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Original Article

The occurrence of ST elevation myocardial infarction (STEMI) and non-STEMI in patients with post traumatic stress disorder (PTSD) using the large nationwide inpatient sample (NIS)

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Abstract: Background: PTSD leads to increased levels of stress hormones and dysregulation of the autonomic nervous system which may trigger cardiac events. The goal of this study is to evaluate any association between PTSD and the occurrence of STEMI and NSTEMI using a large database. Method: Using the Nationwide Inpatient Sample (NIS) and ICD-9 codes from 2005 to 2014 (n=1,621,382), we performed a univariate chi-square analysis of in-hospital occurrence of STEMI and NSTEMI in patients greater than 40 years of age with and without PTSD. We also performed a multivariate analysis adjusting for baseline characteristics including age, gender, diabetes, race, hyperlipidemia, hypertension, and tobacco use. Results: The 2005-2014 dataset contained 401,485 STEMI patients (745, or 0.19%, with PTSD) and 1,219,897 NSTEMI patients (2,441, or 0.15%, with PTSD). In the 2005 dataset, 0.5% of PTSD patients had STEMI compared to 1.0% of non-PTSD patients (OR=0.46, 95% C.I., 0.36-0.59). Similarly, 0.6% of patients with PTSD and 2.2% of patients without PTSD had NSTEMI (OR=0.28, 95% C.I., 0.23-0.35). In the 2014 dataset, 0.3% of PTSD patients had STEMI compared to 0.7% of non-PTSD patients (OR=0.43, 95% C.I., 0.35-0.51). Similarly, 1.4% of patients with PTSD versus 2.9% of patients without PTSD had NSTEMI (OR=0.48, 95% C.I., 0.44-0.52). Similar trends were seen throughout the ten-year period. After adjusting for age, gender, diabetes, race, hyperlipidemia, hypertension, and tobacco use, PTSD was associated with a lower occurrence of STEMI (2005: OR=0.50, 95% C.I., 0.37-0.66; 2014: OR=0.35, 95% C.I., 0.29-0.43) and NSTEMI (2005: OR=0.44, 95% C.I., 0.34-0.57; 2014: OR=0.63, 95% C.I., 0.58-0.69). Conclusion: Using a large inpatient database, we did not find an increased occurrence of STEMI or NSTEMI in patients diagnosed with PTSD, suggesting that PTSD is not an independent risk factor for myocardial infarction.

Keywords: STEMI, NSTEMI, myocardial infarction, PTSD, CVD, ischemic heart disease

Introduction

Posttraumatic stress disorder (PTSD) manifests as persistent maladaptive reactions after experiencing severe emotional or physical distress, including but not limited to, violent assault, military combat, and natural or man-made disasters [1]. According to the latest update to the Diagnostic and Statistical Manual of Mental Disorders, DSM-5, all of the following criteria needs to be met for diagnosis of PTSD: (1) Direct or indirect exposure to death or actual/threatened violence or serious injury; (2) Persistently re-experiencing traumatic events through nightmares, flashbacks, memories; (3) Avoidance of trauma-related stimuli following trauma; (4) Negative thoughts or feelings that began or worsened following trauma; (5) Trauma related arousal and reactivity that began or worsened after trauma; (6) Symptoms must last for longer than one month; (7) Symptoms created distress or functional impairment; (8) Symptoms not explained by medication, substance use, or other illness.

Current evidence-based guidelines overwhelmingly lean towards trauma focused psychotherapy as the gold standard for PTSD manage-

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ment. The three most established types of therapy with the strongest evidence are eye movement desensitization and reprocessing (EMDR), cognitive processing therapy (CPT), and prolonged exposure (PE). Further therapy modalities are the subject of newer research and will likely be employed in adjunction to the more common types. In patients with more severe or persistent PTSD, pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) is shown to be effective alongside psychotherapy. The medications fluoxetine, paroxetine, and venlafaxine have proven to show the most benefit for reducing symptoms [2].

