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The Relation of Psychosocial Distress With Myocardial Perfusion and Stress-Induced Myocardial Ischemia

Pratik Pimple, MBBS, MPH,

Department of Epidemiology Rollins School of Public Health, Emory University

Muhammad Hammadah, MD,

Department of Medicine, Division of Cardiology, Emory University

Kobina Wilmot, MD, MSCR,

Department of Medicine, Division of Cardiology, Emory University

Ronnie Ramadan, MD,

Department of Medicine, Division of Cardiology, Emory University

Ibhar Al Mheid, MD,

Department of Medicine, Division of Cardiology, Emory University

Oleksiy Levantsevych, MD,

Department of Medicine, Division of Cardiology, Emory University

Samaah Sullivan, PhD,

Department of Epidemiology Rollins School of Public Health, Emory University

Bruno B. Lima, MD, PhD,

Department of Medicine, Division of Cardiology, Emory University

Jeong Hwan Kim, MD,

Department of Medicine, Division of Cardiology, Emory University

Ernest V. Garcia, PhD,

Department of Radiology & Imaging Science, Emory University School of Medicine

Jonathon Nye, PhD,

Department of Radiology & Imaging Science, Emory University School of Medicine

Amit J. Shah, MD, MSCR,

Department of Epidemiology Rollins School of Public Health, Emory University ; Department of Medicine, Division of Cardiology, Emory University

Laura Ward, MPH,

Department of Biostatistics & Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, Georgia

Address correspondence to Pratik Pimple, MBBS, MPH, Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Rd NE, Atlanta, CA 30322. ppimple@emory.edu.

All the authors had access to the data and a significant contribution in either data collection or design, data analysis, and execution of the article. All authors contributed to the writing of the article.

Paolo Raggi, MD,

Mazankowski Alberta Heart Institute, University of Alberta, Edmonton, Alberta, Canada

J. Douglas Bremner, MD,

Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia.

John Hanfelt, PhD,

Department of Biostatistics & Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, Georgia

Tené T. Lewis, PhD,

Department of Epidemiology Rollins School of Public Health, Emory University

Arshed A. Quyyumi, MD,

Department of Medicine, Division of Cardiology, Emory University

Viola Vaccarino, MD, PhD

Department of Epidemiology Rollins School of Public Health, Emory University ; Department of Medicine, Division of Cardiology, Emory University

Abstract

Objective: Mental stress–induced myocardial ischemia is a frequent phenomenon in patients with coronary artery disease (CAD). The link between an integrated measure of chronic psychosocial distress and mental stress–induced myocardial ischemia, and whether it differs by sex, has not been examined before.

Methods: We used latent class analysis to derive a composite measure of psychosocial distress integrating scales of depression, posttraumatic stress, anxiety, anger, hostility, and perceived stress in 665 individuals with stable CAD. Participants underwent myocardial perfusion imaging with mental stress and perfusion defects were quantified at rest (summed rest score), with mental stress (summed stress score), and their difference (summed difference score), the latter being an index of inducible ischemia.

Results: The M (SD) age was 63 (9) years, and 185 (28%) were women. Latent class analysis characterized the study sample into four distinct classes of incremental psychosocial distress. In women, class 4 (highest distress) had an adjusted 4.0-point higher summed rest score (95% confidence interval = 0.2–7.7) as compared with class 1 (lowest distress), whereas no difference was observed in men (–0.87 points, 95% confidence interval = –3.74 to 1.99, $p = .04$ for interaction). There was no association between the psychosocial distress latent variable and summed difference score in either women or men.

Conclusions: Among patients with CAD, a higher level of psychosocial distress is not associated with mental stress ischemia, but it is associated with more resting (fixed) perfusion abnormalities in women only, as well as with blunted hemodynamic response to mental stress in both men and women.

Keywords

cardiovascular disease; ischemia; psychosocial stress; sex differences

INTRODUCTION

Mental stress–induced myocardial ischemia (MSIMI) is a transient myocardial ischemic response to mental stress (1), which can be induced in patients with coronary artery disease (CAD) during a standardized mental stress challenge (1). MSIMI is associated with a twofold increase in risk of future cardiac events, which is similar to ischemia induced by conventional stress testing (exercise or pharmacological stress testing) (2). MSIMI, however, seems to be a unique phenomenon, because it occurs at lower levels of oxygen demand and is usually not related to severity of CAD (1,3). Furthermore, MSIMI has been associated with myocardial ischemia measured in daily life ambulatory monitoring (3,4). These features suggest that MSIMI is not a direct reflection of underlying CAD severity. Rather, it is possible that the level of psychosocial burden is a unique contributing factor in MSIMI, independent of CAD severity.

