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Analysis of Mental-Stress Induced Arrhythmia in Individuals with Recent Myocardial Infarction

By

Baffour Otchere
Degree to be awarded: Master of Public Health

Epidemiology

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Dr. Amit Shah, MD, MSCR
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Analysis of Mental-Stress Induced Arrhythmia in Individuals with Recent Myocardial Infarction

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University of Ghana
2016

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An abstract of
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Abstract

Analysis of Mental-Stress Induced Arrhythmia in Individuals with Recent Myocardial Infarction
By Baffour Otchere

Background:
Stress has been found to be associated with sudden cardiac death and cardiovascular diseases; however, these associations have not been extensively studied like the traditional risk factors of cardiovascular diseases.

Methods and Results:
A total of 162 individuals were included in this study. The average age of the cohort was 53±6 years and 81 of the study participants (52%) were women. There were 123 cases of myocardial infarction (MI) and 32 controls, who did not have MI, in this study. Cases and controls were subjected to acute mental stress and heart rhythm was recorded using Holter monitors and analyzed using General Electric MARS 8.0.2 software. On average, there were 1.27 (95% CI: 0.46, 2.08) premature atrial contractions (PAC) and 2.56 (95% CI: 1.22, 3.89) premature ventricular contractions (PVC) during the mental stress periods, compared to 0.95 (95% CI: 0.43,1.47) PACs and 2.22 (95% CI: 0.61, 3.83) PVCs during a matched period pre-stress. Participants had an average of 0.32 (95% CI: -0.26, 0.90) more PACs and 0.34 (95% CI: -1.32, 2.00) more PVCs during mental stress compared to pre-stress rest. PAC counts were more likely to increase acutely during mental stress in depressed versus non-depressed individuals (OR= 3.60, 95% CI: 1.31, 9.86); PVC count increases were more likely to occur in the recovery period (OR= 3.01 vs. pre-stress rest, 95% CI: 1.12, 8.08) in depressed vs. non-depressed individuals. However, these associations reduced and lost statistical significance after multivariable adjustment for demographic and cardiovascular risk factors.

Conclusions:
Overall, we observed slight, non-significant increases in PAC and PVC burden during stress versus pre-stress rest. Depression was associated with higher arrhythmia burden during stress and recovery, although these relationships were explained by multivariable adjustment for traditional risk factors. More studies are needed to further explore these relationships and their clinical and public health relevance.

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INTRODUCTION

Heart disease is the biggest cause of disability associated life years even during this pandemic, with some studies suggesting a synergistic relationship between COVID-19 and heart disease with respect to disease prognosis (1). According to the CDC, heart disease is the leading cause of death in the United States (2). About a quarter of deaths yearly in the US are attributed to heart disease (3) (23). Sudden cardiac death, particularly, is estimated to be responsible for a lot of cardiovascular disease-associated deaths (4). Considering sudden circulatory collapse due to cardiac arrhythmias is a hallmark of sudden cardiac deaths (5), it is imperative that cardiac arrhythmias, their associations, and precipitants be extensively studied. One such understudied precipitant is psychosocial stress.

Psychosocial stresses may, in fact directly lead to cardiac dysrhythmias because they have long been anecdotally linked with cardiovascular disease especially sudden cardiac death (6). The problem, however, is that there has not been much attention paid to this area as evidenced by the limited number of studies exploring this relationship. Indeed, the difficulty has previously been the inability to objectively measure and reproduce the psychosocial exposures hypothesized to be responsible for the cardiovascular disease outcomes (7). Additionally, replicating studies that seek to find biologically plausible mechanisms by which acute stress leads to disease in humans have been challenging (8,9).

One important pathway proposed is autonomic dysregulation, which includes upregulation of the sympathetic nervous system and downregulation of vagal tone. This may be followed by downstream functional and structural changes of the cardiovascular system that increase the risk of arrhythmia (10). Depression and chronic anxiety reduce heart variability, increase heart rate, and increase blood pressure, suggesting sympathetic overactivity may occur in those with such conditions (11,12).

Unfortunately, with building evidence suggesting a relationship between stress and heart disease, particularly coronary artery disease and cardiac arrhythmias, stress is still not widely accepted as a known risk factor for heart disease (1,10,13,14) . However, a few studies have found that incorporating interventions aimed at reducing psychosocial stress and treating psychiatric disorders can improve outcomes associated with heart disease (15,16). In this study, our first aim was to examine the overall arrhythmia burden during mental stress, if any. The second aim of this study was to examine sex and race differences in mental stress-induced arrhythmias. The third aim was to examine the associations of depression and post-traumatic stress disorder with total arrhythmia burden.

