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Jacob Germany April 22, 2025

The Relationship Between Mental Stress and Hemodynamic Responses in Patients with Coronary Artery Disease

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The Relationship Between Mental Stress and Hemodynamic Responses in Patients with Coronary Artery Disease

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An abstract of
A thesis submitted to the Faculty of the
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Abstract

The Relationship Between Mental Stress and Hemodynamic Responses in Patients with Coronary Artery Disease

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Background

Cardiovascular disease remains a major cause of mortality worldwide, and growing evidence suggests that stress, particularly mental stress and mental stress-induced myocardial ischemia, may serve as a critical link between stress and adverse cardiovascular outcomes in stable coronary artery disease (CAD) and post-MI patients. Recent efforts to address the gap between self-reported stress and physiological stress have utilized large observational datasets, such as the Myocardial Infarction and Mental Stress Study 2 (MIMS2), and the Mental Stress and Myocardial Ischemia after MI: Sex Differences, Mechanisms, and Prognosis study (MIMS3).

Methods

From a sample of 829 participants from the MIMS2 and MIMS3 databases, blood pressure characteristics and Subjective Units of Distress Scale (SUDS) scores were assessed before, during, and after mental stress proxy test. CAD measurement was examined with coronary angiograms, and Gensini Scores were calculated to assess severity. Pearson correlations and multivariate regression modeling was performed.

Results

In our sample of 829 study participants, 440 (53%) are female with a mean age of 50.9 ± 7.2 years. Mean percent increase for systolic blood pressure (SBP) was 24.4 ± 15.2 mmHg, diastolic blood pressure (DBP) 24.4 ± 15.6 mmHg, and heart rate (HR) 88.0 ± 71.0 mmHg. There was no significant linear association between the subjective stress response and hemodynamic changes (SBP, $r = 0.050$; DBP, $r = 0.054$; HR, $r = -0.030$). No significant regression estimates were observed for predicting SUDS score changes from hemodynamic variables after adjusting for age, race, sex, and MI status. Further analysis with Gensini Scores for the MI investigation arms included a total of 594 participants, and no significant regression estimates were observed.

Conclusion

These findings suggest that self-reported stress and physiological responses to mental stress, as measured by hemodynamic changes, may not represent the same underlying construct in this population and stresses the ongoing need for a multidimensional and time-varying approach to stress assessment that integrates both psychological and physiological markers independently.

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Introduction

Cardiovascular disease (CVD) remains a major cause of mortality worldwide, with ischemic heart disease being a primary driver of morbidity and mortality.[1,2] Among individuals who experience a myocardial infarction (MI), the risk of recurrent events remains high despite advances in medical management, with psychological and physiological stress emerging as key contributors to adverse cardiovascular outcomes.[3,4] Growing evidence suggests that stress, particularly mental stress, plays a significant role in the pathophysiology of CVD by triggering hemodynamic dysfunction, increasing inflammation, and exacerbating myocardial ischemia.[5]

Previous efforts to assess stress from a clinical perspective diverge between physical and self-reported measures. On one front, physiological assessments of stress, such as changes in heart rate and blood pressure, are important autonomic markers of cardiovascular risk and are widely regarded as sensitive indicators of psychological and physiological stress.[6] Both heart rate and blood pressure result from underlying autonomic nervous system activity and offer an objective measure of stress-induced cardiovascular effects. Acute increases in HR and BP in response to laboratory stress tasks have been associated with progression of atherosclerosis.[6,7] These objective responses are reproducible under standardized testing conditions and provide insight into an individual's stress reactivity profile, which has shown predictive utility for long-term cardiovascular outcomes.[8]

On the other front, self-reported stress questionnaires are commonly used in clinical and epidemiological studies due to their accessibility and ease of administration.[9] These tools often capture perceived stress levels acutely and over time, including chronic stress, life events, and emotional coping, using instruments such as the Perceived Stress Scale (PSS), the Beck Anxiety Inventory (BAI), the Subjective Units of Distress Score (SUDS), or the Depression, Anxiety, and