Published literature on the association between indicators of psychosocial distress and MSIMI has provided conflicting results (5-11). In some studies, depression was associated with MSIMI, irrespective of whether ischemia was measured using perfusion imaging (7,11) or echocardiography (5). On the other hand, depression was not associated with MSIMI in the Psychophysiological Investigation of Myocardial Ischemia Study (9). Anger and/or hostility was associated with MSIMI in two studies using nuclear imaging techniques (6,10), but this association was nonsignificant in other studies that used echocardiography (5) or perfusion imaging (9). Neither anxiety (5,9) nor perceived stress (5) was found to be associated with MSIMI in published literature.

Previous studies investigating the association between psychosocial factors and MSIMI treated each psychosocial phenotype as an independent exposure, and none have taken into account and integrated individual psychosocial attributes more broadly. One reason why an integrative approach may be useful is that psychosocial factors may share biological or behavioral substrates, explaining why they tend to correlate and cluster with each other (12). Examining them together may provide new insights onto specific psychosocial profiles that are relevant for MSIMI and cardiovascular risk.

In the current study, we investigated the association between a composite measure of psychosocial distress, derived using latent class analysis (LCA), and myocardial perfusion abnormalities at rest and with mental stress. Our composite measure integrated measures of depression, posttraumatic stress disorder (PTSD), anxiety, anger, hostility, and perceived stress. A similar composite measure of psychosocial distress was recently developed in stable patients with CAD and found to be modifiable (13). Because women with CAD have a higher prevalence of psychosocial distress relative to men (14), as well as a higher prevalence of MSIMI (15,16), we explored whether the previous associations differed by sex.

METHODS

Study Sample

Between June 2011 and October 2014, we enrolled 695 individuals with stable CAD from Emory University–affiliated hospitals and clinics for the Mental Stress Ischemia: Prognosis and Genetic Influences Study. This research was approved by the Emory University Institutional Review Board, and all participants provided informed consent. A detailed protocol with inclusion and exclusion criteria has been previously described (17). Briefly, study participants between ages 30 to 80 years were enrolled if they had significant history of CAD during their lifetime (previous myocardial infarction [MI], bypass surgery or percutaneous intervention, positive nuclear scan/exercise stress test, angiographically proven major coronary vessel disease, or abnormal coronary ultrasound). Participants were excluded if they had a history of unstable angina or acute MI within the previous week of enrollment, severe comorbid medical or psychiatric disorders, uncontrolled hypertension, pregnancy or breastfeeding, chronic inflammatory disorders, organ transplant, or were receiving dialysis.

Stress Testing Procedures

Mental stress was induced by a standardized social stressor using a public speaking task, as previously described (17). Briefly, each individual was asked to imagine a real-life stressful situation and to make up a realistic story around this scenario. They were given 2 minutes to plan the story and 3 minutes to present it in front of a video camera and a small audience wearing white coats. Individuals were told that their speech would be evaluated by the laboratory staff for content, quality, and duration. We conducted continuous blood pressure and heart rate monitoring during the resting stage (every 5 minutes) and during mental stress (every 1 minute). We calculated the rate-pressure product as the mean systolic blood pressure times the mean heart rate at rest. Hemodynamic reactivity was calculated as the rate-pressure product during stress minus the rate-pressure product at rest.

Myocardial Perfusion Imaging

Each study participant underwent two single-photon emission tomography (SPECT) imaging studies; at rest, and with mental stress, with ^{99m}Tc -Sestamibi, at the dose of 10–14 mCi for rest imaging and 30 to 40 mCi for stress imaging, based on weight.

SPECT images were interpreted using accepted methodology by two experienced readers blinded to patients' data using a 17-segment model. Disagreements between the two readers were resolved by consensus and a third reader if needed. Each myocardial segment was scored from 0 (no abnormality) to 4 (absent perfusion), and summed scores were calculated in a conventional fashion, yielding a summed stress scores (SSS) for mental stress, and a summed rest score (SRS) for rest, each with a theoretical range of 0 to 68. A summed difference score (SDS) was calculated for mental stress by subtracting the SRS from the SSS. The SDS is a semiquantitative measure of the number and severity of reversible (ischemic) myocardial perfusion defects (18).

Assessment of Psychosocial Distress

Our global distress measure integrated intrinsic dimensions (i.e., psychological characteristics) previously used in a composite measure developed by Blumenthal et al. (13), which included scales of depression, anxiety, anger, and perceived general stress. To these components, we added scales of PTSD and hostility, given their recognized importance for cardiovascular risk (19,20).

