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Social Support and Mental Stress-Induced Myocardial Ischemia
Following a Myocardial Infarction

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
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ABSTRACT

Social Support and Mental Stress-Induced Myocardial Ischemia
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Introduction: Coronary artery disease (CAD) is an important public health issue. One of the manifestations of CAD is myocardial ischemia, which can be induced through mental stress or physical stressors such as exercise. Lack of social support has been identified as a psychosocial risk factor of CAD. The purpose of this analysis was to evaluate the role of social support in mental stress ischemia (MSI) and determine any sex differences.
Methods: Secondary analysis of the Myocardial Infarction and Mental Stress (MIMS) study, a cross-sectional study of 98 young (<60 years old) patients with a previous MI who have all undergone mental stress testing. Perfusion imaging scores at rest, after mental stress and after exercise stress were used to quantify ischemia under both stress conditions. Social support was measured with the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Social Support Inventory (ESSI). The ESSI score was analyzed as a continuous variable and divided into tertiles.
Results: We found a small inverse relationship between mental stress ischemia and ESSI score, but relationship was not statistically significant. The results were similar in men and women.
Conclusion: No association was found between social support and MSI and no sex differences were evident.

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INTRODUCTION

Chronic diseases in populations are major public health issues. Specifically, coronary artery disease (CAD) is the leading cause of death in both women and men. Myocardial ischemia, which is a decrease in blood flow to the heart relative to demands, can be induced through mental stress or exercise. Both types of ischemia have prognostic significance and can lead to subsequent cardiac events such as a myocardial infarction (MI), or heart attack.

One of the earliest studies on mental stress ischemia (MSI) determined that MSI is due to different mechanisms than that caused by exercise-induced ischemia (1). Several studies have determined that mental stress occurs in daily life from tasks such as presenting a speech, but MSI is usually without symptoms and occurs at low heart rate (1, 2). One study discovered that MSI occurs in about 20 % of CAD patients, but another study determined that acute mental stress could induce myocardial ischemia in approximately 40% to 70% of CAD patients (2, 3). Another recent study discovered that MSI occurs in about 12 % to 55 % of CAD patients but also MSI can possibly worsen exercise-induced ischemia in certain CAD patients (4). In fact, a meta-analysis of peer-reviewed publications determined that the incidence of MSI averaged about 30% in CAD patients but also many patients with MSI additionally have exercise-induced ischemia (5). However, in the most recent study involving mental stress testing of CAD patients, MSI was found to occur more frequently than exercise-induced ischemia, specifically in women, unmarried men and individuals living alone (6).

There are several risk factors for heart disease. Although psychosocial factors are less well studied than traditional risk factors such as blood lipids, high blood pressure and diabetes, they are coming to the fore as important, potentially modifiable risk indicators in patients with CAD. An important psychosocial factor is social support, which has been defined as “being cared for and loved, esteemed, and being a member of a network of mutual obligations”(7). The size, the quality and the perceived adequacy of a person’s social contacts and provision of instrumental and emotional support have all been related to lower risk of CAD and total mortality (7). For instance, a meta-analytic review of more than 100 studies assessing the influence of social relationships on mortality found that stronger social relationships significantly reduced mortality (8). Other meta-analyses and large follow up studies have found that low social support, social networks and social capital (“social value of human interactions”) all have a role in all-cause mortality and CAD-associated mortality (9-12).

Two domains of social support have been theorized, which include functional support and structural support. Functional support refers to the encouragement and support provided by an individual’s social network, but structural support refers to the characteristics of one’s social network (7). Social relationships may improve health in a variety of ways, for example through encouragement towards a healthy lifestyle and health care seeking, and by buffering the adverse effects of psychological stressors through provision of emotional support.

