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Association of psychosocial stress factors and vascular function before and after acute mental stress

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Association of psychosocial stress factors and vascular function before and after acute mental stress

By

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B.S., University of Michigan, 2014

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An abstract of
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Abstract

Association of psychosocial stress factors and vascular function before and after acute mental stress

By Melissa Bruno

Objective: Psychological stress, depression, and trauma are commonly hypothesized as important risk factors for adverse cardiovascular outcomes. In this study, we aimed to determine if a higher burden of psychosocial stress, assessed by means of a summary psychosocial stress score, is associated with worse vascular function before and after acute mental stress in cases with a previous myocardial infarction (MI) and age- and sex-matched community controls.

Methods: 303 cases who were hospitalized for MI and 110 community controls frequency matched on sex and age were included in this analysis. Flow-mediated vasodilation (FMD) and reactive hyperemia index (RHI) were measured before and 30 minutes after mental stress procedures and their association with a psychosocial summary score, including depression, post-traumatic stress disorder (PTSD), perceived stress, childhood trauma, and lifetime trauma, was examined.

Results: Overall, cases had more adverse sociodemographic and clinical profiles compared to controls. Cases exhibited a significant but weak negative correlation between the psychosocial distress summary score and post-mental stress RHI measurements, indicating worse vascular function per increased levels of distress (β -0.14, $p=0.02$). Controls had more significant correlations with vascular function compared to the cases. Among controls, the psychosocial distress summary score had significant correlations with pre- and post-mental health FMD, -0.334 ($p<0.01$) and -0.286 ($p<0.01$), respectively. Among cases there were no significant regressions coefficients for resting FMD or resting RHI. Controls had significant negative coefficients for all resting FMD models. For controls, significant positive interactions between time and stress score were found for RHI percent change in the crude ($\beta= 2.9$) and demographic-adjusted models ($\beta= 2.9$), but not after medical history adjustment.

Conclusions: Psychosocial stress is related more adverse resting vascular function in those without existing CAD, especially at rest. In those who have previously experienced a MI, stress is more related to post-mental stress vascular function. Due to the healthier state of vessels in those without CAD, a more definitive relationship between increasing psychosocial stress burden and impaired vascular function may be more evident in this group as opposed to the post-MI group. This study also demonstrates the importance to consider cumulative effects of psychosocial stress variables on vascular function.

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Table of Contents

INTRODUCTION

Psychological stress, depression, and trauma are commonly hypothesized as important risk factors for adverse cardiovascular outcomes. Meta-analyses have shown that the risk for cardiovascular disease due to psychosocial factors may be of similar magnitude than risks of hypertension and increased cholesterol(1). The underlying mechanisms for the relationship between psychosocial stress and cardiovascular outcomes are not entirely clear and likely multifactorial. Several factors have been proposed, including behavioral/lifestyle factors, underlying cardiac disease severity, and neurobiological, autonomic and immune dysregulation and their effects on the vasculature, the myocardium and cardiac electrophysiology(2,3).

A proposed mechanism through which psychological stress may affect cardiovascular health is impaired vascular function(4-7). Vascular and metabolic effects of the hypothalamic-pituitary-adrenal axis and sympathetic nervous activity can contribute to vascular disease by altering factors such as resting heart rate, inflammation, and basal metabolic energy expenditure(8). Chronic stress and depression have been shown to cause poor vascular function in individuals with no history of vasculopathy(4,5). In addition to depression, exposure to extremely stressful or traumatic events, such as childhood adversity and combat, have been linked to increased risk for adverse cardiovascular outcomes(6). Chronic psychosocial stressors exacerbate physiologic responses to stress leading to vasculopathy(8).

The exact mechanisms through with psychosocial health may affect vascular function remains largely unknown. For example, associations between psychosocial

stress and impaired vascular function have been described, but do not prove that these effects cause poor cardiovascular outcomes(8). There is a paucity of data on the effects of chronic stressors on vascular function measures known to be linked physiologically to cardiovascular health. In addition, many previous studies have examined CVD patients or healthy individuals, not both. There is evidence that psychological stress can precipitate recurrent cardiovascular events in those with CAD by triggering myocardial ischemia(9), while in those without CAD, mechanisms may differ, and vascular function could be more important in this group(8). These differences suggest variations in the pathways through which stress may affect cardiovascular events for those with and without CAD. Examining both groups can shed light on mechanisms linking stress to CVD risk. Because vascular function is already low in persons with CAD, it may be difficult to establish associations with factors that may affect vascular function in this group. A comparison with controls of similar age and sex, without CAD, can help clarify these associations. Insights into the pathways of these relationships may also reveal targets for future interventions.