Stress Scales (DASS). In cardiovascular research, elevated scores on self-reported stress scales have been associated with increased incidence of hypertension, coronary artery disease, and adverse cardiac events[10]. Notably, chronic perceived stress has been linked to elevated inflammatory markers and greater progression of atherosclerosis, suggesting that subjective experiences of stress can reflect underlying biological processes.[10] Additionally, these methods have demonstrated reasonable validity, indicating that they may accurately reflect internal stress states in relation to cardiovascular outcomes.[11,12]

These two approaches offer distinct insights for how researchers aim to measure stress and assess risk for future adverse CVD events. While self-reported and physiological stress measures offer valuable insights on their own, integrating them in cardiovascular research presents a unique opportunity to deepen our understanding of stress-related risk. However, this integration presents several challenges. Self-reported stress reflects subjective appraisal and coping, which may not always align with acute physiological responses driven by autonomic activity.[13,14] Previous research has revealed the difficulty adjusting for confounders such as socioeconomic, behavioral, and environmental factors when measuring acute stress levels among individuals.[15] Differences in timing, context, and the nature of stressors - whether chronic or acute - further complicate their comparison.[16] Despite these challenges, examining the similarities and differences between self-reported and physiological responses is critical for improving risk assessment and tailoring interventions, and few studies have explored these relationships in high-risk individuals such as post-MI populations.[17,18]

This thesis presents a secondary analysis of pooled data from two longitudinal cohort studies – the Myocardial Infarction and Mental Stress Study 2 (MIMS2), and the Mental Stress and Myocardial Ischemia after MI: Sex Differences, Mechanisms, and Prognosis study (MIMS3)

- to investigate the relationship between self-reported stress levels and hemodynamic reactivity impact of mental stress on cardiovascular outcomes. Drawing on a diverse sample of individuals with histories of myocardial infarction and controls without prior cardiovascular events, this study aims to examine the relationship between mental stress and hemodynamic response with specific attention to both self-reported and physiological measures of stress. The findings may improve our understanding of stress-related cardiovascular risk and inform the current development of more personalized strategies for post-MI risk stratification and intervention.

Methods

Data were collected in a combined sample of 829 participants from two Emory University Rollins School of Public Health Emory Program in Cardiovascular Outcomes Research and Epidemiology (EPICORE) observational cohort studies, MIMS2 and MIMS3, to evaluate the effect of our stress proxy on self-reported stress levels and physiological hemodynamic changes. MIMS2 aimed to evaluate whether young women who have recently experienced a myocardial infarction (MI) are more susceptible to myocardial ischemia due to psychological stress compared to men of similar age. It also sought to examine the mechanisms underlying this stress-induced ischemia and assess its role in the poorer prognosis observed in women with MI relative to men. Furthermore, MIMS2 investigated stress-related factors contributing to heart disease by examining how mental stress tasks, such as public speaking and problem-solving, affect the heart in patients with diagnosed heart disease while also analyzing blood biomarkers and conducting heart scans during testing sessions.[17] MIMS3, which was a renewal of MIMS2, allowed the researchers to study a larger sample and conduct an adequately powered analysis of sex differences in risk of long-term adverse outcomes.

Study participants for the MIMS2 and MIMS3 studies 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 within the previous 8 months from February 2018 at Emory-affiliated hospitals in Atlanta, Georgia and who were between the ages of 18 to 60 years at the time of screening.[17] The diagnosis of MI (type 1) was verified by medical record review based on standard criteria of troponin level increase together with symptoms of ischemia and electrocardiogram (ECG) changes or other evidence of myocardial necrosis; presence of obstructive CAD was not a criterion for inclusion.[19] Controls were recruited in the Atlanta area from a community-based study of individuals without established CAD.[20] Inclusion criteria for controls were between 18 and 60 years of age and no past 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.[17]

Subjects were excluded if they had a severe comorbid medical or psychiatric disorder that could interfere with study results. Examples of such exclusion criteria included cancer, renal failure, severe uncontrolled hypertension, current alcohol or substance abuse, schizophrenia, if they were pregnant or breastfeeding, or if they were currently using immunosuppressant or psychotropic medications other than antidepressants.[17] MI patients were also excluded if they had unstable angina, acute MI, or decompensated heart failure within the past week. Additional exclusion criteria included if they weighed more than 450 pounds due to testing limitations on nuclear stress test equipment. Research participants were also excluded if it was deemed to be unsafe by study cardiologists to hold anti-ischemic medications for 24 hours before the testing.[17]