METHODS

Data Source:

Data was obtained from the third Mental Stress and Myocardial Ischemia after MI Study (MIMS 3), which follows a similar protocol as previously described (17). The data obtained included patient demographic data, blood pressure and heart rate data, lab data, ECG data from Holter monitoring, medical history and medication data obtained by reviewing the medical records of the MI admission. Using the MIMS 3 data, this study explored the incidence of cardiac arrhythmia changes during acute mental stress, and also potential moderation by sex and race, as well as post-traumatic stress disorder and depression.

Study Population:

Potential participants were recruited from the pool of patients admitted for myocardial infarction at Emory-affiliated hospitals. We recruited from a clinical pool of men and women ≤ 61 years who were hospitalized for myocardial infarction in the previous 8 months. Patients were pre-screened over the phone and medical records abstracted to confirm the MI prior to testing (18).

Participants:

We excluded participants with a history of unstable angina or MI within the 1 month of visit, systolic blood pressure (SBP) >180mmHg or diastolic blood pressure (DBP) >110 mmHg immediately before stress test; alcohol or substance abuse (past 8 months), or severe psychotic disorder. In addition, we excluded individuals with other serious medical disorders that may interfere with the study results and those deemed unsafe to hold anti-ischemic medications before testing (it is standard protocol to hold these meds before imaging studies) (19) ; on postmenopausal hormone therapy in the past 3 months or on psychotropic medications for severe psychiatric disorder (past month) except anti-depressants were also excluded. Finally, individuals were excluded if they were pregnant or breast feeding (all women with myocardial infarction of childbearing potential receive a pregnancy test), or if they had severe aortic stenosis, or if they weighed more than 360 pounds and/or had a BMI >40 (weight limit of the SPECT imaging table).

Study Design:

All myocardial infarction cases and controls who met the eligibility criteria underwent mental stress testing in the morning. Sociodemographic and psychosocial data were collected before mental stress and cardiac testing. Mental stress testing was done after overnight fast, and anti-ischemic drugs were withheld for 24 hours before mental stress testing. Medical records were abstracted from clinical information. The study protocol was approved by the Emory University Institutional Review Board, and all participants provided informed consent.

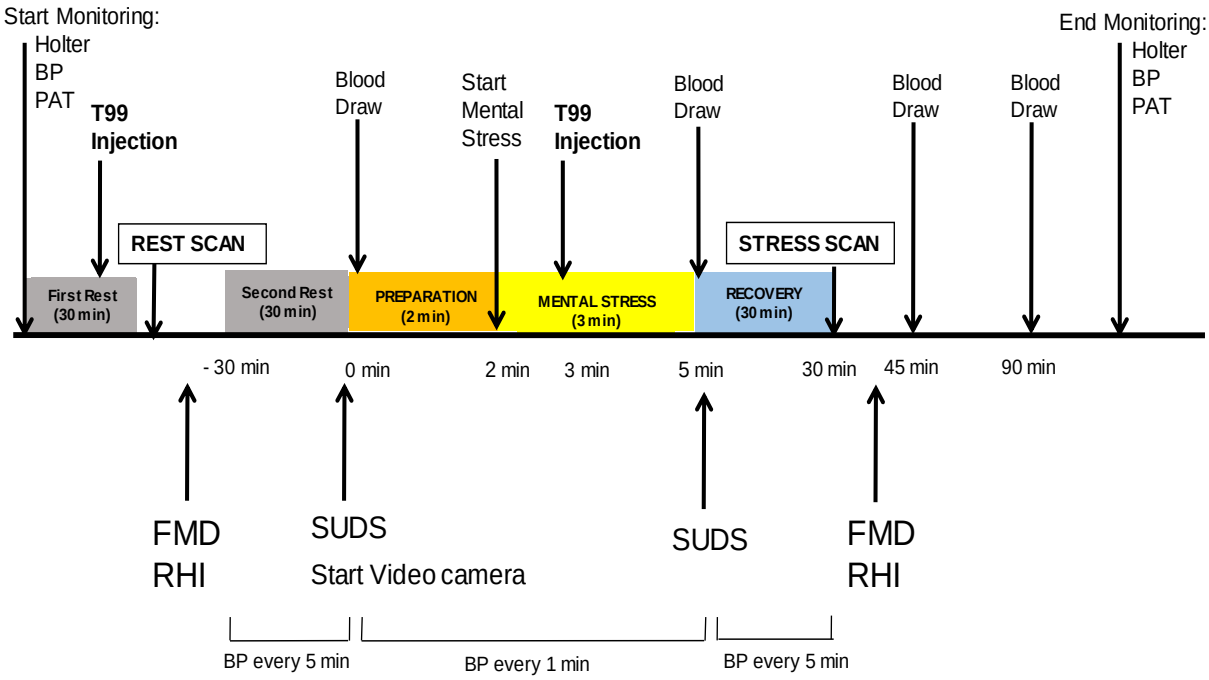
Experimental Protocol and Exposure:

All participants arrive at the lab in the morning after fasting. Following common clinical practice for nuclear cardiology studies (19–21), anti-ischemic medications were held on the morning of the test for myocardial infarction cases. The protocol

timeline is shown in Figure 1 below. While the patient rests, baseline data were obtained, including the rest scan. Afterward, the stress challenge begins. A physician or other staff member wearing a white coat and not known to the patient entered the room and provided instructions. Subjects were asked to imagine a stressful situation: a scenario in which a close relative had been mistreated in a nursing home. They were asked to prepare a statement for 2 min and then present it in front of an audience (≥3 people) and video camera for 3 min. Subjects were told that their speech will be evaluated for quality, content, and duration. Blood pressure and heart rate were recorded at 5-min intervals during the resting phase and at 1-min intervals during mental stress using an automatic device (Datascope Accutorr). Subjects wore a Holter monitor. At 1 min into the stress task, 30-40 mCi for stress imaging, based on weight, is injected. Images are acquired 40 minutes to 1 hour later.

Figure 1:

General diagram of the mental stress protocol.



Measurement of Arrhythmias:

We clinically reviewed Holter ECG files in General Electric MARS 8.0.2 software (22). Labels of premature atrial complexes, premature ventricular complexes, atrial fibrillation, non-sustained supraventricular tachycardia, and paroxysmal supraventricular tachycardia were the first proposed by the software algorithms, and then confirmed by the trained ECG reader. We determined the overall arrhythmia burden by evaluating the entire recording time of the study visit, which was approximately 6-8 hours. Information on the number of arrhythmias during the rest period, during mental stress, and during the recovery period was recorded from ECGs. The rest period was defined as the 5-minute interval from 10 minutes before mental stress starts to 5 minutes before mental

stress starts. The mental stress period was defined as the 5-minute interval between when participants started preparing their speech (2 minutes) to when the speech presentation was complete (3 minutes). The recovery period was defined as the 5-minute interval from 5 minutes after the end of mental stress to 10 minutes after the end of mental stress.

Other Measurements:

Data on sociodemographic characteristics, medical history, and medication history were obtained by a research nurse using standardized questionnaires and by abstracting medical records. Glucose and lipid profiles were measured after an overnight fast.

Psychosocial and mental health information were elicited using standardized psychometric instruments. The Structured Clinical Interview for DSM IV (23) was used to categorize participants based on a lifetime history of mental health disorders like depression, post-traumatic stress disorder.

The covariates of interest for this study include age, race, sex, level of education, cardiac disease risk factors like diabetes, hypertension, hyperlipidemia, chronic psychiatric disorders like depression and PTSD (to be considered as secondary exposure). These were examined by trained clinical staff who conducted interviews and detailed chart reviews.

Statistical Analysis:

We collected data from participants using REDCap (24) and analyzed it with R studio APGL v3 software (25). Demographic, clinical and arrhythmia, psychosocial and mental health disorder variables were stratified by race and sex because of our interest in the race and sex differences in overall arrhythmia burden. These comparisons were made using *Wilcoxon signed-rank test* for continuous variables because the distributions of the PACs and PVCs were skewed, and *chi squared tests* for categorical variables.