We assessed depressive symptoms using the Beck Depression Inventory (BDI-II), a 21-item self-administered scale with excellent internal consistency (Chronbach's $\alpha = 0.91$) (21). Because symptom dimensions of the BDI may differ in their association with cardiovascular outcomes (22), we calculated two separate subscales: negative affect (8 items) and somatic symptoms (13 items) (21). PTSD symptoms were assessed using the PTSD Symptom Checklist (PCL), civilian version, a 17-item scale (Chronbach's $\alpha = 0.94$) (23). Trait anxiety was measured with the State-Trait Anxiety Inventory (STAI) (Chronbach's $\alpha = 0.95$) (24). To measure trait anger, we used the Spielberger's State-Trait Anger Expression Inventory (STAXI) (Chronbach's $\alpha > 0.8$) (25) to measure hostility we administered the Cook-Medley Hostility Scale (CMHS) (26) and to assess general perceived stress we used the Perceived Stress Scale (Chronbach's $\alpha = 0.84$) (27).

Using the previous psychological measures, we developed a latent psychosocial distress construct using LCA (28,29). A latent construct is a variable that is not directly observed or measured but that is constructed through observed related variables (28,29). LCA models are based on the assumption that observed indicator variables are associated with each other because of an underlying unobserved factor, rather than being directly related (28). Using structural equation modeling, LCA creates a categorical latent variable based on the designated observed indicators through maximum likelihood estimation (28,29).

We also performed a sensitivity analysis using the traditional approach of creating a composite score of our psychosocial distress scales. We first converted each psychological scale into a *z* score variable by subtracting the mean of each scale from each individual's reported score and then dividing the resulting score by the standard deviation (SD) of each scale. We then summed these individual *z* scores (a total of seven *z* scores, corresponding to seven psychological scales) to derive a composite psychological distress index.

Other Study Measures

We used validated instruments to collect demographic, behavioral, social, and health status data. Angiographic data and left ventricular ejection fraction were obtained from the most recent coronary angiogram documented in the patient's medical record. CAD severity was quantified using a cutoff of 70% blockage in any major artery. We also assessed a number of extrinsic psychosocial dimensions, i.e., those related to the social environment or other external exposures, which may act as a psychological stressor and/or result in increased levels of perceived psychological distress. These included exposure to traumatic events, which were measured using the Early Trauma Inventory, short form, for events before the age of 18 years and the Lifetime Trauma Inventory (LTI) for events after the age of 18 years (30); exposure to discrimination, assessed through the Everyday Discrimination Scale (31);

and perceived social support, assessed using the Multidimensional Scale of Perceived Social Support (MSPSS) (32).

Statistical Analysis

LCA was carried out using Latent Gold software (33). The seven psychosocial scales mentioned previously (somatic and cognitive depressive symptoms, PTSD symptoms, anxiety, anger, hostility, and perceived stress) were used as the loading factors. To assess the proper fit of the model (i.e., the minimum number of latent classes needed to get the best fit of the maximum likelihood), we used established criteria, including Bayesian information criteria, entropy, the bootstrap likelihood ratio test, and the Integrated Classification Likelihood criteria (28,29).

We compared study participant characteristics according to categories of the psychosocial distress LCA variable using either the analysis of variance test for continuous, normally distributed variables or the χ^2 test for categorical variables. We also examined whether the psychosocial distress LCA variable was associated with hemodynamic responses to stress, by comparing the change in rate-pressure product according to psychosocial distress class using linear regression models. For our main analyses, we performed two separate multivariable linear regression models with resting myocardial perfusion defects (SRS), and ischemia with mental stress (mental stress SDS) as outcomes, and the psychosocial distress LCA categorical variable as the main predictor variable. Because the SDS for mental stress had a skewed distribution, whereas the SRS was approximately normally distributed, we used the SRS score as dependent variables while adjusting for the rest score (SRS). Because of the mathematical relationship between these scores, the coefficient from a model with SRS as dependent variable, adjusted for SRS, is identical to that from a model where the dependent variable is the SDS. This strategy allowed us to obtain less biased standard errors and *p* values. We adjusted for a priori chosen covariates, including sociodemographic characteristics (age, sex, race, education less than or equal to high school education), CAD risk factors, and severity indicators, which might be on the pathway between stress and disease (smoking status, hypertension, dyslipidemia, diabetes, body mass index [BMI], and previous revascularization). We did not consider CAD severity based on angiographic data because of missing values in 84 participants. In separate models, we explored sex as an effect modifier for the association between psychosocial distress and perfusion measures. We used SAS Version 9.3 (Cary, NC) for the analysis, with an α level of 0.05 for statistical significance.

RESULTS

Sample Characteristics

Thirty of the total of 695 participants had missing information on either exposure or outcome, leaving an analytical sample size of 665. The M (SD) age of the study sample was 63 (9) years, 185 (28%) were women, 198 (30%) were African Americans, and 169 (25%) had less than or equal to high school education (Table 1). As expected, the prevalence of cardiovascular risk factors was high in this sample, including hypertension (76%), dyslipidemia (82%), and type 2 diabetes (32%). Furthermore, 37% had a previous MI, and

77% had a previous revascularization procedure. When patient characteristics were examined by sex (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A541>), women were more likely to be African American and had a higher BMI and a higher ejection fraction. Women also had higher levels of psychosocial factors (symptoms of depression and PTSD, anxiety, and perceived stress) than men and a higher use of antidepressant medications.

