1.05)		0.42	0.91 (0.74–1.13)	0.41
Chronic stress tertile (Range)	1 (0)	2 (1)	3 (2–5)					
No. of incident HF events	80	83	76				239	
Total no. of participants	2308	2108	2332				6748	•••
Model 1	1.00 (referent)	1.12 (0.82-1.53)	1.25 (0.90-1.72)			0.04	1.27 (1.01-1.59)	0.04
Model 2	1.00 (referent)	1.13 (0.83–1.53)	1.23 (0.89-1.70)			0.05	1.25 (1.00-1.57)	0.05
Depressive symptoms quintiles (range)	1 (0-2)	2 (3–5)	3 (6–10)	4 (11–15)	5 (16–60)			
No. of incident HF events	72	49	62	27	30			
Total no. of participants	1829	1549	1707	816	872			
Model 1	1.00 (referent)	0.85 (0.59-1.23)	1.01 (0.71-1.42)	0.97 (0.62-1.52)	1.19 (0.76-1.85)	0.35	1.07 (0.93-1.24)	0.35
Model 2	1.00 (referent)	0.90 (0.60-1.35)	0.97 (0.66-1.43)	1.06 (0.65-1.74)	1.18 (0.72-1.93)	0.43	1.06 (0.91-1.22)	0.46
Hostility quartile (range)	1 (0)	2 (1–2)	3 (3–4)	4 (5–8)				
No. of incident HF events	51	37	69	50			207	
Total no. of participants	1440	1741	1544	1437			6162	
Model 1	1.00 (referent)	0.60 (0.39-0.91)	1.30 (0.90-1.89)	0.95 (0.62-1.43)		0.10	1.17 (0.97–1.41)	0.10
Model 2	1.00 (referent)	0.58 (0.38-0.89)	1.28 (0.88-1.86)	0.93 (0.61-1.41)		0.13	1.16 (0.96-1.40)	0.13

Model 1: adjusted for age, sex, race, and field center. Model 2: adjusted for model 1 plus smoking and physical activity. Higher scores on the psychosocial measures represent more severe symptoms. Interquartile range (Q1–Q3): anger, 12–17; anxiety, 12–19; chronic stress, 0–2; depressive symptoms, 2–10; and hostility, 1–4. HF indicates heart failure; and IQR, interquatile range.

self-reported health and adverse psychosocial profiles may be less likely to take medications as directed.

One major limitation of this study is the relatively small number of participants who developed HF, especially when we stratified on self-reported health. Interpretation of these results is difficult because it is unclear whether there is no overall association between psychosocial factors and incident HF or there was not enough power to detect

an association. Relatedly, given the limited number of HF cases, our psychosocial factor categories were somewhat broad. Using finer categories, and therefore conducting more extreme comparisons, may have yielded different results. For instance, we used the commonly used cut point of 16 to define depressive symptoms. Previous work, however, has suggested that using this cut point results in many individuals being falsely classified as having depressive symptoms

6

Table 4. Adjusted Hazard Ratios (95% Confidence Intervals) for Psychosocial Factors and Risk of Incident Heart Failure Stratified by Self-Reported Health: The Multi-Ethnic Study of Atherosclerosis (2000–2012)