In this study, the overall arrhythmia burden, and differences in arrhythmia burden in the rest, stress, and recovery periods were examined. To detect these differences, we created reactivity metrics that were simply a difference between stress (or recovery) and rest PAC or PVC counts. A positive reactivity value meant there were more PACs or PVCs during stress (or recovery) than during rest and a negative stress reactivity value meant there were fewer PACs or PVCs during stress (or recovery) than during rest. After, we examined reactivity by subgroups of sex and race.

We conducted univariate logistic regression analyses to investigate the effect of race and sex on arrhythmia formation. Blacks or African Americans and women were the index groups while Whites or Caucasians and men were the reference groups. In these analyses, we again compared ectopic beats during stress or recovery to ectopic beats during rest. Because of the skewed distribution of the outcome of PAC or PVC reactivity, we dichotomized them. A value of 1 was assigned to the outcome if the reactivity value was greater than zero and a value of 0 was assigned reactivity values less than or equal to zero.

Finally, the associations between depression and post-traumatic stress disorder with total arrhythmia burden were examined in a similar manner to sex and race. To determine the relationship between chronic mental stress (depression and PTSD) and arrhythmias, multiple logistic regressions were used adjusting for hypertension, diabetes mellitus, and dyslipidemia. For these analyses, binary outcomes were created from the reactivity values as described above.

RESULTS

Demographic data and medical history

A total of 162 participants were included in the study. One myocardial infarction (MI) case with missing ECG data was excluded from the final analysis. The average age of the entire cohort was 53±6 years and 81(52%) of the study participants were women. African Americans or Black people made up 38% of the cohort. Participants with a history of myocardial infarction had higher rates of history of hypertension compared to controls. The differences in the rates of diabetes, dyslipidemia, depression, posttraumatic stress disorder, and cigarette smoking across myocardial infarction status were however not statistically significant.

Overall arrhythmia burden during mental stress

Throughout the experiment, there were 3.42 (95% CI: 1.65, 5.19) combined PACs and 6.72 (95% CI: 3.33, 10.11) combined PVCs on average. MI cases had more arrhythmias during the study: [PACs: 3.61 (95% CI: 1.47, 5.75) and PVCs: 6.61 (95% CI: 2.65, 10.57)] in cases versus [PACs: 3.03 (95% CI: -0.61, 6.67) and PVCs: 4.66 (95% CI: -0.81, 9.73)] in controls.

Overall, there were 1.27 (95% CI: 0.46, 2.08) premature atrial ectopic beats and 2.56 (95% CI: 1.22, 3.89) premature ventricular ectopic beats during mental stress. When comparing arrhythmias during mental stress to the rest period, participants had an average of 0.32 (95% CI: -0.26, 0.90) more PACs and 0.34 (95% CI: -1.32, 2.00) more PVCs during mental stress compared to pre-stress rest. When comparing arrhythmias during recovery to rest, there were 0.25 (95% CI: -1.32, 2.00) more PACs and 0.27 (95% CI: -1.22, 0.68) fewer PVCs on average during recovery than rest. The differences between arrhythmias during stress to arrhythmias during rest, using the reactivity metrics, yielded no statistically significant results. Similarly, the differences between arrhythmias during recovery to arrhythmias during rest, using the reactivity metrics, yielded no statistically significant results. These findings are detailed in Tables 2 and 3.

Sex and race differences in mental stress-induced arrhythmias

When focusing on the effect sizes alone, women had more PACs than men, and men had more PVCs than women. Black or African Americans had more PACs and PVCs than any racial group in the cohort. Men had more PACs during mental stress and recovery than rest. Women showed a similar trend but with smaller differences in the number of ectopic beats than men. Men had more PVCs during stress than rest but had fewer PVCs during recovery than during the rest period. Women overall had fewer PVCs during recovery than during rest. These findings were not statistically significant and are summarized in Table 5.

On average, African Americans or Black people had more PACs and PVCs during mental stress and recovery than rest. Caucasians however, had fewer ectopic beats when comparing the different time periods overall except there were more PACs during mental stress than during rest. There were no statistically significant associations in any of these comparisons.

As shown in Tables 7and 8, univariate logistic regression analyses showed no significant association between race and sex, and acute stress arrhythmias. Women had an increased PAC count with mental stress than at rest (OR= 2.50, 95% CI: 0.97, 6.44, p =0.06).