LCA classified the study sample into four classes (Figure 1, Supplemental Table 2, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A541>). Class 1 had 268 participants, with the lowest scores for all psychosocial scales, with the class level mean scores ranging from 0.5 to 0.75 SDs below the sample mean. Class 2 had 112 participants and showed similar psychosocial scale mean scores as class 1, except for depressive symptoms. Class 3 had 208 participants, with all scale mean scores 0.25 to 0.5 SD above the mean. Finally, Class 4 had 77 participants, showing the highest psychosocial burden, with scale mean scores between 1.25 and 1.75 SD above the sample mean of each scale (Figure 1). The choice of a four-class solution was based on Akaike information criterion, Bayesian information criterion, and Integrated Completed Likelihood-Bayesian information criterion (Supplemental Table 3, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A541>). We also took into account differences in within-class distribution of psychosocial distress scale scores for each solution, to have parsimonious classes with satisfactory separation.

Study participants with higher psychosocial distress (higher latent class) were younger (57 years in class 4 versus 65 years in class 1), more likely to be female, and African American (Table 1). Among life-style and medical history factors, only BMI and history of previous MI were significantly different according to psychosocial distress level, with higher distress classes showing greater BMI and a higher frequency of history of MI. Medication use was similar between the groups, except for β -blockers, antidepressants, and anxiolytics, which were more common in higher distress categories. As expected, higher classes of the psychosocial distress latent variable were associated with significantly more traumatic events, more reports of discrimination, and lower perceived social support (Table 1).

Association Between Psychosocial Distress and Hemodynamic Changes With Stress

In the overall study sample, the M (SD) systolic blood pressure increased with mental stress by 26 (16) mm Hg and heart rate increased by 11 (9) beats per minute, with a change in rate-pressure product of 3505 (2,326) units.

Participants with higher psychosocial distress showed a blunted hemodynamic response to mental stress, as shown by a decreasing rate-pressure product as psychosocial distress class increased ($p = .02$ for trend), with no meaningful sex differences (Figure 2). Further adjustment by antidepressant use changed minimally the results (an estimated 3% change in the coefficient for rate-pressure product, $p = .14$ for trend, data not shown).

Association Between Psychosocial Distress and SPECT Perfusion Defects With Mental Stress

In the overall sample, the M (SD) SRS was 5.1 (8.7) units, and the M (SD) SSS with mental stress was 6.0 (9.2) units. The M (SD) SDS, quantifying inducible ischemia with mental stress, was 0.8 (2.0) units. Women had lower SRS (M [SD] = 3.6 [7.2]) and SSS (M [SD] = 4.5 [7.8]) than men (M [SD] = 5.7 [9.2], and 6.5 [9.7], respectively), but no difference was found in SDS in women (M [SD] = 0.9 [2.4]) versus men (M [SD] = 0.7 [1.8]). Overall, 75 (12%) participants had MSIMI (defined as SDS ≥ 3), with no significant differences by sex (11% in men versus 12% in women).

Although the psychosocial distress latent variable was not related to resting perfusion defects in the overall sample (Table 2), there was an interaction by sex (Table 3, Figure 3). In women, higher psychosocial distress was associated with a higher level of resting perfusion defects (SRS score). After adjusting for sociodemographic characteristics, CAD risk factors, and CAD severity indicators, as compared with LCA class 1 (no/low distress), class 4 (high distress) was associated with an adjusted 3.98-point higher SRS (95% confidence interval [CI] = 0.22 to 7.73) among women. Women with higher psychosocial distress also showed more perfusion defects with mental stress (Figure 3), but this difference was driven by resting perfusion defects, because there was no difference in inducible ischemia (SDS score) (Table 3). Among men, there were no differences in resting or inducible perfusion defects by psychosocial distress class; the interaction between sex and psychosocial distress class was significant for resting perfusion ($p = .04$). Similar results were found when we used a composite z score as the indicator of psychosocial distress instead of LCA variable (Table 3). Even after adjusting for hemodynamic changes with mental stress (rate-pressure product), results did not change (data not shown).

When we performed these analyses using individual scales instead of the latent variable, we found, overall, similar results (Table 4). After applying the Bonferroni correction for multiple testing (p cutoff of $0.05/7 = 0.007$), none of the individual scales showed a statistically significant interaction with sex, but in women, there was a significant association between the SRS score and anxiety (STAI anxiety trait score) and perceived stress (Perceived Stress Scale score).