Social support has various effects on coronary artery disease. A review on behavioral cardiology determined that social support is one of many psychosocial risk factors that need to be addressed in behavioral interventions to diagnose and manage CAD (13). Furthermore, several meta-analyses of peer-reviewed publications confirmed that, variously defined social support, is linked to CAD progression and outcomes. A systematic review and meta-analysis of 20 prognostic of studies examining the relationship between social support and CHD determined that low functional support was associated with increased mortality in CAD patients (7). Early meta-analyses determined that social support inversely affects CAD progression, but social support networks and social isolation relate to CAD mortality in a complex mechanism; although more social support networks have led to less CAD outcomes and/or future cardiac events (14-16). A review of prospective cohort studies has determined that social support has an effect on the etiology and prognosis of CAD in combination with other psychosocial risk factors such as depression and anxiety (17). A more recent meta-analysis has shown that the effect of social support on CAD could be moderated by factors such as socioeconomic status and personality (18). Finally, a large randomized clinical trial, the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD), was the first clinical trial to investigate whether implementing interventions on patients with depression and low social support after MI would reduce mortality and recurrent MI. This clinical trial concluded that although social support improved in the intervention group, morality was not affected (19).

Although social support in relation to CAD progression and mortality has been studied, the role of social support in protecting towards MSI has not been evaluated. Further, studies have determined that men and women differ in both amount of social support received and MSI outcomes. Particularly, in meta-analyses women reported less social support received one year following MI (20). Additionally, in a large analysis of MI patients, women had higher rates of mortality during hospitalization following MI than men (21). In the most recent study of sex differences following a MI, using the same sample as the current analysis, young women more frequently had MSI than men (22). Therefore, the purpose of this analysis is to evaluate the role of social support in MSI and determine if sex differences exist that could allow social support to buffer MSI. The hypothesis is that higher levels of social support are associated with lower levels of MSI.

METHODS

As this analysis is a secondary analysis of previously collected data, all study recruitment and procedures are described in the Myocardial Infarction and Mental Stress (MIMS) study (IRB Approval Number AM14_IRB00009248), a cross-sectional study of 98 young (<60 years old) patients with a previous MI who have all undergone mental stress testing at Emory University (22). The MIMS study was a pilot study examining the sex differences in MSI following a MI. The study population was young women and young men who had been hospitalized for a MI in the previous six months in Emory University-affiliated hospitals.

The mental stress procedure included a resting period followed by a social stressor based on delivering a speech on a real-life stressful situation to a video camera and an audience with white coats. Blood pressure and heart rate were recorded at 1-minute intervals during and every five minutes after the mental stress procedure. MSI was measured through SPECT myocardial perfusion imaging scans at rest, during mental stress and during physical stress.

Along with many other clinical and psychosocial factors, social and emotional support was assessed using the ENRICHD Social Support Inventory (ESSI), a seven-item scale well validated and reliable in patients with CAD to measure and screen for low social support (19, 23). Each of the first six questions was scored from one to five points.

The last question was scored four points if the answer was yes and two points if the answer was no. The points from each question were totaled and could range between eight and thirty-four. A higher score indicates more social support. The total score was used to create tertiles with cut-off points of 24, 30, and greater than 31.

Other questionnaires and psychometric instruments were administered in MIMS to assess behavioral, social, and mental health information in addition to collecting demographic data. These include the Beck Depression Inventory-II (BDI-II) (24), Structured Clinical Interview for DSM IV (25), Cohen's Perceived Stress Scale (26), the State-Trait Anxiety Inventory (27) and Early Trauma Inventory (28). A research nurse collected medical history including medications taken. Blood samples were taken to obtain data on lipid profiles. Angiographic data was obtained from the coronary angiogram performed, which also gave the left ventricular ejection fraction. Finally, the disease severity was measured by the Gensini angiographic score, which was obtained from the Gensini semi-quantitative angiographic scoring system (29).

Statistical Analysis

This data was analyzed using the SAS 9.3 program at the 0.05 alpha level. Data cleaning included determining implausible or missing values for each variable through the univariate procedure for continuous variables and the frequency procedure for categorical variables. The primary outcome was the measurement of mental stress ischemia, which was calculated through the perfusion scores from the myocardial perfusion imaging data. These scores include the Summed Stress Score (SSS), Summed Rest Score (SRS) and the Summed Difference Score (SDS), which is the difference between the previous two scores. The main outcome variable was SDS, however the variable was highly skewed. The SSS variable is approximately normally distributed and became the dependent variable. The primary predictor variable was the ESSI score. Other risk factors were considered in the analysis. These factors were demographic and lifestyle factors, CAD severity and depressive symptoms.

