Published in final edited form as:

Am J Med. 2013 December ; 126(12): 1107–1113. doi:10.1016/j.amjmed.2013.07.022.

Anxiety, Anger, and Mortality Risk Among Survivors of Myocardial Infarction

Katherine C. Wrenn, MD^a, Elizabeth Mostofsky, MPH, ScD^{a,b}, Geoffrey H. Tofler, MD^c, James E. Muller, MD^d, and Murray A. Mittleman, MD, DrPH^{a,b}

^aDepartment of Cardiology and Cardiovascular Epidemiology Research Unit, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston

^bDepartment of Epidemiology, Harvard School of Public Health, Boston, MA

^cDepartment of Cardiology, Royal North Shore Hospital, Sydney, Australia

^dInfraReDx, Burlington, Massachusetts

Abstract

Background—Although there is evidence that anxiety and anger are associated with a higher risk of cardiovascular events, studies examining the relationship between these stressors and prognosis following myocardial infarction have been mixed.

Methods—We conducted a prospective cohort study of 1968 participants (average age 60.2, 30.6% women) in the Determinants of Myocardial Infarction Onset Study recruited at the time of admission for myocardial infarction between 1989–1996. We used the state anxiety and anger subscales of the State-Trait Personality Inventory. Participants were followed for all-cause mortality through December 31, 2007 using the National Death Index. We constructed multivariable Cox proportional hazards models adjusted for demographic, behavioral, and clinical confounders and calculated hazard ratios and 95% confidence intervals to examine the relationship between high levels of anxiety and anger and all-cause mortality.

Results—Over 10 years of follow-up, 525 participants died. Compared to those scoring lower, an anxiety score >90th percentile was associated with a 1.31-times (95% CI 0.93–1.84) higher mortality rate. The association was apparent in the first 3 years (HR=1.78; 95% CI 1.08–2.93) but not thereafter. Likewise, an anger score >90th percentile was associated with a 1.25-times (95% CI 0.87–1.80) higher mortality rate. The association was higher in the first 3 years (HR=1.58; 95% CI 0.91–2.74) than in subsequent years, but it was not statistically significant during either follow-up period.

Conclusions—In this study of myocardial infarction survivors, a high level of anxiety was associated with all-cause mortality, with the strongest association in the first 3 years of follow-up.

© 2013 Elsevier Inc. All rights reserved.

Address for Correspondence: Murray A. Mittleman, MD, DrPH, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 375 Longwood Avenue, Room 423, Boston, MA 02215, mmittlem@bidmc.harvard.edu, Tel: (617) 632-7653, Fax: (617) 632-7698.

Conflict of Interest Disclosures: None

All authors had access to the data and a role in writing the manuscript.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

Anxiety; Anger; Myocardial Infarction; All-cause mortality

Introduction

Cardiovascular disease is the leading cause of death in the United States. Approximately 785,000 Americans have a new myocardial infarction each year, and approximately 470,000 have a recurrent myocardial infarction.¹ There is consistent evidence that anxiety²⁻⁴ and anger⁵⁻⁷ are associated with higher rates of cardiovascular events and fatal coronary heart disease. For instance, in a study of 735 healthy older men followed for an average of 12.4 years, there was a 1.43-times higher rate of myocardial infarction for each standard deviation increase in anxiety.² In a study of 12,990 normotensive individuals followed for an average of four years, a strong angry temperament was associated with more than a 2-fold higher rate of acute myocardial infarction and fatal coronary heart disease.⁶

Despite the evidence that anxiety and anger are associated with a higher rate of incident myocardial infarction, studies examining the relationship between psychosocial stressors and prognosis following myocardial infarction have had conflicting results, with some showing higher risk⁸⁻¹⁴ and others showing no association.¹⁵⁻¹⁸ These studies had variable lengths of follow-up periods and used different instruments to measure anxiety and anger, perhaps contributing to the mixed results and leaving uncertainty as to whether there is an association between anxiety, anger, and long-term prognosis following myocardial infarction. Therefore, we conducted a prospective cohort study of 1968 early survivors of acute myocardial infarction followed for up to 10 years to examine whether self-reported anxiety and anger at the time of admission for myocardial infarction are associated with prognosis, as assessed by all-cause mortality.