The associations of depression and post-traumatic stress disorder with total arrhythmia burden

After adjusting for post-traumatic stress disorder, participants with a diagnosis of depression were more likely to have premature atrial complexes in the stress period compared to the rest period (OR= 3.60, 95% CI: 1.31, 9.86, p =0.01). The depression-stratified model also showed that participants with depression were more likely to develop premature ventricular complexes during the recovery period than the rest period after adjusting for post-traumatic stress disorder (OR= 3.01, 95% CI: 1.12, 8.08, p =0.03). Other models, however, in the tables did not show significant results.

TABLE 1: PARTICIPANT CHARACTERISTICS

	Cases (N=123)	**Controls (N=32)**	**p**
Age at baseline			
Mean (SD) years	52.0 (6.70)	54.4 (5.10)	0.07
Sex			<0.001
Female Male	49 (39.8%) 74 (60.2%)	32 (100%) 0 (0%)	
Race			0.72
White/Caucasian Black/ African American Other/More than one race American Indian/Alaskan Asian Hawaiian Native	61 (49.6%) 49 (39.8%) 3 (2.4%) 1 (0.8%) 8 (6.5%) 1 (0.8%)	18 (56.3%) 13 (40.6%) 1 (3.1%) 0 (0%) 0 (0%) 0 (0%)	
Education			0.21
Less than 9th grade 9th-11th grade High School Graduate Some College/ AA degree College Graduate & above	1 (0.8%) 7 (5.7%) 22 (17.9%) 37 (30.1%) 56 (45.5%)	0 (0%) 0 (0%) 2 (6.3%) 10 (31.3%) 20 (62.5%)	
Diabetes	42 (34.1%)	7 (21.9%)	0.21
Hypertension	83 (67.5%)	13 (40.6%)	0.006
Dyslipidemia	71 (57.7%)	12 (37.5%)	0.56
Currently Smoking	14 (11.4%)	1 (3.1%)	0.27
Depression	18 (14.6%)	7 (21.9%)	0.22
Post-Traumatic Stress Disorder	8 (6.5%)	5 (15.6%)	0.07

TABLE 2: OVERALL ARRHYTHMIA BURDEN IN ALL PERIODS COMBINED (REST, STRESS, and RECOVERY)

	Cases (N=123)	**Controls (N=32)**	**Overall (N=162)**
Total PACs			
Mean (CI)	3.61 (1.47, 5.75)	3.03 (-0.61, 6.67)	3.42 (1.65, 5.19)
Total PVCs			
Mean (CI)	6.61 (2.65, 10.57)	4.66 (-0.81, 9.73)	6.72 (3.33, 10.11)

PAC – Premature Atrial Complexes; PVC – Premature Ventricular Complexes

TABLE 3: OVERALL ARRHYTHMIA BURDEN DURING MENTAL STRESS

	Overall (N=162)
PACs	
Mean (CI)	1.27 (0.46, 2.08)
PVCs	
Mean (CI)	2.56 (1.22, 3.89)

PAC – Premature Atrial Complexes; PVC – Premature Ventricular Complexes

TABLE 4: COMPARING ARRHYTHMIA BURDEN DURING MENTAL STRESS TO THE REST PERIOD AND DURING RECOVERY TO THE REST PERIOD IN THE COHORT

	Cases (N=123)	**Controls (N=32)**	**Overall (N=162)**
PAC			
Stress vs Rest, Mean (CI)	0.48 (-0.22, 1.18)	0.09 (-0.94, 1.13)	0.32 (-0.26, 0.90)
Recovery vs Rest, Mean (CI)	0.50 (-0.28, 1.28)	-0.34 (-0.87, 0.19)	0.25 (0.36, 0.86)
PVC			
Stress vs Rest, Mean (CI)	0.79 (-1.26, 2.84)	-0.44 (-2.99, 2.11)	0.34 (-1.32, 2.00)
Recovery vs Rest, Mean (CI)	-0.11 (-1.27, 1.05)	-0.72 (-2.51, 1.07)	-0.27 (-1.22, 0.68)

PAC – Premature Atrial Complexes; PVC – Premature Ventricular Complexes

TABLE 5: SEX DIFFERENCES IN MEAN ARRHYTHMIA BURDEN: STRESS VS REST AND RECOVERY VS REST

	Male (N=74)	**Female (N=81)**
PAC		
Stress vs Rest, Mean (CI) **Recovery vs Rest,** Mean (CI)	0.59 (-0.11, 1.29) 0.41 (-0.27, 1.09)	0.24 (-0.71, 1.19) 0.25 (-0.78, 1.28)
PVC		
Stress vs Rest, Mean (CI) **Recovery vs Rest,** Mean (CI)	1.26 (-2.00, 4.52) -0.16 (-1.98, 1.66)	-0.12 (-1.48, 1.24) -0.23 (-1.16, 0.70)