Most studies of the effects of psychological stressors and CVD have examined several psychosocial measures separately (such as depression, anxiety, perceived stress). However, these measures are often inter-correlated and may also have cumulative effects. It is often difficult to isolate the effects of independent psychosocial variables because they interact and tend to cluster together(10). Additionally, multiple psychosocial variables mediate various pathways in the relationship between stress and impaired vascular function(11). In general, the more adverse the psychosocial profile, the greater the risk for CAD and these relationships may be further mediated by social support(10).

Failure to study cumulative psychosocial effects may lead to underestimation in their role or oversight of important contextual situations(12). Furthermore, most previous studies have examined vascular function at the resting state. An assessment of vascular responses to acute stress, using a standardized, laboratory-based protocol, can shed new light on the effects of stress on vascular function in individuals with and without CAD.

In this study, we aimed to determine if a higher burden of psychosocial stress, assessed by means of a summary psychosocial stress score, is associated with worse vascular function before and after acute mental stress in cases with a previous myocardial infarction (MI) and age- and sex-matched community controls. We hypothesized that higher psychosocial burden scores would result in poorer overall vascular function in both cases and controls, as well as a decrease in function from pre- to post-mental stress due to lower-functioning vessels from greater stress.

METHODS

Population

Data for this study were taken from the MIMS2 (Myocardial Infarction and Mental Stress 2) dataset. Participants included early onset MI cases and community controls without a history of CAD. The MI cases were recruited from the pool of patients who were admitted with a documented history of MI in the previous 8 months at Emory-affiliated hospitals in Atlanta, Georgia, and who were 18 to 60 years of age at the time of screening. The diagnosis of MI was verified by medical record review based on standard criteria of troponin level increase together with symptoms of ischemia and ECG changes or other evidence of myocardial necrosis; presence of obstructive CAD was not a criterion for inclusion(13). Controls were recruited in the Atlanta area from a community-based study of individuals without established CAD(14). Inclusion criteria for controls were between 18 and 60 years of age and no history of MI, unstable or stable angina pectoris, congestive heart failure, or stroke. Controls were frequency matched for age and sex to the MI cases, with the goal of achieving ≈50% women and a similar mean age in both samples.

Subjects were excluded if they had a severe comorbid medical or psychiatric disorder that could interfere with study results, such as cancer, renal failure, severe uncontrolled hypertension, current alcohol or substance abuse, or schizophrenia; if they were pregnant or breastfeeding; or if they were currently using immunosuppressant or psychotropic medications other than antidepressants. MI patients were also excluded if they had unstable angina, acute MI, or decompensated heart failure within the past week; if they weighed >450 pounds (because of limits on the weight bearing of the nuclear

stress test equipment); and if it was deemed to be unsafe by study cardiologists to hold anti-ischemic medications for 24 hours before the testing.

Both MI cases and healthy controls underwent a standardized mental stress test and vascular testing as described below and following published methodology(15).

Sociodemographic and psychosocial data were collected for all participants before all testing. At the end of the study protocol, medical records for the patients with MI were abstracted for clinical information, including catheterization data. The Emory University Institutional Review Board approved the protocol, and all participants provided written informed consent.

Psychosocial Questionnaires

We used validated instruments to assess behavioral, social, and health status information for both patients with MI and controls. Depressive symptoms were assessed with the Beck Depression Inventory-II(16), a reliable and valid self-report measure that has been widely used in cardiac as well as non-cardiac populations. In addition, we administered the Structured Clinical Interview for DSM−IV(17) to derive a lifetime diagnosis of major depression and posttraumatic stress disorder. The Structured Clinical Interview for DSM−IV was administered by a trained research nurse under the supervision of the study psychiatrist, who reviewed psychiatric diagnoses. We also administered the Cohen's Perceived Stress Scale,(18) a 10-item survey of general stress validated in multiethnic populations, and the Spielberger's State-Trait Anxiety Inventory, a 40-item questionnaire to measure anxiety as an emotional state or a personality trait.(19) Post-traumatic stress disorder was assessed using the PTSD check list (PCL).

Childhood Trauma was measured through self-report on the Early Trauma Inventory Short Form (ETI)(20) and Lifetime Trauma using the Lifetime Trauma Inventory (LTI)(21).