Methods

Enrollment and Data Collection

Between 1989 and 1996, 1968 people (1366 men and 602 women, mean age 60.2 years) in the Determinants of Myocardial Infarction Onset Study (MIOS) were enrolled from 64 medical centers and completed an interview including questions about anxiety and anger a median of 4 days after admission for myocardial infarction. The cohort was followed prospectively for all-cause mortality through December 31, 2007. As previously described, trained interviewers identified eligible patients by reviewing coronary care unit admission logs and patient charts.⁵ Inclusion criteria were: creatine kinase levels higher than the upper limit of normal for the clinical laboratory at each center, positive MB isoenzymes, an identifiable onset of pain or other symptoms typical of acute myocardial infarction, and the ability to complete a structured interview. Interviewers used structured data abstraction and questionnaire forms. The institutional review board of each center approved this protocol, and all participants provided informed consent. Subsequent approval was obtained from the Beth Israel Deaconess Medical Center Committee on Clinical Investigations to search publicly available mortality records.

Exposure and Covariate Assessment

Trained interviewers administered the state anger and anxiety subscales of the State-Trait Personality Inventory (STPI), a research instrument that has been widely used and extensively validated.^{19,20} The state anxiety and anger scores for this study ranged from 10-40, with higher scores indicating more severe symptoms. Although we previously dichotomized these scores at the 75th percentile,⁵ we dichotomized the scores at the 90th

percentile in this analysis, as the 75th percentile was a score of 11, which is not a meaningful difference from the lowest score of 10. Among the 1968 people with information on anxiety or anger, 1944 had information on anxiety and 1957 had information on anger. We excluded patients from the analysis who did not complete the anxiety subscale (n=62) or anger subscale (n=49).

Trained research personnel reviewed medical records to collect information including patient age, sex, race, marital status, medical history (history of hypertension, diabetes mellitus, prior myocardial infarction, prior congestive heart failure, angina, and non-cardiac comorbidities including respiratory disease, renal failure, cancer and stroke), and regular use of several medications (angiotensin converting enzyme inhibitors, aspirin, beta blockers, calcium channel blockers, digoxin, diuretics, and hypolipidemic agents). We used the 2000 United States census data to derive median household income from census block groups.^{21,22} We calculated body mass index (BMI) using self-reported height and weight. We collected information on habitual physical activity, educational attainment, smoking status, and alcohol consumption.

Outcome Assessment

We searched the National Death Index for deaths of Myocardial Infarction Onset Study participants and requested death certificates from state offices of vital records for all probable matches using a previously validated algorithm that included name, date of birth, sex, race, marital status, and state as previously described.²³ Three physicians independently verified the determination of each death and disagreements among raters were resolved by discussion. All-cause mortality was the primary outcome in all analyses and cardiovascular mortality was a secondary outcome. Using the National Death Index cause of death recodes, we classified deaths as due to cardiovascular causes or not. For patients that died between 1989 and 1998, death certificates with International Classification of Diseases, Ninth Revision (ICD-9) recodes of 300 to 490 represented cardiovascular death. For patients that died in 1999 and later, International Classification of Diseases, Tenth Revision (ICD-10) recodes of 53 to 75 represented cardiovascular death.²³ All participants were administratively censored on December 31, 2007 or date of death, whichever came first.

Statistical Analysis

We constructed Cox proportional hazards models and calculated hazard ratios (HR) and 95% confidence intervals (CI) to examine the relationship between anxiety and all-cause mortality and between anger and all-cause mortality. In all analyses, we allowed the baseline hazard to vary by age. In an initial model, we adjusted for age and sex. In a second model, we further adjusted for covariates selected a priori based on their plausible relationship with anxiety, anger, and all-cause mortality: age (continuous), sex, race (white versus other), marital status (married versus other), educational attainment (<12, 12-14, 14 years of school), body mass index (continuous and quadratic terms), neighborhood median household income (continuous), smoking status (never, former, current), alcohol consumption (servings per week), usual frequency of physical activity (0, 1-4, 5 times per week), hypertension, diabetes mellitus, prior myocardial infarction, prior congestive heart failure, angina, non-cardiac comorbidities (respiratory disease, renal failure, cancer and stroke), thrombolytic therapy (yes/no) and current use of angiotensin-converting enzyme inhibitors, aspirin, β -blockers, calcium-channel blockers, digoxin, diuretics, and hypolipidemic agents (yes/no).

In the primary analysis, we examined the association between anxiety and anger and the rate of all-cause mortality over 10 years of follow-up. Based on the crude Kaplan-Meier curves, the association appears to decline after the third year of follow-up, so we constructed

separate Cox models for the first 3 years and years 3-10 of follow-up. In a secondary analysis, we constructed similar models for the association between anxiety and anger and the rate of cardiovascular mortality. We also performed an analysis to examine the risk of all-cause mortality among participants with both low anger and low anxiety scores compared to those scoring high on the anger scale, high on the anxiety scale, or high on both scales.