DISCUSSION

Among individuals with stable CAD, we observed that psychosocial distress, defined as a composite measure of psychosocial scales (depression, PTSD, anxiety, anger, hostility, and perceived stress) using LCA, was not associated with MSIMI, overall and in sex-stratified analysis. However, women with higher psychosocial distress showed significantly higher resting perfusion defects, whereas there was no such association in men. These findings were independent of traditional CAD risk factors.

Although this is the first study examining the relationship between a composite measure of psychosocial distress and myocardial perfusion, previous investigations that evaluated individual psychosocial risk factors have provided conflicting results (5-11). For example,

depression was found to be associated with MSIMI in some studies (5,7,11), but not in others (9).

Higher hemodynamic response to stress is one of the postulated mechanisms for MSIMI (1). In a published study from the same cohort, a higher increase in rate-pressure product with mental stress, a measure of hemodynamic response to stress, was independently associated with MSIMI (34). In our analysis, higher psychosocial distress was associated with blunted hemodynamic response to stress, which is consistent with previous studies (35). These findings could be partially due to underlying differences among distress groups (like health behaviors and medication use), but a blunted hemodynamic response has gained recognition as being potentially unhealthy (36). However, even after adjusting for rate-pressure product with mental stress, we found no association between psychosocial distress and MSIMI.

Another reason for a lack of association between psychosocial distress and MSIMI might be the presence of collider bias. Because all our participants have a history of CAD, there could be selection bias affecting the results, and traditional confounding adjustment may not be sufficient to correct for this bias (37).

Although our psychosocial distress composite variable was not associated with ischemia, it was related to a higher degree of resting perfusion abnormalities among women. Few previous studies have examined this issue. Boyle et al. (5) found a significant association between resting wall-motion abnormalities and depression, whereas Burg et al. (7) did not find a relationship between depression and resting myocardial perfusion; both these studies, however, reported an association between depression and a measure of MSIMI. However, these studies did not examine sex differences. Our results of a positive association between psychosocial distress and resting perfusion abnormalities in women may underline the influence of chronic stressors on CAD burden in this group (38). The fact that we found this association in women only may underscore a vulnerability of women with CAD toward the chronic effects of stress on the cardiovascular system. Alternatively, because of the cross-sectional nature of our analyses, the psychosocial distress indicator could index distress that is a consequence of previous infarcts, especially among women. However, our results mirror previous findings of an association of depression with CAD burden and cardiovascular outcomes that was stronger in women than in men (39,40). Furthermore, in the large interheart study, a composite measure of psychosocial distress yielded a 40% population attributable risk for acute MI in women, whereas for men, the same attributable risk was only 25% (41).

Our study has several strengths. To the best of our knowledge, this is the first study to investigate the association between a comprehensive measure of psychosocial distress and myocardial ischemic responses to acute emotional stress using LCA of multiple observed psychosocial phenotypes. This is also the largest study of mental stress ischemia using myocardial perfusion imaging, because previous studies had sample sizes of less than 500 participants. Myocardial perfusion imaging remains the state-of-the-art method for ischemia assessment, and scans were read by experienced readers according to established protocols.

Our study has also some limitations. Because the LCA variable is not directly observed, there is a possibility that our psychosocial distress construct was not a proper representation of true underlying distress. However, we believe that our latent class variable was a valid measure, because there was a clear separation of psychological scale score levels across classes. Furthermore, results for each observed psychosocial phenotype showed similar trends when analyzed separately. Another limitation is that the extent of ischemia with mental stress was relatively mild, which may have influenced our study power. We used a validated public speaking task as mental stressor in conjunction with myocardial perfusion imaging; this technique did not allow us to use multiple mental stressors, which could have contributed to underdiagnosing MSIMI. However, perfusion imaging is the criterion standard for evaluation of myocardial ischemia. An important advantage of this method is that [^{99m}Tc] sestamibi, once injected during mental stress, is trapped in the myocyte, and thus, it provides a “snapshot” of perfusion unobtrusively during the speech task, whereas scanning occurs later. This eliminates measurement errors because of patients' position and other logistical and distracting factors related the scanning procedure, such as having to lay down still in the scanner. A disadvantage, however, is that only one stress task is feasible with this method. The validity of using multiple tasks in a single session has been questioned, however, given the known protracted effects of mental stress on vascular regulation (42). Another limitation is the lack of correction for breast artifacts and diaphragmatic attenuation. However, each perfusion image was independently evaluated by two experienced readers with disagreements resolved by a third reader. The readers were blinded to the sex of the patient and to any other study factors. Thus, this bias would likely lead to nondifferential misclassification, which would bias results toward the null. Finally, because this is a cross-sectional study, we cannot infer casualty and it is not possible to ascertain whether some of the risk factors adjusted for in the analysis are mediators or confounders of the associations.