Descriptive statistics were examined for baseline clinical and demographic characteristics. Hemodynamic responses and patient stress assessment rankings were recorded. The stress test started with a 30-minute rest in a quiet, temperature-controlled room as participants underwent a standardized mental stress task involving a simulated public speaking scenario. Participants were given 2 minutes to prepare and 3 minutes to speak about a distressing situation involving a mistreated family member while being recorded and observed by an evaluative audience of researchers in white coats. Blood pressure characteristics were assessed before the stress test (30 min rest-period), during the stress test (every minute), and after the stress test (30 min rest period). Subjective Units of Distress Scale (SUDS) was administered before and after stress test, scoring stress from 0 to 100; minimum blood pressure during rest-period and maximum blood pressure during stress test were used in the analysis. Coronary artery disease assessment and progression was examined with coronary angiograms, and Gensini Scores were calculated to measure severity. Pearson correlations were computed, and multivariate regression modeling was used with SAS 9.4 statistical software to examine the relationship between change in blood pressure characteristics and change in SUDS score.

Results

Descriptive statistics of the cohort are presented in Table 1. In our sample of 829 study participants, there were 284 (34%) participants in the female MI group, 335 (40%) in the male MI group, 156 (19%) in the female control group, and 54 (7%) in the male control group. Overall, 440 (53%) study participants were female with a mean age of 50.9 ± 7.2 years, 458

(55%) identified as Black/African American, and 414 (50%) had a Body Mass Index (BMI) greater than 30 kg/m².

Descriptive hemodynamic and SUDS score statistics are presented in Table 2. Mean percent increase for systolic blood pressure (SBP) was 24.4 ± 15.2 mmHg, diastolic blood pressure (DBP) 24.4 ± 15.6 mmHg, and heart rate (HR) 88.0 ± 71.0 mmHg. The average SUDS score increase was 30.6 ± 30.0 points. Overall, women who have experienced an MI were younger and had the lowest percent increase in blood pressure characteristics while also recording the highest resting and stress-test blood pressure characteristics than both MI men and both control groups. On average, women who have experienced an MI had the highest baseline SUDS scores of 15.1 ± 23.0 points and highest post stress-test SUDS score of 46.7 ± 31.5 points. However, the female control group had the largest difference in SUDS scores with an average of 34.0 ± 28.1 points compared to the other groups.

Changes in hemodynamics and SUDS scores were approximately normally distributed (Figure 1). For the entire cohort, no significant correlations were observed between percent increase in hemodynamic variables (SBP, $r = 0.050$; DBP, $r = 0.054$; HR, $r = -0.030$) and the change in SUDS score (Table 3). Additionally, no significant correlations were observed after stratifying by group. Figure 2 displays the correlation matrices between hemodynamic responses and SUDS score differences. No significant regression estimates were observed for predicting SUDS score changes from hemodynamic variables after adjusting for age, race, sex, and MI status (Table 4). Further analysis was conducted by including Gensini Scores for the MI investigation arms which included a total of 594 participants from the MI investigation arms, and no significant regression estimates were observed (Table 5).

Discussion

In our sample of 829 study participants, there was no significant linear association between recorded stress response and hemodynamic changes. After adjusting for age, sex, race, and MI diagnosis, the association remained non-significant. Furthermore, adjusting for level of coronary artery disease did not result in statistically significant linear associations. These findings suggest that self-reported stress and physiological responses to mental stress, as measured by hemodynamic changes, may not represent the same underlying construct in this population. To clarify, the subjective, perceived stress and the cardiac stress that is autonomically driven occur together during the speech task – however, the intensity and change in one does not control the intensity and change of the other, suggesting that the underlying mechanisms are different.

Although prior studies have demonstrated that both subjective stress and physiological reactivity independently predict adverse cardiovascular outcomes, few studies have investigated this relationship together; after thorough search through the relevant literature, one study assessed daily high and low-frequency heart rate changes and self-reported stress changes via diary proxy entrances in patients with CAD over a 48-hour period;[21] none have directly compared the level of agreement or disagreement between these two domains completely within the same individuals with CAD against controls. These findings add clarity to the current literature by revealing a lack of correlation between self-reported and physiological stress responses, suggesting these measures may tap into fundamentally different dimensions of the stress experience.[16] This divergence challenges the assumption that subjective reports can reliably proxy for physiological stress load in cardiovascular risk assessment and vice versa.