We tested the assumption of proportional hazards by testing the significance of interaction terms between the indicator variables of exposure and the natural log of time in our adjusted model. We did not find statistically significant evidence that the association between all-cause mortality and anger ($P=0.33$) varied over time, but it was borderline significant for anxiety ($P=0.08$). We used SAS version 9.2 (SAS Institute, Cary, NC). All P values presented are 2 sided, and we considered values <0.05 to be statistically significant.

Results

The characteristics of the participants included in the Determinants of Myocardial Infarction Onset Study are listed in Table 1. The majority of study participants were men (69.4%), and participants were predominantly white. Approximately 25.8% had a history of prior myocardial infarction. Among the 1944 participants who completed the State-Trait Personality Inventory anxiety scale, those with a higher level of anxiety were slightly younger (average age 56.2 versus 60.6) and more likely to be current smokers than those with low anxiety scores. Similar to those who completed the anxiety scale, among the 1957 participants who completed the State-Trait Personality Inventory anger scale, those with a higher level of anger were slightly younger (average age 54.9 versus 60.7) and more likely to be current smokers than those with low anger scores.

Over 10 years of follow-up, 525 (27%) participants died, including 326 that died of cardiovascular disease. Compared to those scoring 90th percentile on the State-Trait Personality Inventory anxiety scale, a higher score was associated with a 1.31-times (95% CI 0.93-1.84) higher mortality rate over 10 years (Table 2). Although this overall association was not statistically significant, there was a statistically significant association for higher mortality in the first 3 years (HR=1.78; 95% CI 1.08-2.93) but not in years 3-10 of follow-up. Scoring high on the anger scale was associated with a 1.25-times higher mortality rate over 10 years (Table 2), with a stronger association in the first 3 years than in subsequent years, but the association was not statistically significant in any of the examined time periods.

In a secondary analysis of cardiovascular mortality, there was a higher rate of cardiovascular death among those with higher anxiety scores. Compared to those scoring low on the anxiety scale, a score above the 90th percentile was associated with a HR of 1.17 (95% CI 0.74-1.86) over 10 years (Table 3). Similar to the findings on all-cause mortality, this association was stronger in the first 3 years (with a 1.49-times higher cardiovascular mortality rate), but not thereafter. On the other hand, a high score on the anger scale was not associated with a higher cardiovascular mortality rate over 10 years, even in the analysis restricted to the first three years of follow-up (Table 3).

In an additional analysis, we found that compared to participants scoring low on both the anxiety and anger scales, those scoring high on either the anger or anxiety scale or high on both scales had a 1.30-times (95% CI 0.96-1.75) higher mortality rate over 10 years, particularly in the first 3 years of follow-up (HR=1.79; 95% CI 1.14-2.79) (Table 4).

Discussion

In this study of myocardial infarction survivors, high levels of anxiety were associated with a higher rate of all-cause and cardiovascular mortality, with the strongest association in the first 3 years of follow-up. The association between higher levels of anger and all-cause mortality was of similar magnitude, but was not statistically significant during either period, and there was no apparent association with cardiovascular mortality.

Studies on the relationship between anxiety and myocardial infarction prognosis have been mixed, with some reporting no association,^{15,16,18,24} and others showing that, similar to our findings, anxiety negatively influences prognosis among people that had a myocardial infarction^{12,13} or that have coronary heart disease.^{8,11,14} For example, Frasure-Smith et al. found that among a cohort of 222 patients with myocardial infarction, anxiety was associated with a more than 3-fold higher rate of cardiac events (OR 3.13; 95% CI 1.57-6.21).¹² Similar to our findings that the higher risk is only apparent in the first few years following a myocardial infarction, a study of 275 patients who survived their first myocardial infarction found that the higher risk of all-cause mortality associated with anxiety was strongest in the first 5-6 years of follow-up.¹⁶ This suggests that higher anxiety measured at the time of the myocardial infarction may be less predictive of mortality over time, although it is possible that the effect may be due to “depletion of susceptibles”; the risk of all-cause mortality may have declined over time because those at highest risk died soon after their myocardial infarction, leaving fewer high-risk individuals remaining in the population at later time periods.²⁵