Mental Stress Testing

After resting for 30 minutes in a quiet, dimly lit, temperature-controlled room, mental stress was induced in both patients with MI and controls by a standardized public speaking task as previously described(14,22,23). Participants were asked to imagine a real-life stressful situation, in which a close relative had been mistreated in a nursing home and asked to make up a realistic story around this scenario. They were given 2 minutes to prepare a statement and then 3 minutes to present it in front of a video camera and an audience wearing white coats. Subjects were told that their speech would be evaluated by the laboratory staff for content, quality, and duration. We recorded blood pressure and heart rate at 5-minute intervals during the resting phase and at 1-minute intervals during the mental stress task, and we calculated the rate-pressure product as peak systolic blood pressure times peak heart rate. We also obtained subjective ratings of distress with the Subjective Units of Distress Scale(24) on a linear scale of 0 to 100, with 100 being the highest level of distress.

Vascular Testing

Among both patients with MI and controls, we assessed peripheral vasoconstriction and microvascular function using the Endo-PAT2000 (Itamar Medical),

which measures finger pulse volume amplitude (PVA), reflecting peripheral blood volume changes using volume plethysmography technology(25,26). PVA signals detected by a finger probe were filtered, amplified, and analyzed in an operator-independent manner. The baseline PVA was determined by averaging the last 3 minutes of recording that preceded the mental stress test. The stress amplitude was determined as the lowest PVA during the speaking period. The peripheral arterial tonometry (PAT) ratio was then calculated by the software as the ratio of PVA during the speaking task over the resting baseline, with a ratio <1 signifying a vasoconstrictive response. After removing participants with excessive artifacts, the PAT ratio was available in in 76% of MI cases and 72% of controls.

Before and 30 minutes after the mental stress test, we also used the EndoPAT device to assess the digital reactive hyperemia index (RHI), a measurement of peripheral microvascular function. For this test, PVA is obtained in resting condition and during reactive hyperemia, which is elicited by the release of an upper arm blood pressure cuff inflated to suprasystolic pressure for 5 minutes. The RHI is then calculated as the ratio of post deflation to baseline pulse amplitude in the hyperemic finger divided by the ratio in the contralateral finger(27). This metric is calculated by a computer algorithm and has been associated with cardiovascular outcomes(28). Before and 30 minutes after the mental stress test, patients with MI and controls also underwent measurement of flow-mediated vasodilation (FMD) of the brachial artery via bimode ultrasound to assess endothelial function using standard methodology(29).

Statistical Analysis

We calculated a composite score of observed psychosocial scales related to stress and trauma using ranks. For psychosocial scales measuring dimensions related to trauma-spectrum symptoms and disorders, including depression (BDI), PTSD (PCL), perceived stress (PSS), childhood trauma (ETI), and lifetime trauma (LTI), study subjects were ranked according to their score, producing 5 ranks for each subject, corresponding to 5 scales. We then calculated a global measure of psychosocial stress by taking the mean of these ranks for each subject following the approach used by other authors (30).

We compared study variables (demographic factors, cardiovascular risk factors, medications, and clinical characteristics) between MI cases and community controls using t tests and chi-square tests according to their distribution. Hemodynamics and vascular function measures were compared between groups with two sample t-tests. Spearman methods were used to generate correlation coefficients for psychosocial stress score, its components scores, and vascular measurements, given that they were approximately normally distributed. Significant interaction between study group and sex for FMD and RHI percent change was assessed by dividing psychosocial stress score into even quartiles and conducting a two-way ANOVA analysis.

The relationship between psychosocial summary score and resting vascular function (FMD and RHI) was analyzed using linear regression models. Model adjustments included subsequent addition of demographic factors (age, sex, and race), medical history and lifestyle factors (hypertension, diabetes, dyslipidemia, smoking, and physical activity), and MI severity for cases only (ejection fraction).

Mixed model regression models for repeated measures, with a pre- and post-mental stress time point variable, were used to assess the relationship between the

psychosocial summary score and pre- and post-mental stress measurements of FMD and RHI percent change. Model adjustments included subsequent addition of demographic (age, sex, and race), medical history (hypertension, diabetes, dyslipidemia, smoking, and physical activity), and MI severity variables for cases (ejection fraction).

RESULTS

Study sample and baseline characteristics

Between August 2012 and March 2016, 313 MI cases and 112 controls were enrolled in the MIMS2 study. Two controls and 10 cases were excluded for missing psychosocial stressor data, leaving a final analytic sample of 110 controls (57 men and 53 women) and 303 cases (152 men and 151 women). The median age for MI cases was 52 years with a range of 25 to 61, and 51.5 for controls with a range of 22 to 61 years. Table 1 shows the study population characteristics by study group. Overall, cases had more adverse sociodemographic and clinical profiles compared to controls. Cases were more likely to be black and to have an income less than $25,000 compared to controls. Fifty-five percent of cases were ever smokers, while 27% of controls reported ever smoking. As expected, cases were more likely to have a history of diabetes, hypertension, and dyslipidemia than controls, as well as higher rates of use of cardiovascular medications, including aspirin, statins, beta blockers, and angiotensin-converting-enzyme (ACE) inhibitors. However, there was no case/control difference in rates of antidepressants.