Like most psychiatric disorders, long term prognosis is dependent on multiple factors, including but not limited to degree of trauma, one's support system, treatment compliance and presence or absence of substance abuse. Thus, studies are highly variable with regards to recovery rates, ranging from unto 30% of PTSD patients usually recover with one or more treatment modalities, with a slightly higher number reporting partial recovery [3].

PTSD has been shown to have an association with a multitude of medical conditions. The link between psychological disorders and cardiovascular disease in particular is a growing area of research, owing mainly to the bidirectional relationship between the two [4]. A majority of these studies show that patients with PTSD are more likely to develop cardiovascular disease (CVD) and eventually die from it [5-9]. There are multiple current hypotheses to explain the underlying mechanism of association between PTSD and CVD. A common theory studied so far is related to persistent autonomic dysregulation in PTSD, which leads to higher catecholamine release and consequently lower resting heart rate. Another concept studied so far implicates the sharp rise of pro inflammatory cytokines in PTSD as a cause of cardiovascular disease. Heightened inflammation can accelerate atherosclerosis and increase risk of plaque rupture [10]. This relationship could develop to become a crucial target for screening and education of patients with PTSD about CVD and vice versa in patients recovering from STEMI or NSTEMI to improve post-MI outcomes. However, it remains unclear whether these associations are causal or confounded by other cardiovascular risk factors. Furthermore, a recent literature review by Habbal et al. identified that most research in this area is limited to populations exposed to particular traumatic events and/or from certain geographic areas or demographics [11].

Our study aims to add to the growing literature on PTSD as an independent risk factor for cardiovascular events in the general population. Using a large national inpatient database, we retrospectively analyzed the data to investigate the association between PTSD and STEMI or NSTEMI.

Methods

Data source

This study utilized the Nationwide Inpatient Sample (NIS) database to obtain patient data. The NIS is a component of the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS database is the largest all-payer inpatient database in the United States and accounts for over seven million admissions annually across approximately 1,000 hospitals. The database is publicly available to researchers and is exempt from Institutional Review Board (IRB) approval.

Data collection

We utilized International Classification of Diseases, Ninth Revision, and Clinical Modification (ICD-9-CM) codes to identify patients in the NIS database with PTSD (309.81) and without PTSD. Inclusion criteria were as following: patients > 40 years of age in the inpatient setting between the years 2005 and 2014, diagnosed with STEMI or NSTEMI identified by ICD-9 codes. The study excludes patients less than 40 years of age without history of either STEMI or NSTEMI. The following ICD-9 codes were used for STEMI (410.0-410.6 and 410.8) and NSTEMI (410.7 or 410.9). A multivariate analysis was also conducted, adjusting for age, race, gender, tobacco use, hypertension (401.0, 401.1, 401.9), hyperlipidemia (272.0, 272.1, 272.2, 272.4), and diabetes (250).

Statistical analysis

The Statistical Package for Social Sciences (SPSS) software was utilized to perform retro-

Table 1. Comorbidities and demographic data for STEMI patients from 2005-2014

	PTSD	Non-PTSD
N	745	400740
Mean Age (years)	58.60 ± 9.37 SD	64.95 ± 13.24 SD
Gender %		
Male	84.30%	65.61%
Female	15.70%	34.39%
Race %		
White	74.77%	72.45%
Black	7.93%	6.88%
Hispanic	3.03%	6.62%
Asian/Pac Isl	1.01%	2.13%
Native-American	1.30%	0.52%
Others	11.96%	11.40%
Diabetes %	28.46%	26.30%
Hypertension %	57.72%	51.18%
Hyperlipidemia %	62.82%	53.85%
Smoking %	55.97%	37.21%