Although our results did not reach statistical significance, our data suggested that anger is associated with a higher rate of all-cause mortality following myocardial infarction, particularly in the first 3 years of follow-up. This is consistent with several prior studies showing a higher risk with higher anger levels,^{9,10} though other studies have reported no association^{12,16} or lower cardiovascular risk with higher anger levels.^{18,26,27} A study following 92 patients for one year post-myocardial infarction found that those who experienced anger were more likely to experience re-infarction or death ($p = 0.03$),¹⁰ though the study used several different subscales to measure anger, and only the Total Anger Expression scale had a statistically significant association with worse prognosis.^{10,28} It is possible that only certain anger constructs are associated with higher risk,^{29,30} while other forms of anger may be associated with lower cardiovascular risk.^{26,27} For instance, anger suppression has been associated with a higher risk of coronary heart disease³⁰ and cardiac death or myocardial infarction among patients with established coronary heart disease,²⁹ whereas anger expression has been associated with a lower risk of nonfatal myocardial infarction²⁶ and a lower risk of all-cause mortality among myocardial infarction survivors.²⁷

There are several potential mechanisms linking anxiety and anger to postmyocardial infarction survival. Anxiety and anger are associated with increases in sympathetic nervous system activity, resulting in higher blood pressure and platelet aggregation.³¹ Chronic stress is associated with hypertension,³² and anger is associated with higher levels of total cholesterol, low-density lipoprotein,³³ and arterial stiffness.³⁴ Compared to patients scoring low on anxiety in the days following myocardial infarction, those with high anxiety scores have a lower probability of reducing smoking in the following 2 years,¹³ which may also result in a worse prognosis for more anxious individuals.

The limitations of this study warrant discussion. We used information from the state component of the State-Trait Personality Inventory instrument, which measures symptoms at the present moment, and not as an overall trait of an individual. However, previous studies have shown that the two State-Trait Personality Inventory sub-scores (state versus trait) have

high concordance.¹⁹ We did not collect information on different constructs of anger (suppressed versus expressed) to examine whether the association depends on the anger construct, but our findings on the general construct of anger may be useful since health professionals interacting with myocardial infarction survivors may be more likely to recognize indicators of general anger, rather than a specific subtype of anger expression or suppression. Although we did not have information on depression, which is associated with worse prognosis following myocardial infarction,^{12,18} previous studies have shown that anxiety is associated with poor prognosis independent of concurrent depression.³⁵ Finally, this study is based on individuals that had a myocardial infarction between 1989 and 1996, before the current standards of post-myocardial infarction care were established. There are also several strengths to our study. The MIOS study includes a large sample of myocardial infarction survivors followed for up to 10 years, with information on many demographic, lifestyle, and health characteristics, and information on anxiety and anger from the validated State-Trait Personality Inventory instrument. Additionally, although data on anxiety and anger were collected at the time of the index myocardial infarction and it is possible that participants' levels of anxiety and anger changed over time, this measure presents a unique opportunity to assess psychological state close to the time of the index event and provides clinically relevant prognostic information.

Although there is evidence that psychosocial factors impact cardiovascular disease incidence and prognosis,¹⁴ there is limited evidence on the efficacy of psychosocial interventions to improve prognosis among those with coronary heart disease. Among people with coronary heart disease, there is evidence that psychological interventions improve psychological symptoms and may lower the risk of cardiovascular mortality, but there is not strong evidence that they reduce total deaths, risk of re-vascularization, or non-fatal infarction.³⁶ In a study following 1376 post-myocardial infarction patients for one year to assess the effects of a program intended to reduce psychological distress, Frasure-Smith et al. found that the intervention had a small impact on depression and anxiety among the participants, no impact on overall survival in men, and higher cardiac and all-cause mortality among women.³⁷ In another study, 2328 myocardial infarction patients were randomized to either usual care or a rehabilitation program with psychological therapy, counseling, relaxation training, and stress management training. Compared to those receiving usual care, the treatment arm was not associated with a statistically significant difference in reported anxiety or depression at 6 months and there was no difference in clinical outcomes or mortality at 12 months.³⁸

In summary, our results show that high levels of anxiety were associated with all-cause mortality, with the strongest association in the first 3 years of follow-up. There was also a suggestion that high levels of anger were associated with a higher mortality rate, particularly in the first 3 years following a myocardial infarction. Future research is needed to determine whether specific psychosocial interventions may help to reduce mortality among patients with acute myocardial infarction.

Acknowledgments

Funding/Support: This work was supported by grant T32-HL098048 from the National Institutes of Health.

Role of the Sponsor: No funding organization had any role in the design and conduct of the study; collection; management, analysis and interpretation of the data; and preparation of the manuscript.