Several analyses were completed to determine the role of social support in MSI using ESSI scores as an indicator of social support and also if ESSI scores following a MI varied by age and sex. The SDS determines if MSI is present, which is defined as SDS $\geq$3 and SDS $\geq$ 4 for physical stress ischemia. Since the MIMS study focused on young participants, age was categorized into less than or equal to 50 years and greater than 50 years. First, a complete descriptive analysis of demographic and patient characteristics was done. These variables include demographics, medical history and CHD risk factors, CAD severity, psychosocial factors, and medications. Next, differences in patient characteristics were examined through stratification by ESSI tertiles using Mantel-Haenszel Chi-Square tests and Fisher's Exact test for categorical variables and simple linear regression for continuous variables. Stratified analysis of the relationship between ESSI score and mental stress ischemia or physical stress ischemia by age and sex was completed using unadjusted linear regression with SSS as the dependent variable while adjusting for SRS. Finally, multiple linear regression models were used to assess the association between ESSI scores and mental stress ischemia as well as physical stress ischemia, adjusting for possible confounders. The SSS was the dependent variable while adjusting for SRS. The primary predictor was ESSI scores as a continuous variable (primary focus), ordinal variable, and tertiles, with the last tertile (ESSI score greater than or equal to 31) as the reference. Four models were constructed for mental stress and physical stress, respectively, adjusting for factors considered *a priori* as possible confounding factors. Model 1 was the unadjusted model. Model 2 adjusted for socio-demographic and lifestyle factors (age, race, income below poverty level, current cigarette smoking, and sex). Model 3 adjusted for all of the factors in Model 2 and also disease severity (Gensini angiographic score and left ventricular ejection fraction). Model 4 adjusted for all the factors in Model 3 and also depressive symptoms (BDI-II score and Trait Anxiety Inventory score).

RESULTS

During 2009 and 2012, 49 males and 49 females with a mean age of 50 years (SD 5.9) were recruited for the MIMS study (Table 1). Over half of the participants were African American. Overall, 40 % of the sample was married with a mean of 13.8 total years of education (SD 3.1). Approximately 32 % of the 98 participants had an income level below poverty. About 85 % of participants had a previous revascularization. As for psychosocial factors, about 38 % of the sample had a lifetime history of major depression with mean BDI-II score of 11.2 (SD 8.6). As for the State-Trait Anxiety Inventory, participants had a mean score of 39 (SD 10.7) on the Trait Anxiety Inventory.

As shown in Table 2, patients differed by several characteristics when stratified by the ESSI score tertiles, which are ESSI total score less than or equal to 24, between 25 and 30 and greater than or equal to 31. Age was approximately the same in each tertile with mean ages of 51.8, 49.3 and 50.1 years, in ascending tertiles (p=0.22). The percentage of women in each tertile from lowest tertile to highest tertile was 51.5 %, 55.9% and 41.9 %. Percent of those who were married increased with increasing ESSI tertile but differences were not statistically significant in this pilot study with 27.3 %, 44.1 % and 51.6 % ($p=0.53$). Total years of education were similar among the tertiles with 13.4 years, 14.2 years and 13.7 years, respectively. The percent of income level below poverty differed slightly among the tertiles but was not statistically significant with 38 %, 27 % and 32 % ($p=0.65$). However, regarding medical history, there was a statistically significant difference in the percent of patients who had a previous revascularization according to ESSI tertile, with the most patients scoring in the highest social support tertile ($p=0.03$). Additionally, psychosocial factors showed differences among the ESSI tertiles such that the lowest social support tertile had the highest burden of psychosocial risk factors such as depressive symptoms (BDI-II score), self-reported stress (Cohen's Perceived Stress Scale), and anxiety (State-Trait-Anxiety Inventory) $p=0.005$, $p<0.0001$, $p<0.0001$ and $p<0.0001$, respectively.