Table 2. Comorbidities and demographic data for NSTEMI patients from 2005-2014

	PTSD	Non-PTSD
N	2,441	1,217,456
Mean Age (years)	61.06 ± 10.22 SD	71.08 ± 13.27 SD
Gender %		
Male	78.94%	54.89%
Female	21.06%	45.11%
Race %		
White	73.15%	70.03%
Black	8.68%	1013.00%
Hispanic	4.89%	6.71%
Asian/Pac Isl	1.11%	2.14%
Native-American	0.81%	0.54%
Others	11.36%	10.46%
Diabetes %	35.80%	35.29%
Hypertension %	53.34%	46.39%
Hyperlipidemia %	62.02%	49.55%
Smoking %	44.33%	24.18%

spective uni- and multivariate analysis on NIS data from 2005 to 2014 to evaluate any association between PTSD and the occurrence of STEMI and NSTEMI. For univariate analysis, chi squared test was performed for 10 consecutive years. For multivariate analysis, we adjusted for age, race, gender, tobacco use, hypertension, hyperlipidemia, and diabetes. Odds ratios and 95% confidence intervals were calculated for both analyses. A p-value of ≤ 0.05 was considered statistically significant.

Results

The 2005-2014 dataset contained a total of 401,485 STEMI patients (745, or 0.19%, with PTSD) and 1,219,897 NSTEMI patients (2,441, or 0.15%, with PTSD). The demographic breakdown of patients with STEMI and NSTEMI can be seen in **Tables 1** and **2**, respectively.

Univariate analysis

PTSD patients had a higher prevalence of diabetes, hypertension, hyperlipidemia, and tobacco use. Patients with a diagnosis of PTSD did not have a higher rate of STEMI or NSTEMI in comparison to patients without PTSD (**Tables 3** and **4**). In fact, univariate analysis showed an increased occurrence of STEMI and NSTEMI in patients without PTSD in every year during the ten-year period (**Figures 1** and **2**). For example, in the 2005 dataset, STEMI occurred in 0.5% of PTSD patients and 1.0% of non-PTSD patients (OR=0.46, 95% C.I., 0.36-0.59). NSTEMI occurred in 0.6% of patients with PTSD compared to 2.2% of patients without PTSD (OR=0.28, 95% C.I., 0.23-0.35). Similarly, in the 2014 dataset, STEMI occurred in 0.3% of PTSD patients versus 0.7% of non-PTSD patients (OR=0.43, 95% C.I., 0.35-0.51). NSTEMI occurred in 1.4% of patients with PTSD compared to 2.9% of patients without PTSD (OR=0.48, 95% C.I., 0.44-0.52). Similar trends were seen throughout the ten-year period.

Multivariate analysis

After performing a multivariate analysis adjusting for age, gender, diabetes, race, hyperlipidemia, hypertension, and tobacco use, PTSD was associated with a lower occurrence of

Table 3. Occurrence of STEMI in patients with and without PTSD from 2005-2014

Year	PTSD	Non-PTSD	Odds Ratio	95% CI	*p*-value
2005	0.5%	1.0%	0.46	0.36-0.59	< 0.001
2006	0.4%	1.0%	0.36	0.27-0.46	< 0.001
2007	0.4%	0.9%	0.40	0.31-0.52	< 0.001
2008	0.3%	0.9%	0.38	0.29-0.48	< 0.001
2009	0.3%	0.8%	0.39	0.31-0.50	< 0.001
2010	0.3%	0.8%	0.40	0.32-0.50	< 0.001
2011	0.3%	0.7%	0.43	0.34-0.53	< 0.001
2012	0.3%	0.7%	0.37	0.30-0.46	< 0.001
2013	0.3%	0.7%	0.43	0.35-0.52	< 0.001
2014	0.3%	0.7%	0.43	0.35-0.51	< 0.001