References

1. Roger VL, Go AS, Lloyd-Jones DM, et al. Executive summary: heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation*. 2012; 125(1): 188–197. [PubMed: 22215894]

2. Shen BJ, Avivi YE, Todaro JF, et al. Anxiety characteristics independently and prospectively predict myocardial infarction in men the unique contribution of anxiety among psychologic factors. *J Am Coll Cardiol.* 2008; 51(2):113–119. [PubMed: 18191733]
3. Januzzi JL Jr, Stern TA, Pasternak RC, DeSanctis RW. The influence of anxiety and depression on outcomes of patients with coronary artery disease. *Arch Intern Med.* 2000; 160(13):1913–1921. [PubMed: 10888966]
4. Kubzansky LD, Cole SR, Kawachi I, et al. Shared and unique contributions of anger, anxiety, and depression to coronary heart disease: a prospective study in the normative aging study. *Ann Behav Med.* 2006; 31(1):21–29. [PubMed: 16472035]
5. Mittleman MA, Maclure M, Sherwood JB, et al. Triggering of acute myocardial infarction onset by episodes of anger. Determinants of Myocardial Infarction Onset Study Investigators. *Circulation.* 1995; 92(7):1720–1725. [PubMed: 7671353]
6. Williams JE, Nieto FJ, Sanford CP, Tyroler HA. Effects of an angry temperament on coronary heart disease risk : The Atherosclerosis Risk in Communities Study. *Am J Epidemiol.* 2001; 154(3):230–235. [PubMed: 11479187]
7. Boyle SH, Michalek JE, Suarez EC. Covariation of psychological attributes and incident coronary heart disease in U.S. Air Force veterans of the Vietnam war. *Psychosom Med.* 2006; 68(6):844–850. [PubMed: 17079707]
8. Shibeshi WA, Young-Xu Y, Blatt CM. Anxiety worsens prognosis in patients with coronary artery disease. *J Am Coll Cardiol.* 2007; 49(20):2021–2027. [PubMed: 17512358]
9. Chida Y, Steptoe A. The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. *J Am Coll Cardiol.* 2009; 53(11):936–946. [PubMed: 19281923]
10. Julkunen J, Idanpaan-Heikkilä U, Saarinen T. Components of Type A behavior and the first-year prognosis of a myocardial infarction. *J Psychosom Res.* 1993; 37(1):11–18. [PubMed: 8421256]
11. Frasure-Smith N, Lesperance F. Depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease. *Arch Gen Psychiatry.* 2008; 65(1):62–71. [PubMed: 18180430]
12. Frasure-Smith N, Lesperance F, Talajic M. The impact of negative emotions on prognosis following myocardial infarction: is it more than depression? *Health Psychol.* 1995; 14(5):388–398. [PubMed: 7498109]
13. Benninghoven D, Kaduk A, Wiegand U, et al. Influence of anxiety on the course of heart disease after acute myocardial infarction - risk factor or protective function? *Psychother Psychosom.* 2006; 75(1):56–61. [PubMed: 16361875]
14. Roest AM, Martens EJ, Denollet J, de Jonge P. Prognostic association of anxiety post myocardial infarction with mortality and new cardiac events: a meta-analysis. *Psychosom Med.* 2010; 72(6):563–569. [PubMed: 20410247]
15. Mayou RA, Gill D, Thompson DR, et al. Depression and anxiety as predictors of outcome after myocardial infarction. *Psychosom Med.* 2000; 62(2):212–219. [PubMed: 10772399]
16. Welin C, Lappas G, Wilhelmsen L. Independent importance of psychosocial factors for prognosis after myocardial infarction. *J Intern Med.* 2000; 247(6):629–639. [PubMed: 10886484]
17. Lane D, Carroll D, Ring C, et al. Mortality and quality of life 12 months after myocardial infarction: effects of depression and anxiety. *Psychosom Med.* 2001; 63(2):221–230. [PubMed: 11292269]
18. Nakamura S, Kato K, Yoshida A, et al. Prognostic value of depression, anxiety, and anger in hospitalized cardiovascular disease patients for predicting adverse cardiac outcomes. *Am J Cardiol.* 2013; 111(10):1432–1436. [PubMed: 23433760]
19. Stanley MA, Beck JG, Zebb BJ. Psychometric properties of four anxiety measures in older adults. *Behav Res Ther.* 1996; 34(10):827–838. [PubMed: 8952126]
20. Spielberger CD, Jacobs G, Crane R, et al. Preliminary manual for the State-Trait Personality Inventory. Tampa. 1979
21. Krieger N, Chen JT, Waterman PD, et al. Choosing area based socioeconomic measures to monitor social inequalities in low birth weight and childhood lead poisoning: The Public Health Disparities