Table 2 shows the study population's psychosocial risk factor characteristics by study group. Overall, cases had poorer psychosocial risk factor profiles compared to controls. The largest disparity between cases and controls was in the prevalence of depression and PTSD with a percent difference of 222%, i.e., more than 3-fold higher, in cases than in controls. Cases had an average psychosocial distress summary score that was almost 3 times higher than the controls: 149 vs. 54. Figure 1 illustrates the distribution of psychosocial stress scores stratified by study group. Cases had stress

scores ranging from 16.7 to just under 290, while scores for controls ranged from 10.3 to 107.

Cases had higher resting blood pressure measurements compared to controls (Table 3). Controls experienced greater change in hemodynamics in response to stress, including SBP, heart rate, and RPP, but not DBP. Vascular function, measured both by FMD and RHI, was lower in cases compared with controls, both at rest and after mental stress. Cases experienced an average significant decrease in FMD percent measurement of 1.7 from pre- to post-mental stress ($p<0.001$). Controls experienced an average decrease in FMD percent of 1.8 which was also significant ($p<0.001$). Cases had an average decrease in RHI measurement from pre- to post-mental stress of 0.09 which was not significant. Controls had an average decrease RHI measurement change of 0.097 which was also insignificant.

Psychosocial stress score and vascular function

There was significant correlation between BDI score and PCL score and post-mental stress RHI measurement with correlations -0.15 ($p=0.01$) and -0.123 ($p=0.04$), respectively (Table 4). Among cases, there were no significant correlations between psychosocial variables and FMD, or between psychosocial variables and changes in either FMD or RHI with stress. Cases also exhibited a significant but weak negative correlation between the psychosocial distress summary score and post-mental stress RHI measurements, indicating worse vascular function per increased levels of distress (β -0.14, $p=0.02$).

The community controls had more significant correlations with vascular function compared to the cases. Controls had significant negative correlations with resting FMD and all individual stress score components except lifetime trauma. Additionally, PTSD and childhood trauma had significant correlations with post-mental stress FMD, resting RHI, and RHI percent change. The psychosocial distress summary score had significant correlations with pre- and post-mental health FMD, -0.334 ($p<0.01$) and -0.286 ($p<0.01$), respectively. There were no significant correlations between stress scores and FMD percent change or RHI percent change for controls. These negative correlations again indicate worse vascular function among controls as the psychosocial stressor score increases.

Regression analysis

Figure 2 shows the results of the interaction assessment for study group and sex. This test showed significant interaction between study group and RHI percent change ($p=0.02$) showing that when regressed on psychosocial stress score, the absolute RHI percent change was significantly greater in cases compared to controls. No significant interaction was found between study group and FMD percent change. There was also no significant interaction between either of the vascular function outcomes and sex.

Tables 6 & 7 report the regression coefficients for psychosocial distress score and resting FMD and RHI measurements respectively. Among cases there were no significant regressions coefficients for resting FMD or resting RHI. Controls had significant negative coefficients for all resting FMD models. Controls also had significant negative regression coefficients for resting RHI in the crude analysis ($r= -0.22$) and adjusting for

demographics (r= -0.21), but not when adjusting form medical history factors. These negative coefficients indicate a poorer resting FMD and RHI function as psychosocial distress score increases.

In general, the regression analyses revealed blunted relationships in cases compared to controls when assessing the significance of the mixed model interaction of time and stress score regressed on FMD and RHI vascular measurements (Tables 8 & 9). In the analyses of the association between psychosocial stressor score and FMD percent change, there were no significant interaction coefficients found among cases or controls for the time and stress score variables. There were also no significant coefficients among cases in the mixed regression models for RHI percent change, indicating no significant change in RHI measurements for pre- and post-mental stress testing. For controls, significant positive time by stress score coefficients were found for RHI percent change in the crude (β=2.9) and demographic-adjusted models (β= 2.9), but not after medical history adjustment. These positive coefficients indicate an increase in RHI (improvement) as psychosocial distress score increases among controls.

DISCUSSION

The main findings in this study are that psychosocial stress is more strongly related to resting vascular function among controls, but more related to post-stress values among cases, particularly RHI. Neither study group demonstrated a relationship between stress and change (post-stress minus pre-stress) in vascular function.

Overall, our analyses found that community controls had stronger relationships between psychosocial stressor score and vascular function at rest compared to cases with a previous MI. In general, cases had a poorer psychosocial, hemodynamic, and vascular function profile compared to controls. Cases also had poorer vascular function measurements both pre- and post-mental stress. The overall lower function in cases due to their disease status may affect our ability to see a clear relationship between stress and resting FMD and RHI measurements. The healthier vessels in controls, however, indicate a more definitive relationship of increased psychosocial stress associations with poorer baseline vascular function for both FMD and RHI at rest.