Table 4. Occurrence of NSTEMI in patients with and without PTSD from 2005-2014

Year	PTSD	Non-PTSD	Odds Ratio	95% CI	*p*-value
2005	0.6%	2.2%	0.28	0.23-0.35	< 0.001
2006	0.7%	2.3%	0.33	0.27-0.40	< 0.001
2007	0.7%	2.3%	0.29	0.24-0.35	< 0.001
2008	0.8%	2.4%	0.33	0.28-0.39	< 0.001
2009	0.9%	2.5%	0.35	0.31-0.41	< 0.001
2010	1.0%	2.5%	0.39	0.35-0.44	< 0.001
2011	1.1%	2.6%	0.42	0.37-0.47	< 0.001
2012	1.1%	2.7%	0.41	0.37-0.45	< 0.001
2013	1.3%	2.8%	0.46	0.41-0.50	< 0.001
2014	1.4%	2.9%	0.48	0.44-0.52	< 0.001

STEMI (2005: OR=0.50, 95% C.I., 0.37-0.66; 2014: OR=0.35, 95% C.I., 0.29-0.43) and NSTEMI (2005: OR=0.44, 95% C.I., 0.34-0.57; 2014: OR=0.63, 95% C.I., 0.58-0.69) (**Tables 5** and **6**).

Discussion

Ischemic heart disease continues to be the leading cause of mortality worldwide, accounting for over 15% of global deaths in 2019 [12]. Thus, the recognition of modifiable risk factors for ischemic heart disease is an important public health issue. Psychological disease has emerged as one of the lesser-known triggers of heart disease, and numerous studies have shown an increased prevalence of CVD in patients with preexisting psychiatric conditions. The INTERHEART study by Yusuf et al., which assessed population risk factors for CVD, estimated that psychosocial risk factors including life stressors account for about one-third of the population-attributable risk of myocardial infarction [13]. A growing area of research is the association between psychological trauma and its cardiovascular consequences. After conducting a retrospective analysis of a large nationwide inpatient sample of over 1 million (1,621,382) patients, our study did not find an increased association between PTSD and the occurrence of STEMI or NSTEMI. In fact, both univariate and multivariate analyses revealed a decreased association between PTSD and STEMI/NSTEMI throughout the ten-year period of study. However, given the large sample size of our study and relatively small population of patients with documented PTSD, this may be a type I error.

Previous studies on PTSD and cardiovascular disease have mostly demonstrated a significant positive association with some conflicting results. Multiple studies have reported that patients with PTSD are at higher risk of morbidity from CVD compared to the general population [6, 8, 9, 14]. A vast majority of these studies were conducted on veterans, and many showed that increased PTSD severity correlated with an increased risk of coronary artery disease, even after adjusting for coronary risk factors. For instance, a study conducted by Kubzansky et al. on 2,000 male war veterans displayed an increase in all coronary heart disease (CHD) outcomes (angina, nonfatal myocardial infarction, and fatal CHD) with each standard deviation rise in PTSD symptoms [14]. Other studies also reaffirm the dose-dependent nature of the association between PTSD severity and coronary artery disease outcomes [6, 7, 15].

Most studies in the extant literature are retrospective analyses of patient records or self-reports. This might overinflate the association between PTSD and CVD as PTSD patients seek medical attention more frequently than the general population [16]. Ahmadi et al. published the first objective study that analyzed coronary artery calcium (CAC) score and PTSD. This study found that PTSD patients had higher CAC scores than non-PTSD patients, suggesting an increased risk of heart disease in patients with PTSD [17]. More recent studies using different objective measures, including