- Geocoding Project (US). *J Epidemiol Community Health*. 2003; 57(3):186–199. [PubMed: 12594195]
22. Krieger N, Chen JT, Waterman PD, et al. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of areabased measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am J Epidemiol*. 2002; 156(5):471–482. [PubMed: 12196317]
 23. Rosenbloom JI, Wilker EH, Mukamal KJ, et al. Residential proximity to major roadway and 10-year all-cause mortality after myocardial infarction. *Circulation*. 2012; 125(18):2197–2203. [PubMed: 22566348]
 24. Lane D, Carroll D, Ring C, et al. In-hospital symptoms of depression do not predict mortality 3 years after myocardial infarction. *Int J Epidemiol*. 2002; 31(6):1179–1182. [PubMed: 12540719]
 25. Rothman, KJ.; Greenland, S.; Lash, TL. *Modern Epidemiology*. 3. Philadelphia: Lippincott Williams & Wilkins; 2008.
 26. Eng PM, Fitzmaurice G, Kubzansky LD, et al. Anger expression and risk of stroke and coronary heart disease among male health professionals. *Psychosom Med*. 2003; 65(1):100–110. [PubMed: 12554821]
 27. Thomas SA, Friedmann E, Wimbush F, Schron E. Psychological factors and survival in the cardiac arrhythmia suppression trial (CAST): a reexamination. *Am J Crit Care*. 1997; 6(2):116–126. [PubMed: 9172848]
 28. Spielberger, CD.; Johnson, EH.; Russell, SF., et al. The experience and expression of anger: Construction and validation of an anger expression scale. In: Rosenman, RH., editor. *Anger and hostility in cardiovascular and behavioral disorders*. Washington, D.C: 1985. p. 5–30.
 29. Denollet J, Gidron Y, Vrints CJ, Conraads VM. Anger, suppressed anger, and risk of adverse events in patients with coronary artery disease. *Am J Cardiol*. 2010; 105(11):1555–1560. [PubMed: 20494661]
 30. Haynes SG, Feinleib M, Kannel WB. The relationship of psychosocial factors to coronary heart disease in the Framingham Study. III. Eight-year incidence of coronary heart disease. *Am J Epidemiol*. 1980; 111(1):37–58. [PubMed: 7352459]
 31. Strike PC, Magid K, Whitehead DL, et al. Pathophysiological processes underlying emotional triggering of acute cardiac events. *Proc Natl Acad Sci U S A*. 2006; 103(11):4322–4327. [PubMed: 16537529]
 32. Sparrenberger F, Cicheler FT, Ascoli AM, et al. Does psychosocial stress cause hypertension? A systematic review of observational studies. *J Hum Hypertens*. 2009; 23(1):12–19. [PubMed: 18615099]
 33. Engebretson TO, Stoney CM. Anger expression and lipid concentrations. *Int J Behav Med*. 1995; 2(4):281–298. [PubMed: 16250769]
 34. Williams JE, Din-Dzietham R, Szklo M. Trait anger and arterial stiffness: results from the Atherosclerosis Risk in Communities (ARIC) study. *Prev Cardiol*. 2006; 9(1):14–20. [PubMed: 16407698]
 35. Watkins LL, Koch GG, Sherwood A, et al. Association of anxiety and depression with allcause mortality in individuals with coronary heart disease. *J Am Heart Assoc*. 2013; 2(2):e000068. [PubMed: 23537805]
 36. Whalley B, Thompson DR, Taylor RS. Psychological Interventions for Coronary Heart Disease: Cochrane Systematic Review and Meta-analysis. *Int J Behav Med*.
 37. Lesperance F, Frasere-Smith N. Negative emotions and coronary heart disease: getting to the heart of the matter. *Lancet*. 1996; 347(8999):414–415. [PubMed: 8618478]
 38. Jones DA, West RR. Psychological rehabilitation after myocardial infarction: multicentre randomised controlled trial. *BMJ*. 1996; 313(7071):1517–1521. [PubMed: 8978226]

Clinical Significance Statement

- Anxiety and anger have been associated with higher rates of cardiovascular events and coronary heart disease, but studies examining the relationship between psychosocial stressors and prognosis following myocardial infarction have had conflicting results.
- In this study of myocardial infarction survivors, high levels of anxiety were associated with a higher rate of all-cause mortality, and there was a suggestion that high levels of anger were associated with a higher mortality rate.

Table 1

Clinical Characteristics of the Determinants of Myocardial Infarction Onset Study Population. Data are expressed as mean $\pm$ SD or as number (percentage).