	Good Self-Reported Health			Poor Self-Reported Health			
_	Low	High	Per IQR	Low	High	Per IQR	
Anger (range)	(10–14)	(15–40)		(10–14)	(15–40)		
No. of incident HF events	121	86	207	22	12	34	
Total no. of participants	3358	2742	6100	352	325	677	
Model 1	1.00 (referent)	1.16 (0.88-1.54)	1.09 (0.90-1.33)	1.00 (referent)	0.78 (0.37-1.65)	0.73 (0.44-1.21)	
Model 2	1.00 (referent)	1.14 (0.86-1.52)	1.07 (0.88-1.31)	1.00 (referent)	0.72 (0.34-1.53)	0.69 (0.42-1.14)	
Anxiety (range)	(10-15)	(16-37)		(10–15)	(16–37)		
No. of incident HF events	129	78	207	12	22	34	
Total no. of participants	3286	2806	6092	283	395	678	
Model 1	1.00 (referent)	0.86 (0.65-1.15)	0.83 (0.65-1.05)	1.00 (referent)	2.11 (1.00-4.47)	1.39 (0.86–2.25)	
Model 2	1.00 (referent)	0.85 (0.64-1.14)	0.82 (0.64-1.04)	1.00 (referent)	2.03 (0.97-4.27)	1.31 (0.81-2.13)	
Chronic stress (range)	(0-1)	(2-5)		(0-1)	(2-5)		
No. of incident HF events	150	55	205	13	21	34	
Total no. of participants	4085	1987	6072	331	345	676	
Model 1	1.00 (referent)	1.01 (0.74-1.38)	1.10 (0.85-1.43)	1.00 (referent)	2.25 (1.08-4.67)	2.12 (1.25-3.60)	
Model 2	1.00 (referent)	1.00 (0.73-1.37)	1.09 (0.85-1.42)	1.00 (referent)	2.15 (1.04-4.47)	2.04 (1.21-3.44)	
Depressive symptoms (range)	(0-15)	(16–60)		(0-15)	(16–60)		
No. of incident HF events	187	19	206	23	11	34	
Total no. of participants	5411	685	6096	490	187	677	
Model 1	1.00 (referent)	1.01 (0.62-1.63)	1.02 (0.86-1.20)	1.00 (referent)	2.15 (0.98-4.68)	1.21 (0.90-1.63)	
Model 2	1.00 (referent)	0.98 (0.61-1.59)	1.00 (0.85-1.19)	1.00 (referent)	1.98 (0.90-4.34)	1.18 (0.88–1.58)	
Hostility (range)	(0-2)	(3–8)		(0-2)	(3–8)		
No. of incident HF events	76	102	178	12	17	29	
Total no. of participants	3006	2589	5595	175	392	538	
Model 1	1.00 (referent)	1.63 (1.20-2.23)	1.25 (1.02-1.53)	1.00 (referent)	0.60 (0.27-1.33)	0.73 (0.45-1.19)	
Model 2	1.00 (referent)	1.65 (1.20-2.25)	1.25 (1.02-1.53)	1.00 (referent)	0.59 (0.26-1.31)	0.71 (0.43-1.17)	

Model 1: adjusted for age, sex, race, and field center. Model 2: adjusted for model 1 plus smoking and physical activity. Higher scores on the psychosocial measures represent more severe symptoms. Interquartile range (Q1–Q3): anger, 12–17; anxiety, 12–19; chronic stress, 0–2; depressive symptoms, 2–10; and hostility, 1–4. HF indicates heart failure; and IQR, interquatile range.

and that a higher cut point should be used. 32,33 Studies with a larger number of cases may be able to more precisely determine the magnitude of the relationship between psychosocial factors and risk of incident HF. In addition, there is the potential for error in the measurement of the exposures and the outcome. For the exposures, we would expect this error to be unrelated to the outcome because there were no prevalent HF cases at baseline and disease status is ascertained in the future. Because this misclassification is nondifferential, estimates obtained from this study would likely be biased toward the null. For the outcome, because exposure status is determined before the outcome occurs, any error in the measurement of the outcome is likely to be unrelated to exposure and is expected to bias the results toward the null. This study also has several noteworthy strengths, including a multiethnic representative population-based sample, ascertainment of multiple psychosocial factors, and adjudicated HF outcomes.

Overall, this study found no strong statistically significant relationships between psychosocial factors and incident HF. However, adverse levels of psychosocial factors may play a role in, or be an indicator of, HF development among those who perceive themselves as having poor health. Future research with greater power is necessary to reach more definitive conclusions.

Acknowledgments

We thank the other investigators, the staff, and the participants of the Multi-Ethnic Study of Atherosclerosis (MESA) study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Sources of Funding

Research reported in this publication was supported by grants and contracts T32-HL-007779, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, and N01-HC-95169 from the National Heart, Lung, and Blood Institute and by grants UL1-TR-000040 and UL1-TR-001079 from the National Center for Research Resources.

Disclosures

None.