Linear regression models were constructed to assess the relationship between ESSI score (as a continuous variable) and SDS with mental stress and physical stress (Table 3). All models showed a slight inverse relationship between mental stress SDS and ESSI score, however none of the results were statistically significant. Although the coefficients were numerically lower, they were not significantly different from zero. Physical stress SDS and ESSI score had a direct, but statistically non-significant relationship.

Table 4 shows the relationship between SDS and ESSI tertiles (ESSI as an ordinal variable) with mental stress and physical stress. According to Model 3, which adjusted for demographic factors, lifestyle factors, and disease severity, mental stress SDS decreases by 0.30 points for every tertile increment ($p=0.43$). However, when additionally adjusting for depressive symptoms (Model 4), mental stress SDS increased by 0.04 points for every tertile increment (p=0.92). While not statistically significant, physical stress SDS showed increase in SDS for every tertile increment.

While the primary analysis involved the ESSI score as a continuous variable, in secondary analyses the ESSI score was also considered as a categorical variable and as an ordinal variable according to tertiles. When modeled as a categorical variable, the highest tertile was set as the reference. Table 5 shows the unadjusted and adjusted relationship between ESSI score tertiles (as a categorical variable) and SDS. The model adjusting for demographic and lifestyle factors, disease severity and depressive symptoms showed that those who had an ESSI score of ≤ 24 (lowest tertile) had 0.10 points decrease in mental stress SDS than those who scored greater than or equal to 31 (highest tertile) on the ESSI, but this difference was not statistically significant (p=0.91). The fully adjusted model for those scoring 25-30 (middle tertile) on the ESSI had 0.19 points increase in mental stress SDS than those scoring in the highest ESSI tertile (p=0.80). As for physical stress SDS, those scoring in both the lowest and middle tertile showed decrease in SDS compared to the highest tertile, but the results were not statistically significant in this pilot study.

The ESSI score was stratified by sex in patients with mental stress and physical stress (Table 6). Overall, there was no association between mental stress and ESSI score by sex. In women, mental stress SDS increased by 0.03 point for every unit increase in ESSI score (p=0.67). However, in men, mental stress SDS decreased by 0.08 point for every unit increase in ESSI score (p=0.20). However, the interaction by sex was not statistically significant. There also was no association between physical stress and ESSI score by sex.

As shown in Table 7, mental stress SDS also was not associated with ESSI score in each of the two age strata. For participants less than or equal to 50 years, mental stress SDS increased by 0.07 point for every unit increase in ESSI score (p=0.36), while in participants older than 50 years mental stress SDS decreased by 0.08 point for every unit increase in ESSI score (p=0.21). This difference by age strata was not statistically significant. Physical stress SDS also was not significantly related to ESSI within age strata.

DISCUSSION

In this pilot study, no association was found between social and emotional support, measured with the ESSI scale, and mental stress-induced myocardial ischemia as measured by the SDS. Irrespective of whether the ESSI score was treated as a continuous, ordinal or categorical variable, the results indicated that more social support does not affect the propensity for developing MSI. Depression, stress and anxiety were all more elevated in patients having the lowest social support. Additionally, no sex or age differences were found between social support and MSI in our study. Although the lowest social support tertile had the highest mean age, the differences between ESSI tertiles were not statistically significant.