In conclusion, we found that among patients with CAD, a higher level of psychosocial distress is not associated with ischemia provoked by mental stress, but, in women only, it is associated with more resting perfusion abnormalities, as well as with a blunted hemodynamic response to mental stress in both men and women. Although the exact implications of these findings need to be evaluated in the context of future outcome studies, they suggest that chronic psychosocial distress, considered as a global measure, may affect the severity of CAD more than ischemia provoked by acute stress exposure, especially among women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Glossary

BDI	Beck Depression Inventory
BMI	body mass index
CAD	coronary artery disease
CMHS	Cook-Medley Hostility Scale
ETI	early trauma inventory
LCA	latent class analysis
LTI	Lifetime Trauma Inventory
MI	myocardial infarction
MSIMI	mental stress-induced myocardial ischemia
PTSD	posttraumatic stress disorder
SDS	summed difference score
SPECT	single-photon emission tomography
SRS	summed rest score
SSS	summed stress score
STAI	State-Trait Anxiety Inventory
STAXI	State-Trait Anger Expression Inventory

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FIGURE 1.

Panel plot of the psychosocial distress LCA variable, according to individual scale levels. The graph shows the distribution of each latent class according to the individual psychosocial scale z scores (scale score – sample mean/sample SD). Color image is available only in online version (www.psychosomaticmedicine.org).

FIGURE 2.

Hemodynamic change with stress (rate-pressure product difference), stratified by sex, according to Psychosocial Distress Latent Classes. Estimates are adjusted for age, sex, race, education, smoking, and body mass index. Color image is available only in online version (www.psychosomaticmedicine.org).

FIGURE 3.

Perfusion defect severity (mean summed scores) at rest and with stress, stratified by sex, according to Psychosocial Distress Latent Classes. In women, but not in men, higher psychosocial distress was associated with more perfusion defects (denoting abnormal myocardial perfusion), which were already present at rest. Color image is available only in online version (www.psychosomaticmedicine.org).

TABLE 1.
Descriptive Characteristics of the Study Sample According to Latent Classes of Psychosocial Distress

Variables	Class 1 (No/Low Symptoms) (<i>n</i> = 268)	Class 2 (Mild Symptoms) (<i>n</i> = 112)	Class 3 (Moderate Symptoms) (<i>n</i> = 208)	Class 4 (High Symptoms) (<i>n</i> = 77)	Total Sample (<i>N</i> = 665)
Demographic factors					
Age, M (SD) *	65 (8)	66 (8)	61 (9)	57 (9)	63 (9)
Women, <i>n</i> (%) *	62 (23)	21 (19)	71 (34)	31 (40)	185 (28)
African American, <i>n</i> (%) *	70 (26)	21 (19)	77 (37)	30 (39)	198 (30)
Education high school, <i>n</i> (%)	64 (24)	21 (19)	57 (27)	27 (35)	169 (25)
Lifestyle factors and medical history					
Current smokers, <i>n</i> (%)	33 (12)	8 (7)	42 (20)	11 (14)	94 (14)
Hypertension, <i>n</i> (%)	202 (75)	87 (78)	158 (76)	61 (79)	508 (76)
Dyslipidemia, <i>n</i> (%)	220 (82)	91 (81)	166 (80)	67 (87)	544 (82)
Diabetes, <i>n</i> (%)	83 (31)	30 (27)	76 (36)	27 (35)	216 (32)
BMI, M (SD) *	29 (5)	29 (4)	30 (6)	32 (6)	30 (5)
Previous MI, <i>n</i> (%) *	91 (34)	34 (30)	93 (44)	31 (40)	249 (37)
History of heart failure, <i>n</i> (%)	29 (11)	15 (13)	32 (15)	17 (22)	93 (14)
Previous revascularization, <i>n</i> (%)	207 (77)	85 (76)	158 (76)	60 (78)	510 (77)
Ejection fraction in %, M (SD)	70 (14)	67 (14)	68 (13)	69 (14)	69 (14)
CAD 70% stenosis, <i>n</i> (%) ^a	210 (86)	84 (85)	139 (82)	55 (83)	488 (84)
Current medications					
Statins, <i>n</i> (%)	225 (84)	97 (87)	183 (89)	62 (81)	567 (86)
β-Blockers, <i>n</i> (%) *	185 (69)	82 (73)	163 (79)	65 (85)	495 (75)
ACE inhibitors, <i>n</i> (%)	126 (47)	52 (46)	89 (43)	35 (45)	302 (46)
Aspirin, <i>n</i> (%) *	233 (87)	98 (87)	186 (90)	55 (71)	572 (86)
Antidepressants, <i>n</i> (%) *	34 (13)	20 (18)	58 (28)	40 (52)	152 (22)
Anxiolytics, <i>n</i> (%) *	12 (4)	14 (13)	21 (10)	9 (12)	56 (8)
Extrinsic psychosocial factors					
ETI score, M (SD) *	5 (4)	6 (4)	8 (5)	10 (6)	7 (5)
LTI score, M (SD) *	16 (9)	18 (9)	20 (10)	23 (13)	18 (10)