The observed differences across sex and MI status further emphasize the well-documented importance of contextual, demographic, socioeconomic, and social factors in shaping stress responses. Although subgroup differences were observed, such as higher SUDS scores and lower percent BP increases among women with MI, they were not statistically significant and were outside the original scope of this study. Therefore, these specific findings should be interpreted cautiously and warrant further investigation. Nevertheless, they are consistent with the prior research from the MIMS2 and MIMS3 research projects, which have reported sex-based disparities in both stress perception and cardiovascular outcomes following MI.[17]

The absence of significant findings in this study may point to the limitations of using acute stress tests in controlled settings as a proxy for cardiovascular hemodynamic changes. Another limitation is the reliance on self-reported distress ratings, which are influenced by social desirability bias and reduce the accuracy of their assessment of stress. However, this limitation stems from the well-known reality of self-reported data and begets the original purpose of this study. In a similar theme, having different stress proxies rather than a single mental stress assessment may improve the internal consistency of the testing protocol and strengthen the comparisons to hemodynamic reactivity.

Finally, this study highlights the need for multidimensional and time-sensitive approaches that capture perceived and biological markers across varying contexts. While acute lab-based assessments of stress offer standardized conditions, they do not fully encompass the effect of the cumulative nature of psychosocial stress encountered over weeks, months, and years of life. While these findings revealed a divergence between subjective and physiological stress responses, these results do not diminish the importance of each type of stress in cardiovascular

health. Rather, it suggests that the pathways through which stress influences disease risk are likely multifaceted and involve independent but complementary processes as currently measured. Future studies should examine stress through separate frameworks that capture both psychological and physiological responses alongside varying interventions based on whether they target subjective stress or autonomic stress activation. Additionally, further analysis should explore the role of neurobiological markers, inflammatory profiles, and long-term stress exposure to better elucidate the varying and differing mechanisms linking stress and cardiovascular outcomes.

Table 1: Demographic Characteristics of MIMS2 and MIMS3 Participants, Stratified by Investigation Arm

Sample Characteristic	Full Cohort (N=829)	MI Female (N=284)	MI Male (N=335)	Control Female (N=156)	Control Male (N=54)
Age (years) --- mean (SD)	50.9 (7.2)	50.9 (7.1)	511.2 (6.6)	51.3 (7.1)	48.3 (10.3)
Race --- no. of participants (%)					
Black/AA	458 (55.25)	201 (70.77)	163 (48.66)	75 (48.08)	19 (35.19)
White	312 (37.64)	69 (24.3)	140 (41.79)	72 (46.15)	31 (57.41)
Asian	23 (2.77)	2 (0.7)	18 (5.37)	1 (0.64)	2 (3.70)
Am Ind/Alaska Native	5 (0.60)	2 (0.7)	2 (0.6)	1 (0.64)	0 (0)
Multiracial	10 (1.21)	4 (1.41)	2 (0.6)	3 (1.92)	1 (1.85)
Unknown, Hispanic	12 (1.45	3 (1.06)	8 (2.39)	1 (0.64)	1 (1.85)
West Indian	6 (0.72)	2 (0.7)	0 (0)	3 (1.92)	0 (0)
Hawaii/Pacific Is	1 (0.12)	0 (0)	1 (0.3)	0 (0)	0 (0)
Indian (Asian)	1 (0.12)	0 (0)	1 (0.3)	0 (0)	0 (0)
Other, no specified	1 (0.12)	1 (0.35)	0 (0)	0 (0)	0 (0)
Body Mass Index (BMI) (kg/m²) --- no. of participants (%)					
<25	165 (19.93)	45 (15.9)	61 (18.21)	47 (30.13)	12 (22.22)
25<30	249 (30.07)	55 (19.43)	128 (38.21)	42 (26.92)	24 (44.44)
>=30	414 (50.0)	183 (64.66)	146 (43.58)	67 (42.95)	18 (33.33)
missing	1	1	0	0	0
H/o Coronary Artery Bypass --- no. of participants (%)	88 (10.62)	42 (14.79)	46 (13.73)	0 (0)	0 (0)
Hypertension --- no. of participants (%)	555 (66.95)	235 (82.75)	257 (76.72)	48 (30.77)	15 (27.78)
Diabetes Mellitus --- no. of participants (%)	227 (27.38)	108 (38.03)	99 (29.55)	17 (10.9)	3 (5.56)
Hyperlipidemia --- no. of participants (%)	546 (65.86)	212 (74.65)	266 (79.40)	53 (33.97)	15 (27.78)
Autoimmune Disease --- no. of participants (%)	61 (7.36)	33 (11.62)	13 (3.88)	15 (9.62)	0 (0)
Human Immunodeficiency Virus --- no. of participants (%)	30 (3.62)	8 (2.82)	18 (5.39)	3 (1.92)	1 (1.85)