PAC – Premature Atrial Complexes; PVC – Premature Ventricular Complexes

TABLE 6: RACE DIFFERENCES IN MEAN ARRHYTHMIA BURDEN: STRESS VS REST AND RECOVERY VS REST

	White or Caucasian (N=79)	**Black or African American (N=62)**	**Other/More than one race (N=4)**	**Asian (N=8)**
PAC				
Stress vs Rest, Mean (CI)	0.50 (-0.10, 1.10)	0.36 (-0.92, 1.64)	-0.25 (-0.74, 0.24)	0.25 (-0.74, 0.24)
Recovery vs Rest, Mean (CI)	-0.04 (-0.26, 0.18)	0.89 (-0.65, 2.43)	-0.50 (-1.48, 0.48)	0 (0)
PVC				
Stress vs Rest, Mean (CI)	-0.19 (-2.46, 2.08)	1.55 (-1.59, 4.69)	0 (0)	0.13 (-0.37, 0.11)
Recovery vs Rest, Mean (CI)	-0.49 (-1.99, 1.01)	0.05 (-1.55, 1.65)	-0.25 (-0.74, 0.24)	0 (0)

PAC – Premature Atrial Complexes; PVC – Premature Ventricular Complexes

TABLE 7: ODDS OF STRESS-INDUCED PAC AND PVC INCREASES IN WOMEN VERSUS MEN

	OR (95% CI)	**p**
Premature atrial complexes		
Increased PAC Counts with Stress vs Rest	2.50 (0.97, 6.44)	0.06
Increased PAC Counts with Recovery vs Rest	0.99 (0.39, 2.49)	0.98
Premature ventricular complexes		
Increased PVC Counts with Stress vs Rest	0.67 (0.29, 1.55)	0.35
Increased PVC Counts with Recovery vs Rest	0.75 (0.72, 4.25)	0.22

Model includes Sex only as the exposure (Female =1).

TABLE 8: ODDS OF STRESS-INDUCED PAC AND PVC INCREASES IN AFRICAN AMERICANS/BLACKS VERSUS CAUCASIANS/ WHITES

	OR (95% CI)	**p**
Premature atrial complexes		
Increased PAC Counts with Stress vs Rest	1.80 (0.73, 4.45)	0.20
Increased PAC Counts with Recovery vs Rest	1.84 (0.72, 4.70)	0.20
Premature ventricular complexes		
Increased PVC Counts with Stress vs Rest	0.91 (0.38, 2.14)	0.82
Increased PVC Counts with Recovery vs Rest	1.46 (0.61, 3.47)	0.39

Model includes Sex only as the exposure (Blacks or African Americans =1).

TABLE 9: ODDS OF STRESS-INDUCED PAC AND PVC INCREASES IN PARTICIPANTS WITH DEPRESSION AND PTSD

	aOR (95% CI) PTSD	**p**	**aOR (95% CI)** Depression	**p**
Premature atrial complexes				
Increased PAC Counts with Stress vs Rest	0.37 (0.04, 3.16)	0.37	3.60 (1.31, 9.86)	0.01
Increased PAC Counts with Recovery vs Rest	3.56 (0.97, 13.13)	0.06	0.47 (0.10, 2.23)	0.34
Increased PAC Counts with Stress vs Rest + Comorbidities	0	0.99	2.81 (0.62, 11.81)	0.16
Increased PAC Counts with Recovery vs Rest + Comorbidities	1.78 (0.08, 16.33)	0.64	0.78 (0.08, 16.33)	0.83
Premature ventricular complexes				
Increased PVC Counts with Stress vs Rest	0.86 (0.18, 4.15)	0.85	0.90 (0.28, 2.88)	0.86
Increased PVC Counts with Recovery vs Rest	0.82 (0.16, 4.07)	0.80	3.01 (1.12, 8.08)	0.03
Increased PVC Counts with Stress vs Rest + Comorbidities	0	0.99	0.31 (0.01, 1.66)	0.24
Increased PVC Counts with Recovery vs Rest + Comorbidities	1.10 (0.05, 7.84)	0.96	3.15 (0.75, 12.69)	0.11

Comorbidities include Hypertension, Diabetes mellitus, and Dyslipidemia.