Although there have not been previous studies assessing the relationship between social support and mental stress ischemia, other studies have examined the effect of social support on coronary heart disease morbidity and mortality with varying conclusions. Some studies have determined social support to be an independent risk factor of CHD. Particularly, research had focused on social support in relation to depression as an independent risk factor. In a prospective cohort study involving patients following a myocardial infarction, several psychosocial variables, such as social support, depression, and anxiety, were considered in relation to coronary mortality. After 10 years of follow-up, the study concluded that lack of social support (measured by the Interview Schedule for Social Interaction questionnaire) and high depression scores independently increased the risk for coronary events (30). Another study found similar results. A follow-up study that recruited participants from the ENRICHD study did not find the same relationship between functional support and health outcomes in people with varying levels of depression (high vs. low) (31). However, further research had discovered that depression and social support may interact with regards to coronary outcomes. In a large follow-up study (one year post-MI) that recruited patients from a randomized controlled trial, high social support as measured through the Perceived Social Support Scale (PSSS) seemed to buffer the effects of depression on mortality (32). In a subsequent study by the same researchers social support measures appeared to interact with depression scores (Beck Depression Inventory) in a complex relationship but any measures of social support from the study did not predict cardiac-related mortality (33). Additionally, the original ENRICHD study and a reanalysis of the study found that social support did not influence mortality or recurrent myocardial infarction (19, 34). Conversely, a prospective 5-year study found that patients with small social support networks (measured by the Mannheim Social Support Interview questionnaire) had increased risk of mortality; in this study a small social network was defined as containing three or fewer persons in the network (35). In a prospective study that followed women for five years, both social isolation (measured by the Interview Schedule for Social Interaction questionnaire) and depressive symptoms did not interact, but rather had an additive effect on the risk of recurring cardiac events such as myocardial infarction and revascularization procedures (36). A more recent meta-analysis of prognostic studies confirmed that low functional support negatively affects CHD-related mortality (pooled RR, range, 1.59-1.71), but there was substantial heterogeneity of findings across studies (7). Overall, the relationship between social support and coronary artery disease mortality is unclear.

There are several strengths and limitations of this secondary analysis. A large amount of data was collected on these participants through questionnaires, psychometric instruments, laboratory tests and mental stress testing. Thus, the sample was well characterized. Additionally, an established experimental protocol was used to measure mental stress ischemia and also physical stress ischemia was measured as a control condition. Also, contrary to previous studies, the sample of participants included a large number of women and minorities. The main limitation of the MIMS study is the small sample size that limited the number of patients with MSI. Another limitation is that the ESSI questionnaire is composed of only seven questions and may not have completely measured social support as other questionnaires in other studies have done. However, this is a validated instrument that has been specifically developed for post-MI patients.

In conclusion, this study did not find an association between social support and mental stress ischemia. Furthermore, there was no association between social support and mental stress ischemia by sex. Since a number of previous have demonstrated an association between social support and increased risk of coronary artery disease events, it is likely that the underlying mechanisms for this association involve pathways other than ischemia induced by emotional stress.

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TABLES

Table 1. Demographics and clinical characteristics of MIMS study participants (N=98)

Characteristic	N (%)	Mean (SD)
Demographics		
Age, years	-	(50.4) 5.9
Female	49 (50.0)	-
Black race	53 (54.1)	
Married	40 (40.8)	-
Education, total years	-	13.8 (3.1)
Income below poverty level (≤ $20,000)	31 (32.3)	-
Current smoking	28 (28.6)	-
Medical History and CHD Risk Factors		
ST-elevation MI	44 (44.9)	-
Angina in past 4 weeks	58 (59.2)	-
Hypertension	67 (69.1)	-
Hyperlipidemia	71 (73.2)	-
Diabetes	20 (20.6)	-
Previous revascularization	84 (85.7)	-
BMI	-	31.0 (6.4)
BMI ≥ 30	45 (45.9)	-
Triglycerides, mg/dl	-	132.8 (99.7)
HDL Cholesterol, mg/dl	-	47.1 (13.2)
LDL Cholesterol, mg/dl	-	92.4 (33.5)
Coronary Angiography Data (at time of MI)		
Gensini score	-	37.9 (33.8)
Left ventricular ejection fraction	-	51.6 (10.9)
Psychosocial Factors		
Lifetime history of major depression	36 (37.5)	-
Beck Depression Inventory	-	11.2 (8.6)
Cohen's Perceived Stress Scale	-	16.1 (7.6)
State-Trait Anxiety Inventory		
State	-	37.8 (11.3)
Trait	-	39.0 (10.7)
Medications		
Statins	85 (87.6)	-
Beta blockers	85 (87.6)	-
ACE Inhibitors	53 (54.6)	-
Aspirin	85 (87.6)	-

Table 2. Differences in patient characteristics stratified by ESSI Score Tertiles