Table 2: Hemodynamic and SUDS Score Descriptive Statistics

Hemodynamic Characteristic	Full Cohort (N=829)	MI Female (N=284)	MI Male (N=335)	Control Female (N=156)	Control Male (N=54)
Systolic Pressure (mmHg) --- mean (SD)					
Min	129.6 (21.3)	135.1 (24.1)	129.6 (20.2)	121.7 (16.8)	123.6 (14.5)
Max	159.8 (25.5)	162.8 (26.9)	160.6 (25.7)	154.8 (23.0)	153.8 (20.8)
% Increase	24.4 (15.2)	22.1 (16.0)	24.7 (14.8)	27.9 (14.5)	24.8 (13.8)
Diastolic Pressure (mmHg) --- mean (SD)					
Min	81.5 (13.3)	83.8 (13.9)	81.8 (13.8)	77.5 (11.2)	79.5 (10.5)
Max	100.2 (15.1)	101.5 (16.2)	101.3 (15.1)	96.8 (13.8)	97.1 (10.5)
% increase	24.4 (15.6)	22.6 (16.8)	25.6 (15.9)	25.8 (13.6)	23.0 (11.6)
Heart Rate (bpm) --- mean (SD)					
Min	62.4 (10.9)	65.0 (10.7)	61.4 (11.5)	61.3 (9.5)	58.6 (9.0)
Max	114.7 (39.5)	117.7 (43.0)	113.5 (40.4)	105.3 (31.2)	133.3 (27.5)
% Increase	88.0 (71.0)	85.0 (73.1)	89.7 (75.4)	74.4 (54.1)	131.9 (57.7)
SUDS --- (scale 0-100)					
Pre --- mean (SD)	11.8 (18.3)	15.1 (23.0)	9.5 (14.7)	12.0 (16.8)	8.6 (9.9)
Pre --- median (IQR)	5 (0, 15)	3 (0, 20)	5 (0, 10)	5 (0, 20)	10 (0, 10)
Post --- mean (SD)	42.4 (29.8)	46.7 (31.5)	37.0 (28.0)	45.97 (28.9)	42.1 (29.1)
Post --- median (IQR)	40 (20, 65)	50 (20, 70)	30 (10, 60)	45 (20, 70)	35 (20, 60)
Difference --- mean (SD)	30.6 (30.0)	31.5 (34.2)	27.7 (26.2)	34.0 (28.1)	33.4 (26.9)