References

- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014;129:399–410. doi: 10.1161/01.cir.0000442015.53336.12.
- Hemingway H, Marmot M. Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. *BMJ*. 1999;318:1460–1467.
- Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. *J Am Coll Cardiol*. 2006;48:1527–1537. doi: 10.1016/j.jacc.2006.06.055.
- MacMahon KM, Lip GY. Psychological factors in heart failure: a review of the liteure. Arch Intern Med. 2002;162:509–516.
- Johnson TJ, Basu S, Pisani BA, Avery EF, Mendez JC, Calvin JE Jr, Powell LH. Depression predicts repeated heart failure hospitalizations. J Card Fail. 2012;18:246–252. doi: 10.1016/j.cardfail.2011.12.005.
- van den Broek KC, Defilippi CR, Christenson RH, Seliger SL, Gottdiener JS, Kop WJ. Predictive value of depressive symptoms and B-type natriuretic peptide for new-onset heart failure and mortality. *Am J Cardiol*. 2011;107:723–729. doi: 10.1016/j.amjcard.2010.10.055.
- Williams SA, Kasl SV, Heiat A, Abramson JL, Krumholz HM, Vaccarino V. Depression and risk of heart failure among the elderly: a prospective community-based study. *Psychosom Med.* 2002;64:6–12.
- 8. Abramson J, Berger A, Krumholz HM, Vaccarino V. Depression and risk of heart failure among older persons with isolated systolic hypertension. *Arch Intern Med*. 2001;161:1725–1730.
- May HT, Horne BD, Carlquist JF, Sheng X, Joy E, Catinella AP. Depression after coronary artery disease is associated with heart failure. J Am Coll Cardiol. 2009;53:1440–1447. doi: 10.1016/j.jacc.2009.01.036.
- Garfield LD, Scherrer JF, Hauptman PJ, Freedland KE, Chrusciel T, Balasubramanian S, Carney RM, Newcomer JW, Owen R, Bucholz KK, Lustman PJ. Association of anxiety disorders and depression with incident heart failure. *Psychosom Med.* 2014;76:128–136. doi: 10.1097/ PSY.00000000000000027.
- Gustad LT, Laugsand LE, Janszky I, Dalen H, Bjerkeset O. Symptoms of anxiety and depression and risk of heart failure: the HUNT Study. Eur J Heart Fail. 2014;16:861–870. doi: 10.1002/ejhf.133.
- Kamphuis MH, Kalmijn S, Tijhuis MA, Geerlings MI, Giampaoli S, Nissinen A, Grobbee DE, Kromhout D. Depressive symptoms as risk factor of cardiovascular mortality in older European men: the Finland, Italy and Netherlands Elderly (FINE) study. Eur J Cardiovasc Prev Rehabil. 2006;13:199–206. doi: 10.1097/01.hjr.0000188242.64590.92.
- Kucharska-Newton AM, Williams JE, Chang PP, Stearns SC, Sueta CA, Blecker SB, Mosley TH. Anger proneness, gender, and the risk of heart failure. *J Card Fail*. 2014;20:1020–1026. doi: 10.1016/j.cardfail.2014.09.010.
- Cené CW, Loehr L, Lin FC, Hammond WP, Foraker RE, Rose K, Mosley T, Corbie-Smith G. Social isolation, vital exhaustion, and incident heart failure: findings from the Atherosclerosis Risk in Communities Study. Eur J Heart Fail. 2012;14:748–753. doi: 10.1093/eurjhf/hfs064.
- Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and