Demographics	**ESSI Total Score ≤ 24 (N=33)**	**ESSI Score 25-30 (N=34)**	**ESSI Score ≥ 31 (N=31)**	**p value [b]**
Age, years [a]	51.8 (5.5)	49.3 (6.2)	50.1 (5.8)	0.22
Female, %	51.5	55.9	41.9	0.46
Black race, %	51.5	61.8	48.4	0.82
Married, %	27.3	44.1	51.6	0.53[c]
Education, total years	13.4 (3.7)	14.2 (2.4)	13.7 (3.2)	0.65
Income below poverty level (≤ $20,000), %	37.5	27.3	32.3	0.65
Current smoking, %	42.4	14.7	29.0	0.22
Medical History and CHD Risk Factors				
ST-elevation MI, %	42.4	38.2	54.8	0.33
Angina in past 4 weeks, %	69.7	58.8	48.4	0.08
Hypertension, %	69.7	66.7	71.0	0.92
Hyperlipidemia, %	78.8	63.6	77.4	0.88
Diabetes, %	18.2	21.2	22.6	0.66
Previous revascularization, %	87.9	73.5	96.8	0.03[c]
BMI	30.0 (5.9)	33.1 (6.7)	29.7 (6.1)	0.87
BMI ≥ 30, %	45.5	50.0	41.9	0.79
Triglycerides, mg/dl	142.2 (87.1)	114.7 (83.2)	143.5 (126.6)	0.98
HDL Cholesterol, mg/dl	45.2 (16.0)	48.3 (11.8)	47.8 (11.5)	0.44
LDL Cholesterol, mg/dl	92.5 (31.5)	88.8 (31.3)	96.7 (38.4)	0.65
Coronary Angiography Data (at time of MI)				
Gensini score	41.4 (39.9)	39.5 (32.2)	32.5 (28.5)	0.30
Left ventricular ejection fraction	51.0 (11.9)	52.9 (10.5)	51.0 (10.3)	0.96
Psychosocial Factors				
Lifetime history of major depression, %	43.8	42.4	25.8	0.15
Beck Depression Inventory	14.8 (9.1)	9.9 (8.1)	8.8 (7.4)	0.005
Cohen's Perceived Stress Scale	19.7 (7.1)	16.6 (5.7)	11.8 (8.0)	<0.0001
State-Trait Anxiety Inventory				
State	44.0 (10.9)	36.1 (10.2)	32.9 (10.2)	<0.0001
Trait	46.3 (8.8)	36.9 (10.4)	33.5 (8.6)	<0.0001
Medications				
Statins, %	84.9	90.9	87.1	0.80[c]
Beta blockers, %	87.9	84.9	90.3	0.93[c]
ACE Inhibitors, %	57.6	57.6	48.4	0.47
Aspirin, %	87.9	84.9	90.3	0.93[c]

[a] All values are means (standard deviation), unless otherwise specified
[b] All are Mantel-Haenszel Chi-Square test except for continuous variables, which are linear regression and where noted
[c] Fisher's Exact test

Table 3. Unadjusted and adjusted relationship between ESSI Score and Summed Difference Score (SDS) with mental stress and physical stress

	ESSI Score [a]		
Mental Stress	β	95 % CI	*p*
Model 1: Unadjusted	-0.03	-0.12 − 0.05	0.47
Model 2: Adjusted for demographic and lifestyle factors [b]	-0.03	-0.13 − 0.06	0.47
Model 3: Adjusted for the above plus disease severity [c]	-0.04	-0.14 − 0.06	0.40
Model 4: Adjusted for the above plus depressive symptoms [d]	-0.005	-0.11 − 0.10	0.93
Physical Stress			
Model 1: Unadjusted	0.03	-0.07 − 0.14	0.53
Model 2: Adjusted for demographic and lifestyle factors [b]	0.04	-0.08 − 0.15	0.52
Model 3: Adjusted for the above plus disease severity [c]	0.04	-0.08 − 0.16	0.49
Model 4: Adjusted for the above plus depressive symptoms [d]	0.004	-0.14 − 0.15	0.95

[a] ESSI Score as a continuous variable
[b] Age, Race (black versus non-black), income below poverty level, current cigarette smoking, sex
[c] Gensini angiographic score and left ventricular ejection fraction
[d] Beck Depression Inventory-II and Trait Anxiety Inventory

