

## EDITORIAL COMMENT

# Addressing the Heart-Mind Connection\*



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*The world breaks everyone and afterward  
many are strong at the broken places.  
But those that will not break it kills.*

—Ernest Hemingway, A Farewell to Arms

While research has focused on the relationship between ischemic heart disease (IHD) and traditional cardiovascular (CV) risk factors such as hypertension, diabetes, and hyperlipidemia, there is a growing body of evidence that psychologic health and socioeconomic determinants of health also contribute to CV morbidity and mortality. The connection between adverse psychologic conditions and cardiac disease is being increasingly recognized by organizations such as the National Heart, Lung, and Blood Institute and the American Heart Association both of which have recognized the need for further research in this field of behavioral cardiology.<sup>1,2</sup> Post-traumatic stress disorder (PTSD) is a well-defined and recognized psychologic condition that may affect 6 out of every 100 persons according to the national center of Post-traumatic stress disorder with disproportionate impact on women. Since the late 60s, professional and military experts have recognized this disorder and became aware of its consequences on affected individuals. The violent outcomes (suicide, homicide, and domestic partner abuse) were often acute/subacute and relatively easy to measure. The chronic morbidities of this high adrenergic state, poor self-care, poor sleep hygiene, and lack of stable employment and access to quality health care are now being finally

appreciated. The best studied cohort of PTSD individuals comes to us from the United States Veterans Administration where exposure to stressful/adverse events is easier to measure by time of deployment, proximity to violence, real and repetitive exposure to war carnage, and duration of deployment.

To further our understanding of this condition and this time uniquely in female veterans, the paper by Ebrahimi et al<sup>3</sup> in this issue of *JACC: Advances* conducted a retrospective longitudinal study on 398,769 female veterans following these patients to incident IHD diagnosis, which was defined as coronary artery disease, angina, or myocardial infarction. Propensity 1:2 matching was used to compare the cohort with PTSD to those without based on age and baseline CV risk factors. Cox regression with time-varying covariates was analyzed along with a single-model significance test to include PTSD and other CV risk factors. In the cohort, 2.5% were diagnosed with IHD over a mean follow-up of 4.92 years. Despite the low incidence of IHD likely due to this younger cohort, PTSD was associated with a significantly higher rate of IHD.

The association between PTSD and IHD was influenced by all risk factors excluding pregnancy-related risk factors. PTSD was most associated with tobacco use, obesity, and hyperlipidemia, all of which have strong behavioral component. Furthermore, PTSD had a strong association with other psychiatric conditions including depression, which appeared to impact the relationship between PTSD and IHD. The study found that traditional CV risk factors and psychiatric risk factors accounted for 48.5% of IHD, the former of which included female-specific risk factors such as gestational hypertension and diabetes. Prior studies confirm this with the Nurses' Health study showing women with  $\geq 4$  PTSD symptoms having a 60% higher incidence in both myocardial infarction and stroke.<sup>4</sup> These findings call for further investigation into the pathophysiology linking PTSD and IHD.

Unfortunately, the connection between PTSD and IHD is neither direct nor causal. As reflected in the

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study design, the mechanisms underlying the relationship between PTSD and CV risk factors remain elusive. Proposed mechanisms revolve around a dysregulated response to perceived stresses leading to increased levels of inflammatory markers and elevated sympathetic response, the latter of which may be regulated by the hypothalamic pituitary adrenal axis.<sup>5,6</sup> In addition, the link between PTSD and traditional IHD risk factors may be mediated by behavioral aspects linked to PTSD including sleep disruption, obesity, physical inactivity, and substance use.

Future studies should also examine if there are gender differences in the association between PTSD and IHD. Psychologic disturbances tend to be more prevalent in females including PTSD and depression. Prior studies have conflicting results. Remch et al<sup>7</sup> reported PTSD carried similar risk in men and women diagnosed with myocardial infarction and stroke over a similar period of follow-up. Interestingly, the risk was not attenuated after adjusting for depression. In contrast, in a group of predominantly male veterans with PTSD, adjustment for psychiatric comorbidities including depression and traditional CV risk factors negated the association between PTSD and the development of CV disease.<sup>8</sup>

Lastly, with increased recognition of the role of mental health on CV outcomes, the impact of psychiatric treatment on CV events should also be studied.<sup>9</sup> This includes both medication and behavioral interventions such as cognitive behavioral therapy. This requires further collaboration between psychologists and cardiologists. Attainable in-office guidance encompasses discussions regarding smoking cessation, addressing modifiable risk factors (hypertension, lipids, and dietary habits) and the importance of physical activity.

The current study adds another layer to our understanding of PTSD and CV morbidity. The short follow-up period in a very young cohort in diseases where risk factors have a long latent period and where most of the measured outcomes (myocardial infarction, revascularization, death) occur in middle age and beyond may lead us to underestimate the

potential CV risks of PTSD. Furthermore, the complicated multifactorial and multistep maze of PTSD leading to poverty, increased rates of smoking, untreated hypertension, sleep apnea, obesity, poor living conditions, unstable family structure, among many known risk factors for coronary artery disease makes a direct connection (PTSD leads to heart disease) more a “butterfly effect” rather than a smoking gun evidence.

The diagnosis of PTSD as a result of war is now well studied and more long-term insights on physical health outcomes will for sure be evident overtime. Other risk factors for PTSD are less studied. Overtime, more attention is needed to assess the impact of chronic poverty, intimate partner violence, war and forced migration in civilian populations, endemic gun violence, school shooting on development of PTSD, incident development of CV risk factors and CV risky practices and ultimately major CV morbidities and mortality.

Overall, much remains to be elucidated on how psychiatric conditions affect the heart. For now, the diagnosis of PTSD should alert clinicians that these patients may be at higher risk of developing IHD. Clinicians should also be screening patients for psychiatric conditions and connecting these patients with the appropriate resources. Future studies should aim to identify mechanisms linking the 2 conditions, examine impact of psychiatric treatment on CV risk and explore gender differences.

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