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### PTSD May Raise Risk of Heart Disease

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The idea that post-traumatic stress disorder (PTSD) may be a risk factor for coronary heart disease received more support from a study of twin military veterans from the Vietnam War era.

Through a median of 13 years of follow-up, twins who had PTSD at baseline had a significantly higher rate of incident coronary heart disease compared with those without PTSD (22.6% versus 8.9%), according to Viola Vaccarino, MD, PhD, of Emory University in Atlanta, and colleagues.

The difference was not due to established risk factors, since the association remained significant after adjustment for sociodemographic factors, service in Southeast Asia, lifestyle factors, coronary heart disease risk factors, major depression, and other psychiatric diagnoses (OR 2.1, 95% CI 1.1-3.9), the researchers reported online in the *Journal of the American College of Cardiology*.

The study joins others in supporting a link between PTSD and coronary heart disease, according to Stephen Sidney, MD, MPH, of the Kaiser Permanente Northern California Division of Research in Oakland.

"Overall, there are considerable data supporting an association that is likely causal between PTSD and coronary heart disease outcomes," he wrote in an accompanying editorial. "While, on the one hand, [the studies] often utilize self-reported data with risk factor measurement and self-reported outcomes without validation, the strong associations with subclinical outcomes, the studies that show a dose relationship, and the evidence for plausible mechanistic associations suggest that the relation is real and clinically important."

He added that "our consciousness should be raised to the importance of obtaining a history of exposures that are associated with PTSD risk, and to perform or refer patients for screening, diagnosis, and treatment, when appropriate."

Over the course of a lifetime, PTSD affects 10% to 12% of women and 5% to 6% of men in the



#### Action Points

Note that this cohort study of twins from the Vietnam era demonstrated that post-traumatic stress disorder (PTSD) is associated with an increased risk of coronary heart disease.

Be aware that just under half of the twin pairs in the registry participated in this study, potentially biasing the results.

general population. Rates are higher among military personnel exposed to combat, however, reaching 15% to 19% among those who served during the Vietnam War, and even higher for those who served in the more recent conflicts in Iraq and Afghanistan.

"A characteristic of PTSD is enhanced sympathetic nervous system response with trauma-reminiscent stimuli coupled with chronic dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis," Vaccarino and colleagues wrote. "These biological perturbations could affect the cardiovascular system."

To explore the relationship between PTSD and coronary heart disease, the researchers turned to the Vietnam Era Twin Registry, a national study of male monozygotic and dizygotic twins who served on active duty in any military branch during the Vietnam War era (1964 to 1975).

The current analysis included 281 twin pairs who were born from 1946 to 1956, including 177 pairs in which only one twin reported a history of PTSD. Rates of participation in the study were similar among groups (range 38% to 46%). At baseline, all of the participants (mean age 42.6) were free from cardiovascular disease.

The higher rate of incident coronary heart disease during follow-up among those with PTSD was consistent for each component of the endpoint, including acute myocardial infarction, other hospitalizations for coronary heart disease, and revascularization procedures.

In addition, in fully adjusted models, twins with PTSD had a stress total severity score measured by positron emission tomography (PET) that was 123% higher compared with those without PTSD ( $P<0.001$ ), indicating a greater number of myocardial perfusion defects.

The percentage of individuals with a stress total severity score of at least 100 -- which has been associated with about a 10% decrease in event-free survival at 2 years in patients with established coronary artery disease -- was greater among those with PTSD (59.5% versus 38.6%,  $P=0.001$ ).

Although an assessment of coronary flow reserve indicated worse myocardial perfusion in individuals with PTSD, the difference was not statistically significant in the fully adjusted model. However, an abnormal coronary flow reserve (less than 2.0) was more frequent in the PTSD group (43.5% versus 24.7%,  $P<0.001$ ).

When the analyses were restricted to the twin pairs with discordant PTSD histories, all of the relationships were weakened; however, the associations between PTSD, incident coronary heart disease, and stress total severity score remained statistically significant.

"Future studies should address mechanisms underlying the increased cardiovascular risk in persons with PTSD, as this information will help guide effective prevention and treatment strategies aimed at reducing cardiovascular morbidity and mortality in persons with PTSD," the researchers wrote.

They acknowledged some limitations of the study, including the "modest" participation rate stemming from the need for participants to travel for the in-person examination, the lack of access to medical records to validate the clinical endpoints, the lack of PET data at baseline, and a study population that included mostly non-Hispanic white men, which limits generalizability of the findings.

The study was supported by the National Institutes of Health and the American Heart Association. It received additional support from the National Center for Advancing Translational Sciences and the Emory University General Clinical Research Center. The U.S. Department of Veterans Affairs has provided financial support for the development and maintenance of the Vietnam Era Twin Registry.

Vaccarino reported that she had no conflicts of interest. One co-author, who is now deceased, was a consultant and shareholder and received royalties from Syntermed, which licenses the Emory Cardiac Toolbox used for some analyses in the study.

Sidney did not report any conflicts of interest.

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**Primary source:** Journal of the American College of Cardiology

Source reference:

Vaccarino V, et al "Post-traumatic stress disorder and incidence of coronary heart disease: a twin study" *J Am Coll Cardiol* 2013.**Additional source:** Journal of the American College of Cardiology

Source reference:

Sidney S "Post-traumatic stress disorder (PTSD) and coronary heart disease" *J Am Coll Cardiol* 2013.

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