Variables	Class 1 (No/Low Symptoms) (<i>n</i> = 268)	Class 2 (Mild Symptoms) (<i>n</i> = 112)	Class 3 (Moderate Symptoms) (<i>n</i> = 208)	Class 4 (High Symptoms) (<i>n</i> = 77)	Total Sample (<i>N</i> = 665)
EDS score, M (SD) ^a	13 (4)	13 (4)	16 (4)	20 (6)	15 (5)
Perceived social support score, M(SD) ^{a,b}	73 (12)	70 (11)	64 (15)	53 (17)	67 (15)

SD = standard deviation; MI = myocardial infarction; BMI = body mass index; CAD = coronary artery disease; ETI = early trauma inventory (total score); LTI = life-traumatic events (total score); EDS = Everyday Discrimination Scale (total score).

^a *p* < .05.

^a CAD severity based on coronary angiography results before revascularization procedures (if any); 86 observations missing.

^b For perceived social support scale, a higher score indicates better social support.

TABLE 2.

Association of Latent Classes and the Composite Score of Psychosocial Distress With Perfusion Defect Severity at Rest (SRS) and Induced Ischemia Severity (SDS) With Mental Stress in the Overall Sample

Exposure Comparison	Full Sample: Unadjusted β (95% CI)	Full Sample: Adjusted ^a β (95% CI)
SRS		
LCA class 1 versus 2	0.31 (−1.62 to 2.23)	0.35 (−1.54 to 2.25)
LCA class 1 versus 3	0.71 (−0.88 to 2.30)	0.80 (−0.78 to 2.39)
LCA class 1 versus 4	0.73 (−1.49 to 2.95)	0.88 (−1.41 to 3.16)
Composite z score	0.17 (−0.50 to 0.84)	0.11 (−0.59 to 0.81)
SDS		
LCA class 1 versus 2	0.01 (−0.44 to 0.45)	0.04 (−0.41 to 0.48)
LCA class 1 versus 3	0.10 (−0.27 to 0.46)	0.04 (−0.34 to 0.41)
LCA class 1 versus 4	−0.19 (−0.71 to 0.32)	−0.31 (−0.86 to 0.23)
Composite z score	−0.14 (−0.29 to 0.02)	−0.20 (−0.37 to −0.03)

CI = confidence interval; SRS = summed rest score; LCA = latent class analysis; SDS = summed difference score.

β represents estimated point increase in perfusion defect score (either SRS for rest or SDS for stress) when comparing class 1 (reference) to class 2, 3, or 4 for LCA comparison and represents estimated point increase with 1 SD increase in composite z score.

^aResults adjusted for age, sex, race, education, history of smoking, hypertension, hyperlipidemia, diabetes, revascularization, body mass index, and summed rest score (for the SDS analysis only).

TABLE 3.

Association of Latent Classes and the Composite Score of Psychosocial Distress With Perfusion Defect Severity at Rest (SRS) and Induced Ischemia Severity (SDS) With Mental Stress, According to Sex

Exposure Comparison	Men: Unadjusted β (95% CI)	Men: Adjusted ^d β (95% CI)	Women: Unadjusted β (95% CI)	Women: Adjusted ^d β (95% CI)	p Value for Sex Interaction
SRS					
LCA class 1 versus 2	0.03 (-2.23 to 2.30)	-0.02 (-2.14 to 2.10)	0.71 (-2.76 to 4.19)	1.62 (-2.63 to 5.87)	0.50
LCA class 1 versus 3	0.64 (-1.35 to 2.64)	0.41 (-1.45 to 2.28)	1.88 (-0.53 to 4.29)	1.98 (-0.99 to 4.96)	0.38
LCA class 1 versus 4	-0.26 (-3.22 to 2.71)	-0.87 (-3.74 to 1.99)	3.61 (0.59 to 6.64)	3.98 (0.22 to 7.73)	0.04
Composite z score	-0.17 (-0.97 to 0.63)	-0.41 (-1.24 to 0.41)	1.30 (0.11 to 2.50)	1.26 (0.05 to 2.46)	0.02
SDS					
LCA class 1 versus 2	-0.11 (-0.57 to 0.34)	-0.08 (-0.57 to 0.42)	0.50 (-0.70 to 1.70)	0.44 (-0.56 to 1.44)	0.37
LCA class 1 versus 3	-0.14 (-0.53 to 0.27)	-0.15 (-0.59 to 0.29)	0.58 (-0.25 to 1.42)	0.52 (-0.18 to 1.22)	0.11
LCA class 1 versus 4	-0.27 (-0.87 to 0.33)	-0.30 (-0.98 to 0.38)	-0.06 (-1.13 to 1.00)	-0.16 (-1.06 to 0.73)	0.81
Composite z score	-0.16 (-0.34 to 0.03)	-0.19 (-0.39 to 0.01)	-0.17 (-0.46 to 0.11)	-0.22 (-0.50 to 0.07)	0.90

CI = confidence interval; SRS = summed rest score; LCA = latent class analysis; SDS = summed difference score.