	Anxiety		Anger	
	Low (90th percentile) (n=1765)	High (>90th percentile) (n=179)	Low (90th percentile) (n=1777)	High (>90th percentile) (n=180)
Age, years	60.6 $\pm$ 12.4	56.2 $\pm$ 12.2	60.7 $\pm$ 12.4	54.9 $\pm$ 11.7
Female	529 (30.0)	69 (38.6)	534 (30.1)	62 (34.4)
White race	1564 (88.6)	161 (89.9)	1581 (89.0)	158 (87.8)
Body mass index, kg/m ²	27.7 $\pm$ 5.0	27.7 $\pm$ 4.6	27.7 $\pm$ 5.0	27.5 $\pm$ 4.6
Married	1182 (67.0)	103 (57.5)	1187 (66.8)	109 (60.6)
Years of School				
<12	351 (19.9)	43 (24.0)	356 (20.0)	44 (24.4)
12–<14	739 (41.9)	66 (36.9)	744 (41.9)	64 (35.6)
14	649 (36.8)	65 (36.3)	649 (36.5)	68 (37.8)
Median household income (\$k)	39.0 $\pm$ 16.7	36.7 $\pm$ 17.5	38.9 $\pm$ 16.9	37.8 $\pm$ 15.4
Smoking status				
Never	437 (24.8)	46 (25.8)	443 (24.9)	43 (23.9)
Former	737 (41.8)	60 (33.5)	754 (42.4)	49 (27.2)
Current	585 (33.1)	73 (40.8)	574 (32.3)	88 (48.9)
Weekly alcohol consumption (servings)	4.7 $\pm$ 14.5	4.5 $\pm$ 15.6	4.6 $\pm$ 14.3	4.3 $\pm$ 14.3
Episodes of physical activity per week				
None	1302 (73.8)	126 (70.4)	1309 (73.7)	123 (68.3)
1 to 4	214 (12.1)	25 (14.0)	225 (12.7)	20 (11.1)
5	249 (14.1)	28 (15.6)	243 (13.7)	37 (20.6)
History of				
Hypertension	763 (43.2)	74 (41.3)	767 (43.2)	76 (42.2)
Diabetes mellitus	357 (20.2)	37 (20.7)	362 (20.4)	28 (15.6)
Previous MI*	447 (25.3)	45 (25.1)	459 (25.8)	39 (21.7)
Angina	424 (24.0)	52 (29.1)	436 (24.5)	42 (23.3)
Congestive heart failure	32 (1.8)	2 (1.1)	32 (1.8)	2 (1.1)
Non-cardiac comorbidities	82 (4.7)	9 (5.0)	84 (4.7)	11 (6.1)
Regular use of				
ACE inhibitor**	226 (12.8)	19 (10.6)	222 (12.5)	21 (11.7)
Aspirin	680 (38.5)	62 (34.6)	696 (39.2)	53 (29.4)
Beta-blocker	382 (21.6)	38 (21.2)	390 (22.0)	32 (17.8)
Calcium channel blocker	410 (23.2)	42 (23.5)	416 (23.4)	37 (20.6)
Digoxin	102 (5.8)	7 (3.9)	102 (5.7)	9 (5.0)
Diuretic	262 (14.8)	28 (15.6)	267 (15.0)	25 (13.9)
Hypolipidemic agent	161 (9.1)	24 (13.4)	171 (9.6)	16 (8.9)
Thrombolytic therapy	745 (42.2)	71 (39.7)	754 (42.4)	75 (41.7)

* MI = myocardial infarction.

**
ACE inhibitor = Angiotensin converting enzyme inhibitor.

Adjusted hazard ratios and 95% confidence intervals (CI) for the association between anxiety and all-cause mortality and anger and all-cause mortality among patients in the Myocardial Infarction Onset Study followed for 10 years.

Table 2

Anxiety and All-Cause Mortality (n=1944)					
Follow-Up	STPI*	# Deaths	Person-Years	Age/Sex Adjusted	Hazard Ratio (95% CI) Fully Adjusted**
0-10 years	90th	475	15,143	1.00 (reference)	1.00 (reference)
	>90th	44	1,533	1.21 (0.88-1.66)	1.31 (0.93-1.84)
0-3 years	90th	180	4,982	1.00 (reference)	1.00 (reference)
	>90th	21	493	1.49 (0.93-2.38)	1.78 (1.08-2.93)
3-10 years	90th	295	10,161	1.00 (reference)	1.00 (reference)
	>90th	23	1,040	1.03 (0.66-1.59)	1.06 (0.65-1.71)
Anger and All-Cause Mortality (n=1957)					
Follow-Up	STPI*	# Deaths	Person-Years	Age/Sex Adjusted	Hazard Ratio (95% CI) Fully Adjusted**
0-10 years	90th	482	15,216	1.00 (reference)	1.00 (reference)
	>90th	41	1,576	1.15 (0.82-1.60)	1.25 (0.87-1.80)
0-3 years	90th	183	5,014	1.00 (reference)	1.00 (reference)
	>90th	17	503	1.29 (0.77-2.15)	1.58 (0.91-2.74)
3-10 years	90th	299	10,202	1.00 (reference)	1.00 (reference)
	>90th	24	1,073	1.07 (0.69-1.65)	1.05 (0.65-1.70)