Figure 1: Hemodynamic and SUDS Change Distributions

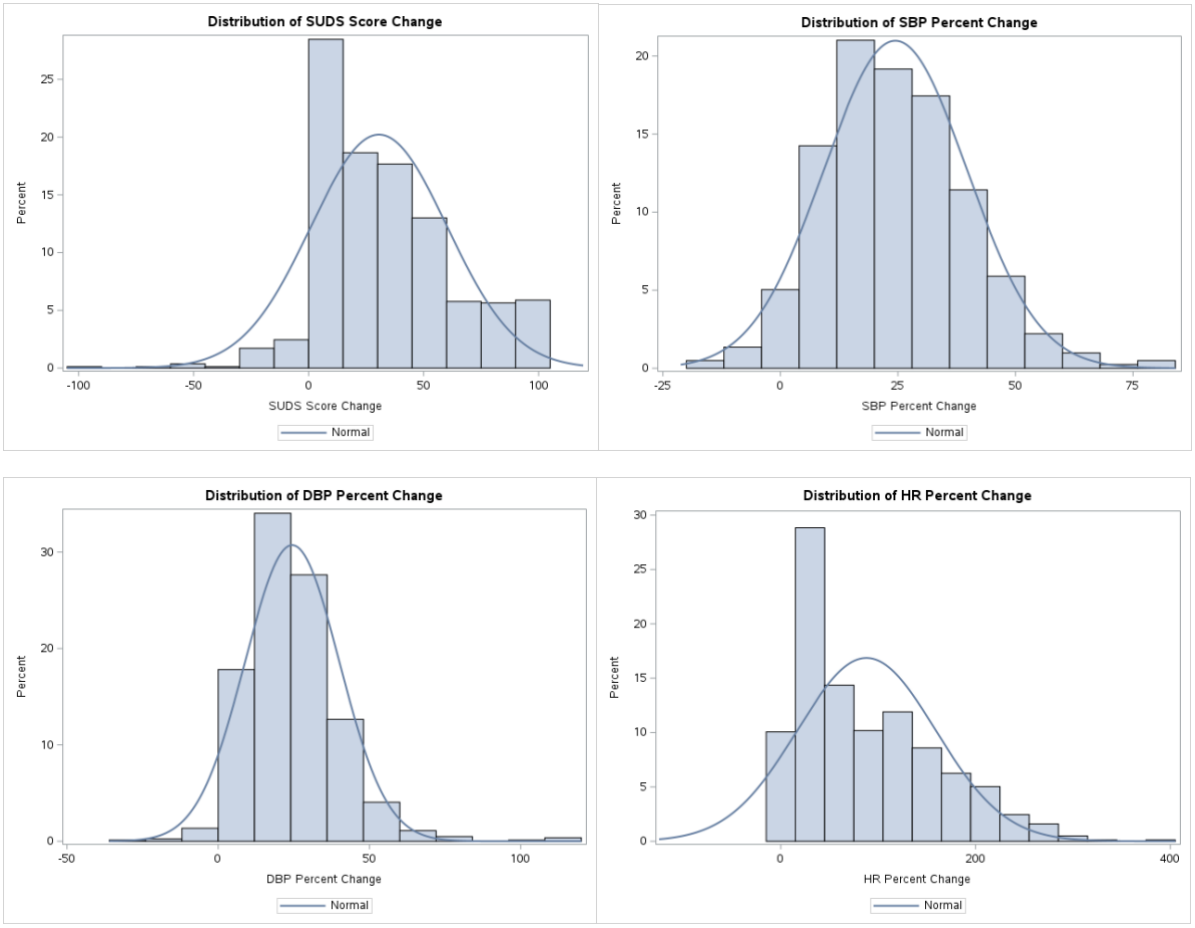


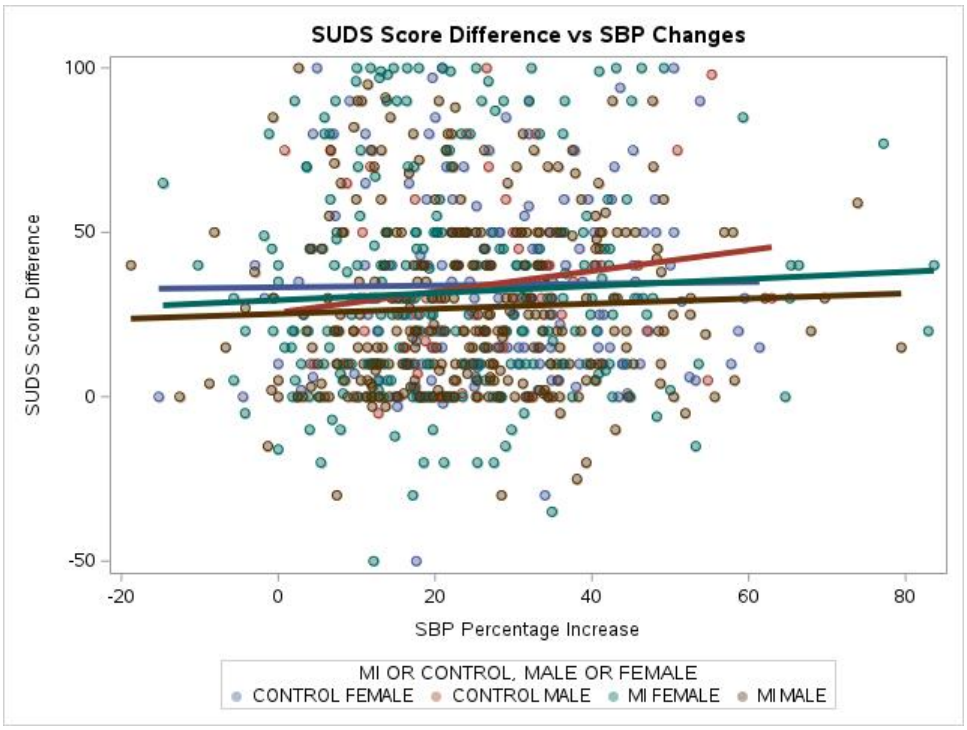
Table 3: Correlation between Change in SUDS Score and Hemodynamic Changes in Blood Pressure Characteristics