- diagnosis. Cardiovasc Psychiatry Neurol. 2013;2013:695925. doi: 10.1155/2013/695925.
- Gold PW, Goodwin FK, Chrousos GP. Clinical and biochemical manifestations of depression. Relation to the neurobiology of stress (2). N Engl J Med. 1988;319:413–420. doi: 10.1056/NEJM198808183190706.
- Chrousos GP, Gold PW. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *JAMA*. 1992;267:1244–1252.
- Packer M. New concepts in the pathophysiology of heart failure: beneficial and deleterious interaction of endogenous haemodynamic and neurohormonal mechanisms. *J Intern Med.* 1996;239:327–333.
- Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress. Lancet. 2007;370:1089–1100. doi: 10.1016/S0140-6736(07)61305-1.
- Kop WJ, Synowski SJ, Gottlieb SS. Depression in heart failure: biobehavioral mechanisms. *Heart Fail Clin*. 2011;7:23–38. doi: 10.1016/ j.hfc.2010.08.011.
- Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-Ethnic Study of Atherosclerosis: objectives and design. Am J Epidemiol. 2002;156:871–881.
- Spielberger CD. Preliminary Manual for the State-Trait Personality Inventory. Palo Alto, CA: Consulting Psychologist Press; 1980.
- Bromberger JT, Matthews KA. A longitudinal study of the effects of pessimism, trait anxiety, and life stress on depressive symptoms in middleaged women. *Psychol Aging*. 1996;11:207–13.
- Radloff LS. The CES-D Scale. A self-report depression for research in the general population. Appl Psychol Meas. 1977;1:385–401.
- Greenglass ER, Julkunen J. Cook-Medley hostility, anger, and the type A behavior pattern in Finland. *Psychol Rep.* 1991;68(3 pt 2):1059–1066. doi: 10.2466/pr0.1991.68.3c.1059.
- Radloff LS, Teri L. Use of the Center for Epidemiological Studies-Depression Scale with Older Adults. Clinical Gerontologist. 1986;5:119–136.
- Bluemke DA, Kronmal RA, Lima JA, Liu K, Olson J, Burke GL, Folsom AR. The relationship of left ventricular mass and geometry to incident cardio-vascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. *J Am Coll Cardiol*. 2008;52:2148–2155. doi: 10.1016/j.jacc.2008.09.014.
- Everson-Rose SA, Roetker NS, Lutsey PL, Kershaw KN, Longstreth WT Jr, Sacco RL, Diez Roux AV, Alonso A. Chronic stress, depressive symptoms, anger, hostility, and risk of stroke and transient ischemic attack in the multi-ethnic study of atherosclerosis. *Stroke*. 2014;45:2318–2323. doi: 10.1161/STROKEAHA.114.004815.
- Low CA, Thurston RC, Matthews KA. Psychosocial factors in the development of heart disease in women: current research and future directions. *Psychosom Med.* 2010;72:842–854. doi: 10.1097/ PSY.0b013e3181f6934f.
- Chamberlain AM, Manemann SM, Dunlay SM, Spertus JA, Moser DK, Berardi C, Kane RL, Weston SA, Redfield MM, Roger VL. Self-rated health predicts healthcare utilization in heart failure. *J Am Heart Assoc*. 2014;3:e000931. doi: 10.1161/JAHA.114.000931.
- Chamberlain AM, McNallan SM, Dunlay SM, Spertus JA, Redfield MM, Moser DK, Kane RL, Weston SA, Roger VL. Physical health status measures predict all-cause mortality in patients with heart failure. Circ Heart Fail. 2013;6:669–675. doi: 10.1161/ CIRCHEARTFAILURE.112.000291.
- Boyd JH, Weissman MM, Thompson WD, Myers JK. Screening for depression in a community sample. Understanding the discrepancies between depression symptom and diagnostic scales. *Arch Gen Psychiatry*. 1982;39:1195–1200.
- Zich JM, Attkisson CC, Greenfield TK. Screening for depression in primary care clinics: the CES-D and the BDI. *Int J Psychiatry Med*. 1990;20:259–77.

CLINICAL PERSPECTIVE

Previous research has examined how psychosocial factors are related to coronary heart disease, but their association with heart failure is understudied. This study investigated whether anger, anxiety, chronic burden, depression, and hostility are related to the development of the new heart failure cases. In the overall sample, we found no relationship between psychosocial factors and heart failure. However, among those reporting fair or poor health, several psychosocial factors (ie, anxiety, chronic burden, and depression) may be related to heart failure risk. From a clinical perspective, although there is evidence of an association between psychosocial factors and other cardiovascular outcomes, the influence of psychosocial factors on incident heart failure is less clear but may be influenced by baseline health status, with stronger effect in those with poorer baseline health.