Table 4. Unadjusted and adjusted relationship between ESSI Score Tertiles and SDS with mental stress and physical stress

	ESSI Tertiles [a]		
Mental Stress	β	95 % CI	*p*
Model 1: Unadjusted	-0.29	-0.99 − 0.40	0.40
Model 2: Adjusted for demographic and lifestyle factors [b]	-0.29	-1.00 − 0.42	0.43
Model 3: Adjusted for the above plus disease severity [c]	-0.30	-1.05 − 0.45	0.43
Model 4: Adjusted for the above plus depressive symptoms [d]	0.04	-0.80 − 0.88	0.92
Physical Stress			
Model 1: Unadjusted	0.46	-0.37 − 1.30	0.27
Model 2: Adjusted for demographic and lifestyle factors [b]	0.51	-0.36 − 1.39	0.25
Model 3: Adjusted for the above plus disease severity [c]	0.69	-0.26 − 1.63	0.15
Model 4: Adjusted for the above plus depressive symptoms [d]	0.57	-0.55 − 1.68	0.32

[a] ESSI Score as an ordinal variable
[b] Age, Race (black versus non-black), income below poverty level, current cigarette smoking, sex
[c] Gensini angiographic score and left ventricular ejection fraction
[d] Beck Depression Inventory-II and Trait Anxiety Inventory

Table 5. Unadjusted and adjusted relationship between ESSI Score Tertiles and SDS with mental stress and physical stress

	ESSI Score ≤ 24[a]			ESSI Score 25-30		
Mental Stress	β	95 % CI	*p*	β	95 % CI	*p*
Model 1: Unadjusted	0.59	-0.80 − 1.98	0.40	0.45	-0.92 − 1.83	0.51
Model 2: Adjusted for demographic and lifestyle factors [b]	0.57	-0.86 − 2.00	0.43	0.37	-1.03 − 1.78	0.60
Model 3: Adjusted for the above plus disease severity [c]	0.59	-0.92 − 2.11	0.44	0.23	-1.28 − 1.74	0.76
Model 4: Adjusted for the above plus depressive symptoms [d]	-0.10	-1.79 − 1.60	0.91	0.19	-1.30 − 1.68	0.80
Physical Stress						
Model 1: Unadjusted	-0.94	-2.61 − 0.74	0.27	-0.97	-2.61 − 0.67	0.24
Model 2: Adjusted for demographic and lifestyle factors [b]	-1.02	-2.78 − 0.74	0.25	-0.83	-2.55 − 0.89	0.34
Model 3: Adjusted for the above plus disease severity [c]	-1.39	-3.29 − 0.51	0.15	-1.09	-2.98 − 0.79	0.25
Model 4: Adjusted for the above plus depressive symptoms [d]	-1.11	-3.36 − 1.14	0.33	-0.89	-2.85 − 1.08	0.37

[a] ESSI Score ≥ 31 as reference
[b] Age, Race (black versus non-black), income below poverty level, current cigarette smoking, sex
[c] Gensini angiographic score and left ventricular ejection fraction
[d] Beck Depression Inventory-II and Trait Anxiety Inventory

Table 6. Unadjusted relationship between ESSI Score and SDS with mental stress and physical stress stratified by sex

	Women			Men		
Mental Stress	β	95 % CI	*p*	β	95 % CI	*p*
ESSI score	0.03	-0.10 − 0.16	0.67	-0.08	-0.20 − 0.04	0.20
Physical Stress						
ESSI score	0.002	-0.16 − 0.16	0.98	0.05	-0.09 − 0.19	0.51

Table 7. Unadjusted relationship between ESSI Score and SDS with mental stress and physical stress stratified by age group

	Age ≤ 50 years			Age > 50 years		
Mental Stress	β	95 % CI	*p*	β	95 % CI	*p*
ESSI score	0.07	-0.08 − 0.21	0.36	-0.08	-0.20 − 0.05	0.21
Physical Stress						
ESSI score	-0.01	-0.21 − 0.18	0.89	0.04	-0.10 − 0.18	0.56