* STPI = State-Trait Personality Inventory Score

** Adjusted for age, sex, body mass index, body mass index², marital status, race, educational attainment, smoking, previous myocardial infarction, previous congestive heart failure, previous angina, diabetes mellitus, hypertension, non-cardiac comorbidities (respiratory disease, renal failure, cancer, stroke), previous cardiac medication use (aspirin, beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors, lipid drugs, diuretics), thrombolysis, frequency of physical activity, neighborhood household income, and alcohol consumption.

Adjusted hazard ratios and 95% confidence intervals (CI) for the association between anxiety and cardiovascular mortality and anger and cardiovascular mortality among patients in the Myocardial Infarction Onset Study followed for 10 years.

Table 3

Anxiety and Cardiovascular Mortality (n=1944)					
Follow-Up	STPI*	# Deaths	Person-Years	Hazard Ratio (95% CI) Age/Sex Adjusted	Hazard Ratio (95% CI) Fully Adjusted**
0-10 years	90th	300	15,143	1.00 (reference)	1.00 (reference)
	>90th	24	1,533	1.06 (0.69-1.62)	1.17 (0.74-1.86)
0-3 years	90th	131	4,982	1.00 (reference)	1.00 (reference)
	>90th	11	493	1.07 (0.57-2.01)	1.49 (0.77-2.89)
3-10 years	90th	169	10,161	1.00 (reference)	1.00 (reference)
	>90th	13	1,040	1.05 (0.59-1.88)	1.05 (0.55-2.00)
Anger and Cardiovascular Mortality (n=1957)					
Follow-Up	STPI*	# Deaths	Person-Years	Hazard Ratio (95% CI) Age/Sex Adjusted	Hazard Ratio (95% CI) Fully Adjusted**
0-10 years	90th	305	15,216	1.00 (reference)	1.00 (reference)
	>90th	21	1,576	0.95 (0.60-1.50)	1.08 (0.65-1.78)
0-3 years	90th	134	5,014	1.00 (reference)	1.00 (reference)
	>90th	7	503	0.69 (0.32-1.51)	0.99 (0.44-2.21)
3-10 years	90th	171	10,202	1.00 (reference)	1.00 (reference)
	>90th	14	1,073	1.16 (0.66-2.05)	1.15 (0.60-2.21)

* STPI = State-Trait Personality Inventory Score

** Adjusted for age, sex, body mass index, body mass index², marital status, race, educational attainment, smoking, previous myocardial infarction, previous congestive heart failure, previous angina, diabetes mellitus, hypertension, non-cardiac comorbidities (respiratory disease, renal failure, cancer, stroke), previous cardiac medication use (aspirin, beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors, lipid drugs, diuretics), thrombolysis, frequency of physical activity, neighborhood household income, and alcohol consumption.

Adjusted hazard ratios and 95% confidence intervals (CI) for the association between a high score on anxiety, anger, or both scales and all-cause mortality among participants of the Myocardial Infarction Onset Study followed for 10 years.

Table 4

Follow-Up	STPI*	# Deaths	Person-Years	Hazard Ratio (95% CI)	
				Age/Sex Adjusted	Fully Adjusted**
0-10 years	Low Anxiety/Low Anger	455	14,341	1.00 (reference)	1.00 (reference)
	High Anxiety, High Anger, or Both	62	2,241	1.19 (0.90-1.57)	1.30 (0.96-1.75)
0-3 years	Low Anxiety/Low Anger	172	4,726	1.00 (reference)	1.00 (reference)
	High Anxiety, High Anger, or Both	28	720	1.44 (0.95-2.18)	1.79 (1.14-2.79)
3-10 years	Low Anxiety/Low Anger	283	9,615	1.00 (reference)	1.00 (reference)
	High Anxiety, High Anger, or Both	34	1,521	1.04 (0.72-1.51)	1.02 (0.68-1.54)

* STPI = State-Trait Personality Inventory Score

** Adjusted for age, sex, body mass index, body mass index², marital status, race, educational attainment, smoking, previous myocardial infarction, previous congestive heart failure, previous angina, diabetes mellitus, hypertension, non-cardiac comorbidities (respiratory disease, renal failure, cancer, stroke), previous cardiac medication use (aspirin, beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors, lipid drugs, diuretics), thrombolysis, frequency of physical activity, neighborhood household income, and alcohol consumption.