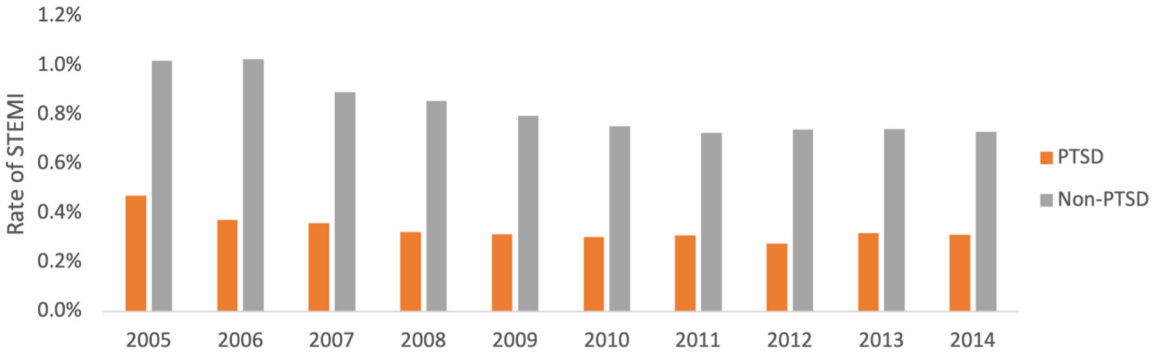

Figure 1. Rate of STEMI in PTSD patients vs. non-PTSD patients in 2005-2014.

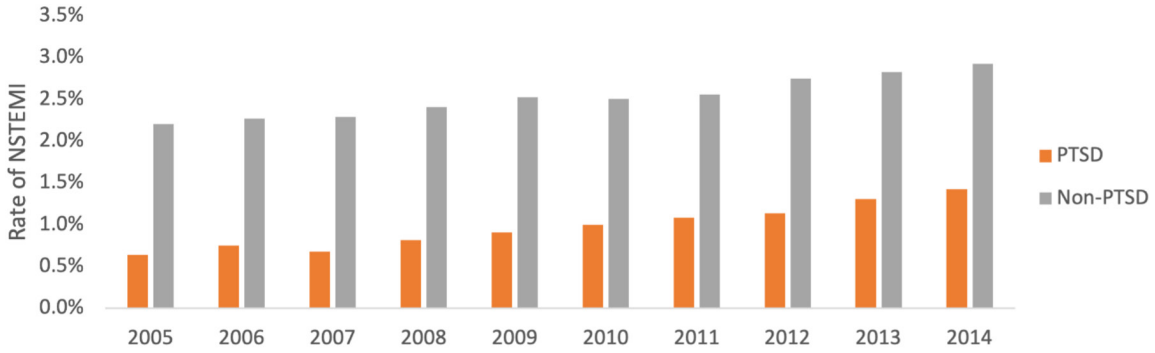

Figure 2. Rate of NSTEMI in PTSD patients vs. non-PTSD patients in 2005-2014.

Table 5. Multivariate adjusted odds ratios evaluating any association between PTSD and STEMI

Year	Odds Ratio	95% CI	*p*-value
2005	0.50	0.37-0.66	< 0.001
2006	0.35	0.25-0.48	< 0.001
2007	0.35	0.26-0.48	< 0.001
2008	0.33	0.25-0.42	< 0.001
2009	0.34	0.27-0.44	< 0.001
2010	0.33	0.27-0.42	< 0.001
2011	0.35	0.28-0.43	< 0.001
2012	0.31	0.25-0.39	< 0.001
2013	0.36	0.29-0.43	< 0.001
2014	0.35	0.29-0.43	< 0.001

Table 6. Multivariate adjusted odds ratios evaluating any association between PTSD and NSTEMI

Year	Odds Ratio	95% CI	*p*-value
2005	0.44	0.34-0.57	< 0.001
2006	0.52	0.41-0.64	< 0.001
2007	0.44	0.35-0.55	< 0.001
2008	0.47	0.40-0.55	< 0.001
2009	0.49	0.43-0.56	< 0.001
2010	0.53	0.46-0.60	< 0.001
2011	0.56	0.50-0.63	< 0.001
2012	0.54	0.48-0.60	< 0.001
2013	0.59	0.53-0.65	< 0.001
2014	0.63	0.58-0.69	< 0.001

myocardial perfusion PET scans and carotid intima medial thickness (CIMT), concur with the notion of increased atherosclerotic risk in patients with PTSD [18, 19]. An increased cardiovascular risk may be tied to evidence of chronic autonomic dysfunction in PTSD, such as higher levels of circulating catecholamines and decreased resting heart rate variability [20]. Whether autonomic dysfunction can serve as a marker for the onset and progression of PTSD has not been determined. Furthermore, studies have shown a twofold increase in inflammatory markers as well as proinflammatory cytokines in patients with PTSD which could potentially increase susceptibility to CVD [21].