The stronger negative correlation between the summary score and resting FMD compared to the score components give insight into a stronger cumulative effect these psychosocial factors may have on vascular function. These findings suggest that the relationships between psychosocial stress variables and vascular function are more complex and will require further research to understand mechanisms and pathways. It is important for future studies to consider cumulative effects of stress rather than simply a single psychosocial stress factor.

In cases, there was no significant relationship between increasing psychosocial stress score and change in vascular function with mental stress. In controls, significant

relationships were found between increasing psychosocial score and both resting FMD and RHI. Increasing distress score was associated with decreased FMD and RHI function at rest. The ability to see these associations in healthy participants compared to cases with a previous MI is likely due to differences in vascular function. In healthy individuals, blood flow increases in response to mental stress as a result of microvascular dilation(25). These responses, however, are attenuated in individuals with CAD. The attenuated responses in those with CAD account for the blunted relationship between stress and vascular function seen in the cases compared to controls.

STRENGTHS AND WEAKNESSES

A strength of this study is its consideration of a cumulative effect of multiple psychosocial factors allowing for a more robust analysis of the relationship between stress and vascular function. The inclusion of both MI cases and community controls in the analysis also allows for comparison of the effects of psychosocial stress in both diseased and non-diseased vessels.

Our study also has limitations to consider. The limited range of psychosocial values among community controls may have affected our results. Future studies may consider focusing on a larger population (with a wide range of stress scores) among those without existing cardiovascular disease. Finally, the specific study population of a single institution affects the generalizability of these results.

CONCLUSION

Psychosocial stress is related more to resting vascular function in those without existing CAD. In those who have previously experienced a MI, stress is more related to post-mental stress function. Due to the healthier state of vessels in those without CAD, a relationship between increasing psychosocial stress burden and impaired vascular function may be easier to detect in the resting state among healthy individuals, suggesting chronic effects of daily stress exposures on vascular function. Acute stress, however, does not seem to further worsen vascular function among healthy controls.

This study also demonstrates the importance to consider cumulative effects of psychosocial stress variables on vascular function. Further research is needed to better

characterize the pathways and interaction occurring between multiple psychosocial factors and vascular function.

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TABLES & FIGURES

Table 1. Characteristics of Study Population by study group.

	Cases	Controls
Demographic Factors		
Age, years, mean (SD)	52 (6.6)	51.5 (9.1)
Sex, % female	49.8	51.8
Black/African American %	65.7	41.8
Married or living with partner %	41.9	53.6
Income, $\leq$ 25,000, %	40.7	10.4
Years of education, mean (SD)	13.7 (2.9)	16.4 (2.7)
Cardiovascular Risk Factors		
BMI, kg/m2, mean (SD)	31.3 (7.2)	28.8 (6.0)
Ever smoker, %	55.1	27.3
History of diabetes, %	31.4	7.3
History of hypertension, %	81.5	30.9
History of dyslipidemia, %	80.2	31.8
Medications		
Aspirin, n (%)	247 (81.8)	11 (10.1)
Beta Blocker, n (%)	259 (85.8)	6 (5.5)
ACE Inhibitors, n (%)	141 (46.7)	14 (12.8)
Antidepressants, n (%)	51 (16.9)	18 (16.5)
Statins, n (%)	255 (84.4)	16 (14.7)
Clinical Characteristics (MI Patients Only)		
ST-segment MI, %	28.7	
History of MI prior to index MI, %	20.9	
History of congestive heart failure, %	9.6	
History of coronary revascularization, %	80.2	
LV ejection fraction (%), mean (SD)	50.8 (12.1)	
Obstructive CAD (stenosis $\geq$70%), %	84.1	

Table 2. Psychosocial characteristics of study population by study group.

	Cases	Controls	% difference
Lifetime history of major depression, %	35.9	19.1	88%
Lifetime history of PTSD, %	14.8	4.6	222%
Beck Depression Inventory, mean (SD)	12.4 (10.7)	6 (7.3)	107%
PSTD Symptom Checklist, mean (SD)	32.1 (14.8)	24.2 (10.7)	33%
Perceived Stress Scale, mean (SD)	16.5 (8.5)	10.3 (6.4)	60%
State Anxiety, mean (SD)	36.1 (13.1)	29.7 (9.7)	22%
Trait Anxiety, mean (SD)	38 (12.2)	31.6 (9.6)	20%
Childhood Trauma, mean (SD)	3.5 (2.6)	2.7 (2.2)	30%
Lifetime Trauma, mean (SD)	19.0 (12)	14.3 (9.7)	36%
Hostility, mean (SD)	18.5 (9)	12.7 (6.5)	46%
Discrimination, mean (SD)	16.9 (6)	15.8 (5.1)	7%
Psychosocial stressor summary score, mean (SD)	148.6 (66.4)	54.3 (23)	174%

Table 3. Study population resting hemodynamics and vascular function characteristics by study group.