Hemodynamic Characteristic	Pearson Correlation Coefficient (r)	95% Confidence Interval	p-value (α=0.05)	Investigation Arm
SBP % Increase	0.05	-0.02, 0.12	0.16	MI Female
DBP % Increase	0.054	-0.02, 0.12	0.13	
HR % Increase	-0.03	-0.10, 0.04	0.39	
SBP % Increase	0.05	-0.07, 0.17	0.41	MI Female
DBP % Increase	0.03	-0.09, 0.15	0.66	
HR % Increase	-0.03	-0.15, 0.09	0.61	
SBP % Increase	0.05	-0.06, 0.15	0.42	MI Male
DBP % Increase	0.08	-0.03, 0.19	0.16	
HR % Increase	-0.05	-0.15, 0.06	0.41	
SBP % Increase	0.01	-0.14, .17	0.86	Control Female
DBP % Increase	0.06	-0.10, 0.22	0.45	
HR % Increase	0.05	-0.10, 0.21	0.5	
SBP % Increase	0.16	-0.11, 0.41	0.24	Control Male
DBP % Increase	0.19	-0.08, 0.44	0.17	
HR % Increase	-0.13	-0.38, 0.14	0.35	

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate

Figure 2. Correlation Matrices of SUDS Score Change vs SBP Changes (a), DBP Changes (b), and HR Changes (c) by Investigation Arm

(a)



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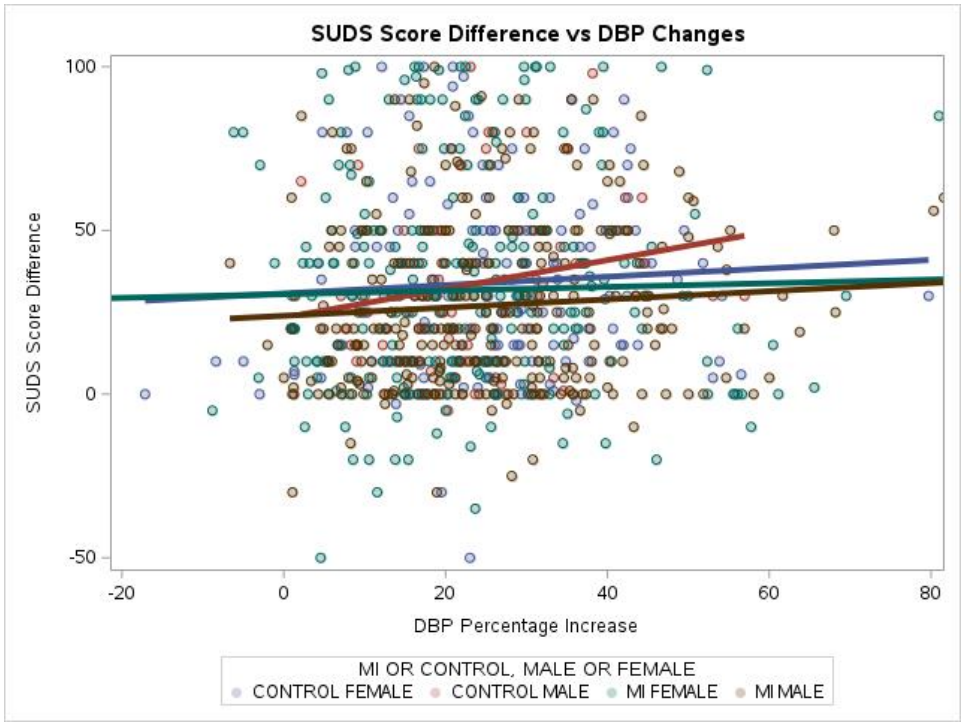