Yet other studies found no significant association between PTSD and CVD or a decreased prevalence of CVD in PTSD patients, similar to our results. Schnurr et al. reported that PTSD symptoms in male veterans had a significant positive association with arterial disorders but not ischemic cardiovascular disease or other cardiovascular disease, after adjusting for age, BMI, tobacco, and alcohol use [22]. Likewise, Scherrer et al. found that PTSD is not an independent risk factor for incident cardiovascular disease (including MI, ischemic heart disease, or hypertensive heart disease) after controlling for comorbid conditions such as tobacco use and depression. Unlike prior studies which controlled for similar confounders, this study modeled the variables as time-dependent, so longer exposure to comorbidities may at least in part explain the lack of significant association between PTSD and incident CVD observed in multivariate analysis [23]. Furthermore, in a cross-sectional study by Dobie et al., there was a slightly higher prevalence of self-reported MI or CAD among PTSD screen negative patients than PTSD screen positive patients, albeit the results did not reach statistical significance and may be limited by self-reporting bias [24]. Similarly, in another study, Dutch Resistance veterans with and without PTSD reported similar rates of prior MI [25].

The reason for the discrepancy in results of studies investigating a connection between PTSD and CVD is unclear. This could be attributed to differences in baseline characteristics of the populations studied. Much of the current research in this area is focused on particular patient populations, which may limit the generalizability of their findings. Our study uses the NIS database which provides a diverse patient sample from various demographics and geographic areas within the U.S., as well as PTSD patients with likely exposure to a variety of traumatic events, although this specific information is not available in the database. Additionally, prior studies vary significantly in their study design, including primary outcomes, sample size, and duration of follow-up. Our findings from a large database suggest that PTSD is not an independent risk factor for STEMI or NSTEMI. The increased risk of CVD in PTSD patients reported in prior studies may be mediated through other known risk factors such as sedentary lifestyle or medication noncompliance leading to a greater impact of chronic comorbidities [10, 11]. While some studies have reported higher levels of pro-inflammatory markers in PTSD patients, another study by Sondergaard et al. reported lower levels of CRP in PTSD patients than non-PTSD patients, which challenges the notion of heightened inflammation leading to accelerated atherosclerosis in PTSD patients [26]. Furthermore, a recent systematic review by Dyball et al. found conflicting results on heart rate variability in PTSD patients, with some studies reported increased heart rate variability, which has been thought to prevent the progression of atherosclerosis to manifest CAD [27, 28]. Interventions can also minimize the potential impact of PTSD on CVD. While the NIS database does not include information regarding whether the PTSD patients received psychotherapy or pharmacotherapy, a number of studies including clinical trials, quasi-experimental studies, and observational studies demonstrated improvements in blood pressure, heart rate, heart rate variability, and cholesterol levels following evidence-based psychotherapies such as cognitive behavioral therapy and/or exposure therapy [29-32].

Overall, the findings of this study and many others indicate that an association between PTSD and CVD may not be as clear cut as initially thought, warranting further investigation. Since many initial studies portrayed the link between PTSD and CVD as independent from traditional cardiovascular risk factors, it may be important to consider other behavioral and psychosocial comorbidities of PTSD as predisposing factors in these patients.

Limitations

This was a retrospective study and utilized ICD-9 codes which are limited by potential coding inaccuracies. As this study used an inpatient database, the time and method of diagnosis of PTSD is not known. We were unable to exclude ACS-induced PTSD due to the limitations of the database and lack of a separate ICD-9 code. The database also does not include information regarding psychotherapy and/or medical treatment. Additionally, the results may not be reflective of the outpatient population.

Conclusion

Using a large inpatient database over a ten-year period did not reveal an increased occurrence of STEMI or NSTEMI in PTSD patients. This suggests that PTSD is not an independent risk factor for myocardial infarction.

Disclosure of conflict of interest

None.

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