Resting Hemodynamics	Cases	Controls	*p*
Systolic blood pressure, mmHg, mean (SD)	133.6 (21.7)	121.2 (13.1)	<.0001
Diastolic blood pressure, mmHg, mean (SD)	83.6 (12.5)	77.7 (9.1)	<.0001
Heart rate, beat/min, mean (SD)	64.3 (10.7)	62.1 (9.2)	0.04
RPP, beat x mmHg/min per 1,000, mean (SD)	7364.7 (1981.4)	6562.4 (1361.6)	<.0001
Change in Hemodynamics			
Systolic blood pressure, mmHg, mean (SD)	40.3 (16.5)	43.0 (15.3)	0.12
Diastolic blood pressure, mmHg, mean (SD)	28.6 (11.6)	27.2 (10.1)	0.23
Heart rate, beat/min, mean (SD)	23.2 (14.6)	29.8 (14.9)	<.0001
RPP, beat x mmHg/min per 1,000, mean (SD)	13550.3 (3807.3)	13797.9 (3716.4)	0.55
Resting Vascular Function			
FMD percent, mean (SD)	3.9 (2.8)	5.1 (2.6)	<0.01
RHI, mean (SD)	1.79 (0.55)	1.86 (0.51)	0.19
Post-mental stress Vascular Function			
FMD percent, mean (SD)	2.2 (2.4)	3.2 (2.1)	<.0001
FMD percent difference, mean (SD)	0.07 (0.08)	0.11 (0.07)	<0.01
RHI, mean (SD)	1.7 (0.60)	1.9 (0.57)	0.06
Change in Vascular Function			
FMD percent change, mean (SD)	-1.7 (.21)	-.18 (.22)	0.55
RHI percent change, mean (SD)	-0.09 (5.2)	-0.097 (5.7)	0.45

Table 4. Correlation for psychosocial stressor score (and components) and vascular function measures stratified by cases and controls.

Cases	Vascular function measures					
	Resting FMD	Post-mental stress FMD	FMD percent change	Resting RHI	Post-mental stress RHI	RHI percent change
Psychosocial Variables	Spearman Correlation Coefficients					
Summary Score	-0.032	-0.066	-0.032	-0.08	-0.14**	-0.086
BDI	0.007	-0.057	-0.073	-0.11*	-0.15**	-0.086
PCL	-0.018	-0.035	-0.003	-0.061	-0.12**	-0.097
PSS	-0.031	-0.039	0.012	-0.096	-0.11*	-0.066
Childhood Trauma	-0.015	-0.06	-0.042	-0.041	-0.07	0.007
Lifetime Trauma	-0.075	-0.066	-0.004	0.008	-0.078	-0.09
Controls	Vascular function measures					
	Resting FMD	Post-mental stress FMD	FMD percent change	Resting RHI	Post-mental stress RHI	RHI percent change
Psychosocial Variables						
Summary Score	-0.33**	-0.29**	0.025	-0.18*	0.075	0.16
BDI	-0.19**	-0.12	0.079	-0.11	0.063	0.11
PCL	-0.3**	-0.25**	0.031	-0.22**	0.051	0.2**
PSS	-0.22**	-0.15	0.032	-0.089	0.061	0.076
Childhood Trauma	-0.3**	-0.3**	-0.012	-0.21**	0.046	0.18**
Lifetime Trauma	-0.19*	-0.16	0.011	-0.065	0.004	-0.012

* $p < 0.10$

** $p < 0.05$

Table 5. p-values for interaction assessment for psychosocial stressor score quartiles with study group and sex.

	Outcome	
Modifier	FMD percent change	RHI percent change
Sex	0.79	0.57
Study group	0.73	0.02

Table 6. Regression coefficients for psychosocial stressor score and resting FMD percent.

	Regression coefficients			
	Cases	p	Controls	p
Model adjustments				
No adjustment	-0.052	0.68	-1.7	0.002
Age, sex, race	0.038	0.76	-1.6	0.004
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity	0.079	0.56	-1.6	0.02
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity, MI severity	0.061	0.65		

Table 7. Regression coefficients for psychosocial stressor score and resting RHI.