DISCUSSION

In this study of 161 participants, we found that PAC and PVC counts were, on average, slightly increased during stress and recovery periods compared with rest, although this difference was not statistically significant and therefore may be due to chance. These differences may be affected by depression, although in adjusted subgroup analyses the effects of depression were no longer significant. Non-significant trends were also seen for increase PAC counts in Black participants, men, and those with CAD versus controls. Overall, this preliminary analysis supports a larger study in which smaller differences can be explored and subgroup analyses can be performed with more statistical power.

Most of the analyses in this study showed no statistically significant association. However, depression was associated with the increased odds of premature atrial contractions during mental stress (compared to the rest period) and premature ventricular contractions during the recovery period (compared to the rest period). The presence of arrhythmias during the recovery period are likely to be because of the residual effects of acute mental stress-induced autonomic imbalance on the heart. After multivariate adjustment of comorbidities, which included hypertension, diabetes and dyslipidemia, there was a loss of significance. Post-traumatic stress disorder showed no association with the increased likelihood of any mental stress or recovery periods.

Certain conditions facilitate the occurrence of mental stress-induced arrhythmias. These include myocardial electrical instability through ion channel effects, myocardial ischemia, and autonomic effects such as sympathetic activation and parasympathetic withdrawal (26). Stress directly impacts several pathways that may disrupt normal cardiac rhythm. Cardiac ion channel function is disrupted by a stressful precipitating event (27). This results in increased calcium influx and a consequent delay in after-depolarizations. This process increases cardiac excitability which can trigger an arrhythmia. In addition, atrial potassium channels are downregulated, and this reduces cardiac excitability during stress.

Although many of our findings did not reach statistical significance, other studies have found arrhythmogenic effects in chronic stress conditions. Overall, the evidence is mixed. A cohort study of over 63,000 nurses showed that depressive symptoms more than double the likelihood of sudden cardiac death (28). In another study, spectral analysis of 24-hour ambulatory Holter ECGs of middle-aged male twins showed that depression was associated with decreased heart rate variability (29). Whang et al., found that depression severity was associated with the risk of shock for ventricular arrhythmias (30). Behavioral effects of depression like smoking, accompanied hypercholesterolemia and truncal obesity, as well as poor patient compliance also predispose affected individuals to cardiac arrhythmias (26).Contrary to some reports, we found no significant association between post-traumatic stress disorder and arrhythmia formation during mental stress (6,32). However, a study looking at the emotional precipitants of ventricular arrhythmias among 277 patients with implantable cardioverter-defibrillators showed no association between anxiety and ventricular arrhythmias (16).

Investigations into race differences in the prevalence of arrhythmias and their risk factors have not been extensively done (33). This study looked at mental stress arrhythmia differences by race and sex categories. While our investigations did not demonstrate any significant race and sex differences in mental stress-induced arrhythmias, Lampert and colleagues have previously found that men with coronary artery disease and implantable cardioverter-defibrillators were more likely to have

ventricular arrhythmias than women (34). In another study that provided evidence that abnormal p-wave axis (aPWA) was associated with mental stress, women had an increased risk of aPWA (35). Additionally, though racial, and ethnic minorities have a higher burden of atrial fibrillation associated risk factors, studies have found a lower incidence of atrial fibrillation in these groups (36,37).

Unfortunately, the small sample size of the study prevented us from detecting small or medium effect size differences between groups. Another limitation is the unrecorded entries for some of the demographic data and medical history. Additionally, the findings from the models may have been affected by residual confounding because few potential confounders were adjusted for in this analysis.

Despite several limitations, this study provided evidence of an association between depression and acute mental stress-induced arrhythmias that may be mediated by traditional risk factors. Arrhythmogenic effects of both depression and acute mental stress are mediated by an increase in sympathetic tone and low parasympathetic activity. Given that ectopic beats have been previously linked to atrial and ventricular fibrillation, ventricular tachycardia, and cardiomyopathy, our results add more evidence to the mechanism linking depression to these cardiovascular endpoints. Finally, these results provide more justification for the inclusion of stress management and psychosocial therapy into cardiovascular disease prevention and care in those with depression (38).

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