(c)

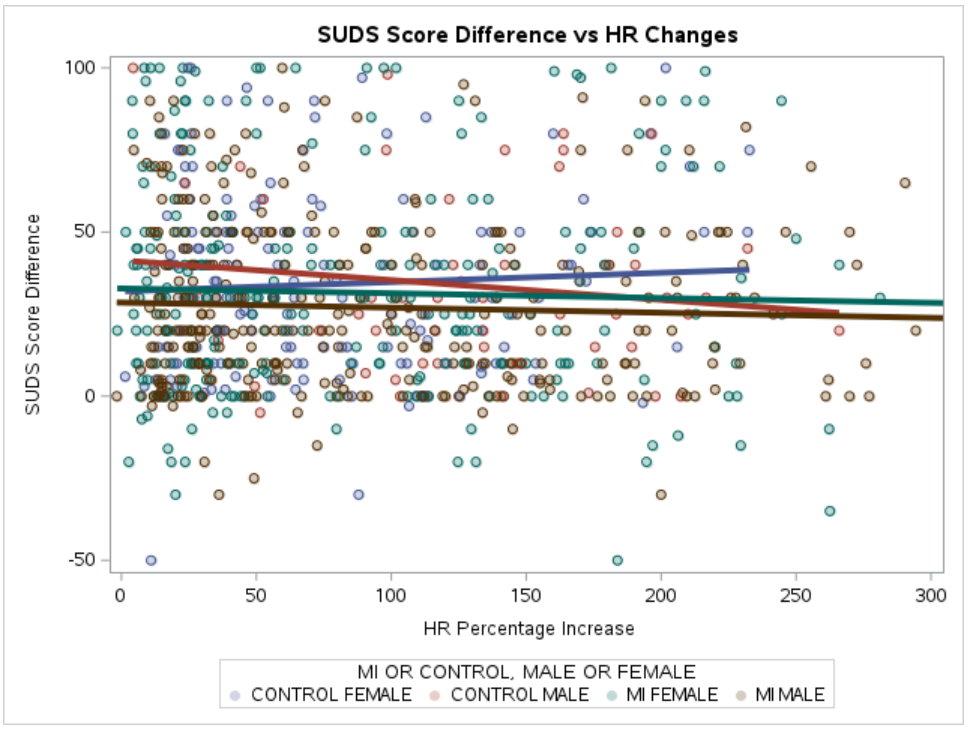

Table 4: Regression Estimates between Change in SUDS Score and Hemodynamic Changes in Blood Pressure Characteristics

Hemodynamic Characteristic	Mean (SD)	Adj. Regression Coefficient Estimate (95% CI)
SBP % Increase	24.4 (15.2)	0.03 (-0.15, 0.21)
DBP % Increase	24.4 (15.6)	0.06 (-0.11, 0.24)
HR % Increase	88.0 (71.0)	-0.01 (-0.04, 0.01)

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate. Model adjusted for age, sex, race, and MI status.

Table 5: Regression Estimates between Change in SUDS Score and Hemodynamic Changes in Blood Pressure Characteristics with Gensini Score Adjustment

Hemodynamic Characteristic	Mean (SD)	Adj. Regression Coefficient Estimate (95% CI)
SBP % Increase	24.4 (15.2)	-0.01 (-0.15-0.22, 0.21)
DBP % Increase	24.4 (15.6)	0.05 (-0.15, 0.26)
HR % Increase	88.0 (71.0)	-0.02 (-0.06, 0.01)

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate. Model adjusted for age, sex, race, and Gensini Score.

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