	Regression coefficients			
	Cases	p	Controls	p
Model adjustments				
No adjustment	-0.024	0.32	-0.22	0.05
Age, sex, race	-0.005	0.85	-0.21	0.05
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity	-0.013	0.63	-0.15	0.20
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity, MI severity	-0.015	0.56		

Table 8. Mixed model regression coefficients for psychosocial stressor score and FMD percent change (interaction between psychosocial score and time).

	Regression coefficients			
	Cases	p	Controls	p
Model adjustments				
No adjustment	-0.072	0.94	4.7	0.33
Age, sex, race	-0.071	0.94	4.7	0.33
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity	0.14	0.89	5.8	0.27
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity, MI severity	0.14	0.89		

Table 9. Mixed model regression coefficients for psychosocial stressor score and RHI percent change (interaction between psychosocial score and time).

	Regression coefficients			
	Cases	p	Controls	p
Model adjustments				
No adjustment	-0.41	0.35	2.9	0.02
Age, sex, race	-0.40	0.08	2.9	0.02
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity	-0.37	0.11	1.9	0.12
Age, sex, race, hypertension, diabetes, dyslipidemia, smoking, physical activity, MI severity	-0.37	0.11		

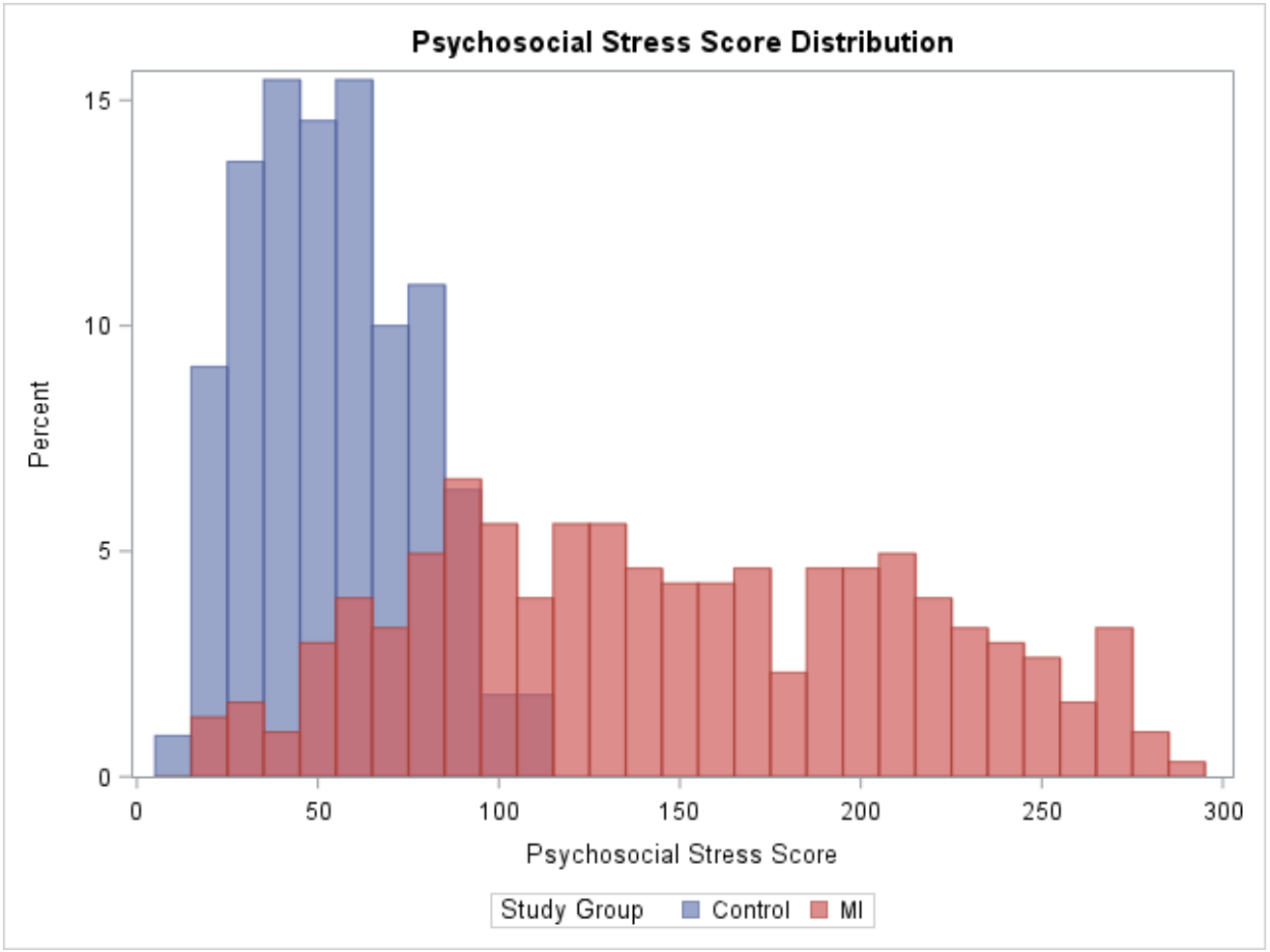

Figure 1. Distribution of psychosocial stressor scores by study group. Psychosocial stressor score summarizes scores of depression, PTSD, perceived stress, childhood trauma, and lifetime trauma.