β represents estimated point increase in perfusion defect score (either SRS for rest or SDS for stress) when comparing class 1 (reference) to class 2, 3, or 4 for LCA comparison and represents estimated point increase with 1 SD increase in composite z score.

^dResults adjusted for age, sex, race, education, history of smoking, hypertension, hyperlipidemia, diabetes, revascularization, body mass index, and summed rest score (for the SDS analysis only).

TABLE 4.

Association of Individual Psychosocial Indicators With Perfusion Defect Severity at Rest (SRS) and Induced Ischemia Severity (SDS), Overall and According to Sex

Exposure Comparison	Full Sample: Unadjusted β (95% CI)	Full Sample: Adjusted β (95% CI)	Men: Adjusted ^a β (95% CI)	Women: Adjusted ^a β (95% CI)	<i>p</i> for Sex Interaction
SRS					
BDI somatic score	0.10 (−0.56 to 0.77)	0.18 (−0.50 to 0.86)	−0.17 (−0.99 to 0.64)	0.89 (−0.26 to 2.05)	.13
BDI negative affect score	0.14 (−0.53 to 0.81)	0.09 (−0.59 to 0.77)	−0.25 (−1.05 to 0.55)	0.95 (−0.32 to 2.23)	.11
PCL score	−0.24 (−0.91 to 0.42)	−0.16 (−0.84 to 0.52)	−0.55 (−1.39 to 0.28)	0.60 (−0.55 to 1.75)	.10
STAI anxiety trait score	0.41 (−0.25 to 1.08)	0.30 (−0.39 to 0.99)	−0.23 (−1.04 to 0.57)	1.61 (0.37 to 2.84)	.01
STAXI anger trait score	0.02 (−0.64 to 0.68)	0.08 (−0.59 to 0.74)	−0.20 (−0.98 to 0.57)	0.84 (−0.42 to 2.10)	.17
CMHS hostility score	0.23 (−0.44 to 0.89)	−0.02 (−0.72 to 0.67)	−0.32 (−1.13 to 0.48)	0.80 (−0.48 to 2.08)	.14
Perceived stress score	0.23 (−0.43 to 0.90)	0.19 (−0.51 to 0.88)	−0.40 (−1.23 to 0.44)	1.38 (0.19 to 2.55)	.02
SDS					
BDI somatic score	−0.02 (−0.17 to 0.13)	−0.06 (−0.23 to 0.10)	−0.09 (−0.29 to 0.10)	−0.01 (−0.28 to 0.28)	.60
BDI negative affect score	−0.08 (−0.24 to 0.08)	−0.12 (−0.28 to 0.04)	−0.13 (−0.32 to 0.06)	−0.08 (−0.38 to 0.23)	.77
PCL score	−0.08 (−0.23 to 0.08)	−0.11 (−0.27 to 0.05)	−0.07 (−0.26 to 0.13)	−0.19 (−0.46 to 0.09)	.52
STAI anxiety trait score	−0.14 (−0.30 to 0.01)	−0.21 (−0.37 to −0.05)	−0.19 (−0.38 to −0.01)	−0.25 (−0.55 to 0.04)	.73
STAXI anger trait score	−0.17 (−0.32 to −0.01)	−0.18 (−0.34 to −0.03)	−0.20 (−0.38 to −0.02)	−0.15 (−0.44 to 0.15)	.78
CMHS hostility score	−0.19 (−0.34 to −0.04)	−0.24 (−0.40 to −0.08)	−0.16 (−0.34 to 0.03)	−0.44 (−0.74 to −0.14)	.11
Perceived stress score	−0.05 (−0.21 to 0.11)	−0.12 (−0.29 to 0.05)	−0.14 (−0.34 to 0.06)	−0.08 (−0.36 to 0.21)	.71

CI = confidence interval; SRS = summed rest score; BDI = Beck Depression Inventory; PCL = PTSD Symptom Checklist (Civilian); STAI = State-Trait Anxiety Inventory; STAXI = State-Trait Anger Expression Inventory; CMHS = Cook-Medley Hostility Score; SDS = summed difference score.

β represents estimated point increase in perfusion defect score (either SRS for rest or SDS for stress) with 1 SD increase in each psychosocial scale.

^aResults adjusted for age, sex, race, education, history of smoking, hypertension, hyperlipidemia, diabetes, revascularization, body mass index, and summed rest score (for the SDS analysis only).