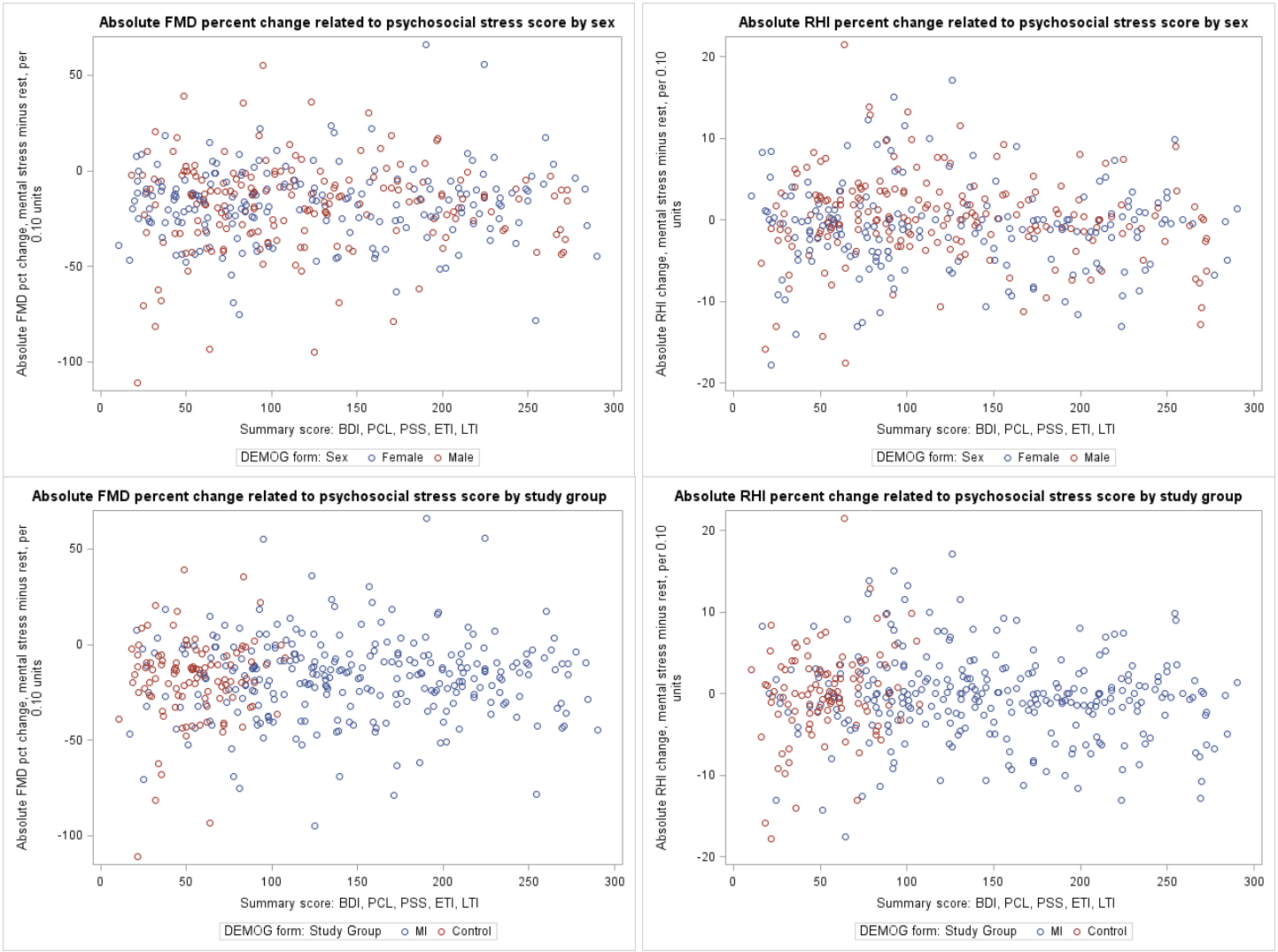

Figure 2. Absolute FMD and RHI percent change stratified by sex and study group.